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Annals of the XX Brazilian Congress of the Brazilian Society of Bone Marrow Transplant August 24 – 27, 2016, Fortaleza – Ceará – Brazil

XX CONGRESSO
DA SBTMO 2016
SOCIEDADE BRASILEIRA DE TRANSPLANTE DE MEDULA ÓSSEA

Hotel Gran Marquise . Fortaleza . Ceará
24 a 27 de agosto de 2016

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XVI Encontro de Histocompatibilidade e Imunogenética – Presidente: Carmen Silvia Vergueiro

X Congresso da Associação Brasileira de Terapia Celular – Presidente: Sérgio Paulo Bydlowski

I Encontro SBTMO, ABTCEL e ISCT – Presidente: Sérgio Paulo Bydlowski

XIV Encontro de TMO em Pediatria da SOBOPE – Coordenação: Liane Daudt

XVIII Encontro de Enfermagem e Equipe Multidisciplinar em TMO – Coordenação: Natália B. Costa Freire

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Associação Brasileira de Histocompatibilidade
President: Carmen Silvia Vergueiro
Associação Brasileira de Terapia Celular
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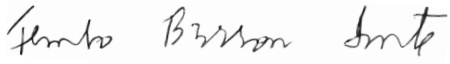
Message from the President of the Congress

The Brazilian Society of Bone Marrow Transplant has prepared the XX SBTMO Congress 2016 which takes place from 24 to 27 of August 2016 in Hotel Gran Marquise in Fortaleza, Ceará.

The event will be marked by the educational sharing of experiences, with the strong participation of leading experts from the country and abroad.

The Land of the Sun will be ready to receive the participants of the Congress with all the infrastructure of a large capital, and the warm, typical openness of the people from Ceará.

Welcome to Fortaleza!



Dr. Fernando Barroso Duarte
President of the XX Congress of the Brazilian Society of Bone Marrow Transplant

Message from the President of SBTMO

After more than 30 years of activity, the Hematopoietic Stem Cell Transplantation (HSCT) program has now 45 hospitals accredited to operate in the area, with different levels of complexity, more than 15 accredited services for performing HSCT with alternative donors. There are more than 60 teams working in the country, performing over 2000 procedures per year, 800 allogeneic, of these 300 with unrelated donors, with progressively better results, currently compatible with those found in international records.

Difficulties and limitations have always existed; perhaps now, increased by the financial crisis that we face they are more present, increased costs of inputs, unavailability of existing resources to reform or expansion of beds in productive units. Even the publication of an ordinance, already updated, is delayed.

In this context, it is noteworthy the commitment and determination of the different teams involved in development of HSCT in Brazil, always interested in producing more and better. We are very encouraged with the increase of newly accredited centers that are already in operation, as well as the larger number of residents belonging to medical residency programs accredited by the CNRM, now available in several HSCT centers.

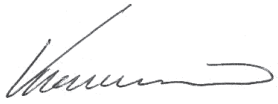
The Brazilian Society of Bone Marrow Transplantation, SBTMO, has stimulated the integration and cooperation between the several active units in the country, as well as participation in educational programs with the ABHH, and has been developing productive relationships with LABMT, WBMT, CIBMTR and EMBT.

The SBTMO Congress will take place this year, in August, in Fortaleza, chaired by Dr. Fernando Barroso, who has spared no effort to reach the desired success, and last but not least, with its established economic viability. Personally, considering the already available programming, in addition to the presence of international and national prominent speakers, I believe the Fortaleza event will score a favorable position in the successful history of the SBTMO Congresses, as many others before.

Next year, in the XXI Congress of SBTMO in Campinas, which will be chaired by Dr Nelson Hamerschlak, we will have the accomplishment of the HSCT Consensus, which unlike other years, was strategically placed next to the Congress.

This year, within the continuing education program of SBTMO, we started the regional meetings, which should have their frequency expanded next year, contributing to a greater integration and cooperation between the different services. In the face of the current difficulties, we propose to maintain the development of the HSCT Brazilian Program, always stimulated by our fraternal cooperation.

I wish you all a great XX SBTMO Congress in Fortaleza.



Vergilio Colturato
President of SBTMO

SUMMARY

Educational articles and Updates

Best Scientific Papers

SUMMARY

SUMMARY

POSTER PRESENTATIONS

Mobilization of hematopoietic progenitor cells for autologous transportation: consensus recommendations

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Meeting in Valencia, Spain, April 2016

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SUMMARY

Selected patients with certain hematological malignancies and solid tumors have the potential to achieve long-term survival with autologous hematopoietic progenitor cell transplant. The collection of these cells in peripheral blood avoids multiple bone marrow aspirations, results in faster engraftment and allows treatment of patients with infection, fibrosis, or bone marrow hypocellularity. However, for the procedure to be successful, it is essential to mobilize a sufficient number of progenitor cells from the bone marrow into the blood circulation. Therefore, a group of Brazilian experts met in order to develop recommendations for mobilization strategies adapted to the reality of the Brazilian national health system, which could help minimize the risk of failure, reduce toxicity and improve the allocation of financial resources.

Keywords: Hematopoietic stem cell mobilization; Autologous transplantation; Plerixafor; G-CSF

Introduction

Autologous transplantation of hematopoietic progenitor cells from peripheral blood is a well-established therapy for some hematological malignancies, such as multiple myeloma, non-Hodgkin's and Hodgkin's lymphoma, as well as for some solid neoplasms, such as germ cell tumors.[1,2] Mobilization and collection are crucial steps in this procedure, which aim not only at obtaining enough stem cells for transplantation but also at minimizing the number of apheresis sessions, reducing the risk of complications, preventing failure and optimizing resource allocation.[3] The choice of the mobilization regimen should take into account factors such as efficacy, safety, convenience and cost-effectiveness.[4] Even though they are well established in everyday practice of Hematology and Transplant centers, mobilization regimens can vary greatly from one institution to another and differ in terms of clinical and pharmacoeconomic outcomes.[5-7]

Of the currently available regimens, the one most commonly used involves the isolated use of the granulocyte-colony stimulating factor (G-CSF), which has the advantages of being well tolerated and allowing the programming of apheresis procedures.[8,9] The combination of chemotherapy and G-CSF has shown to improve the collection of CD34 + cells and reduce tumor activity, but at the expense of increased risk of complications such as fever and neutropenia. In turn, the combination of G-CSF and plerixafor has been shown to result in reduced risk of mobilization failure, improves the collection of CD34 + cells and a favorable tolerability profile, but at a higher cost.

Thus, the combination of G-CSF and plerixafor has been used as the initial regimen for patients with risk factors for poor mobilization, preemptively in patients with early signs of mobilization failure, as well as a rescue strategy in cases of failed mobilization with other regimens.[9-12] Other currently available rescue strategies include the re-mobilization with the same regimen used previously, the segmentation of the G-CSF doses and collection of cells directly from bone marrow.[13]

Recently, the American Society for Blood and Marrow Transplantation[4] and a panel of US experts[3] published their guidelines and recommendations to optimize the mobilization of hematopoietic stem cells from peripheral blood. Considering the peculiarities of the Brazilian public health system and the need for more standardized approaches in our country, a panel of national experts was summoned to meet and develop consensus recommendations adapted

to our reality and that could serve as a starting point for broader efforts to improve clinical outcomes of patients submitted to autologous hematopoietic stem cell transplantation from peripheral blood in Brazil.

Predictive factors of poor mobilization

The identification of risk factors associated with the disease and the patient that can predict poor mobilization of hematopoietic progenitor cells is of utmost importance for the optimization of both the therapy and resource allocation. Several studies carried out to investigate this question showed that the diagnosis of lymphoma,[14-19] thrombocytopenia,[14,20-23] older age[18-21,23-25] and polytreatment[14,16,19,25,26], among other factors, emerged as the main potential factors for the prediction of poor recruitment of hematopoietic stem cells.

However, the retrospective characteristic of these studies, the relatively low number of assessed patients, the heterogeneity of the studied populations, the use of different mobilization regimens and lack of uniform criteria for the definition of failure contributed to the achievement of conflicting results,[11,27-29] making data interpretation and the drawing of definitive conclusions about the role of these factors in therapeutic decision-making difficult. The most robust factor for the prediction of collection efficiency is the CD34+ cell count in peripheral blood before apheresis and its implementation in daily practice has the added potential to save financial resources.[7,30-34]

Recommendation: the isolated use of pre-treatment clinical and laboratory factors to identify patients at risk of poor mobilization and to select the best therapeutic approach shows conflicting results in the literature. However, potentially more effective mobilization strategies – such as chemo-mobilization and plerixafor-based regimens should be considered for patients who have these factors. A low number of CD34+ cells in peripheral blood before apheresis is the most robust predictor of collection failure; thus, the cell count should be performed in all patients submitted to autologous transplantation of hematopoietic progenitor cells.

Measurement of CD34+ cell count in peripheral blood

The use of flow cytometry for CD34 + cell count in peripheral blood has become a standard technique to evaluate the recruitment of these progenitor cells and to optimize mobilization strategies,[3,4,7] having been implemented in the routine practice in the vast majority of treatment centers.[35,36] Although several methodologies and cytometric assays have been described, there can be great variability among the observed cell counts and the lack of standardized methods has led to the obtaining of widely differing results.[35,37] The sample type and condition, the used reagent and the characteristics of the employed anti-CD34 monoclonal antibodies are some potential error sources for the cytofluorimetric measurement of CD34 + cell count.[38]

The three main techniques of hematopoietic progenitor cell count include the Milan/Mullhouse two-platform protocol and the two-platform and single-platform analysis systems of ISHAGE (International Society of Hematotherapy and Graft Engineering). In the two-platform method, the percentage of CD34 + cells is determined by flow cytometry and the leukocyte count is performed in an automated hematology analyzer. The development of single-platform methods allowed the absolute count of CD34+ cells through a single device - the flow cytometer.[39] The results obtained with the three methods are apparently comparable, with a low rate of divergence.[39,40] Given their presumed interchangeability, the choice between these three methods can be based on subjective criteria, such as convenience, cost, and simplicity.[39]

Recommendation: the exact quantification of CD4+ cells in peripheral blood is currently a highly relevant factor for a successful autologous hematopoietic stem cell transplantation. The purchase notices of kits for the analysis of this parameter should be carefully prepared, aiming at the acquisition of accurate, reliable products that have been submitted to quality control testing.

Mobilization with G-CSF

G-CSF is the most commonly used mobilizing agent, either alone or in combination with chemotherapy. The generally applied dose is 10 μg/kg subcutaneously, with apheresis being started on the fifth or sixth day, until the number of target cells is achieved.[41,42] Some studies postulated that G-CSF dose division could result in better mobilization. The pharmacological profile of G-CSF demonstrates a maximum serum concentration within 2 to 8 hours after subcutaneous administration.[43]

Considering an elimination half-life of 3 to 4 hours, the dose division could result in higher basal serum concentrations and, consequently, better mobilization.[44] However, studies comparing a single daily dose versus divided dose of G-CSF showed conflicting results.[5,44] Higher doses of G-CSF (8 to 12 μg/kg/12h) resulted in the collection of a higher number of CD34 + cells with fewer apheresis procedures, suggesting the existence of a dose-effect response.[45-47]

The use of G-CSF has the advantage of allowing the mobilization planning, resulting in more predictability,

when compared to chemotherapy. Moreover, G-CSF can be administered at home, resulting in greater convenience for patients. G-CSF also has a favorable toxicity profile, with the most frequent adverse events being mild to moderate musculoskeletal pain (usually controlled with conventional analgesics), as well as dysuria, fever, headache, nausea and asymptomatic increase in alkaline phosphatase and gamma-glutamyl transferase.[48,49] Retrospective and prospective randomized studies suggest that the granulocyte--monocyte colony stimulating factor (GM-CSF) is less effective than G-CSF in mobilizing hematopoietic progenitor cells, either alone or in combination with chemotherapy, with an additional less favorable profile of safety and tolerability.[48,50] The combination of G-CSF and GM-CSF did not result in significant clinical benefits in comparison with isolated G-CSF.[51] Pegfilgrastim has not been widely accepted by transplant centers, due to the fact that G-CSF is easy to use and the accumulated experience using it, as well as cost-related matters.[42]

Recommendation: G-CSF can be used alone to mobilize hematopoietic progenitor cells at doses of 10 to 20 µg/kg, divided into 2 to 4 equal daily applications, or with a higher dose in the morning.

Chemomobilization

The decision between mobilization with G-CSF alone or a combination of chemotherapy and G-CSF should take into account factors such as the remission status of the underlying disease and the probability of poor mobilization.[52] The combination of G-CSF with chemotherapy accomplishes the double purpose of promoting both the mobilization of hematopoietic progenitor cells and the reduction of antitumor activity, with the latter effect being demonstrated in cases of lymphoma and also of multiple myeloma. Moreover, the combination of chemotherapy and G-CSF has the advantage of resulting in the collection of a higher number of CD34 + cells and requiring fewer apheresis procedures, when compared with the isolated use of G-CSF. In contrast, chemomobilization is associated with lower predictability to the start of apheresis, as well as the toxicity and complications from the chemotherapy regimen used, including febrile neutropenia and need for hospitalization.[10,42,50,52] Moreover, when the chemomobilization is used as a cycle of part of the induction or rescue therapy, additional expenses with the chemotherapy itself and also hospitalization for treatment administration and management of complications result in higher costs related to the isolated use of G-CSF.[6]

The combination of G-CSF with high-doses cyclophosphamide was shown to improve the efficiency of collection and increase the correlation between the CD34+ cell counts in peripheral blood and in the final collection.[8,49] Etoposide, in turn, has shown to be effective in the treatment of Hodgkin's and non-Hodgkin's lymphoma; thus, its inclusion in the mobilization regimens of patients with these tumors has the advantage of providing treatment during the mobilization phase[49]. The combination of vinorelbine and G-CSF is an excellent alternative in comparison with G-CSF alone or in combination with cyclophosphamide, showing a more favorable toxicity profile, resulting in earlier collection and lower costs. Furthermore, outpatient administration with one in bolus injection and better predictability of apheresis improve patient comfort and simplify the collection procedure, both in multiple myeloma and in malignant lymphoma.[53-55]

The use of several cytotoxic combination regimes have also been described, including cisplatin, cytosine arabinoside, dexamethasone (DHAP); ifosfamide, carboplatin and etoposide (ICE); etoposide, methylprednisolone, cytarabine and cisplatin (ESHAP); cyclophosphamide, mitoxantrone, dexamethasone (CMD); dexamethasone, carmustine, etoposide, cytarabine, melphalan (Dexa-BEAM); ifosfamide, epirubicin, etoposide (IEE); cyclophosphamide and etoposide with or without cisplatin; and etoposide and rituximab.[8]

Recommendation: mobilization with chemotherapy combined with G-CSF (beginning on the day after completion of chemotherapy) can be performed with cyclophosphamide 2 to 3 g/m² or vinorelbine 35 mg/m² in a single dose[61] or etoposide 375 mg. The selection of other chemomobilization regimens should preferably take into account the sensitivity of the underlying malignancy to the different cytotoxic agents.

Mobilization with plerixafor

Plerixafor is a reversible antagonist of chemokine receptor type 4 (CXCR4), which blocks the interaction between the receptor and its ligand - the CXC chemokine type 12 - and causes the release of CD34+ cells from the bone marrow into blood circulation. The efficacy and tolerability of the combination of Plerixafor and G-CSF in promoting the mobilization of progenitor cells in patients with previous failed mobilization attempts has been demonstrated in several prospective trials, with success rates ranging from 60 to 90%, even among patients aged ≥60 years.

Furthermore, the combination of Plerixafor and G-CSF has also been successfully used in patients with poor mobilization risk factors. Compared to chemomobilization, the combination of Plerixafor and G-CSF provides

greater predictability of the time to obtain CD34+ cell count peak, resulting in improved collection efficiency and fewer apheresis sessions. In the absence of a clear chemotherapy indication, the combination of Plerixafor and G-CSF may be preferred to chemomobilization in patients at high risk of failure. On the other hand, only one formal phase II study on the combination of plerixafor, chemotherapy and G-CSF has been published to date, so that the evidence for the use of this regimen is scarce.[10,56,57]

Plerixafor can also be used preemptively in patients with early signs of poor mobilization, even in the absence of known risk factors. Several algorithms have been developed to guide the preemptive use of plerixafor. Evidence indicates that the number of collections and failure rates can be substantially reduced with the use of this strategy, although a group of patients may still develop with poor mobilization. In patients undergoing mobilization with G-CSF alone, the decision to preemptively add plerixafor usually occurs after 4 days of the mobilization onset and depends on the target for collection. Usually, the addition of plerixafor is indicated for patients with CD34+ cell count <10/mm^3 on day +4. This strategy has been shown to result in similar or lower total costs compared to traditional mobilization methods, when taking into account the management of adverse events and complications associated with alternative regimens of mobilization and mobilization failure.[56-58]

Recommendation: plerixafor, at a dose of 240 mg/kg subcutaneously, should be preemptively administered in patients undergoing mobilization with G-CSF and <10 CD34 + cells per mm³ at day +5, between 6 and 11 hours before apheresis. Patients showing failure mobilization with chemotherapy and G-CSF are also candidates for rescue with plerixafor and G-CSF. There are no conclusive data for the use of chemotherapy in combination with plerixafor.

Mobilization failure approaches

G-CSF, alone or in combination with chemotherapy is still the most common approach to mobilize hematopoietic progenitor cells for autologous transplantation candidates. Considering that a proportion of patients have insufficient mobilization and are therefore deprived of the transplantation benefit, at least at a first moment, the costs associated with failure are many, including the inconvenience and the psychological impact of mobilization failure on the patient, in addition to the costs of morbidity and mortality associated with subsequent attempts at mobilization. Therefore, strategies are crucial to minimize the risks of failure at the second or third mobilization. Options for remobilization include dividing the G-CSF dose, remobilization with chemotherapy and G-CSF, remobilization with the same previous regimen, the combination of plerixafor and G-CSF and bone marrow collection.[10,42,59]

Mobilization failures are generally defined as <2*106 CD34+ cells collected per kg in a single mobilization or more than 4 sessions of apheresis to collect this minimum number of cells.[10] The division of the G-CSF dose seems to be effective in approximately 1/3 of the patients; however, confirmatory data regarding the effectiveness of this strategy are scarce.[60] Evidence from different centers suggest that remobilization with the combination of intensive chemotherapy and growth factor may result in an increase in the number of progenitor cells in patients with poor pre--mobilization; however, the benefit of this strategy must be weighed against its toxicity and cost. For cases in which the mobilization has been performed earlier – before complete recovery from the previous chemotherapy – and mobilization is poor, a second mobilization with the same regimen may be useful. Regarding the combination of plerixafor and G-CSF, this strategy is more likely to be successful than other rescue strategies[0], allowing obtaining the target CD34+ cell count in >70% of cases. Finally, isolated reports seem to indicate that the addition of bone marrow cells to peripheral blood progenitor cells may benefit patients with poor mobilization.[10,42,59]

Recommendation: in cases of mobilization failure, it is recommended to allow at least 3 weeks for recovery before a new attempt, particularly in cases of unsuccessful chemomobilization. In cases of failure with G-CSF alone, it is recommended to carry out the remobilization by dividing the G-CSF dose, or chemomobilization. In case of chemomobilization failure, it is recommended to carry out the remobilization with plerixafor and G-CSF, or with the growth factor alone. In case of failure using plerixafor and G-CSF, remobilization is recommended using the same strategy, or to perform bone marrow collection.

Conclusions

The presence of risk factors for poor mobilization should be carefully investigated and it may have an impact on the selection of the most appropriate mobilization regimen. The counting of the number of CD34+ cells in peripheral blood should be performed prior to apheresis in all patients submitted to autologous hematopoietic stem cell transplantation through an accurate and reliable laboratory test, of which quality is controlled. Patients with cell count <10 CD34+ cells per mm^3 on day +5 are candidates for the preemptive use of plerixafor in combination with G-CSF. The selection of other mobilization regimens

should take into account efficacy, safety, convenience and cost-effectiveness. Algorithms to minimize mobilization failure risks should be used to reduce complications and additional costs associated with treatment failure.

In cases of poor mobilization (collection resulting in <2*106 CD34+ cells per kg, in a single mobilization or >4 apheresis sessions), remobilization strategies should also take into account the previously used system. Pharmacoeconomic evaluations should include not only the cost of drugs, but also resource savings associated with the reduction in the number of apheresis sessions, complications of treatment, need for hospitalization, mobilization failure risks, as well as morbidity and mortality associated to remobilization.

Resumo

Mobilização de células progenitoras hematopoéticas para transplante autólogo: recomendações de consenso

Pacientes selecionados com certas neoplasias hematológicas e tumores sólidos têm o potencial de alcançar sobrevida de longo prazo com o transplante autólogo de células progenitoras hematopoéticas. A coleta dessas células no sangue periférico evita múltiplas aspirações de medula óssea, resulta em enxertia mais rápida, e permite o tratamento de pacientes com infiltração, fibrose ou hipocelularidade medular. Contudo, para o sucesso desse procedimento, é essencial mobilizar um número suficiente de células progenitoras da medula óssea para a circulação sanguínea. Por isso, um painel de especialistas brasileiros se reuniu com o objetivo de desenvolver recomendações para estratégias de mobilização adaptadas à realidade do sistema de saúde nacional, que pudessem contribuir para minimizar os riscos de falha, reduzir a toxicidade e melhorar a alocação de recursos financeiros.

Palavras-chave: Mobilização de células-tronco hematopoéticas; Transplante autólogo; Plerixafor; G-CSF.

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Allogenic bone narrow transplantation in sickle-cell diseases.

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SUMMARY

Sickle-cell diseases are the most common inherited hemoglobinopathies worldwide. Improvement in survival has been seen in the last decades with the introduction of careful screening and prevention of complications and the introduction of hydroxyurea. Stem-cell transplantation is currently the only curative option for these patients and has been indicated for patients with neurological events, repeated vaso-occlusive crisis, any organ damage or presence of red blood cell antibodies. Related bone-marrow or cord-blood transplant has shown an overall survival of more than 90% with a disease-free survival of 90% in 1,000 patients transplanted in the last decades. The use of unrelated donors unfortunately has not shown the same good results, but better typing methods and improved support may improve the outcome with this source of stem cells in the future. In Brazil, only recently stem cell transplant from related donors has been included in the procedures performed in the public health system. The use of related bone marrow or cord blood and a myeloablative conditioning regimen are considered standard of care for patients with sickle-cell diseases. Transplants with non-myeloablative regimens, unrelated donors or haploidentical donors should be performed only in controlled clinical trials.

Keywords: Sickle Cell Disease; Stem Cell Transplantation; Hemoglobinopathies.

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Introduction

Hemoglobinopathies constitute the most frequent monogenic diseases. It is estimated that approximately 300,000 children are born annually with some type of hemoglobinopathy, with sickle-cell diseases being the most common of them, accounting for over 80% of these cases.[1] However, these figures are underestimated, considering that they often come from retrospective data of individual institutions and not from neonatal screening programs.

In Brazil, it is estimated that 4% of the population is a carrier of the S gene, a number that could reach 10% in Afro-descendants. Sickle-cell disease is caused by a mutation, resulting in a mutant beta protein called hemoglobin S (HbS). In HbS, there is an exchange of an amino acid at position 6, replacing glutamic acid by valine. In homozygous form or in combination with other hemoglobinopathies, deoxygenated HbS form polymers that make the cell rigid, less deformable and that sometimes damages the cell membrane, leading to hemolytic anemia.[2] Disease severity depends on the genotype, with the most severe form being the homozygous one for HbS (HbSS), i.e., sickle-cell anemia. Combinations with thalassemia may be milder in cases of persistence of some normal beta chain production (HbSβ+) or more similar to the homozygous form, if there is no production of the normal beta chain (HbSβ0). Other combinations, such as with hemoglobinopathy C, the HbSC, usually have a milder clinical picture (Table 1). From a pathophysiological point of view, the repeated vaso-occlusive crises lead to tissue infarction in several organs. The interaction of circulating cells and altered vascular endothelium of patients with sickle-cell disease also plays an important role in the disease pathophysiology.[2]

Sickle-cell diseases are systemic diseases that result in damage to all organs. The clinical picture evolution is extremely unpredictable and can vary from mild to severe forms as early as in childhood.[2] The most common complications are vaso-occlusive crises that can occur anywhere, but are more common in the bone marrow, causing intense bone pain; in the lung, as the so-called acute chest syndrome and in the central nervous system. Strokes are especially feared and may be apparent or silent, being related to high morbidity and mortality.[3] Neurological complica-

TABLE 1. Common genotypes and severity of sickle cell diseases

Genotype	Abbreviation	Name	Hb (gdL)	Severity
β^S/β^S	HbSS	Sickle-cell anemia	6-9	+++
β^S/β^0	Hb Sβ^0	S-beta thalassemia	6-9	+++
β^S/β^C	HbSC	SC hemoglobinopathy	9-12	++
β^S/β^+	Hb Sβ^0	S beta talassemia	10-13	+

tions, such as silent infarctions, transient ischemic attacks (TIA), ischemic or hemorrhagic strokes have a prevalence of approximately 5% in children with HbSS and HbSβ0. Strokes occur in up to 10% of children with HbSS, with risk factors being a previous TIA, low hemoglobin levels, increased vascular flow on transcranial Doppler[4] Recurrence of cerebral ischemic events occurs in 60 to 90% of patients that do not receive secondary prophylaxis measures (chronic transfusions, bone marrow transplantation).[5] Repeated splenic infarctions lead to organ atrophy (autosplenectomy), with subsequent splenic hypofunction.[6]

The treatment consists of the introduction of antibiotic prophylaxis as soon the diagnosis is made and family guidance regarding the care and recognition of more severe pictures, preventing dehydration and hypo-oxygenation.[2] The use of hydroxyurea, a drug able not only to increase fetal hemoglobin levels, but also to reduce leukocytes and inflammatory mediators has changed the natural history of the disease. Its use has been recommended from early childhood in order to prevent irreversible organ damage.[7]

Despite these advances in the treatment of sickle-cell disease, some patients do not show adequate responses to hydroxyurea and may develop severe complications at a young age. The great challenge has been to identify predictors of severity that can be used to stratify patients for different types of treatment earlier. Some factors such as persistently lower hemoglobin and severe dactylitis have been associated with worse clinical outcome.

Other markers, such as increased lactate dehydrogenase, as a result of hemolysis, has also been associated with more severe clinical pictures. Although these risk factors are already known, not all of them are accurate enough to guide the therapeutic decision-making.[8] Currently, the most important factor from the clinical point of view is the alteration in the transcranial Doppler, which is a predictor of vascular lesion in the central nervous system.[5] Early and routine use of ultrasound assessment can predict the occurrence of stroke, leading to changes in the therapeutic strategy.[9]

Indications of allogeneic BMT in sickle-cell diseases

The first facts and the vast majority of currently available data on allogeneic BMT in sickle-cell disease (SCD) are on children. The age of 16 years, which appears in several older publications, is derived from rationale on allogeneic BMT in thalassemia. Children with thalassemia major that receive chronic transfusions since the first months of life will have a significant iron accumulation if not submitted to adequate iron chelation. Therefore, the Pesaro group demonstrated that inadequate iron chelation and liver alterations, especially hemosiderosis, led to inferior BMT outcomes.[10] Children older than 16 years, due to the prolonged time of transfusion and consequent accumulation of iron in the 1990s, consequently had these inferior outcomes after BMT. Therefore, restrictions regarding BMT in patients with thalassemia were then assumed for patients with sickle-cell disease (SCD). The pathophysiology of sickle-cell diseases, however, can be very different and the clinical outcome is not as predictable as in the constant iron accumulation. For this reason, the vast majority of data on allogeneic BMT in SCD are obtained from children. Additionally, children with SCD had, at the time, few therapeutic options beyond the general and antibiotic prophylaxis measures. Considering the unpredictability of the clinical course and few predictive factors of severity, it is presumed as a rule that only patients with unfavorable evolution and some organ damage must undergo allogeneic BMT.

Table 2 shows the main indications for allogeneic BMT recognized by international BMT Societies.[11,12] All of them agree that all patients with symptomatic disease and that has an identical HLA donor should be transplanted as soon as possible. Other tools, such as the routine use of transcranial Doppler (TCD) in the early evaluation of cerebral blood flow alterations can be crucial to identify patients that can benefit from allogeneic BMT before irreversible symptoms or lesions occur. Therefore, in addition to the presence of organ damage in both the central nervous system or another organ and an unfavorable evolution with repeated vaso-occlusive crises, it is accepted today the transplantation of patients with TCD alterations. Another indication would be the increase in tricuspid valve regurgitation velocity ≥2.7 m/sec at the conventional echocardiography, as it indicates the need for catheterization assessment for possible pulmonary hypertension.[13]

TABLE 2. Alo BMT indications according to the North American groups of BMT (CIBMTR) and the European Group of BMT (EBMT)

Established Alo BMT indications
Stroke
Isquemia Cerebral
Cerebral ischemia – neurological event lasting > 24 hs
Velocity in TCD ≥ 200 m/s
Repeated Thoracic Syndromes
Recurrent priaprism
Allosensitization
Osteonecrosis
Sickle-cell nephropathy

Allogeneic bone marrow transplantation

bone marrow transplantation is currently the only curative option for patients with sickle cell disease and aims to restore normal hematopoiesis and thus prevent damage by successive sickling episodes. The first description of allogeneic bone marrow transplantation for the treatment of sickle cell anemia dates from 1984, in a patient with acute leukemia.[14] This transplantation showed it was possible to cure SCD patients with this therapy. After this first report, two groups in the USA and Belgium published the first series of patients with sickle-cell disease submitted to allogeneic BMT, with overall survival outcomes >90% and event-free survival > 85%.[15,16]

Myeloablative Conditioning

Large part of the initial data comprises myeloablative conditioning and related donors. The first two series are from the Belgian group in 1996 and the North-American group in 1998 (Table 2).[15,17] After these first publications, other groups reported similar experiences.[18-20] The most often used regimen was the one with busulfan 16 mg/kg and cyclophosphamide 200 mg/kg with or without antithymocyte globulin (ATG) or anti-CD52 antibody (Alemtuzumab). More recently, the introduction of Treosulfan and Thiotepa showed similar efficacy with a slightly superior safety profile related to early complications, such as sinusoidal obstruction syndrome.

The data, however, are similar in terms of overall survival and event-free survival.[21] Table 3 shows the data of the largest published series with myeloablative regimen and identical HLA (human leucocyte antigen) sibling donors. These data clearly demonstrate the benefit of allogeneic bone marrow transplantation in the treatment of patients with sickle-cell disease. Low mortality related to BMT and the low incidence of both acute (aGVHD) and chronic (cGVHD) graft-versus-host-disease (GVHD) demonstrate the curative potential of this therapeutic approach, as well as its safety.

The largest sample of allogeneic BMT in patients with sickle-cell disease was recently presented in a congress.[22] One thousand transplantation cases were reviewed in the USA, Europe and Brazil. The transplants were carried out in 90 centers from 23 countries. All patients received transplantation from an identical HLA sibling donor. The median age was 9 years (1-54 years) and 85% of patients were younger than 16 years. More than half of transplantations, 53%, were carried out after 2007. Most patients had HbSS and stroke was the most common indication for BMT. Regular transfusions and use of hydroxyurea were carried out in 93% and 53% of patients, respectively, pre allogeneic BMT. The most commonly used conditioning regimen was myeloablation (87%) and the most widely used regimen consisted of busulfan and cyclophosphamide. The source of hematopoietic stem cells was the bone marrow in 85% of cases.

The median follow-up time was 45 (1.1-324.6) months. Twenty-six patients had primary graft failure and 47 had late graft loss. The probability of overall survival and event-free survival at 3 years was respectively 94% (95% CI: 92-95) and 90% (95%CI 68-82). The use of peripheral blood hematopoietic stem cells was significantly associated with worse overall survival (BM 94% vs. PB 80%, p <0.0001). Death occurred in 6.7% of patients primarily due to infection or GVHD. At the multivariate analysis, each year of age (HR 1.1, 95% CI: 1.07-1.14, p <0.001) and the use of peripheral blood (HR 3:43, 95% CI: 1.49-7.88, p = 0.004) were associated with higher mortality.

The use of a myeloablative regimen in the univariate analysis was associated with better event-free survival (91 ± 1% vs. 82 ± 1%, respectively; p <0.001). The confidence interval for aGVHD grades 2-4 was 14.4% (12.2-16.7) and for chronic GVHD it was 13.3% (11-15.8). This large series demonstrates the efficacy and safety of allogeneic BMT in patients with sickle-cell disease, even in established lesions. Thus, the allogeneic BMT with identical HLA sibling donor and myeloablative conditioning is now considered the treatment of choice and routine for individuals with sickle-cell disease with indication for BMT. The use of intravenous busulfan should always be the route of choice and the bone marrow should be the source of hematopoietic stem cells.

Some specific care of these patients is important, such as the maintenance of anticonvulsants throughout the period of calcineurin inhibitor use (preferably Lamotrigine, as it does not interfere with serum cyclosporine levels), maintaining platelet levels throughout the BMT period >50,000/μL, maintaining hemoglobin levels bet-

ween 9 and 11 g/dL and no higher, maintaining adequate levels of magnesium and be quite assertive regarding blood pressure control.

Non-myeloablative conditioning

The idea that a mixed chimerism would be enough to prevent the vaso-occlusive crises and the fear of submitting patients already showing extensive organ lesions to transplantation with myeloablative regimens, especially adult ones, has made several non-myeloablative regimens be tested in patients with sickle-cell disease. The first results, more often seen in case reports than in series of patients, were quite disappointing with high engraftment failure rate and delayed engraftment loss. On the other hand, more recent series with better support measures and new conditioning regimens (see Table 4) have started to show better results.

The most recent series with better immunoablative regimens have shown results that are superior to those published in previous decades, with lower rates of rejection and low toxicity. Several groups have tested different conditioning regimens, with the greatest experience being that of the US group with low grafting failure rate and excellent overall survival and event-free survival.[23,24] However, it is known that some of these patients require immunosuppressive maintenance to keep the grafting[23]. Therefore, transplantation with non-myeloablative conditioning should still be considered only in clinical trials and should not be indicated as routine.

Sources of alternative hematopoietic stem cells

The exceptional outcomes with related donors resulted in the search for the cure of the disease with alternative donors. The use of related cord blood, despite showing a delayed neutrophil and platelet engraftment, subsequently showed in the largest series published by the European group of BMT (EBMT), a disease-free survival after 6 years of follow-up 90%, comparable with that of related BM.[22] Also, the data from these 90 cases showed no difference in terms of overall and event-free survival when compared with bone marrow use.[22] Therefore, the use of related umbilical cord blood can be also considered a source of hematopoietic stem cells for allogeneic BMT in sickle-cell disease.

In turn, the use of unrelated umbilical cord blood did not show satisfactory results. The graft rejection rate was 46% in two studies. Although the overall survival rate was 94%, the incidence of aGVHD was 20%, much higher than that found in related umbilical cord blood.[25] The use of unrelated cord blood must be considered only in clinical trials.

TABLE 3. Main series of myeloablative allogeneic BMT with related donor for treatment of sickle-cell diseases.

Author	Vermylen 1998	Walters 1996	Bernaudin 2007-2010	Panepinto 2007	Lucarelli 2012	Mc Pherson 2011	Locatelli 2013
N	50	26	121	67	40	27	160
Overall survival	96%	94%	98%	97%	91%	96%	97%
Sobrevida Livre de Eventos	82%	84%	95%	85%	91%	96%	88%
BRM*	7%	6%	7%	0%	9%	4%	4,5%
Grafting failure	10%	10%	7%	13%	0%	0%	7% MO 10% SCU
Idades	1-23	3-15	2-22	2-27	2-17	3-17	3-17
aGVHD**	20%	3%	17%	10%	17,5%	12%	21% MO 11% SCU
cGVHD***	10%	3%	11%	22%	5%	4%	12% MO 5% SCU

*BRM – BMT-related mortality; aGVHC – acute graft versus host disease
***cGVHD – chronic graft versus host disease; UCB – umbilical cord blood; BM: bone marrow

TABLE 4. Main series of non-myeloablative allogeneic BMT for treatment of sickle-cell diseases.

Author	Van Besien 2000	Iannone 2003	Hsie H 2009	King AA 2015	Saraf S 2016	Strocchio 2015
N	2	6	30	43	13	15
Overall survival	1 caso	100%	97%	93%	100%	100%
Event-free survival	1 caso	0%	87%	90%	92%	93%
BRM*	50%	0%	4%	5,7%	0	0
Grafting failure	0%	100%	13%	1 Case SCU	8%	7%
Ages	40 e 56	3-20	17 - 65	0,8 - 20	17 - 40	< 16
aGVHD**	1 caso grave	-	0	23%	0	
cGVHD***	-	-	0	13%	0	

*BRM – BMT-related mortality; aGVHC – acute graft versus host disease
***cGVHD – chronic graft versus host disease; UCB – umbilical cord blood.

The first obstacle of using unrelated donors is finding the donors for these patients. The probability of finding donors in this group is significantly lower than in Caucasians populations and is only 19% at allelic level.[25] Therefore, there are few data with unrelated donors in the literature and there are only studies in progress, without definitive results. This source should be considered only in clinical trials and cannot be recommended for routine use.

The introduction of haploidentical allogeneic BMT with the use of cyclophosphamide after hematopoietic stem cell infusion has dramatically increased the availability of donors for patients with hematological malignancies. With the favorable data and the low incidence of aGVHD and cGVHD, the first data on hemoglobinopathies appeared. The Johns Hopkins group described the first 14 cases, aged 15 to 42 years, who were transplanted with haploidentical related donors. With a median follow-up of two years, 11 patients maintained a stable graft (14 haploidentical and 3 related donors) and in 6 cases it was possible to discontinue immunosuppression. Although there were no deaths in the described cases, 6 of 14 patients had graft rejection. [26] The group has been carrying out minor protocol modifications to allow better grafting in patients with non-malignant diseases. Nevertheless, the allogeneic BMT with related haploidentical donors should be performed only in the context of a clinical trial.

Table 5 summarizes the main series with alternative hematopoietic stem cell sources.[25]

The treatment of sickle-cell diseases in Brazil

Brazil has a comprehensive public health system (SUS) legislation regarding the treatment of sickle-cell diseases. Even though these were initiated only after 2005, several decrees have been published, covering different aspects of the treatment of these individuals. Table 6 summarizes the main decrees published regarding the treatment of patients with sickle-cell disease. Despite this comprehensive legislation, access to this type of treatment is still very irregular in different parts of the country. The socioeconomic status of the population also hinders access to all available treatments through SUS.[27]

The introduction and scope of the neonatal screening program (NSP) in the whole country after 2014 has not resulted yet in improved survival for patients with sickle-cell diseases in Brazil.[28] Nonetheless, the introduction of allogeneic BMT as a therapeutic option in SUS for patients with sickle-cell diseases was a step forward in the

TABLE 5. Outcomes of unrelated or haploidentical allogeneic BMT in individuals with sickle-cell diseases

Author	N	Mean age	HST source	OS (%)	Rejection	DFS	BRM
Bolanos-Maede	14	22	Haplo	100	43%	57%	0
Dallas	8	9	Haplo	75	38%	38%	38
De la Fuente	13	10	Haplo	94			
Eckrich	15		CD34	75	7%	67%	
Kamani	8	13,7	Cord	87	63%	37%	13
Ruggeri	16	6	Cord	94	-	50%	6
Shenoy	29	14	BM	86	10%	76%	21

HST: hematopoietic stem-cell; BM: bone marrow; Haplo: haploidentical donor

TABLE 6. Ministry of Health Decrees related o sickle-cell diseases in Brazil

Decrees	Description
Decree n. 1.391/GM of August 16, 2005	Institutes, within the National Health System, the guidelines for the National Comprehensive Care Policy for People with sickle cell disease and other hemoglobinopathies.
Decree n. 12.104, of December 1, 2009	Provides for the establishment of the National Action Day for the Rights of People with Sickle Diseases, to be celebrated annually on October 27.
Decree n. 55, of January 29, 2010	Approved the Clinical Protocol and Therapeutic Guidelines - Sickle Cell Disease, considering the need to improve Sickle Cell Disease parameters in Brazil and to update national guidelines for the diagnosis and monitoring of patients with this disease. Hydroxyurea for patients with >3 years.
Decree n. 1459, of June 24, 2011	Institutes, within the Brazilian Unified Health System - SUS - the Stork Network. In December 2013, through a technical communication, hemoglobin electrophoresis was included in the prenatal screening in the Stork Network.
Decree n. 473, of April 26, 2013	Establishes the protocol for Transcranial Doppler use as an outpatient procedure in stroke prevention in patients with sickle-cell disease.
Decree n. 27, of June 12, 2013.	Incorporates hydroxyurea in children with sickle-cell disease in the Brazilian Unified Health System – SUS.
Decree n. 1321, of December 21, 2015.	Includes in the list of Procedures, Drugs, Orthoses, Special Prostheses and Materials of SUS, the compatibility of allogeneic transplant with related donor of bone marrow, peripheral blood or umbilical cord blood for the treatment of sickle cell disease, and establishes guidelines and type of transplantation for this purpose.

fight against this not so benign disease. Table 7 depicts the codes to be used for billing purposes in SUS.

Decree N. 1321 of December 21, 2015, summarized in Table 8, includes in the Technical Regulations of the National Transplant System, the indication for allogeneic transplantation with related donor of bone marrow, peripheral blood or umbilical cord blood, with myeloablative regimen, for the treatment of sickle-cell disease.

According to the decree, the allogeneic hematopoietic stem cell transplantation (HSCT) with related donor, of bone marrow, peripheral blood or umbilical cord blood, with myeloablative regimen, for the treatment of sickle-cell disease may be indicated and performed in patients who meet the following criteria:

I – Patient aged up to 16 years with sickle-cell disease type S, homozygous or type S beta thalassemia (Sbeta) using hydroxyurea, with at least one of the following conditions:

a. neurological alterations due to stroke, neurological alteration that persists for more than 24 hours or alterations at imaging tests;

TABLE 7. SUS codes for allogeneic BMT in sickle-cell diseases

SUS code	Source	ICD
05.05.01.001-1	Allogeneic BMT with related donor	D57.0 Sickle-cell anemia with crisis D57.2 Double heterozygous sickle cell disorders
05.05.01.003-8	Allogeneic transplantation with related donor of umbilical cord blood	D57.0 Sickle-cell anemia with crisis D57.2 Double heterozygous sickle-cell disorders
05.05.01.005-4	Allogeneic transplantation with related donor of peripheral hematopoietic stem cells	D57.0 Sickle-cell anemia with crisis D57.2 Double heterozygous sickle-cell disorders

TABLE 8. Indications for allogeneic BMT with related donor according to decree n. 1321 of December 21, 2015'

Patient aged up to 16 years old with homozygous sickle cell disease type S or type S beta thalassemia (Sbeta) using hydroxyurea that has at least one of the following conditions.
a. Neurological alteration due to stroke, neurological alteration that persists for more than 24 hours or alteration at imaging assessment;
b. cerebrovascular disease associated with sickle cell disease;
c. more than two severe vaso-occlusive crises (including Acute Thoracic Syndrome – ATS) in the previous year;
d. more than one episode of priaprism;
e. presence of more than two antibodies in patients undergoing hypertransfusion or one high-frequency antibody;
f. osteonecrosis in more than one joint.

b. cerebrovascular diseases associated to sickle-cell disease;

c. more than two severe vaso-occlusive crises (including Acute Thoracic Syndrome - ATS) in the last year;

d. more than one episode of priapism;

e. presence of more than two antibodies in patients submitted to hypertransfusion or one high-frequency antibody; or

f. osteonecrosis in more than one joint.

The use of hematopoietic stem cell sources (bone marrow, peripheral blood or umbilical cord blood) should consider the risks to the donor and the risks and benefits to the recipient.

Conclusions

A better understanding of the pathophysiology of sickle-cell disease has brought significant advances to the treatment of these individuals. Early identification of affected individuals by neonatal screening, the introduction of drug preventive measures, such as antibiotic prophylaxis and hydroxyurea and careful monitoring of patients could provide important benefits in terms of survival. Allogeneic BMT with related donors is still the only curative option for sickle-cell disease and has shown excellent results. The incorporation of allogeneic BMT into the Brazilian public health system, SUS, will provide patients with organic complications and patients with an unfavorable evolution with a real hope of cure. Unfortunately, there are no clear predictors of unfavorable evolution that may predict patients who will benefit most from the procedure, but all affected patients that show more severe signs of evolution should be tested to search for possible donor in the family. Universal access to available treatment and follow-up assessment to all patients with sickle-cell disease is still a major challenge in our country.

Resumo

Transplante alogênico de medula óssea em doenças falciformes

As doenças falciformes são as hemoglobinopatias mais frequentes mundialmente. Nas últimas décadas vivenciamos melhora na sobrevida de portadores destas patologias com a introdução de medidas preventivas e o uso precoce da hidroxiurea. O transplante de medula óssea alogênico (alo TMO) é a única opção terapêutica curativa para as hemoglobinopatias. O mesmo tem sido indicado para pacientes com complicações neurológicas, crises vasoclusivas repetidas, alguma lesão orgânica e alosensibilizados. O uso de doadores

relacionados de medula óssea ou cordão umbilical mostrou em 1000 procedimentos realizados sobrevida global de 95% e sobrevida livre de ventos de 90%. O uso de doadores não aparentados não mostrou resultados tão expressivos, mas no futuro métodos melhores de tipagem de HLA e de medidas de suporte podem melhorar estes resultados. No Brasil apenas recentemente o alo TMO foi incluído no âmbito do sistema único de saúde (SUS) como opção terapêutica para portadores de doenças falciformes. O uso de doadores aparentados de MO ou de SCU com regime mieloablativo é considerado hoje tratamento estabelecido, sendo que o uso de doadores alternativos não aparentados ou haploidenticos e o uso de transplante com regime não mieloablativo deve ser considerado apenas em estudos clínicos.

Palavras-Chave: Anemia Falciforme; Transplante de Medula Óssea; Hemoglobinopatias

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Immunotherapy with natural killer cells: a possible approach for the treatment of Acute Myeloid Leukemia also in Brazil

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SUMMARY

The allogeneic hematopoietic stem cell transplantation (HSCT) can cure intermediate and high-risk acute myeloid leukemia. Even with the development of strategies to reduce HSCT toxicity, this is still a complex treatment with high morbidity and mortality. Knowledge of the graft versus leukemia effect of HSCT has prepared the way for the development of Adoptive Immunotherapy or *in vitro* expansion of activated lymphocytes without alloreactivity, with subsequent intravenous infusion. The infusion of genetically modified T lymphocytes and haploidentical natural killer cells has been tested as an alternative to HSCT with very interesting results worldwide and in Brazil, as we not only have the technology of *in vitro* expansion of clinical grade lymphocytes available, but also do it according to the Good Manufacturing Practices that have been determined internationally.

Keywords: NK cells, graft versus leukemia effect, adoptive immunotherapy, acute myeloid leukemia.

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The Hematopoietic Stem Cell Transplantation (HSCT) is currently the curative option for intermediate and high-risk acute myeloid leukemia (AML); procedure toxicity and complexity can, however, result in a series of harmful consequences for the body – even when cured of the malignancy. Since the beginning of the 1990s, it has been known that the curative action of HSCT depends on the effect of graft immune cells on residual malignant disease - the graft-versus-leukemia effect - consolidating the knowledge of the immune system role in eradicating malignancy[1].

Immunotherapy based on the use of activated immune cells, also known as Adoptive Immunotherapy (AI), aims to use the patient's own immune cells or those of a selected donor, in order to eradicate the malignant disease without the risk of graft-versus-host-disease (GVHD) development observed in the HSCT scenario. The results of AI, tested initially and for many years in the treatment of solid cancers, particularly melanoma, have become consistent after Rosenberg[2] demonstrated that it is essential to eliminate or attenuate the activity of the patient's immune cells prior to the lymphocyte infusion, as to allow the *ex-vivo* activated lymphocytes, when infused, to find an environment rich in growth factors and thus proliferate and perform their antitumor action markedly and continuously.

The recent development of T-lymphocytes modified by inserting Chimeric Antigen Receptors (CAR) into them and their infusion after the patient's immune system ablation demonstrates the principle that AI is a promising treatment[3]. However, the infusion of CAR lymphocytes, with significant antitumor activity, it followed by tumor lysis syndrome that results in a cytokine storm, of which the patient, if not adequately treated with specific immunological blockers, may die. Fortunately, these are preliminary results obtained in the treatment of patients with significant tumor mass. Perhaps the use of immune effectors in a residual tumor disease scenario might minimize these effects and thus, phase II studies including patients in complete remission of the disease are needed to test this hypothesis.

In the treatment of AML, particularly when using the haploidentical HSCT, the role of natural killer (NK) cells in eradicating the disease dissociated from GVHD was demonstrated[4]. Therefore, NK cells seem to be natural candidates for AI in the treatment of this disease and their infusion, without HSCT, in patients with AML, has shown to be effective[5].

The great challenge has been, however, to achieve the *in vitro* expansion of a population of purified NK cells, with no contamination by T lymphocytes – a very difficult

task, because NK cells are relatively rare in peripheral blood. The development of cells with artificial antigens that received the insertion of adhesion molecules and specific cytokines, when co-cultured with mononuclear cells previously depleted of T lymphocytes, has been shown to be a promising technique to obtain up to 1010 NK cells with purity levels >90%[6].

This technology is established in Brazil, more precisely in the Technology and Cell Therapy Center of Porto Alegre University Hospital. A clinical trial about the safety and feasibility of AI with expanded NK cells for the treatment of recurrent or treatment-refractory AML has already been approved in Brazil and ongoing at MD Anderson Cancer Center (MDACC), in Houston, TX, USA. The first three patients that have already treated in Houston have shown that not only the infusion of these cells is not accompanied by any adverse effects, but also that the answer seems to be slow and gradual, as four months after treatment the disease residual levels remain decreased, demonstrating not only the antitumor action of these cells but also the permanence of these cells or their effect for a prolonged period. The inclusion of the first patient treated in Brazil should take place within a few weeks. In a review recently published by our group[7] it is possible to have a broader and more comprehensive view of the role of NK cells in the treatment of neoplasms.

Resumo

Imunoterapia com células *natural killer*: um caminho possível para o tratamento da Leucemia Mielóide Aguda também no Brasil

O transplante de células-tronco hematopoéticas (TCTH) alogênico é curativo para leucemia mielóide aguda de risco intermediário e alto. Mesmo com o desenvolvimento de estratégias para minorar a toxicidade do TCTH, este ainda é um tratamento complexo com elevada morbi-mortalidade. O conhecimento sobre o efeito enxerto contra leukemia do TCTH pavimentou o caminho para o desenvolvimento da Imunoterapia Adotiva ou expansão *in vitro* de linfócitos ativados, sem alo-reatividade, com posterior infusão endovenosa. A infusão de Linfócitos T geneticamente modificados e de células Natural Killer haploidenticas tem sido testada como alternativa ao TCTH com resultados bastante interessantes no mundo e no Brazil já que não apenas dominamos a tecnologia de expansão *in vitro* de linfócitos em grau clínico, como o fazemos segundo as Boas Práticas de Manufatura determinadas internacionalmente.

Palavras-chave: Células NK, efeito enxerto contra leucemia, imunoterapia adotiva, leukemia mieloide aguda.

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Relevance of prognostic factors in the decision-making of stem cell transplantation in Myelodysplastic Syndromes

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Abstract

The hematopoietic stem cell transplantation (HSCT) is the only curative alternative for Myelodysplastic Syndrome (MDS), but many patients are not eligible for this treatment, as there are several limiting factors, especially in the case of patients with low-risk MDS. The aim of this study is to discuss the factors that can guide the decision-making on referring or not a patient to HSCT. Three cases of MDS, two of which were submitted to HSCT are presented. We intend to report the difficulties in referring patients with MDS to transplant and the prognostic factors that contribute to define eligibility.

Keywords: Myelodysplastic Syndrome; Hematopoietic Stem Cell Transplantation; Prognosis

Introduction

Myelodysplastic Syndrome (MDS) is a clonal disorder characterized by cytopenia and it may be accompanied by dysmyelopoiesis cytogenetic changes, which may define prognosis[1,2]. Approximately one third of the patients develop acute leukemia, in most cases, acute myelogenous leukemia, making it necessary to use prognostic scoring systems, such as IPSS, IPSS-R and WPSS. The latter has been enhanced with improved cytogenetic stratification[3,4]. Despite this refinement, as we better understand the molecular changes, we found that the prognostic scores, as they do not incorporate the mutations, do not fully contemplate this risk characterization[1]. In fact, when we are treating high-risk patients, who present with refractory anemia with excess blasts (RAEB) I and II, there is no doubt that, if the patient has the medical condition, he should be referred to hematopoietic stem cell transplantation (HSCT). However, in low-risk patients, for whom the recommendation is a more conservative approach, we often deal with an adverse context, as due to the cytopenia many of these patients depend on transfusions of packed red blood cells and platelets, which, despite classifications, behave as high risk, with an unfavorable quality of life and life expectancy.

The study of TET2, DNMT3, TP53, JAK2, RUNX1, SF3B1, AF1 and ASXL1 mutations has shown to be significant, as it identifies the association between the tumor genomic profile and the phenotypic and clinical characteristics of the disease, thus having significant prognostic value[5]. The p53 gene mutation can be found in 8 to 12% of all subtypes of MDS and is independently associated with poor prognosis, more frequently in patients with complex karyotype and 5q deletion (15 to 20%), which may predict resistance to lenalidomide or be associated with recurrence[6-9]. The protein encoded by the TP53 tumor sup-

pressor gene is a key factor in regulating the cell cycle and tumor pathogenesis. Its overexpression is related with the presence of TP53 mutations and both have been associated with poor prognosis and shorter survival[10]. The analysis by the immunohistochemistry of p53 protein has been considered a useful and easily applicable tool, having been observed in up to 34.4% of patients with low-risk MDS[11]. In addition to correlating with the presence of the mutation and indicating poor prognosis and shorter survival[12-14], p53 has been identified as a parameter that can help in the indication and the outcome of HSCT[12-15].

Case 1

A 70-year-old male patient was diagnosed with MDS, of refractory cytopenia with multilineage dysplasia (RCMD) subtype, according to the WHO 2008[16], with intermediate-1 risk according to IPSS and very low risk, according to the R-IPSS after blood count assessment: hemoglobin, 11.4 g/dL, hematocrit, 34.4%, Leukocytes-3.030x10^9/L, platelets 9.13x109/L; myelogram: hypercellular with dysplasia >10% in all lineages, 0.2% blasts and normal iron levels; biopsy: grade I/II diffuse fibrosis; Immunohistochemistry: CD34 + labeling in precursor cells and in some megakaryocytes,

presence of lymph nodes, CD20 labeling. Strong nuclear staining of 40% in p53 was observed in blast cells. The karyotype was normal (46, XY). The patient did not respond to therapy with erythropoietin and granulocyte colony-stimulating factor (G-CSF). The disease progressed to acute leukemia with pancytopenia: Hemoglobin-9.91 g/dL, hematocrit, 29.3%, leukocyte, 1.41x10^9/L, platelets, 8.0x10^9/L and 10% blasts in peripheral blood. Six months after the first admission, the patient died.

Case 2

A 51-year-old male patient was diagnosed with MDS, of refractory anemia with excess blasts I (RAEB-1)[16] subtype, after careful analysis of blood count: hemoglobin – 4.84g/dL, hematocrit, 14.4%, leukocytes, 2.03x10^9/L, platelets, 6.52x10^9/L and myelogram: markedly hypocellular, presence of 5% blasts. Bone biopsy showed hypercellularity with marked dysmegakaryopoiesis, mild dyserythropoiesis and grade I/II myelofibrosis. No metaphases were obtained at the cytogenetic analysis. Immunohistochemistry was positive for CD34 in several precursor cells and megakaryocytes. Lymphoid nodules were observed, labeling CD20. The p53 expression was positive in 4% of analyzed cells and the hypomethylating azacitidine was requested, but it was not available. The patient was referred to related allogeneic HSCT. The conditioning regimen consisted of fludarabine 120 mg/m^2 and melphalan 180 mg/m^2. After the HSCT, the patient developed a severe infectious condition and died.

Case 3

A 56-year-old male patient was diagnosed with hypocellular MDS after ruling out aplasia. The blood count showed pancytopenia: hemoglobin, 8.0 g/dL, hematocrit, 24.2% and leukocytes, 3.0x10^9/L. The myelogram and bone marrow biopsy showed hypocellular marrow with reticulin stain, indicating the presence of grade II marrow fibrosis (MF-2). Cytogenetics did not provide enough metaphases for analysis. The immunohistochemistry was positive for CD34, with megakaryocyte labeling and there were lymphoid nodules, labeling CD20. The p53 protein labeling was negative. The patient was referred to HSCT with related donor. The conditioning regimen consisted of fludarabine 120 mg/m^2 and melphalan 180 mg/m^2. Six months after transplantation, the patient is stable and in complete remission.

Discussion

Although an increased understanding of MDS has led to the emergence of new approaches to clinical manage-

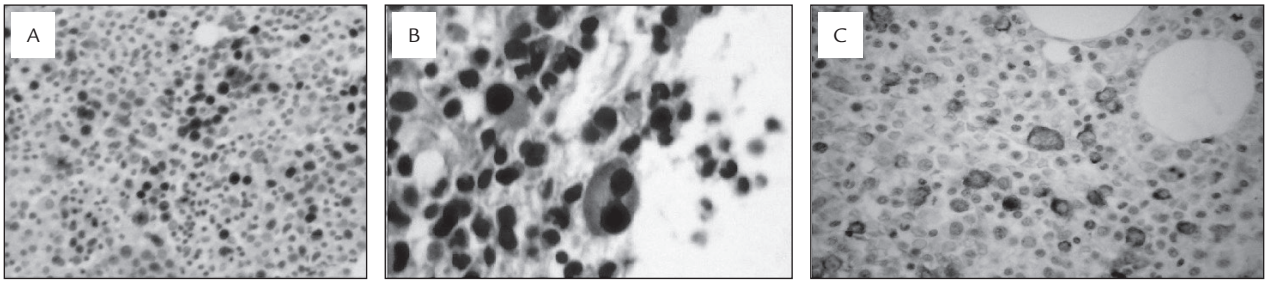

FIGURE 1. Images from Case 1. A- Strong nuclear staining (40%) of p53 protein in granulocytic precursors. B- Myelogram showing cellularity of approximately 70%. Dysplastic megakaryocytes, erythroblasts in the peritrabecular position (ALIP). Hematoxylin. Magnification: 1000x. C- Positive CD34+ labeling in precursor cells and in some megakaryocytes. Streptavidin-Biotin. Magnification: 400x.

ment and new therapeutic modalities, allogeneic hematopoietic cells is still the only curative therapy[1,17]. In MDS, factors considered critical in HSCT indication such as age, comorbidities, ideal transplantation time and conditioning regimen have limited its practice to less than 5% of patients, after careful selection[18-21]. Regarding therapeutic regimens, protocols with low doses of radiation or alkylating agents have been used in an attempt to minimize treatment effects related to toxicity and graft-versus-host disease[22.23]. It is expected that, with the development of new preventive and therapeutic strategies for better post-transplantation management, most patients with MDS can benefit from better survival. Generally, HSCT is indicated for patients with unfavorable prognostic features, according to the World Health Organization and classification systems such as IPSS and IPSS-R. Some characteristics have been reported as being indicative of HSCT, such as complex karyotype, bone marrow fibrosis markers and immature cells in the bone marrow. Clinical conditions such as intense need for transfusion, iron overload or recurrent clinical infections are also important factors in determining the possibility of HSCT[24-26]. Although increased frequency of high-risk disease phenotypes, such as unfavorable cytogenetics and possibly higher rates of mortality due to transplantation limit its use in older patients,[27] McClune et al., analyzed the results of 1.080 patients with AML or MDS undergoing HSCT and concluded that age alone should not be considered as a contraindication to HSCT. Patients undergoing HSCT can benefit from approximately 30 to 50% disease-free survival, depending on patient and disease characteristics, conditioning regimen, hematopoietic cell donors and transplantation procedure strategies[28,29]. In patients with low-risk MDS, HSCT constitutes a challenge, as the best time to perform it has not been well-established yet and it is a relevant issue to be discussed, considering the most significant factors that may indicate the viability and success of the procedure[21].

This article reports two cases of low-risk patients and one high-risk case, which according to the literature, showed clinical and hematological indications favorable to HSCT. The striking characteristic in all cases was the presence of fibrosis and lymphoid nodules in the bone marrow. Two patients were positive for the p53 protein expression and died. The first died before undergoing HSCT and the second died twenty days after the procedure, due to a severe infection. The third case is a patient who was negative for p53 expression, had not previously use antithymocyte globulin[3], but was submitted to HSCT, progressed well and, nine months later, had no complications.

There are few studies that investigate the role of p53 expression in patients with low-risk MDS. In a previous study, we observed that patients with p53 expression had a higher frequency of bone marrow fibrosis and lower survival[12].

Studies have suggested the participation of MDS patients in research protocols, particularly those with complex karyotypes and mutations that can indicate HSCT, for risk assessment and potential benefits of each available therapeutic approach[10,30]. Considering the outcome of each reported patient, added to the literature data, we suggest that the expression of p53 protein, in addition to being an important prognostic marker, can help in HSCT indication associated with the presence of fibrosis. However, further studies are needed to confirm this hypothesis.

Resumo

Relevância dos fatores prognósticos na decisão do transplante de células-tronco na Síndrome Mielodisplásica

O transplante de células-tronco hematopoéticas (TCTH) é a única alternativa curativa para Síndrome Mielodisplásica (SMD), porém muitos pacientes não são elegíveis para esta opção, pois existem diversos fatores limitantes, principalmente no caso de pacientes com SMD de baixo risco. O objetivo do estudo é discutir os fatores que podem orientar a decisão no encaminhamento ou não para o TCTH. São apresentados três casos de SMD, dos quais dois foram submetidos ao TCTH. Nos propomos a relatar as dificuldades no encaminhamento dos pacientes com SMD ao transplante e os fatores prognósticos que contribuem para definir a elegibilidade.

Palavras-Chave: Síndrome Mielodisplásica; Transplante de Células-Tronco Hematopoéticas; Prognóstico.

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Haploidentical transplantation of hematopoietic stem cells

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SUMMARY

Objective: To review and discuss the literature on hematopoietic stem cell transplantation (HSCT) with haploidentical donors in Brazil.
Method: Literature review.
Results: The haploidentical hematopoietic stem cell transplantations have become a safe option in hematology since the 80s, with the possibility of *ex-vivo* T-cell depletion. However, its broad use worldwide occurred with the advent of haploidentical non-myeloablative transplants using *in vivo* T-cell depletion with the administration of post-transplant cyclophosphamide. The results were encouraging, despite the increased risk of infection and post-transplantation recurrence. Recent publications on acute myeloid leukemia, myelodysplastic syndrome and Hodgkin's lymphoma have shown similar results among haploidentical, unrelated and related full-match transplants. Obviously, these findings of retrospective studies should be confirmed by clinical trials.
Conclusions: Transplantation with haploidentical donor has shown to be feasible in Brazil and the first publications and results are showing encouraging results.

Keywords: Bone Marrow Transplantation. Stem cells. Transplants.

Introduction

The haploidentical transplantation initiatives in the 1970s were catastrophic and prohibitive, with an incidence of graft-versus-host-disease (GVHD) >70% and grafting failure of 20%.[1] In the 1980s, with the use of T-cell depletion with sheep erythrocytes, the methodology started to show greater acceptance.[1]

In 1994, the Italian group with the CD34 cell selection equipment, demonstrated decreased risk of rejection using high doses of cells ("mega dose": 13.8 x 10^6 CD34 with 1x10^4 CD3).[2] The initiatives of Chinese researchers with stringent conditioning have shown excellent results since 2006.[3] In 2007, the Duke University group led by Nelson Chao presented a protocol without selection of CD34+ cells *in vitro* and *in vivo* depletion using Campath (alemtuzumab) in the conditioning regimen.[4] However, a major breakthrough occurred in 2008 when the group of Baltimore, led by Ephraim Fuchs, consolidated the use of cyclophosphamide on days +3 and +4 post-transplantation, also with depletion of T cells *in vivo*.[5] The authors published results using this type of regimen in several types of malignant diseases, such acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplasia and non-Hodgkin and Hodgkin's lymphoma, with an overall survival >50% in Hodgkin's lymphoma, reaching 76%.[5] From that point onward, what we saw was a constant search for methodologies that would further improve the results of haploidentical transplants.[5-7]

The advantages of using this type of transplant is the immediate donor availability, instant access to the donor for cell therapy after transplantation and the possibility of selecting several family members according to clinical characteristics and alloreactivity of NK (natural killer) cells. As disadvantages, we can mention the higher potential risk of GVHD, the need for depletion of T cells *in vivo* or *ex vivo*, leading to a higher incidence of infection due to the slow immuno-reconstitution and high incidence of recurrence.[6,7]

But undoubtedly, the great advantage is that, considering that 40-50% of patients have no related or unrelated compatible donors, HLA "mismatch" or haploidentical transplants of first-degree relatives can be found in over 95% of patients.[7-9]

In Brazil, the use of post-transplantation cyclophosphamide is the one most often used to perform haploidentical transplants. This choice is not made by chance.

First, it results from the high cost of processing, which is restricted to a few treatment centers that have specific protocols to be used in, for instance, congenital immunodeficiencies. Secondly, literature reports indicate that the results tend to be better, since only alloreactive lymphocytes are affected.[5,8,9,10]

Initial studies seeking to compare the haploidentical transplantation with other alternatives, such the umbilical cord or unrelated mismatch transplants, have not shown great superiority between one form or another of transplanting. Given that factors such as mismatch, presence of anti-HLA antibodies, KIR reactivity, NIMA and HLA C in umbilical cord can help in the decision-making, Table 1 has been widely used as a guide.[11-15]

Recently, the MD Anderson group, led by Dr. Stefan Ciurea, showed comparable results between haploidentical and unrelated transplants, even fully compatible. This fact opens the possibility of using the haploidentical transplant primarily when compatible related donor cannot be found and when it takes longer to find unrelated donors due to genetic or operational difficulties. This finding, which has been demonstrated by other groups, will obviously change – if confirmed by clinical studies – the way we choose the best donor for hematopoietic cell transplantation, significantly modifying Table 1 and establishing the haploidentical transplant option or unrelated transplant as fully compatible for most clinical situations[16,17].

Advantages and disadvantages of using haploidentical donors

Compared to other sources of donors, the main advantages of using haploidentical transplants are:[6,7,9]

a) Availability: it is estimated that a patient has 2.7 potential haploidentical donors among their first-degree relatives. This number is compared to a 25 to 30% chance of an HLA-identical family donor and the variable chances between 16% and 75% of a fully compatible donor (8 x 8) in a donor registry, depending on the genetic difficulty of each case.
b) Immediate availability: in urgent cases, when compatible family donors cannot be found, a haploidentical donor will be selected quickly, compared with the mean time for search and confirmation of an unrelated donor, which is around three to four months.

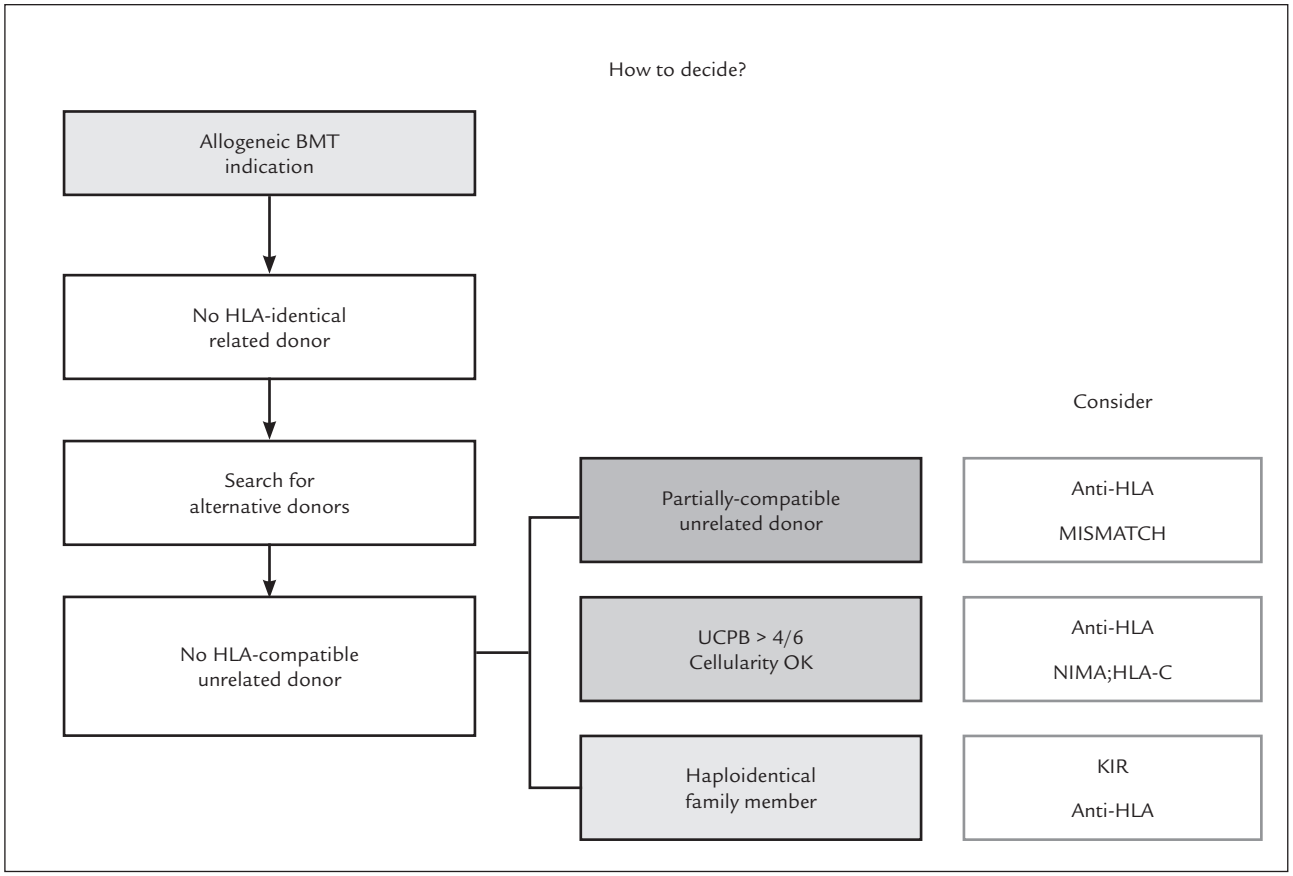


CHART 1. Decision process between alternative transplants

c) Low cost: compared with unrelated donors and umbilical cord blood, the costs are significantly lower in the search for haploidentical donors.
d) Possibility of using the donor cells for immunotherapy (lymphocyte infusion): this strategy is impossible in the case of umbilical cords.

However, the use of methods that target T-cell depletion decreases the incidence of GVHD, but increases the risk of rejection, infection and reduces graft-versus-leukemia reaction.[11-13]

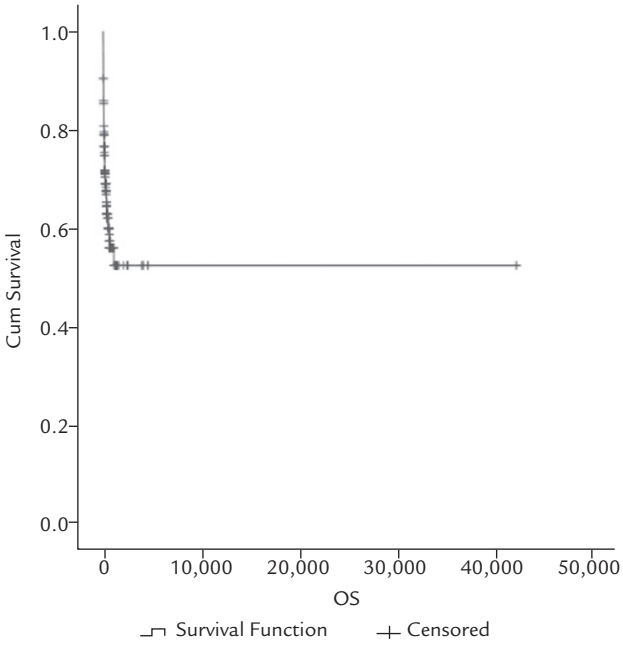
Main current strategies for haploidentical transplants

a) In vitro T-cell depletion: This methodology employs megadoses of CD34 and is used by the Perugia group.[1,2,12,13]
b) GIAC: uses G-CSF (G) granulocyte colony stimulating factor to stimulate the donor and extensive post-transplantation immunosuppression (I), using ATG (A) (antithymocyte globulin) and the combined use (C) of bone marrow and peripheral blood. This methodology is used almost exclusively in China, where there is extensive experience in haploidentical transplants.[13]
c) Post-transplantation cyclophosphamide: this is the main form of T-cell depletion used worldwide, with adaptations to the first works with non-myeloablative transplants using fludarabine, low-dose (200 Gy) total body irradiation and cyclophosphamide. Cyclophosphamide 50 mg/kg is used on days +3 and +4 and the prophylaxis of graft-versus-host disease is made with MMF and tacrolimus.[4,16,18]
d) Choice of the best donor: According to a study published by the Chinese group, the best donor is young and male.[19] The father has precedence over the mother. It is also important to assess the blood group, perform serology for cytomegalovirus, assess the presence of HLA donor-specific antibodies, NIMA (non-inherited maternal antigens) and KIR reactivity.[20] These data have not been reproduced by others and we do not know whether their use is valid for other conditioning regimens. The most important factor in all the works and for any type of methodology, is the assessment of the presence of anti-donor specific antibodies.

Brazilian experience with haploidentical transplantation

The number of haploidentical transplants have been increasing in Brazilian centers. Until mid-2013, 85 transplants had been performed. From that date until mid-2015, over 100 transplants were performed, totaling 185 cases and this number is increasing.[21] Most were performed in cases of acute leukemia (90 patients), severe aplastic anemia (24 patients) and Hodgkin's lymphoma (20 patients), with the remaining patients scattered among other indications of malignant and nonmalignant diseases. The overall survival of these patients can be seen in Graph 1. The presence of hepatic veno-occlusive disease was the only factor that had an impact on survival in the multivariate analysis of Brazilian cases as shown in Table 1.[21]

Regarding specific initiatives, the Brazilian group published a series of severe aplastic anemia cases (16 patients) with interesting results (Graph 2) and presented the results of 20 patients with Hodgkin's lymphoma



GRAPH 1. Overall survival of patients undergoing haploidentical transplants in Brazil[21]

TABLE 1. Multivariate analysis of impact on survival[21]

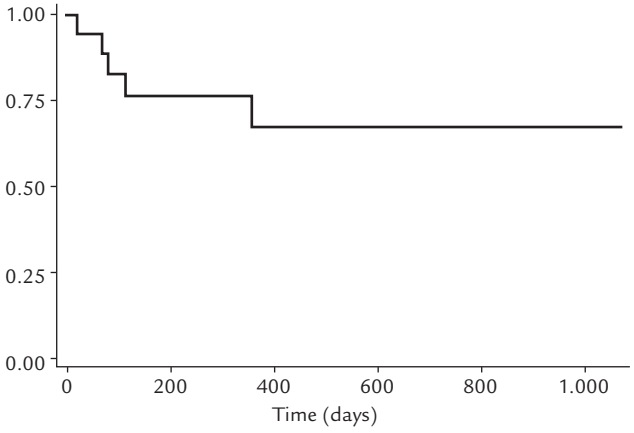
Variable	Hazard ratio	P
Diagnosis		
Lymphoma/Myeloma (*versus* non-malignant)	1.99	0.625
Acute leukemia (*versus* non-malignant)	2.28	0.12
Age (contínua)	1.01	0.10
High-risk disease (*versus* standard risk)	1.16	0.63
Bone marrow use (*versus* peripheral blood)	1.22	0.49
Myeloablative conditioning	1.00	0.98
Total body irradiation use	0.70	0.48
Onset of hepatic veno-occlusive disease	2.85	0.008
Chronic GVHD (time-dependent)	0.87	0.78

GVHD = graft-versus-host disease.

(Figure 3) at the Congress of the Brazilian Association of Hematology (ABHH) in 2015.[22,23] The main initiatives in haploidentical transplants of the Brazilian Society of Bone Marrow Transplantation (SBTMO) were established at the society meetings, with members interested in the area and the creation of uniform protocols for the following situations: acute myeloid leukemia and myelodysplasia, acute lymphocytic leukemia, Hodgkin's lymphoma and severe aplastic anemia.[24]

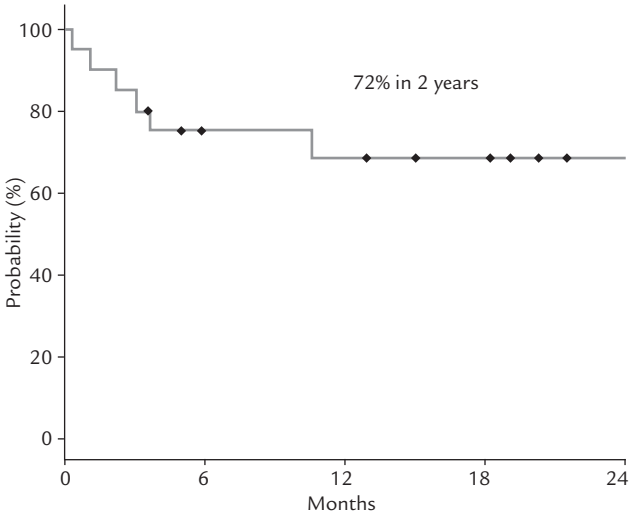
Conclusion

The haploidentical transplantation is a type of procedure that has become more and more popular among specialists in the area. The use of post-transplant cyclophosphamide has popularized its use. In some pathologies, the results are as good as in related and unrelated transplants. In Brazil, its use has gained much acceptance.



Bone Marrow Transplantation 50, 685-689 (May 2015)

GRAPH 2. Overall survival in severe aplastic anemia: 67.1% (95% confidence interval: 36.5% -85.4%).[22]



Lacerda MP, Rodrigues CA, Rocha V et al submitted ABHH 2015

GRAPH 3. Overall survival in Hodgkin's Lymphoma.[23]

Resumo

Transplantes haploidênticos de células-tronco hematopoieticas

Objetivo: Revisar e discutir a literatura sobre transplantes de células-tronco hematopoiéticas (TCTH) com doador haploidêntico no Brasil.

Métodos: Revisão da literatura médica.

Resultados: Os transplantes haploidênticos de células-tronco hematopoiéticas tornaram-se uma opção segura na hematologia a partir dos anos 1980, com a possibilidade de depleção de células T *ex-vivo*. No entanto, sua ampla utilização em todo mundo ocorreu após os trabalhos com os transplantes haploidênticos não mieloablativos, com depleção de células T *in-vivo*, utilizando ciclofosfamida pós-transplante. Os resultados se mostraram encorajadores, apesar do maior risco de infecções e recidiva pós-transplante. Estudos em determinadas patologias, principalmente na leucemia mieloide aguda, mielodisplasia e linfoma de Hodgkin, mostram resultados semelhantes entre transplantes haploidênticos e não aparentados e aparentados totalmente compatíveis. Logicamente, esses achados de estudos retrospectivos precisam ser confirmados por estudos clínicos.

Conclusões: No Brasil, a modalidade de transplante com doador haploidêntico se mostrou factível e as primeiras publicações e resultados mostram resultados animadores.

Palavras-chave: Transplante de medula óssea. Células-tronco. Transplantes.

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Hodgkin's Lymphoma - evaluation of patients submitted to Autologous transplantation of hematopoietic cells in the Hematology Service of the Hospital Walter Cantídio – Fortaleza, Brazil.

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SUMMARY

The Autologous HSCT is an important alternative for refractory or recurrent HL patients in terms of survival and improved quality of life. This study analyzes the results of autologous BMT performed in HL patients in the Transplant Unit of the HUWC/HEMOCE (Fortaleza - CE, Brazil). Fifty-two transplanted patients were studied from January 2009 to October 2015, among them, 30 men and 22 women, mean age of 28.2 years. All of them received GCS-F during the mobilization, in some cases associated with Vinorelbine or Plerixafor, with CD34 collection averaging 4.8 CD34/kg. The conditioning was performed with BEAC, NEAM or BEAM and the grafting with an average of 10 days. The evaluation on D + 100 showed: CR - 42 (82.7%), PR - 08 (13.5%) and 02 (3.8%) deaths, three and six days after cell infusion. After the D+100, 08 patients in CR showed HL recurrence from 06 to 36 months; 03 died and 05 are being treated with brentuximab; among the 08 patients in PR, 01 died due to HL activity, 04 months after BMT and 07 patients are undergoing treatment. The final evaluation of HL transplant patients showed an OS of 88.5% and a DFS of 61.5% in 6 years, with OS of the chemosensitive patients of 81% and of the chemoresistant ones, of 72.6%. It is possible to conclude that the Autologous HSCT has shown to be an excellent rescue therapy regarding tolerance, as well as the overall survival.

Keywords: Hematopoietic Stem Cell Transplantation; Hodgkin's lymphoma; Autologous transplantation.

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Introduction

Hodgkin's lymphoma (HL) is a B lymphoid neoplasia, with a higher incidence in young adults, curable in up to 80% of cases. Advancements in HL therapy have been documented since the introduction of combination chemotherapy protocols and changes in irradiation strategies.[1,2,3] Despite these advancements, approximately 10% of refractory patients and 20 to 25% with lymphoma recurrence should be carefully re-evaluated for a second attempt at remission. Several studies have shown that autologous hematopoietic stem cell transplantation (HSCT) is one of the most important alternatives for such patients in terms of survival and improved quality of life. The allogeneic transplant does not have a well-defined role in this new treatment strategy.[4] More recent studies have shown the importance of haploidentical transplantation in the rescue of refractory HL patients non-responsive to autologous transplantation.[5]

The objective of this study is to analyze the results of autologous BMT performed in LH patients at the Transplant Unit of SH of HUWC/HEMOCE.

Métodos

Patients originating from the state of Ceará and treated in several medical services are referred to the

Hematology Service, where they are seen in the Pre-Transplantation Outpatient Clinic for reassessment of BMT indication. Patients are referred with their respective medical records from the original service, containing the biopsy diagnosis report, immunohistochemistry, chemotherapy and radiotherapy protocols performed, date of recurrence or whether the patient is refractory to treatment. With these first recommendations the patient is enrolled in the BMT waiting listing, after which medical history and complete physical examination, hematological, biochemical and imaging evaluations are performed. A dental assessment, consultations with a nutritionist and psychologist are also requested.

The results are then analyzed for the patient to be referred to the transplantation team to schedule the mobilization and collection of hematopoietic stem cells and subsequent hospitalization for cell conditioning and infusion.

Results

A total of 54 patients were submitted to autologous transplantation from January 2009 to April 2016, of which 31 were men, aged between 17 and 63 years (mean 28.1 years) and 23 women, aged 16 to 51 years (mean 28.2 years); 21 were originally from Fortaleza and 33 from other cities in the state of Ceará. The present analysis includes 52 patients treated up to October 2015. Clinical and epidemiological characteristics are shown in Chart 1.

Regarding the first treatment, all patients received the ABVD polydrug regimen (Adriamycin, bleomycin, vinblastine, dacarbazine), of which 16 underwent associated field radiotherapy. In response, 21 patients went into complete remission, 16 into partial remission and 15 did not respond. Of the 21 in CR, recurrence ranged from 5 months to 14 years, whereas two had HL recurrence after less than 6 months, seven between 6 and 12 months and twelve more than 12 months (Chart 2).

As the second treatment due to recurrence or no response/refractory patient, 35 (62.5%) patients received the ICE regimen 12 (20.8%) ICE associated to another polychemotherapy regimen, five received DHAP, two received ESHAP and one received ABVD. The analysis of the response at this step of treatment showed that 27 (51.9%) achieved CR, whereas 25 (48.1%) had PR.

All patients received GCS-F during mobilization, and 35 were mobilized only with G-CSF, 15 with Vinorelbine and G-CSF, two with Plerixafor and G-CSF. CD34 collection ranged from 2.03 to 18.39 $X10^6$ CD34 cells/kilogram, with a mean of 4.8. The waiting time until transplantation ranged from 26 to 274 days, with a mean of 86.3 days.

Conditioning was performed with BEAC in 34 (65.4%), NEAM in 13 (25.0%) and BEAM in five (9.6%) patients. Grafting varied from 7 to 15 days, occurring in 19 (36.6%) patients in less than 10 days, in 28 (50%) between 10 and 12 days, in 3 (5.7%) more than 12 days and 2 (3.8%) showed no grafting.

The post-BMT results up to D+100 showed: CR - 42 (82.7%), PR - 8 (13.5%) and 2 (3.8%) deaths, which occurred 3 and 6 days after cell infusion. After D+100, 8 patients in CR showed HL recurrence between 6 and 36 months; 3 died and 5 are being treated with brentuximab; of the 8 patients in PR, 1 died due to HL activity four months after the BMT and 7 are undergoing treatment (2 with allogeneic transplant indication).

Charts 3 and 4 show the results considering patient clinical status (CR and PR) before BMT, the assessment on D+100 and the last report (May 2016).

CHART 1. Distribution of HL patients according to the clinical and epidemiological characteristics

Characteristics	N	%
Age at diagnosis		
mean (Range)	16 a 51	
<25	21	40.4
25 – 44	29	55.8
>44	02	3.8
Origin		
Fortaleza	21	40.4
Other cities	31	69.6
Gender		
Male	30	57.6
Female	22	43.4
Histological types		
LP	01	1.9
MC	01	1.9
NS	46	88.6
LD	02	3.8
NI	02	3.8
Initial clinical staging (Ann Arbor)		
I + II	29	55.8
III + IV	19	36.6
NI	04	7.6
Constitutional symptoms		
A	16	30.8
B	34	65.4
NI	02	3.8
Immunophenotyping		
CD30+ CD15+ CD20+	33	63.5
CD30+ CD15neg CD20+	02	3.8
CD30+ CD15+ CD20neg	10	19.3
NI	07	13.4
First treatment		
ABVD	36	69.3
ABVD + radiotherapy	16	30.7

Seven years after the first and seven months after the last evaluated BMT (October 2015), the following results were observed: CR - 32 (61.6%) patients, PR and treatment – 14 (26.9%) and 6 (11.5%) deaths. The overall survival, disease-free curves and chemosensitive and chemoresistant cases are shown in graphs 1, 2, 3 and 4.

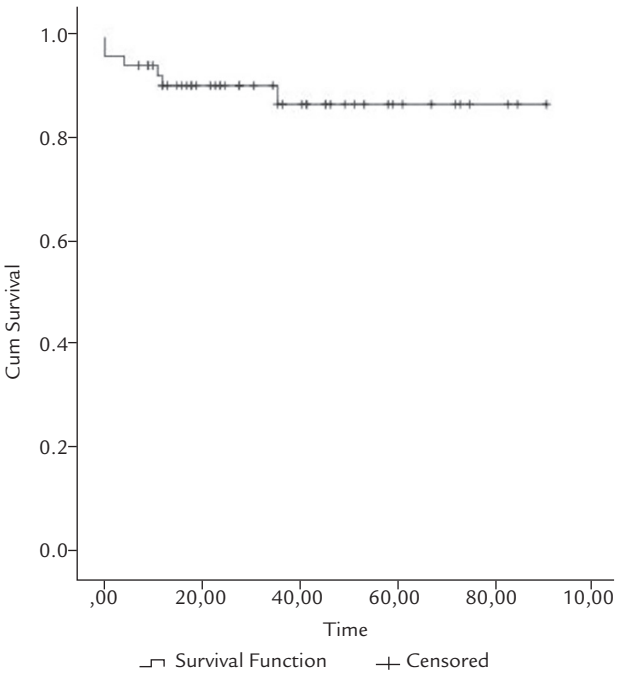
Discussion

The Hematological Service of HUWC/UFC/HEMOCE has 50 years of experience with HL and 1045 followed cases. Eight years ago, a Bone Marrow Transplant Unit was implemented, a procedure that brought a new dimension to patients with refractory disease.

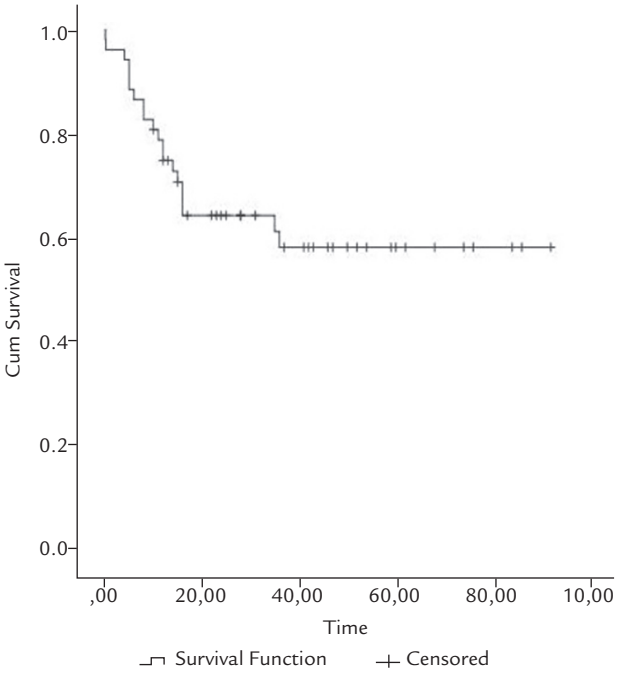
The prognosis of Hodgkin's lymphoma has improved considerably with the new chemotherapy regimens and advancements in radiotherapy techniques, allowing young patients to have a disease-free survival rate of approximately 80% and even achieving the cure.[2,3,6] Currently, it is worth mentioning the new forms of treatment, including targeted therapy and the possibility of bone marrow trans-

CHART 2. Distribution of patients according to the responses at several stages of transplantation

Characteristics	N	%
Response to first treatment		
Complete remission	21	40.4
Partial remission	15	28.8
Non-responder/Refractory	16	30.8
Recurrence (after the first CR – 21 patients)		
< 6 months	02	9.5
6 – 12 months	09	42.9
> 12 months	10	47.6
Response to the second treatment (Pré TMO)		
Complete remission	26	50.0
Partial remission	26	50.0
Mobilization		
GCS-F	35	67.3
Plerixafor+GCS-F	02	3.8
Vinorelbine+GCSF	15	28.8
Conditioning		
BEAC	34	65.4
BEAM	05	9.6
NEAM	13	25.0
Grafting (days)		
Variation	07 – 15	
<10 days	18	34.7
10 – 12 days	29	55.8
>12 days	03	5.7
Grafting failure	02	3.8
Status pós TMO (D+100)		
Complete remission	42	80.9
Partial remission	08	15.3
Deaths	02	3.8



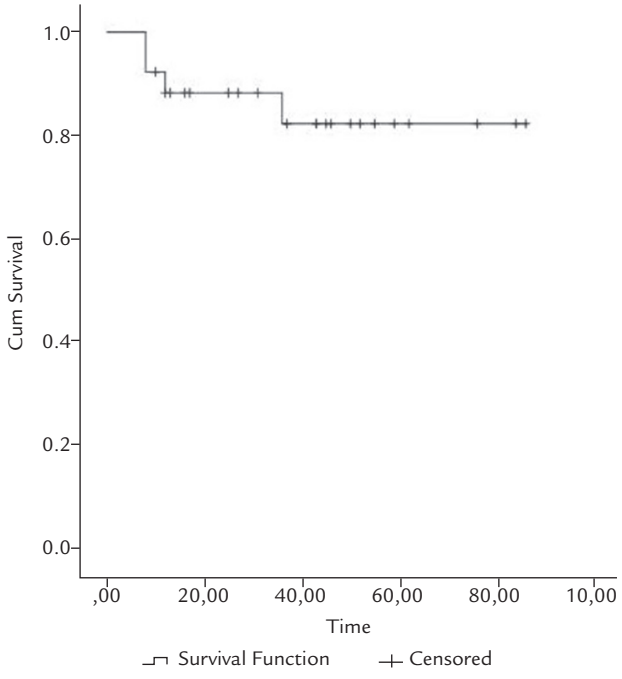
GRAPH 1. Overall survival of 52 patients with Hodgkin's lymphoma submitted to autologous bone marrow transplantation (2009-2015)



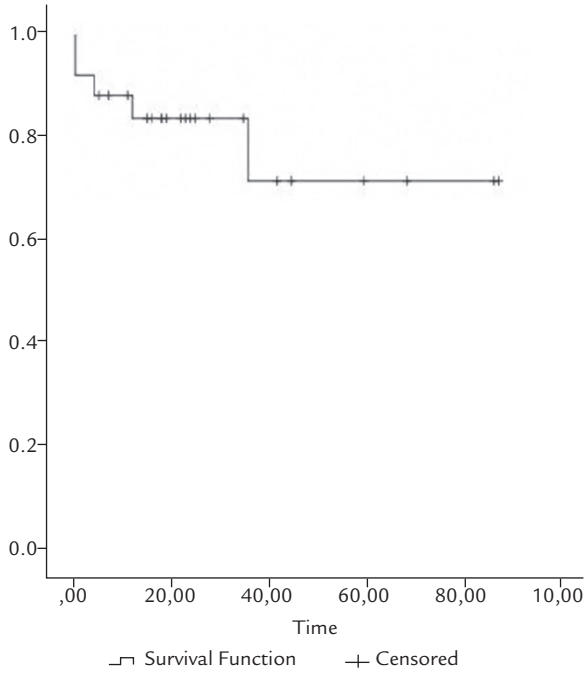
GRAPH 2. Disease-free survival of 52 patients with Hodgkin's lymphoma submitted to autologous bone marrow transplantation (2009-2015)

plant indication not only in young patients, but also in those at older age groups.[7,8,9,10,11,12]

The present analysis of transplanted patients at UTMO/HUWC/UFC shows a young population (mean age of 28 years), with a predominance of localized disease (I+II), mostly B, initially treated with standard regimen (ABVD) and who did not respond or had recurrence, becoming candidates for a new treatment regimen and the possibility of BMT indication. However, 50.0% of them came to transplantation in partial remission of the lymphoma, showing much lower results when considering the patient coming to the BMT in complete remission (64.7% vs. 35.3%). These data show the importance of trying to perform the transplant with the patient in the best possible



GRAPH 3. Survival of 26 chemosensitive patients with Hodgkin's lymphoma submitted to autologous bone marrow transplantation (2009-2015)



GRAPH 4. Overall survival of 26 chemoresistant patients with Hodgkin's lymphoma submitted to autologous bone marrow transplantation (2009-2015)

CHART 3. Distribution of patients according to the clinical criteria and the evolution of pre-BMT to the latest report (May 2016)

Criteria	RESULTS		
	PRE-BMT N %	D+100 N %	Current N %
Complete remission	27 (51.9)	42 (80.9)	34 (65.4)
Partial remission	25 (48.1)	08 (15.3%)	14 (29.6)
Deaths	–	02 (3.8)	04 (7.7)
Total	52 (100.0)	52 (100.0)	52 (100.0)

CHART 4. Distribution of patients according to the complete remission criteria in the pre-BMT, on D +100 and the latest report (May 2016)

Critérios	PRE-BMT *Status* de entrada N %		D+100 Complete remission N %		Latest report Complete remission N %	
Complete remission	27	51.9	25	59.6	22	64.7
Partial remission	25	48.1	17	40.4	12	35.3
Total	52	100.0	42	100.0	34	100.0

conditions of absence of disease activity, with chemoresistance being identified as worsening factor of response to BMT[13] (Chart 3).

The conditioning with the BEAC regimen showed to be very effective, as well as the NEAM (91.1% vs. 84.6%) regarding the achievement of CR in patients evaluated at the level of D+100. Some conditioning regimens suggest adding bortezomib to other drugs, but there was no significant difference in the outcome.[14]

The final evaluation of the transplanted HL patients showed an overall survival rate of 88.5% and 61.5% disease-free survival at six years, with an overall survival of chemosensitive patients of 81% and 72.6% in chemoresistant ones, results comparable to other transplant centers [15,16] and even to data from the Center for International Blood & Marrow Transplant Research, or CIBMTR.[17]

It is possible to conclude that autologous HSCT emerges an excellent rescue therapy regarding tolerance and overall survival.

Resumo

Linfoma de Hodgkin – avaliação dos pacientes submetidos a transplante autólogo de células hematopoéticas no Serviço de Hematologia do HUWC

O TCTH autólogo é uma importante alternativa para os pacientes de LH refratários ou recidivados, em termos de sobrevida e melhora da qualidade de vida. O presente trabalho analisa os resultados do TMO autólogo realizado em pacientes de LH na Unidade de Transplante do SH do HUWC/HEMOCE. Foram estudados 52 pacientes submetidos ao TMO de janeiro de 2009 a outubro de 2015, sendo 30 homens e 22 mulheres, média de idade de 28,2 anos. Todos receberam GCS-F na mobilização, em alguns casos associados a Vinorelbine ou a Plerixafor e coleta de CD34 com média de 4,8CD34/kilo. O condicionamento foi realizado com BEAC, NEAM ou BEAM e a enxertia com média de 10 dias. A avaliação no D+100 mostrou: RC – 42 (82,7%), RP – 08 (13,5%) e 02 (3,8%) óbitos ocorridos 3 e 6 dias após a infusão das células. Após o D+100, 08 pacientes em RC apresentaram recidiva do LH entre 6 e 36 meses; 3 foram a óbito e 5 estão em tratamento com brentuximabe; os 8 pacientes em RP, 1 faleceu por atividade do LH, 4 meses após o TMO e 7 estão em tratamento. A avaliação final dos pacientes de LH transplantados mostrou uma SG de 88,5% e SLD de 61,5% em 6 anos, SG dos pacientes quimiossensiveis de 81% e dos quimioresistentes de 72,6%.

É possível concluir que o TCTH Autólogo se coloca como excelente terapia de resgate em relação à tolerância, bem como na sobrevida global.

Palavras-chaves: Transplante de células-tronco hematopoiéticas;

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Association of oxidative stress and DNA damage with grafting time in patients with multiple myeloma and lymphoma submitted to autologous hematopoietic stem cell transplantation

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Abstract

The aim of the study was to investigate the association between oxidative stress and DNA damage with grafting time in patients submitted to autologous hematopoietic stem-cell transplantation (HSCT). The study included 37 patients submitted to autologous HSCT diagnosed with Multiple Myeloma (MM) and lymphoma (Hodgkin's and non-Hodgkin's). Biomarkers of oxidative stress and DNA damage index (DI) were performed at baseline (pre-CR) of the disease and during the conditioning regimen (CR), one day after the HSCT, ten days after HSCT and twenty days after HSCT, as well as in the control group consisting of 30 healthy individuals. The outcomes showed that both groups of patients had an hyperoxidative state with high DI when compared to baseline and to the control group and that the CR exacerbated this condition. However, after the follow-up period of the study, this picture was re-established to the baseline levels of each pathology. The study patients with MM showed a mean grafting time of 10.75 days (8 to 13 days), with 10.15 days (8 to 15 days) for the lymphoma patients. In patients with MM, there was a negative correlation between the grafting time and the basal levels of GPx ($r = -0.54$; $p = 0.034$), indicating that lower levels of this important enzyme are associated with a longer grafting time. For the DI, the correlation was a positive one ($r = 0.529$; $p = 0.030$). In the group with lymphoma, it was observed that the basal levels of NOx were positively correlated with grafting time ($r = 0.4664$, $p = 0.032$). The data indicate the potential of these biomarkers as predictors of toxicity and grafting time in patients with MM and Lymphomas submitted to autologous HSCT.

Keywords: Autologous hematopoietic stem-cell transplantation; Oxidative stress; DNA damage; Multiple myeloma; Lymphoma.

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Introduction

The conditioning regimen with high-dose chemotherapy used for autologous stem cell transplantation (HSCT) has been associated with increased production of reactive oxygen species (ROS) and depletion of important components of the antioxidant system[1-4]. Considering that ROS affect cell cycle progression and signaling of growth factors in several cell types, including stem cells and hematopoietic progenitors, oxidative stress has been reported as one of the proposed mechanisms to explain the damage to several tissues after HSCT[5,6].

The aim of the study was to investigate the association between oxidative stress and DNA damage with the grafting time in patients undergoing HSCT.

Methods

The study included 37 patients submitted to autologous HSCT at Hospital Universitário Walter Cantídio (HUWC) in Fortaleza, Ceará, in 2013. Patients were stratified into two groups: Myeloma, consisting of patients diagnosed with MM (n = 17), and Lymphomas (n = 20), consisting of patients with Hodgkin's lymphoma (n = 10) and non-Hodgkin's lymphoma (n = 10). The control group consisted of 30 healthy subjects with matched age and gender according to the group of patients. Individuals using antioxidants, smokers, those who consumed alcohol, were infected with hepatitis, HIV or HTLV virus were excluded from the study.

The study was approved by the Research Ethics Committee of HUWC under protocol number 08022912.8.0000.5045. All participants in the study agreed to participate by signing the free and informed consent form.

Autologous HSCT

The autologous HSCT procedure followed the standard protocol of the institution. The mobilization of stem cells was performed with granulocyte colony stimulating factor (G-CSF) at a dose of 10-16 mg/kg/day. Subsequently, CD34+ cells were collected and cryopreserved for the HSCT. The patients were submitted to the CR (conditioning regimen) according to the underlying disease: the Myeloma group received melphalan (200 mg/m^2) and the Lymphoma group received polychemotherapy, comprising carmustine 300 mg/m^2, etoposide 600 mg/m^2, cytarabine 1600 mg/m^2, cyclophosphamide 140 mg/m^2 and mesna 168 mg/m^2 (for HL patients) and carmustine 300 mg/m^2, etoposide 600 mg/m^2, cytarabine 1600 mg/m^2 and melphalan 140 mg/m^2 for the other patients.

Peripheral blood samples were collected for determination of the parameters analyzed during the following moments: baseline or pre-CR; during the CR (the last day on which the patient received chemotherapy: D-1); 1 day after autologous HSCT (D+1); 10 days after autologous HSCT (D+10) and 20 days after autologous HSCT (D+20). The Pre-CR time was considered as the moment that reflects the patient's baseline condition before the autologous HSCT intervention.

Oxidative stress analysis

Malondialdehyde (MDA), a lipid peroxidation product, was determined by its reaction with thiobarbituric acid (TBARS) by spectrophotometry at 532-535nm[7].

Nitric oxide levels were determined by the concentration of nitrite/nitrate (NOx) according to the method by Green et al. (1981) using the spectrophotometric method[8]. The reading was performed through absorbance at 560 nm.

The activity of the catalase (CAT) enzyme was measured in hemolysates by monitoring the H_2O_2 reduction rate at 240 nm in a spectrophotometer. The enzymatic activity was expressed as U/L[9].

The activity of the glutathione peroxidase (GPx) and superoxide dismutase (SOD) enzymes was determined in hemolysates using the Ransel Glutathione Peroxidase® and RANSOD® (RANDOX BRAZIL Ltd.) kits, respectively, according to the manufacturer's specifications.

DNA damage Assessment – the Comet assay

The test was performed according to Singh et al (1988)[10], by fixing leukocytes to a slide with low melting-point agarose, subsequently submitted to electrophoresis. The DNA damage index (DI) was determined by fragmented DNA content after ethidium bromide staining.

Statistical analysis

The results obtained in the performed analyses were tabulated and plotted using the GraphPadPrism 5.0 program, which was used for statistical analysis. The differences between the means of the groups were verified by analysis of variance (ANOVA TWO-WAY) followed by Tukey's post-test. Statistically significant differences were considered with $p < 0.05$.

Results

Figure 1 shows the data of oxidative stress parameters at all times of HSCT.

Patients with MM and lymphoma had significantly high basal MDA levels when compared with the control group at all times when peripheral blood collection was performed, with significant differences according to the type of patient diagnosis after the conditioning phase, which implies that the type of approach or the patient's own clinical condition greatly influences MDA increase after the CR.

Regarding NOx analysis, it was observed that this oxidative stress parameter is increased in patients submitted to HSCT. We emphasize that on D+10 to D+20 a trend was observed in patients with lymphoma of having higher NOx values than patients with myeloma.

When comparing the SOD activity, this enzyme showed significantly reduced activity at baseline (pre-CR) in the control group. At the other times, a tendency to having lower values of this marker in patients diagnosed with myeloma was observed, when compared to patients with lymphoma.

Catalase showed an increase profile at baseline (pre-CR), showing significant elevation when compared to the means in the control group. At other times, lymphoma patients tended to have lower values of this enzyme activity when compared to patients diagnosed with myeloma.

Regarding the times of HSCT, the CR was able to raise the MDA levels ($p < 0.01$) and decrease the SOD and CAT activities in both groups of patients. Twenty days after HSCT (D+20), we observed that the MDA levels were restored to the baseline levels of each pathology; however, they were still higher than in the control group ($p < 0.0001$). At times D+1, D+10 and D+20, MDA levels in the Lymphoma group were significantly elevated compared to the MM group ($p < 0.05$).

The CAT activity was re-established at time D+1 for the Myeloma group and time D+10 for the lymphoma group to higher levels than those in the control group ($p < 0.0001$). The SOD activity was restored to levels similar to those in the control group at time D+20 for the two groups of patients.

There was no statistically significant difference between the NOx levels and GPx activity at the different times of HSCT.

Patients with myeloma and lymphoma showed significantly higher DI than the control group. It was also observed that the CR was able to increase the DI in the two groups of patients ($p < 0.05$); however, one day after HSCT (D+1), these values decreased significantly, resembling those observed at baseline, twenty days after HSCT (D+20).

The mean grafting time in patients with MM was 10.75 days, ranging from 8 to 13 days and 10.15 days for the lymphoma group, ranging from 8 to 15 days. The correlation analysis between the oxidative stress parameters and DI with grafting time after HSCT showed that for patients with MM, there was a negative correlation between the grafting time and the basal levels of GPx ($r = -0.54$; $p = 0.034$). For the DI, the correlation was positive ($r = 0.529$; $p = 0.030$). In the group with lymphoma, it was

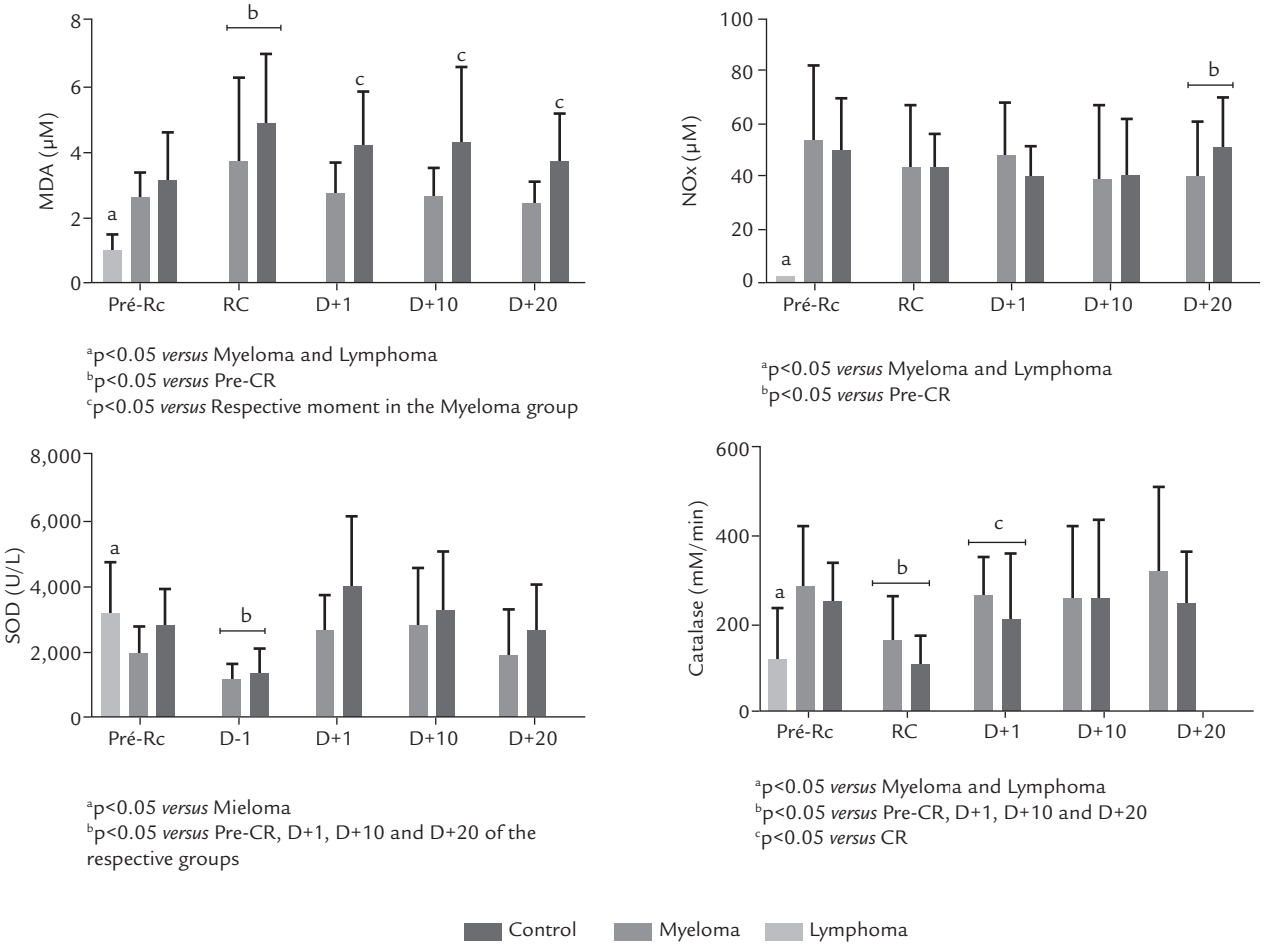

FIGURE 1. Profile of oxidative stress in patients with multiple myeloma (n = 17) and lymphomas (n = 20) submitted to HSCT.

observed that the basal NOx levels were positively correlated with grafting time (r = 0.4664, p = 0.032) (Figure 3).

Discussion

The present study showed that patients with MM and Hodgkin's and non-Hodgkin lymphoma show a state of oxidative stress and conditions consistent with DNA damage, represented by high MDA and DI values, with reduced activity of SOD and CAT anti-oxidative enzymes when compared with the control group. This finding is consistent with several studies reporting that patients with hematological malignancies have a hyperoxidative state before any CR, suggesting an intrinsic process of the underlying disease or inherent to drug treatments prior to HSCT[11-17].

The CR with high-dose chemotherapy, to which the patients had been previously submitted, was able to exacerbate this hyperoxidative state. After HSCT, the evaluated parameters gradually improved until they were restored to similar levels to those seen at patients' baseline, corroborating data observed by Sabuncuoglu et. al (2012)[17].

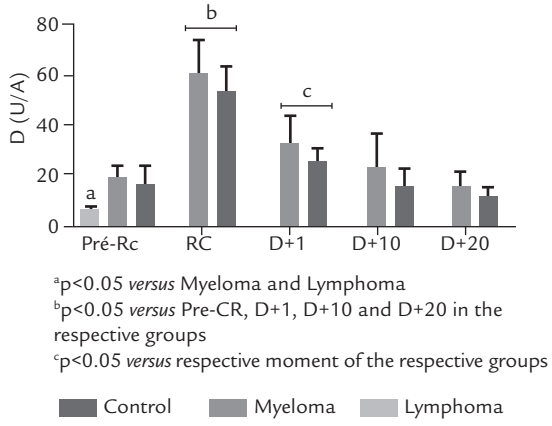

FIGURE 2. DNA damage index in patients with multiple myeloma (n = 17) and lymphomas (n = 20) submitted to HSCT.

In relation to DNA damage assessment, the results of this study corroborate and substantiate the oxidative stress profile at all times of the HSCT, considering that the excess of free radicals readily react with all components of the DNA molecule and can induce a permanent change in the genetic material[18]. Follow-up studies of the patients can be performed to correlate possible oxidative stress exacerbations with patient prognosis and survival, greatly contributing to the understanding of the oxidative process importance in patients undergoing HSCT.

The grafting time is an important indicator during the follow-up of transplanted patient, as it reflects the time of engraftment. The longer the grafting time, the higher is the risk of infections and other complications that can lead to death[19]. The positive correlations between DI and NOx with grafting time, as well as the negative correlation with Gpx, indicate the potential of these biomarkers as predictors of toxicity and grafting time in autologous HSCT in MM and Lymphomas. This study collaborates by giving rise to new studies with this approach and with a larger sample to reinforce the findings, aiming at the monitoring of patients and decreasing complications related to HSCT, demonstrating that the procedure brings significant changes in oxidative stress, as well as the treatment of the diseases discussed here.

Conclusion

The positive correlations of damage index and NOx with grafting time, as well as the negative correlation with Gpx, indicate the potential of these biomarkers as predictors of toxicity and grafting time in autologous HSCT in patients with MM and Lymphomas. These findings allow us to correlate the state of oxidative stress with possible DNA damage, showing evidence that the control of oxidative stress in HSCT could be associated with a less damaging condition for the patient and with a better prognosis, which may be verified by monitoring these patients after they are submitted to the autologous HSCT procedure.

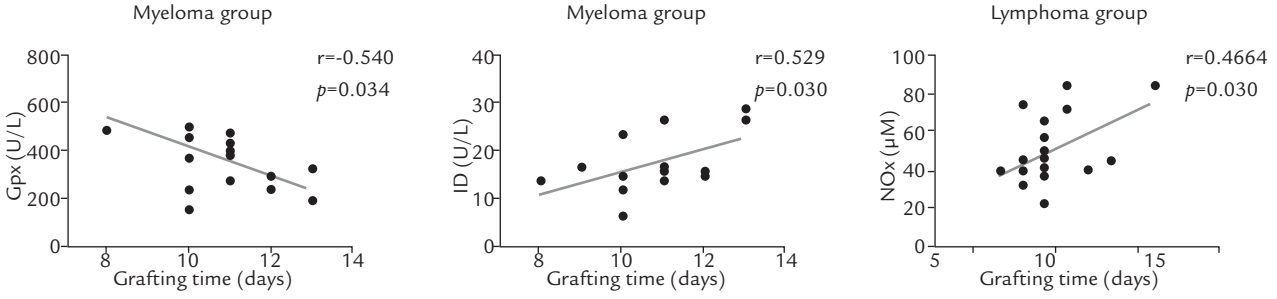

FIGURE 3. Analysis of correlation of oxidative stress and DI parameters at baseline (pre-CR) in patients with MM (n = 17) and lymphomas (n = 20) submitted to HSCT.

Resumo

Associação do estresse oxidativo e dano ao DNA com o tempo de enxertia em pacientes com mieloma múltiplo e linfomas submetidos a transplante autólogo de células-tronco hematopoéticas

O objetivo do estudo foi investigar a associação entre estresse oxidativo e dano ao DNA com o tempo de enxertia em pacientes submetidos ao transplante de células-tronco hematopoéticas autólogo (TCTH). Participaram do estudo 37 pacientes submetidos ao TCTH autólogo com diagnóstico de mieloma múltiplo (MM) e Linfomas (Hodgkin e não Hodgkin). Biomarcadores de estresse oxidativo e índice de dano ao DNA (ID) foram determinados no estado basal (Pré-RC) das doenças e durante o regime de condicionamento (RC), um dia após o TCTH, dez dias após o TCTH e vinte dias após o TCTH e no grupo controle composto por 30 individuos saudáveis. Os resultados demonstraram que os dois grupos de pacientes apresentaram um estado hiperoxidativo com elevado ID quando comparados ao estado basal e ao grupo controle e que o RC exacerbou essa condição. No entanto, após o tempo de acompanhamento do estudo, esse quadro foi reestabelecido ao estado basal de cada patologia. Os pacientes do estudo com MM apresentaram uma média do tempo de enxertia de 10,75 dias (8 a 13 dias), e de 10,15 dias (8 a 15 dias) para o grupo Linfoma. Nos pacientes com MM houve uma correlação negativa entre o tempo de enxertia e os níveis basais de GPx (r=-0,54; *p*=0,034), indicando que níveis mais baixos de GPx estão relacionados a um maior tempo de enxertia, e para o ID, a correlação foi positiva (r=0,529; *p*=0,030). No grupo com Linfoma, observou-se que os níveis basais de NOx correlacionaram-se positivamente com o tempo de enxertia (r= 0,4664; *p*=0,032). Os dados apontam para o potencial desses biomarcadores como preditores da toxicidade e do tempo de enxertia em pacientes com MM e Linfomas submetidos ao TCTH autólogo.

Palavras-chave: Transplante autólogo de células-tronco hematopoéticas; Estresse oxidativo; Dano ao DNA; Mieloma múltiplo; Linfoma.

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Acute and chronic Graft-versus-host disease after hematopoietic stem cell transplantation

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Abstract

graft-versus-host disease (GVHD) is one of the main complications of hematopoietic stem cell transplantation, affecting about 50% to 80% of the patients. Acute GVHD and its clinical manifestations are discussed in this article, as well as the new NIH criteria for the diagnosis and classification of chronic GVHD. Therapy for both chronic and acute GVHD is an important field of discussion, as there is no proven superiority for the majority of therapies used after primary treatment has failed. Hence, this review is meant to be a useful consultation tool for hematologists dealing with this complex transplantation procedure complication.

Keywords: Graft versus host disease, hematopoietic stem cell transplantation.

Introduction

Approximately 50% of the hematopoietic stem cell transplant (HSCT) recipients develop Graft-versus-host disease (GVHD) with varying degrees of severity and mortality, which can affect 20% of transplanted patients[2]. The published data on the incidence and severity of chronic GVHD are heterogeneous, but it is estimated that 60-80% of long-term HSCT survivors have some degree of disease activity with immunosuppressive therapy indication for long periods after transplantation[3].

Acute graft versus host disease (aGVHD)

Diagnosis

In 2005, the National Institutes of Health (NIH) published a consensus document aimed to address several aspects of the diagnosis, classification and treatment of chronic GVHD (cGVHD)[4]. Therefore, it was possible to establish clear distinctions differentiating these two entities through a better characterization of cGVHD. After 2005, patients with the clinical syndrome before the D+100 were considered as having the "classic acute GVHD" and when it appeared after D+100, it was classified as "late, persistent or recurrent GVHD"[4].

Epidemiology and risk factors

Several studies have identified the following risk factors for increased incidence of GVHD: HLA disparity between donor and patient (HLA mismatch, or unrelated donor, donor and patient of different sexes (especially female donor for male recipient); intensity of conditioning regimen; prophylactic regimen used, source of progenitor cells (peripheral blood or bone marrow > cord)[5].

aGVHD: clinical presentation

The skin, gastrointestinal tract and liver are the main target organs affected in aGVHD. The first organ usually affected is the skin, in the form of a maculopapular rash in areas of the neck, ears, shoulders (cephalic end), palms and soles. It can disseminate throughout the body surface (BS) becoming confluent and causing pruritus, sometimes painful. In the severe form, it resembles Stevens-Johnson syndrome with bullous lesions secondary to epidermal necrosis. Regarding the gastrointestinal tract (GIT), the involvement of the upper and lower portions is often observed. The clinical presentation ranges from nausea, vomiting and anorexia to diarrhea and abdominal pain[6]. The involvement of the lower GIT is usually severe, with diarrhea accompanied or not by hematochezia and abdominal cramps. The diarrheal volume may be greater than 10 liters/24h, with an aqueous pattern and frequently progresses to bloody stools[7]. Liver damage caused by aGVHD usually occurs in patients with signs of skin and/or GIT aGVHD. The liver is rarely moderately or severely

affected without involvement of other organs. Liver function tests (LFTs) show alterations, with elevated total bilirubin (predominantly the conjugated form) and alkaline phosphatase levels[8].

aGVHD staging and classification

The first aGVHD staging system was published in 1974 by Glucksberg et al.[6]. Each organ was evaluated separately according to the clinical/laboratory involvement stage and the resulting data provided an overall grading of GVHD (Tables 1 and 2)[6,9].

The initial grading of aGVHD is important to assess response to treatment or prophylaxis, in addition to correlating it to overall survival after hematopoietic stem cell transplantation (HSCT)[10]. Patients who develop the moderate or severe forms of the disease (overall stages II-IV) have a significantly higher mortality rate than those with the mild form. The moderate and severe forms occur in approximately 40% of all allogeneic HSCTs and without effective prophylaxis, it becomes a severe complication[11,12].

aGVHD treatment

The choice of the initial therapy for aGVHD depends on the organs involved, symptom severity, the prophylactic regimen used and, to some extent, the importance of the GVT effect in that particular clinical setting.

aGVHD grade I

The treatment of aGVHD grade I (mild) should comprise the optimization of the prophylactic regimens, for instance, adjusting cyclosporine or tacrolimus levels to therapeutic serum levels, use of topical agents (corticosteroids or tacrolimus) and adjuvant therapy, such as antihistamines to control pruritus. There is no indication for systemic immunosuppression[13].

aGVHD grade II-IV

aGVHD patients with grade II to IV should start treatment with methylprednisolone (MP) at a dose of 2 mg/kg/day of prednisone or equivalent. Its effect is related to lympholythic and anti-inflammatory properties and has been used as standard therapy for several decades[14]. At the same time, the drug used in the prophylaxis (CSA or FK) must not be interrupted. In a retrospective study of 733 patients, the use of MP at a dose of 1 mg/kg/day for the less severe forms of the disease (aGVHD grade II) increasing it to 2 mg/kg if there is symptom worsening after 72 hours, did not bring an adverse impact on survival rate and allowed the use of MP doses that were 50% lower than the standard ones[15].

"Nonabsorbable" glucocorticoids (beclomethasone and budesonide) have been used in the treatment of mild GVHD in the upper or lower GIT (500-1000 mL/24 h) as adjunctive therapy to systemic corticosteroid therapy[16,17]. Only approximately 60% of patients respond to the initial treatment with systemic corticosteroids and many of these responses are not long-lasting[18].

Second-line treatment for grade II-IV aGVHD

If aGVHD progresses within the first 3 days (72h) or if there is no improvement after 5-7 days of the onset of initial therapy with MP 2 mg/kg/day plus calcineurin inhibitor, the disease is considered cortico-refractory and a second-line treatment is indicated. Cortico-refractory aGVHD has a poor prognosis and the second-line therapies have high failure rates. The overall survival of this population at one year is about 20-30%[19].

TABLE 1. aGVHD staging per organ

Staging	Skin findings	Liver findings	Intestinal findings
+	Maculopapular exanthema in <25% of body surface	Bilirubin: 2-3 mg/dL	Persistent diarrhea (500-1000 mL) and nausea
++	Maculopapular exanthema in 25-50% of body surface	Bilirrubina: 3-6 mg/dL	Diarreia (1000-1500 mL)
+++	Generalized erythroderma	Bilirrubina: 6-15 mg/dL	Diarreia > 1500 mL)
++++	Desquamation and blisters	Bilirrubina > 15 mg/dL	Pain with or without obstruction

TABLE 2. Overall graduation of aGVHD

Degree/stage	Skin	Liver	Intestine	Functional disorder
0 (None)	0	0	0	0
I (Mild)	+a++	0	0	0
II (Moderate)	+a+++	+	+	+
III (Severe)	++a+++	++a+++	++a+++	++
IV (Life-threatening)	++a++++	++a++++	++a++++	+++

Few prospective studies have been published with 2nd-line agents and due to their heterogeneity, the results are difficult to compare. As the superiority of one agent over the others has not been demonstrated, the choice should be directed by factors such as the effects of any prior therapy, interaction with other drugs (including those used for prophylaxis) availability, cost and the health team's familiarity with its use. In general, the mean rate of response of these agents is 50% with a median survival of at least 60% at six months after treatment, many without evidence of active aGVHD [19,20]. The results obtained with the most commonly used agents are summarized below.

Mycophenolate mofetil (MMF)

MMF acts by inhibiting the synthesis of guanosine triphosphate, of which lymphocytes depend for proliferation, therefore being preferentially affected. It was one of four drugs used in the phase-II, randomized BMT CTN 0302[21] as the initial therapy together with MP. However, the addition of MMF to the MP in a subsequent, phase III, randomized, double-blind study, with a similar endpoint to the previous study (BMT CTN 0802) did not significantly alter aGVHD-free survival or the cumulative incidence of chronic GVHD at 12 months[22]. Retrospective studies show RC/RP ratios of up to 77% at 6 months, thus being an option to be considered in these cases[23-24].

Extracorporeal photopheresis (ECP)

The ECP consists of the irradiation of circulating lymphocytes in peripheral blood collected by apheresis and incubated with 8-methoxypsoraleno with phototherapy (UV-A). The ECP induces apoptosis in all lymphocytes (including activated T-cells) within 24 hours after the treated blood is returned. The reinfusion of these cells and subsequent phagocytosis by antigen-presenting cells (APCs) can regulate immune homeostasis by modulating cytokine production and tolerance induction by expanding the regulatory component of T lymphocytes (Treg) observed in murine models[25]. A prospective, phase II study was published in 2006, which included 59 patients with cortico-refractory or cortico-dependent aGVHD. Complete responses (CR) were observed in 82% of patients with skin involvement, 61% with hepatic GVHD and in 61% of cases with gastrointestinal disease [26]. Associated opportunistic infections were not reported, or loss of the GVT effect with higher relapse rate of malignancy, as it is an immunomodulatory therapy, not an immunosuppressive one[26].

Antithymocyte globulin (ATG)

Polyclonal or monoclonal antibodies are the worldwide most often used second-line agents. There is considerable experience with ATG, which has been used for more than three decades. However, the literature describes responses in 20 to 50% of cases, especially in skin GVHD[27,28].

Antibodies against IL-2 receptor

The α subunit (CD25) of interleukin-2 (IL-2) receptor is expressed predominantly in activated T lymphocytes. Basiliximab is a chimeric antagonist of IL-2 receptor and has shown promising results by achieving 71% of CR in a phase I study published in 2002 with 17 patients[29]. Funke et al. published in 2005 their experience in 34 patients with refractory aGVHD grade III-IV, with approximately 80% of response and 30% overall five-year survival[30].

Tumor necrosis factor antagonists (Infliximab, Enbrel)

Mainly used in situations of refractory aGVHD involving the gastrointestinal tract, several series have been published, most of them by Couriel et al.[31], who found an overall response of 70% in 37 patients with aGVHD. A complete response in 62% of patients was seen with the use of this agent associated with corticosteroids and tacrolimus as the first line[31].

Chronic graft versus host disease (cGVHD)

cGVHD is a major cause of morbidity and late mortality of allogeneic HSCT occurring in 30-70% of patients[32-34]. The cumulative incidence at 2 years of chronic GVHD, defined according to the National Institute of Health (NIH) after allogeneic HSCT with bone marrow or peripheral blood from related or unrelated donors, in a study that evaluated the risk factors for aGVHD and cGVHD was 34% (32%-35% range)[35]. The clinical manifestations of cGVHD may be restricted to a single organ or can be disseminated, with profound impact on quality of life[36]. The pathophysiology of cGVHD involves inflammation, cell and humoral immunity and fibrosis[36].

This immunological complication resembles autoimmune diseases with clinical manifestations of collagen vascular diseases, such as oral lichen planus, keratoconjunctivitis sicca, xerostomia, polyserositis, esophagitis and esophageal stricture, vaginal ulceration and stenosis, intrahepatic obstructive liver disease, obstructive pulmonary disease, scleroderma, fasciitis and myositis. Clinical manifestations usually appear in the first two years after transplantation[36].

Diagnosis of cGVHD and differentiation from aGVHD

As the 20054 consensus criterion, the consensus of 201436 recognizes two main categories of GVHD (acute

and chronic). aGVHD includes (1) classical aGVHD that occurs before 100 days after HSCT, without diagnostic or distinct signs of cGVHD; (2) late aGVHD, persistent or recurrent: shows changes of the classical aGVHD, but no diagnostic or distinct signs of cGVHD and occurs after 100 days of HSCT. In the 20054 criterion, the cGVHD included (1) classic cGVHD without characteristics of aGVHD; (2) overlap syndrome, in which the characteristics of aGVHD and cGVHD appear concomitantly.

Better clarification of the overlapping cGVHD subcategory definition has been provided in the 201436 criterion. It is the clinical manifestations, and not the time of symptom onset after HSCT, which determine if the GVHD is acute or chronic. Diagnostic signs and symptoms are manifestations establishing the presence of cGVHD without the need for further tests or evidence of other affected organs, generally represented by lichenoid lesions or sclerosis. Distinct signs and symptoms are not commonly found in aGVHD, but are not considered sufficient to establish an accurate diagnosis of cGVHD (e.g., vitiligo, ocular sicca)[36].

Common signs and symptoms are observed in both aGVHD and cGVHD[36]. For the diagnosis of cGVHD, it is necessary to have at least one diagnostic manifestation of cGVHD or at least a distinct manifestation confirmed by appropriate biopsy or laboratory testing, or evaluation by a specialist (ophthalmologist gynecologist) or radiological images, in the same or another organ, unless otherwise stated[36].

Clinical organ scoring system

the organ scoring system of the 20054 consensus has been modified based on the available evidence, or lack thereof, as well as by the questions raised by researchers and clinical practice[37]. The local organs most often considered for the scoring system include the skin, mouth, eyes, GIT, liver, lungs, joints, fascia and genital tract. Each organ or site is scored on a 4-point scale (0-3) with 0 representing no involvement and 3 representing severe impairment. Several studies have shown that the overall severity at diagnosis, according to the NIH 2005 criteria is associated with the overall survival and TRM and some scoring elements have been validated with quality of life measures[37]. The light, moderate and severe classification reflects the degree of impact and functional impairment in each organ or site, due to cGVHD.

Treatment of chronic GVHD (cGVHD)

Mild asymptomatic cGVHD can be often treated with local therapy (e.g., topical corticosteroids for skin involvement). In patients with three or more affected organs or a score of 2 or greater in any organ, systemic treatment should be considered. Although associated with lower recurrence rate, cGVHD remains a major cause of late morbidity and mortality in HSCT recipients[38]. The frequent involvement of several organs and pleomorphic clinical picture of this complication require multidisciplinary management, which includes, in addition to several medical specialties, nutritional counseling, physical and psychological therapy, dental, social and occupational therapy[39]. Sporadic quality of life assessment is recommended in patients with cGVHD, representing an effective treatment response tool[40].

Treatment of mild cGVHD

The symptomatic mild form should generally be treated with topical agents only, but some data should be considered, such as the underlying disease (malignant or non-malignant) and its status at transplantation, presence of high-risk factors for mortality associated with cGVHD (thrombocytopenia, progressive disease onset)[39]. Moreover, mild cGVHD manifestations that do not respond satisfactorily to topical treatment, such as hepatic cGVHD or fasciitis can be treated with corticosteroids alone[39].

Treatment of moderate to severe cGVHD

First-line systemic treatment

The criteria defined in the NIH Consensus for systemic treatment include: score >2 in an organ, involvement of three or more organs and mild cGVHD with high-risk characteristics (platelet count <100,000/mm^3 and use of immunosuppressants at the diagnosis of cGVHD)[4].

The initial standard systemic therapy consists of prednisone 1 mg/kg/day and cyclosporine (CSA) at a dose de10 mg/kg/day in 2 divided doses, administered orally, with CSA dose adjusted by the plasma level[39]. Tacrolimus has also been used to replace cyclosporine, with similar responses. The withdrawal should be initiated, if there is a stable response or manifestations after two weeks of treatment, reducing the dose of prednisone by 25% per week until, at 6 to 8 weeks, the target dose of 1 mg/kg on alternate days is reached, which must be maintained for 2 to 3 months in cases of incomplete response, severe forms or presence of risk factors. Subsequently, it must be reduced by 10 to 20% per month until the total withdrawal at 9 to 12 months according to patient tolerance[39]. The main drugs used in the first-line treatment are listed in Table 2.

Cortico-refractory cGVHD is defined by progression of the disease after 2 weeks of therapy (prednisone at a dose of 1 mg/kg/day); stable disease with prednisone use

(>0.5 mg/kg/day) for 4-8 weeks or inability to reduce the prednisone dose to below 0.5 mg/kg/day[49]. Indication for second-line treatment include worsening of cGVHD manifestations in a primarily involved organ, the absence of any response after one month of treatment, or inability to reduce the prednisone dose to below 1 mg/kg/day within 2 months[39].

Second-line systemic treatment

Several therapeutic options have been tested in patients with cGVHD refractory to first-line treatment. The choice of treatment, therefore, depends on the chosen medication toxicity pattern, the organs involved, the patient's preference and the availability of the transplant center[39].

The main agents used in the treatment of refractory cGVHD are summarized below.

Extracorporeal photopheresis (ECP)

Extracorporeal photopheresis (ECP) is an immunomodulatory cell therapy, in which mononuclear cells are collected and irradiated with UV in the presence of a photosensitizer, 8-methoxypsoralen. It is postulated that during the ECP, in addition to lymphocyte apoptosis, inhibition of proinflammatory cytokine production occurs, with increased production of inflammatory cytokines, reduction of stimulation of effector T cells, changes in dendritic cell function and activation of regulatory T cells, favoring the energy of T41 cells. ECP has been widely used as second-line therapy for mucocutaneous cGVHD, with complete response rates above 80% and significant improvement in cGVHD with sclerosis. Recently, Flowers et al.[41] reported results of a prospective, randomized, double-blind phase II trial in 95 refractory patients, dependent or intolerant cGVHD, treated with FEC in combination with conventional immunosuppressive agents. There was no significant difference in the total skin score (TSS) improvement at week 12; however, there was a higher rate of complete and partial responses of cGVHD in the skin at the ECP arm in comparison to the control arm; more patients in the ECP arm had at least a 50% reduction in the steroid dose and at least a 25% reduction in total skin score (TSS) at week 12[41]. In the extension study, the group submitted to ECP had a significant improvement in the skin score at week 24, when compared to the group without ECP[42]. ECP has the advantage of not increasing the risk of infection and having few adverse effects.

Mycophenolate mofetil

this immunosuppressant, of which prodrug, mycophenolic acid, interferes with purine synthesis and produces a cytostatic effect on T and B lymphocytes, is often used in rescue therapy for refractory cGVHD. The overall response rates vary between 23 and 79% of patients in several case series[43]. Lopez et al.[44] reported in 2005 on the largest series of cases with 35 patients with cortico-refractory cGVHD. There was 79% overall response and 35% complete responses. Seventy-three percent of patients were able to discontinue immunosuppression after the addition of this drug and only 3% of treated patients discontinued it due to toxicity.

Mammalian target of rapamycin (mTOR) inhibitors: sirolimus

These drugs combine immunosuppressive effects and antiproliferative properties in fibroblasts and smooth muscle cells. There are reports of antineoplastic effects. Sirolimus and everolimus bind to mTOR to form a complex that induces cell cycle arrest in G1 by inhibiting DNA transcription and translation and protein synthesis. In contrast to calcineurin inhibitors, these drugs promote the generation of regulatory T cells[45].

Jurado et al.[46] published a series of cases in 2007 of 47 patients using sirolimus as secondary treatment in combination with other drugs. The overall response rate was 81%, with 38% complete responses; 47% of these patients discontinued immunosuppression and the overall survival was 57% in three years. Couriel et al.[47] also reported their experience with sirolimus as rescue therapy in 35 patients with skin and visceral cGVHD. There was an overall response of 63%, being 17% complete and 34% of patients discontinued immunosuppression. The overall survival at 2 years was 41%.

Rituximab

Rituximab binds to the extracellular portion of the CD20 surface molecule and induces apoptosis and cell death mediated by complement or direct of neoplastic B or normal cells[48]. Cutler et al.[49] carried out the first phase I-II prospective study reporting the efficacy of rituximab (375 mg/m^2) in 21 patients receiving a total of 38 cycles. Objective responses were observed in 70% of patients, allowing a significant reduction in the steroid dose. Patients with skin or musculoskeletal manifestations of cGVHD showed better responses. VonBonin et al.[50] used lower doses of 50 mg/m^2/week for 4 weeks in 11 patients with refractory cGVHD and 2 with post-transplantation autoimmune disorders (immune-thrombocytopenia and glomerulonephritis) observing an overall response rate of 69%, including 3 patients (23%) with complete remission (CR). Recently, Arai et al.[51] published a prospective randomized study comparing imatinib and rituximab.

Significant clinical response was observed in 9 of 35 (26%, 95%CI: 13-43%) participants randomized to imatinib and 10 of 37 (27%, 95% CI: 14-44%) randomized to rituximab.

Imatinib

Imatinib, an inhibitor of several kinases and successfully used in positive BCR-ABL malignancies, has recently been used for the treatment of cGVHD based on its antifibrotic activity by blocking platelet-derived growth factor receptor (PDGFR) and Transforming Growth Factor beta (TGFß)[51]. The main adverse events with the drug include hematologic toxicity, fluid retention and dyspnea, which lead to drug discontinuation in 15 to 25% of patients. Responses between 50% and 80% were observed in patients with skin, ocular and bowel involvement in cGVHD for a period of six months. In cases of pulmonary involvement, the best responses were observed in mild bronchiolitis[51,52].

Low-dose methotrexate (MTX)

Methotrexate is an antimetabolite, which at low doses has immunomodulatory and anti-inflammatory properties. Giaccone et al.[53] reported 71% (10/14) of control of refractory cGVHD, with a decrease in prednisone dose to <1 mg/kg/every other day, with a long-term regimen of 7.5 mg/m^2/week of MTX in patients with refractory cGVHD, with five affected sites, on average, survival of 92.8%, median follow-up of 25 weeks and no toxicity grades III/IV. A more recent series of 27 children with refractory GVHD (17 with the chronic form), treated with MTX doses of 3-10 mg/m^2/week showed 58.8% overall response for cGVHD with prednisone withdrawal in 7/17 and decrease (dose <0.4 mg/kg) in 9/17 patients[54].

Resumo

Doença do enxerto contra o hospedeiro aguda e crônica após transplante de células-tronco hematopoiéticas

A doença do enxerto contra hospedeiro (DECH) é uma das principais complicações do transplante de células-tronco Hematopoéticas, acometendo cerca de 50% a 80% dos pacientes. A DECH aguda e suas manifestações clínicas são discutidas neste artigo, bem como a classificação revisada do NIH para diagnóstico e classificação da DECH crônica. A terapêutica para DECH aguda e crônica é um importante campo de discussão uma vez que não há superioridade comprovada para a maioria das terapêuticas utilizadas após o tratamento primário. Assim, esta revisão pretende ser instrumento de consulta para hematologistas transplantadores que lidam com esta complexa complicação do procedimento.

Palavras-chave: Doença do enxerto contra hospedeiro, Transplante de células-tronco hematopoéticas.

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O-001

Infections

Viral infections and lymphocyte reconstitution in haploidentical transplantation with post-transplant cyclophosphamide.

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Introduction: The use of haploidentical transplantation using post-transplant cyclophosphamide without T-cell depletion for patients with no identical HLA donors is increasing. A major problem in incompatible HLA transplantation is the slow immune reconstitution due to the intense immunosuppression and the resulting infectious complications. Objective: To analyze the incidence of viral infections in patients undergoing haploidentical BMT and its correlation with lymphocyte reconstitution in a hospital in Sao Paulo, Brazil. Method: Analysis of patients undergoing the first haploidentical BMT, with a diagnosis of hematological malignancy and severe aplastic anemia (AA) from 2010 to 2015. After the graft infusion, viral monitoring tests were performed weekly for CMV and adenovirus, every 14 days for EBV by PCR. Screening for BK virus and HHV-6 was performed when there was a clinical diagnosis of infection by these agents. The absolute lymphocyte analysis was performed daily and the analysis of T CD4+ lymphocytes was performed between D+100 and D+180. The occurrence of viral reactivation/infection was computed in the first 6 months of BMT, together with incidence of acute GVHD. Results: 31 patients were submitted to BMT, 25 patients with malignant neoplasms (80%) with a median age of 34 years (7-74 a) and 45% (14/31) using non-myeloablative regimen. Thirty patients had positive serology for CMV (96%). Five patients (16.1%) received a graft from a negative-CMV donor. The cumulative incidence of viral reactivation up to the D+180 was 84%. CMV reactivation occurred in 25/31 (80.6%) of the patients, and of these, 25.8% had subsequent reactivations. The median date of the first CMV reactivation was at D+39 (D+21-67). Pneumonia caused by CMV occurred in 4 patients. The second viral complication was cystitis caused by BK virus: 35.5%. The median number of lymphocytes on D+30 and D+100, was 223 x 103/uL and 705 x 103/uL, respectively, being similar in the group with reactivation (p = 0.385) and without CMV reactivation (P = 0.800). The median number of T CD4+ lymphocytes on D+100 and D+180 was 108/mm^3 (20-349 cells/mm^3) and 158/mm^3 (70-1245/mm^3), respectively. The incidence of acute GVHD II-IV in the entire group was 25.8% and it was not a risk factor for viral reactivation. However, all patients with acute GVHD II-IV showed CMV reactivation. Mortality related to viral infection was 10%. Conclusion: reactivations and viral infections in this Brazilian sample submitted to BMT were higher than those found in the literature. This may be due to a higher prevalence of some viruses, such as CMV, in our population. The number of complications, including mortality, suggests that specific strategies for prevention, prophylaxis and monitoring of viral infections should be discussed in the Brazilian centers that perform haploidentical transplants.

Keywords: allogeneic transplantation, haploidentical, viral infection, cytomegalovirus, lymphocyte reconstitution

0-002

Autologous Transplantation

Hematopoietic stem cell mobilization with plerixafor: Experience of Hospital Universitário Walter Cantídio/HEMOCE

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Introduction: Plerixafor (Mozobil®) is an inhibitor of the interaction between SDF-1 and its cognate receptor, CXCR4. This drug has shown to be effective in rescuing patients with poor mobilization, allowing a greater number of autologous transplantations in cases with risk factors or mobilization failure. It can be used as an "up front" strategy after mobilization failure, in patients with risk factors, or as a preemptive approach. Objective: To report the experience in the mobilization of hematopoietic stem cells with plerixafor in a center of north-eastern Brazil. Materials and Methods: The used protocol was the association of filgrastim (G-CSF) at a dose of 10- 16µg/kg with Plerixafor, at a dose of 0.24 mg/kg, starting on D4, 6 to 11 hours before the start of collection by apheresis, with the dose being repeated, if necessary, to attain a collection > 2.0 x 106 CD34/kg cells. Mozobil was used both as rescue after failure of the first mobilization attempt as the preemptive use in patients who failed to mobilize after the use of GCSF, associated or not with first-line chemotherapy. The medical records of all patients undergoing mobilization/collection during the study period were reviewed for data acquisition. Results: A total of 18 patients used plerixafor in the study period: 11 females and 7 males. Age ranged from 26 to 72 years. 10 patients (55.5%) had been diagnosed with multiple myeloma (MM), 2 (11.2%) with Hodgkin's lymphoma (HL) and 6 (33.3%) with non-Hodgkin's lymphoma (NHL). The number of collected CD34 cells ranged from 1.8 to 9.44 x 106 CD34 cells/kg. Only 2 patients failed to achieve 2.0 x 106 CD34 cells/kg, one due to collection failure and the second due to mobilization failure after the use of plerixafor on D4, D5 and D6. Conclusion: This study shows the importance of establishing rescue strategies for patients who failed mobilization with G-CSF associated or not with chemotherapy, with plerixafor being used as rescue or preemptively, a safe and effective drug for patients with difficulties in mobilization.

Keywords: Plerixafor, mobilization, Autologous transplantation, CD34

O-003

Infections

Intestinal colonization by multiresistant (ESBL or CRE) Gram-Negative (GN) Bacteria – importance for the risk of infection and death in patients submitted to hematopoietic stem-transplantation

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The increase in bacterial resistance among Enterobacteria is a global and probably irreversible phenomenon. These infections are difficult to treat and are associated with high mortality rates, especially in neutropenic patients. International treatment guidelines recommend empirical treatment with broad spectrum drugs in patients known to be colonized. However, there are few data in the literature to support this recommendation. In this study we assessed the prevalence and importance of colonization by Gram-negative (GN) bacteria producing ESBL or CRE in patients undergoing BMT in the following clinical outcomes: bacteremia by GN CRE or ESBL and overall mortality. MM: Retrospective cohort of patients undergoing bone marrow transplantation (BMT) between 2012 and 2015 in a single center. Weekly colonization screening for ESBLs and ERC was performed by rectal swab culture in all patients. Results: 267 patients were analyzed, with 232 (87%) and 35 (13%) submitted to autologous and allogeneic BMT, respectively. The most common underlying disease was myeloma (N = 143, 55%), followed by non-Hodgkin's lymphoma (N = 47; 18%). The median age of the group was 54 years (range 4-74 years). The prevalence of patients colonized by ESBL was 28% (N = 75) and by CRE, 6.3% (N = 17). The colonization was identified in the first week of hospitalization in 48% and 50% of patients with ESBL and CRE, respectively. Of the patients colonized by ESBL, 6 developed bacteremia by GN ESBL (8%; OR 5.4; 95%CI 1.33 to 22.4; p = 0.017). Of the patients colonized by CRE, 2 developed bacteremia by GN CRE (11.8%; OR 33.5, 95%CI 2.87 to 390; p = 0.011). Mortality in the group colonized by ESBL and CRE was greater when compared with the non-colonized group (6.7% vs. 1.6%, p = 0.04 and 18% vs. 2%; p = 0.009). The positive (PPV) and negative (NPV) predictive values of the presence of colonization as bacteremia marker was 8% and 98% for colonization by ESBL and 9% and 98% for CRE, respectively. Conclusion: The prevalence of colonization by ESBL among patients undergoing BMT was high (around 30%) and approximately half of patients are admitted to the procedure when they are already colonized. The colonization by CRE, although less frequent, is associated with bacteremia and mortality. As the colonization screening had high NPV as a marker of infection outcome, this information may be used to improve the adequacy of the empirical treatment of BMT febrile neutropenia.

Keywords: infection, bacterial resistance, colonization, transplant, neutropenia

0-004

Autologous Transplantation

NEAM Protocol: an alternative to the lack of carmustine in Brazil

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Introduction: The hematopoietic stem cell (HSC) is an undifferentiated cell capable of dividing itself indefinitely for self-renewal and generating highly specialized cell lines. The HSC can be obtained from bone marrow, peripheral blood and umbilical cord. Bone marrow transplantation (BMT) consists in obtaining HSC followed by the transplantation itself (conditioning, HSC infusion, bone marrow aplasia and recovery). Among the conditioning protocols used in autologous BMT in patients with Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL), the BEAC and BEAM were performed in Hospital Universitário Walter Cantídeo (HUWC); both contain carmustine, an antineoplastic alkylating agent. With the lack of carmustine in Brazil, it was necessary to use another chemotherapy (CT) protocol in BMT. We found in the literature an alternative Korean protocol: NEAM (mitoxantrone, etoposide, cytarabine and melphalan), which was used from April 2014 to February 2015. It is important to analyze the results of NEAM and compare them with the original protocol and the service outcomes using BEAM. Objective: To assess the efficacy of NEAM in BMT of patients with HL and NHL in HUWC. Methods: Retrospective analysis by reviewing the medical records of patients undergoing NEAM in HUWC from April 2014 to February 2015 and follow-up until December 31, 2015. Results: 25 TMOS were performed with NEAM protocol, 13 (52%) for HL and 12 (48%) for NHL; the median age was 34.5 years. Among the patients with HL, 7 (54%) were women and 6 (46%), men; 7 (54%) were in complete remission (CR) pre-BMT and 6 (46%) in partial remission (PR); 8 (61%) had undergone two pre-BMT chemotherapy regimens, and 5 (39%), three regimens. In the NHL group, 2 (17%) were women and 10 (83%) men; 6 (50%) were in pre-BMT CR, 4 (42%) in PR and 1 (8%) with active disease; 5 (42%) had undergone a pre-BMT CT regimen, 1 (8%) two; 4 (33%) three, and 2 (17%) four regimens. The median of pre-BMT therapy was two. At the post-BMT disease reassessment, the following was observed: in the HL group, 6 (46%) had recurrence and 7 (54%) were in CR. Of those who had recurrence, 1 patient was in CR and 5 in PR pre-BMT. Two patients died, with death rate (DR) of 15% at 1 year and 9 months of follow-up. In the NHL group, 4 (33%) had recurrence and 8 (67%) were in CR. One patient died with a DR of 8% at 1 year and 9 months of follow-up. There were no deaths related to transplantation in both groups. In the HL group that received BEAC (30 patients), 19 (63%) were in CR pre-BMT and 11 (37%) were in PR. With the BMT, 23 (79%) patients attained CR; while 6 (21%) had recurrence. Conclusion: There is a trend towards a good response in patients with NHL and HL in CR pre-BMT with NEAM use. Those with HL in PR pre-BMT tended to have an ineffective response with NEAM, due to the high recurrence rate. The disease-free survival in HL patients was 53.8% and in NHL, was 66.7% at 21 months.

Keywords: complete response, partial response, HL, NHL BMT

0-005

Allogeneic Transplantation

Results of the first survey of the Latin American Group of Bone Marrow Transplantation on Transplantation activity in Latin America 2009-2012

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The activity of Hematopoietic Stem Cell Transplantation (HSCT) and indications vary widely worldwide. The Latin American Group of Bone Marrow Transplantation (LABMT) was created aiming to promote excellence in HSCT in Latin America, encouraging the cooperation between centers, identifying regional differences and contributing to treatment access. Methods: The WBMT (Worldwide Network for Blood and Marrow Transplantation) questionnaire was sent to the Hematology and HSCT Societies, consisting of a simple table with the number of transplants according to the type of HSCT, donor and indication. Countries without a Society or HSCT Registry sent the data from Transplant Centers directly to the WBMT. Results: A total of 11,519 transplants were performed between 2009 and 2012 by 94 groups from 12 countries. Autologous HSCT represented 63% of the total number, indicated mainly for cases of myeloma and lymphoma (87%). The main indications for allogeneic HSCT were leukemia (70%) and non-malignant diseases (20%). A total of 3,391 related HSCT were reported; 55% of them used peripheral blood stem cells. In contrast, most unrelated HSCT used umbilical cord blood (n= 447), followed by bone marrow (n = 402) and peripheral blood (N = 246). In 2012, a total of 3,263 HSCT were reported, an increase of 29% compared to 2009. This increase, however, was of 36% of autologous HSCT and 20% of allogeneic ones. The number of transplants per 10 million individuals (HSCT rate) was 61:27 for allogeneic (ranging, in different countries, from 0 to 85) and 32 for autologous transplants (8 to 215). Compared to Asia, the HSCT rate is higher for autologous transplants (32 vs. 17), similar for allogeneic transplants, but much lower for unrelated HSCT (only 2.2, ranging from 0 to 18). HSCT indications in Latin America are similar to those in the USA and Europe. Conclusion: We have documented that the number of transplants performed in Latin America is still very low when compared to developed countries, but this difference is more marked in allogeneic HSCT, especially in unrelated transplants. Training programs and focus on improving the quality of services can contribute to progressively reduce this difference.

Keywords: Latin America, transplant rate, LABMT, Indications, Questionnaire

0-006

Hematology/Pediatric Transplantation

Autologous transplantation of hematopoietic stem cells in Hodgkin's lymphoma. Experience of the Brazilian Group of Pediatric Bone Marrow Transplantation.

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High-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (auto HSCT) is considered the standard treatment for recurrent or refractory Hodgkin's lymphoma (HL). Objective: To evaluate auto HSCT data for HL from different institutions participating in the Brazilian Group of Pediatric Transplantation. Method: Seven pediatric HSCT centers participated in this retrospective analysis. Results: We included 63 patients (pts), transplanted between November 1999 and January 2016, with a median age of 12.8 years (range: 2.9 to 18) of which 61.9% were males. The main histological type was nodular sclerosis in 41 pts, followed by mixed cellularity in 13, lymphocyte predominance in 5 and lymphocyte depletion in only one. The stage at diagnosis was IV in 13 pts, III in 26 and II in 23, whereas B symptoms were present in 31 pts. Auto HSCT indications were: recurrence in 45 pts and progression/refractoriness in 18. The patients were mainly conditioned with the BEAM regimen (55 pts), busulfan (BU) + melphalan (MEL) + gemcitabine (GEN) in 6, BU/MEL in 1 and carbo-platinum + cyclophosphamide + carmustine also in one patient. The source of cells was peripheral blood in 38 cases, followed by bone marrow in 22 and peripheral blood and bone marrow in 3, with a median of infused CD34+ cells of 6x106/kg. Mucositis grade III and IV was observed in 15 pts and severe skin toxicity in 2 of the pts conditioned with BU+MEL+GEN. Fifty-nine pts had febrile neutropenia, with 1 death from sepsis caused by Candida. The median length of hospital stay was 19 days (12-56), the median neutrophilic grafting was 14 days (8-40) and for platelets, 19 days (6-74), with 42 pts using GCSF (Granulocyte-colony stimulating factor). Pre or post-BMT radiation therapy was performed in 62 pts. When assessing the pre-transplantation disease status, we observed that 21 pts were transplanted in partial remission (PR) and 42 in complete remission (CR). Fifty-seven percent of the transplanted pts in PR had recurrence after the transplantation, versus 21% of those in CR ($p<0.001$). Three patients with recurrence after auto HSCT underwent a second allogeneic HSCT and are alive. There were 19 deaths between 74 days and eight years after the transplantation (median of 572 days), with 16 being associated with recurrence, 1 with sepsis and 2 with unreported causes, showing an overall survival of 67.8% with a median follow-up of 2.9 years (ranging from 74 days to 15 years). Conclusion: The auto HSCT for HL was considered a safe procedure with low mortality related to the procedure. Transplanted patients with active disease (PR) have higher recurrence rates, demonstrating the importance in controlling the pre-BMT disease. New conditioning regimens must be assessed regarding their toxicity and impact on survival.

Keywords: autologous transplantation, Hodgkin's lymphoma, pediatric transplantation

O-007

Histocompatibility

Description of a new epitope that explains the reactivity of anti-HLA-B*18:05 antibodies present in two individuals carrying HLA- B*18:01 allele

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The use of the algorithm HLA MatchMaker for the analysis of pattern reactivity in solid phase assays for HLA antibodies is important for information regarding which epitopes are being recognized by the antibodies. There are situations, however, that the HLA MatchMaker fails to produce a conclusive interpretation. The purpose of the present communication is to report two cases of kidney transplant candidates bearing HLA-B*18:05 that presented an antibody, detected by Luminex-single antigen assay, which reacted with HLA-B*18:01. The specificity of this reaction was confirmed by absorption/elution experiments. We sequenced exon 4 of the B*18:05 allele and observed that the sole difference between B*18:05 and B*18:01 alleles was in the position 127 (B*18:05, with 127K, and B*18:01, with 127N). It is interesting to note that the residue 127N was also present in other self-alleles (A*03:01, B*44:02, C*05:01 and C*12:03). The HLA MatchMaker analysis was not capable to indicate any eplet that could be recognized by the anti-B*18:01 antibody. With the aim of understanding the class I Luminex-single antigen test pattern including the reaction against B*18:01, we explored new possibilities of structural determinants. Using the self-nonself paradigm theory and differences in amino acid sequences, we discovered a new epitope that could explain the observed reactivity pattern. This epitope, corresponding to a combination of amino acids in two regions, namely 113H and 127N, was present only in antigens present on beads with MFI > 5000 (B*07:02, B*08:01, B*13:01/02, B*15:01/03/10/11/12/16, B*18:01, B*35:01, B*38:01, B*39:01, B*40:01/02/06, B*41:01, B*42:01, B*46:01, B*48:01, B*51:01/02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01/03, B*58:01, B*59:01, B*67:01, B*78:01, B*81:01, B*82:01, C*15:02) and was not present in any of the self-antigens. On the other hand, one or the other, but not both, of these amino acids were present in different self-antigens. We concluded that the type of analysis that we described was able to uncover a new epitope and represents an additional useful tool for the understanding of epitopes recognized by the antibodies.

Keywords: HLA, MatchMaker, Luminex-single antigen, self-nonself paradigm

0-008

Histocompatibility

Characterization of the epitope reactivity pattern of anti-HLA antibodies associated to Transfusion-Related Acute Lung Injury (TRALI)

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Female patient, 88 years old, diagnosed with myelodysplastic syndrome, showed transfusion-related acute lung injury (TRALI) with acute respiratory failure, bilateral pulmonary edema and severe hypoxia, after receiving blood products from a 34-year-old female donor, with a history of two pregnancies. The anti-HLA antibodies against class I and or class II molecules from multiparous donors are one of the main risk factors associated with TRALI development when passively infused during the transfusion. For this reason, the presence of anti-HLA antibodies specific to the recipient's HLA antigens (RSA=Recipient Specific Antibodies) was investigated in the serum of the donor of blood products. Identification of anti-HLA anti- bodies was performed by solid-phase assay, based on a panel of isolated HLA antigens (LABScreen Single Antigen Beads, One Lambda), considering MFI ≥1,000 as the cut-off. HLA Fusion (TerEps) and HLA MatchMaker (Eplets) software were both used for the epitope reactivity analysis. Patient's HLA typing was performed by Reverse SSO (LABType, One Lambda) and showed the following result: A*03:AGFGN, A*31:AGFHP; B*39:AGJVY, B*44:AGJWR; C*05:AGUVH, C*12:AGUVZ; DRB1*13:AGPCC, DRB1*15:AGJMZ; DRB3*01:AD, DRB5*01:VG; DQA1*01:ARSW, DQA1*05:05; DQB1*03:AGFVH, DQB1*06:ABXCF; DPA1*01:03; DPB1*02:01P, DPB1*03:01P (alleles included in each letter code are available at www.marrow-donor.org/cgi-bin/DNA/dnatyp.pl). The following antibodies specific to HLA antigens expressed by the recipient were found in the donor serum: B39, B44, DR13, DR15, DR51, DQ7, DP2 and DP3. Epitope analysis showed that the reactivity pattern of these RSAs is explained by the following epitopes: TerEp 9 /Eplet 158T shared by B39, B38 and B67 molecules (Average MFI=2,285); TerEp 1018 /Eplet 70D shared by DR13, DR103, DR4 (DRB1*04:02), DR7, DR8, DR11, DR12, DR16 and DR51 (DRB5*01:01) (Average MFI=7,118); TerEp 1603 /Eplet 142M3 shared by DR15 and DR16 (Average MFI=4,784); TerEp 1402 /Eplet 108T is specific to alleles belonging to DR51 group (Average MFI=4,810); also TerEp 2005 /Eplet 45EV that is a DQ7 private epitope (Average MFI=15,588) and/or the broad epitope TerEp 2006 /Eplet 55PP shared by DQ7, DQ8 and DQ9 (Average MFI=9,219); and finally the immunodominant epitope called TerEp 4002/Eplet 56E shared by DP2 (DPB1*02:01), DP3, DP4 (DPB1*04:02), DP6, DP9, DP10, DP14, DP17, DP18, DP20, DP28 and DR11 (average MFI=5,113). The weak reactivity against the B44 molecule (MFI=1,485) is accounted for TerEp 5018C, which is not clinically relevant, as it is a cryptic epitope exposed only on denatured B44 molecules. The identification of RSAs in the serum of the donor of blood products, using solid phase assays and epitope analysis, strongly suggests that these antibodies specific to HLA-B39, DR13, DR15, DR51, DQ7, DP2 and DP3 molecules are implicated in the development of TRALI.

Keywords: TRALI, blood transfusion, anti-HLA antibodies, HLA epitopes

0-009

Histocompatibility

Characterization of HLA antibodies specific to two recipients of hematopoietic stem cell grafts from their haploidentical mother.

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Two brothers with dyskeratosis congenita were referred to the lab for hematopoietic stem cell donor search. The haploidentical mother was the donor, as no compatible donors were found. As the brothers inherited the same paternal haplotype (A*24:02/C*03:04/B*40:02/DRB1*16:02/DQB1*03:01/DPB1*17:01), the mother could have been sensitized by the paternal HLA molecules. Search for recipient-specific antibodies (RSA) in maternal serum was assessed by solid phase assays using isolated HLA antigens and phenotypes panels (LABScreen SAB/PRA) (Cutoff: MFI≥1000). Epitope reactivity analysis was performed with EpVix and HLA Fusion software. Results showed that mother had RSAs against HLA incompatible molecules A24, B61 and DP17 expressed by her children; Epitope specificities were Eplet 62EE/TerEp 28 shared by A23, A24 and A80 (Average MFI=3,250); Eplet 163EW+73TE/TerEp 223 present in B7 CREG including B7, B13, B27, B47, B48, B60, B61, B73 and B81 (Average MFI=10,114); and Eplet 84DEAV/TerEp 4001 shared by DP1, DP3, DP5, DP6, DP9, DP10, DP11, DP13, DP14, DP17, DP19 and DP20 (Average MFI=1,303). Investigation continued with crossmatches (XMs) and adsorption/elution experiments in order to confirm this pattern of reactivity in silico. XMs were performed with the mother's serum and reference cells expressing RSAs targeting HLA molecules. Flow XMs using A24 cells showed weak positive reactions with B+pronase (MCF=325; Cutoff=275.5) and T lymphocytes (MCF=308; Cut- off=269.5); B61 cells showed strong positive reactions with B+pronase (MCF=592; Cutoff=251.25) and Tcells (MCF=425; Cutoff=224). CDC-XMs with T, T+DTT, T+AGH, T+AGH+DTT, B and B+DTT were negative for A24 and B61 cells. Adsorption/elution experiments were performed with maternal serum and the children's T/B lymphocytes and SAB assay was repeated with eluates. The in silico analysis was compared to the eluate epitope reactivity, and results confirmed the RSA anti-A24 against Eplet 62EE/TerEp 28. However, RSA anti-B61 identified in the eluate showed a different pattern of epitope reactivity than that inferred by in silico analysis. Besides reactions with B7, B13, B27, B47, B48, B60, B61, B73 and B81, it also showed positive reactions with A*66:02, B73 and Cw2. The configuration 163EW+self73T explains this unexpected reactivity, despite not being described yet in Epvix and HLA Fusion software nor in HLA Epitope Registry. In regard to RSA anti-DP, eluate analysis confirmed the anti-84DEAV antibody and revealed another type of RSA not detected by the in silico analysis. This second RSA is specific to 57D Eplet, which is shared by DP3, DP6, DP9, DP14, DP17 and DP20. This study shows that only the adsorption/elution experiments were able to demonstrate with accuracy the epitope reactivity of RSAs present in the maternal serum. It also emphasizes the importance of careful epitope analysis when searching for RSAs in the sera of any HLA incompatible donor, because these antibodies are associated with increased risk of GVHD development.

Keywords: RSA, HLA Epitopes, Crossmatch, SAB, GVHD

0-010

Histocompatibility

Anti-HLA antibody evaluation in patients candidates for hematopoietic stem cell transplantation (HSCT)

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Introduction: The presence of anti-HLA donor-specific antibodies (DSA) is associated with failure of engraftment in hematopoietic stem cell transplantation (HSCT) and this fact becomes even more important with the increasing number of haploidentical transplants. Objective: To describe the rate of alloimmunization against HLA antigens and the frequency of DSA in patients candidates to HSCT and treated at HLA Laboratory of the HSCT Service, and the clinical management in cases of DSA identification. Materials and Methods: We retrospectively evaluated 231 patients with related and unrelated donors between January 2013 and March 2016. Serum samples were tested with LABScreen® Mixed reagents, LABScreen® PRA and LABScreen® Single Antigen, Thermo Fisher Sientific, Luminex platform (LuminexTM, Austin, TX), LabScan-100 and HLA FusionTM analysis program. Results with fluorescence intensity (MFI) > 2000 were considered positive. Results: 131 (f = 0.57) of the samples were males and 100 (f = 0.43) were females. Alloimmunization rate was 29% (n = 68), of which 53% (n = 36) of the patients were males and 47% (n = 32) were females. Anti-HLA class I antibodies were detected in 53 patients (f = 0.78), and among the identified specificities, 79% were against HLA-A antigens, 60% against HLA-B and 26% against HLA-C. Anti-HLA class II antibodies were detected in 35 patients (f = 0.51) and the corresponding specificities corresponded to 71% against HLA-DR antigens, 60% against HLA-DQ and 37% against HLA-DP. DSA were identified in 4 female patients (f = 0.017) with offspring donor (haploidentical). For one of the patients, it was decided to replace the haploidentical donor by an unrelated donor with mismatch for HLA-A locus, without DSA. For the other three cases, where there was no other option, haploidentical transplants were performed after desensitization procedures: two cases with plasmapheresis and immunoglobulin administration, and one case with complement of the buffy-coat infusion prepared with the haploidentical donor's own cells. The desensitized patients were monitored and the transplantation was approved after the DSA removal. Discussion and Conclusion: The alloimmunization rate (29%) observed in this study was consistent with literature data, as well as the higher frequency of DSA between women candidates for haploidentical HSCT with offspring donor. HLA-DP typing is not necessarily performed for donor selection; however, a high sensitization rate was observed against these antigens (37%), so the screening for anti-HLA antibodies is essential, even for patients with 10X10 donors. The anti-HLA antibody screening contributed to the clinical strategies previous to the transplantation and grafting failure was not observed in desensitized patients with DSA.

Keywords: hematopoietic stem cell transplantation (HSCT), anti-HLA antibodies, anti-HLA donor-specific antibodies (DSA), desensitization, HLA-DP.

O-011

Histocompatibility

Importance of HLA-DPB1 typing and screening for anti-DP antibodies in the selection of unrelated donors for transplantation of hematopoietic stem cells

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Female patient diagnosed with acute myeloid leukemia, 56 years old, with multiple transfusions, was referred to the laboratory in search of a hematopoietic stem cell donor. There were no compatible donors in the family nucleus, and thus, the patient was enrolled in the search for an unrelated donor. The patient HLA typing showed the following result: A*01:01, * 02:01P; B*08:01, *44:02; C*05:01, * 07:01P; DRB1*13:01P; DQA1*01:03; DQB1*06:03; DPA1*01:03 and DPB1*02:01. Two volunteer donors were found, one national (DV-1) and another an international one (DV-2), both with 10/10 compatibility at high resolution for the HLA-A, B, C, DRB1, DQB1 loci, but no result for the DPB1 locus. Therefore, HLA-DPB1 typing was performed and showed that the two donors had mismatches (DV-1: DPB1*04:01; DV-2: DPB1*04: 02). The use of the DPB1 T-Cell Epitope Version 2.0 algorithm showed that the DPB1 incompatibilities were permissible for both donors. The screening for anti-HLA antibodies with LABScreen Single Antigen Beads - SAB (One Lambda), considering a cut-off of MFI≥1.000, identified several anti-DP antibodies, including a donor-specific antibody (DSA) with moderate reactivity (MFI=12,757) against DP4 (DPB1*04:01) expressed by the DV-1. The presence of DSA against DP4 (DPB1*04: 02) of DV-2 was not verified. The epitope analysis, performed with the aid of HLA Fusion & EpVix software, showed that the DSA reactivity could be explained by the 56A epitope, shared by DP1, DP4 (DPB1*04:01), DP5, DP11, DP13, DP15, DP19 and DP23 (Average MFI = 8,008). This antibody specificity was considered with reservation due to the unusual distribution of MFI values, with reaction forces ranging from 1,936 (DP5) to 16,744 (DP15) in HLA molecules that had the 56A epitope. The presence of this atypical pattern and the fact that the patient had multiple transfusions suggested the possibility of inhibiting the DSA reactivity through the Prozone effect. The serum thermal inactivation was performed and confirmed the Prozone effect, as an increase of 145% in the mean reactivity of 56A epitope (MFI = 19,627) was found after serum heating. The repetition of SAB with serum serial dilutions showed that the anti-56A DSA had a 1/512 titer. Therefore, DV-1 was excluded from the donor selection process and the DV-2 was chosen as donor. This case report shows that, if the search for donors took into consideration only the information of HLA-A, B, C, DRB1 and DQB1 typing, DV-1 could have been chosen as donor and the transplantation would have been at extremely high risk of primary grafting failure, due to the presence of DSA with 1/512 titer. The use of DPB1 T-Cell Epitope algorithm, together with the analysis of immunodominant DP epitopes in the antibody screening, allows a better risk stratification between different available donors, thus minimizing the risk of primary grafting failure or graft rejection.

Keywords: selection of hematopoietic stem cell donors, specific antibodies against donor, HLA-DPB1, DP epitopes.

0-012

Histocompatibility

HLA in vitro chimerism analysis: definition of a model for evaluation of prior transfusion interference on typing of bone marrow receivers

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INTRODUCTION: Several severe conditions can be treated by bone marrow transplant, and most of these diseases progress with the need to perform several blood component transfusions, as is the case of leukemia, medullary aplasia and more recently, sickle-cell anemia. Patients may receive blood products volumes accounting for 10, 20 or even 50% of their initial blood volume, which means a considerable content of genetic material from the blood products. The phenomenon of "false heterozygous" shown in vitro to HLA alleles, may be the cause of typing failure of patients who received blood transfusions previously to blood collection for testing. The evaluation of the possibility of emergence of this feasible in vitro phenomenon with combination of whole blood samples in different concentrations to simulate the donation dilution effect on the blood volume of an individual was the objective of this work. METHODS: Serial dilutions (1: 2, 1:10, 1:20, 1:50) were performed previously using known homozygous samples for HLA-A, B and DRB1 locus. These samples were typed separately and later combined in the proposed dilutions. DNAs were extracted by a purification column, using a chaotropic agent and DNA selective binding to a glass fiber matrix. A spectrophotometer was used to read the amount of light absorption in a specific wavelength, determining the concentration and purity of DNA for each sample. The samples were amplified by conventional PCR using specific primers for the specific locus of the HLA complex. The result of the amplification was demonstrated on an agarose gel electrophoretic run. PCR was followed by hybridization using a probe of specific sequence oligonucleotides linked to beads (intrinsic fluorescence microspheres) to the amplified alleles, based on their allelic differences. RESULTS: For the A locus, a false heterozygote result was found for a dilution up to 1:20, yielding: A*24, A*68. For the B locus, all dilutions obtained heterozygote results: B*07, B*18. Also, for the DRB1 locus, all dilutions showed heterozygote results: DRB1*03, DRB1*15. CONCLUSION: These results show the possibility of occurrence of the "false heterozygous" phenomenon in plausible proportions of blood mixing that occurred in post-transfusion period (1:10, 1:20). The data are relevant for the definition of temporal restriction procedures concerning the collection of samples in patients undergoing frequent and recent transfusions and to guide the research of inconsistent results found in these HLA typing patients.

Keywords: HLA Chimerism, blood transfusion, false heterozygous

0-013

Histocompatibility

Evaluation of C1qScreen ™ assays in the identification of anti-HLA antibodies.

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Introduction: The screening for antibodies against HLA antigens using the current solid phase assays has been a breakthrough in the identification of anti-HLA antibodies and has greatly contributed to the diagnosis of antibody-mediated rejection (AMR). However, the limitation regarding the assay's incapacity to differentiate complement-fixing antibodies is questionable. Objectives: to validate the C1qScreen™ assay and evaluate the performance to identify complement-fixing antibodies against the solid-phase assay (LabScreen® IgG). Material and Methods: We used 05 ASHI proficiency test serum samples (total of 405 analyses of class I antibody and 275 analyses of class II antibodies) and 8 samples (4 samples with antibodies against HLA class I antigens and 4 samples with antibodies against HLA class II antigens) in patients with suspected AMR and participants of the kidney transplant program (KTP). Samples were tested using LabScreen® IgG and C1qScreen™C1qScreen™ methodologies. The C1qScreen tests were performed in two laboratories to assess reproducibility. We used reagents from Thermo Fisher, LabScreen® Single Antigen I and II and C1qScreen, Luminex platform (LuminexTM, Austin, TX), LabScan-100 and HLA FusionTM analysis program. Results with mean fluorescence intensity (MFI) >2000 were considered positive for IgG assays. The cutoff value for C1q to find a delta ≥300 MFI between two adjacent beads, the smallest of the two beads and all below this value will be considered negative. By adding 1000 MFI in the smallest beads, all beads ≥ to this value were considered positive. Results: The analysis of class I antibodies was in agreement with the results of ASHI Proficiency Test (10 positive antibodies and 377 negative antibodies). The results for class II antibodies were all negative. We found a strong correlation between IgG antibody titers and results of C1qScreen™: all antibodies with MFI ≥ 12000 had positive C1q, with MFI <11999 and >8000 they showed both positive and negative C1q, and those with MFI <8000 showed negative C1q. Among the patients in the KTP, discrepancies were detected between the C1qScreen analyses, repeated in two laboratories mainly with results close the cutoff values. We found 100% correlation in DSA analyses between LabScreen®IgG and C1qScreen™ tests, but these antibodies showed MFI ≥ 13000. Discussion: The C1qScreen ™ methodology showed low reproducibility, as there was no consensus among the participating laboratories in the proficiency test and lack of reproducibility between two laboratories. The results between and LabScreen®IgG and C1qScreen ™ methodologies were similar when the fluorescence intensity was high. Conclusion: Further studies are needed to clarify whether the C1q tests are superior to other methodologies and the clinical significance.

Keywords: anti-HLA antibodies, antibody-mediated rejection (AMR), C1q.

0-014

Histocompatibility

Different HLA-DRB1-DQB1 haplotype associations in a group of Brazilian patients

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The HLA-DRB1-DQB1 alleles show a strong bonding imbalance. The variability of this imbalance depends on the HLA-DRB1 allele and studied ethnic group. The aim of this study was to analyze the HLA-DRB1-DQB1 allele and haplotype frequencies in a group of Brazilian patients consisting mostly of mixed-race individuals. 9165 patients with HLA-DRB1 and DQB1 typing were studied between the years 2000 and 2016, from all over the country, with the Southeast being the most representative region. The methods used were: PCR-SSOr (LiPA and/or One Lambda) and PCR-SBT (Thermo-Fisher). The frequency analyses and the Hardy-Weinberg equilibrium were determined by Harlequin software, version 3.5.2.2. We report the 34 HLA-DRB1 alleles of which frequencies were higher than 0.5%. The following describes the HLA-DRB1-DQB1 combinations, detected at least 3 times, in decreasing order of frequency. DRB1 * 07: 01 (13.10%) - (DQB1 * 02: 02, 03:03, 03:02, 03:01, 04:02); DRB1 * 03: 01 (8.33%) - (DQB1 * 02: 01, 03:01, 05:01, 04:02, 02:02); DRB1 * 13: 01P (7.19%) - (DQB1 * 06: 03, 05:01, 03:03, 06:02, 06:04, 03:01, 06:09); DRB1 * 11: 01P (7.05%) - (DQB1 * 03: 01, 06: 02,03: 19, 05:02, 06:11, 03:02, 02:02, 04:02); DRB1 * 15: 01 (7.0%) - (DQB1 * 06: 02, 05:02, 06:03, 06:01, 05:01); DRB1 * 01: 01E (5.0%) - (DQB1 * 05: 01); DRB1 * 13: 02 (4.45%) - (DQB1 * 06: 04, 06:09, 05:01, 05:02, 06:02); DRB1 * 01: 02 (4.04%) - (DQB1 * 05: 01); DRB1 * 15: 03 (3.35%) - (DQB1 * 06: 02, 05:01); DRB1 * 11: 04 (3.22%) - (DQB1 * 03: 01, 06:03, 05:02); DRB1 * 16: 02 (2.68%) - (DQB1 * 03: 01, 05:02); DRB1 * 14: 01P (2.52%) - DQB1 * 05: 03, 05:01, 05:02, 03:01, 06:04, 06:02); DRB1 * 04: 11 (2.11%) - (DQB1 * 03: 02, 04:02); DRB1 * 04: 04 (2.30%) - (DQB1 * 03: 02, 04:02, 03:01); DRB1 * 09: 01P (2.11%) - (DQB1 * 03: 03, 02:02); DRB1 * 04: 05 (2.05%) - (DQB1 * 03: 02, 04:01, 02:02, 03:01, 02:01); DRB1 * 08: 01 (2.05%) - (DQB1 * 04: 02); DRB1 * 04: 01 (1.94%) - (DQB1 * 03: 02, 03:01); DRB1 * 08: 04 (1.87%) - (DQB1 * 04: 02, 03:01, 03:19, 06:02); DRB1 * 10: 01 (1.83%) - (DQB1 * 05: 01); DRB1 * 14: 02 (1.67%) - (DQB1 * 03: 01); DRB1 * 16: 01 (1.53%) - (DQB1 * 05: 02); DRB1 * 11: 02 (1.48%) - (DQB1 * 03: 01, 03:19); DRB1 * 04: 02 (1.43%) - (DQB1 * 03: 02); DRB1 * 12: 01P (1.42%) - (DQB1 * 03: 01, 05:01); DRB1 * 08: 02 (1.33%) - (DQB1 * 04: 02, 03:02, 03:01); DRB1 * 13: 03 (1.27%) - (DQB1 * 03: 01, 02:02); DRB1 * 03: 02 (1.20%) - (DQB1 * 04: 02, 02:03); DRB1 * 04: 03 (1.0%) - (DQB1 * 03: 02, 03:04, 03:05, 04:02, 03:01); DRB1 * 08: 07 (0.85%) - (DQB1 * 04: 02); DRB1 * 04: 07p (0.78%) - (DQB1 * 03: 02, 03:01, 06:03); DRB1 * 15: 02 (0.76%) - (DQB1 * 06: 01, 06:02); DRB1 * 01: 03 (0.67%) - (DQB1 * 05:01, 03:01); DRB1 * 11: 03 (0.56%) - (DQB1 * 03: 01). The HLA-DRB1 *01:01; 01:02; 10:01; 14:02; 16:01; 04:02; 08:07 and 11:03 alleles are closely associated, each of them with its corresponding HLA-DQB1 allele. A variability, however, can be found in rarer conditions. There is a wide haplotype diversity for the other HLA-DRB1 alleles. These data can contribute to estimate the degree of difficulty to be found in the search and selection of a better 7x8 donor, where there is no information for DQB1 alleles.

Keywords: HLA-DRB1-DQB1 haplotypes, Hematopoietic cell transplantation

0-015

Cell Therapy

New procurement protocol for human pancreas aimed at the generation of decellularized pancreatic scaffolds

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Introduction: Type 1 diabetes mellitus (T1DM) is a condition resulting from the autoimmune destruction of pancreatic β cells, leading patients to require life-long insulin therapy, but, often, it does not avoid the most common complications of this disease. Transplantation of isolated pancreatic islets from heart-beating organ donors is a promising alternative treatment for T1DM, which our group introduced in Brazil in 2002; however, this approach is performed by only a few centers around the world, since it is still considered an experimental procedure. Recently, pancreatic bioengineering and Regenerative Medicine have been proposed as potential and powerful alternative therapeutic approaches. The human pancreas may be decellularized, with the remaining bioscaffold, a skeleton of extracellular matrix (ECM), being able to provide the optimal microstructure and microenvironment for islet formation from cultured beta cells or stem cells differentiated into insulin-producing cells, aiming at their transplantation. Therefore, this bioscaffold may be used as an attractive 3D template for several studies aiming to restore pancreas dual endocrine and exocrine functions. Objectives: To develop a new pancreas procurement protocol specially designed for the pancreas decellularization process. Methods: Human pancreas from adult brain-dead donors (mean age 50 ±5 years, n=6) were harvested in accordance with Brazilian regulations and the local Institutional Ethical Committee. After careful selection of brain-dead donors, a medical pancreas harvesting team goes to the hospital in order to remove the organ and send it to our laboratory, where the decellularization process takes place in a bioclean room under cGMP facilities. Pancreas histology: 1. Optical microscopy (Hematoxylin/Eosin, Alcian blue and Picrosirius red), 2. Transmission electron microscopy and 3. Genomic DNA Analysis (TapeStation analysis) were used to evaluate and characterize the integrity of the decellularized matrix. Results: This new protocol consists of discarding the pancreas head and cannulating the remaining organ by three different pathways. The organs were transported from the Surgical Center to the Bioclean facility in a Preservation Solution, instead of the mixture of Organ Preservation Solution plus Perfluorocarbon (PFC), as is currently used in the islet transplantation procurement. These protocol modifications improve the decellularization process by significantly saving time and financial resources when compared to the pancreas procurement protocol used for isolate islet procedure. Conclusions: This new procurement protocol is more feasible for the pancreas decellularization process, maintaining the extracellular matrix structure, aiming to develop an alternative treatment for T1DM.

Keywords: Decellularization, Bioengineering, pancreas procurement, extracellular matrix, type 1 diabetes

0-016

Cell Therapy

Modelling Type 2 Long qT syndrome using iPSC- derived cardiomyocytes.

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Type 2 Long QT syndrome (LQTS2) is a cardiac channelopathy caused by mutations in the hERG channel, characterized by prolonged ventricular repolarization and sudden cardiac death. The generation of induced pluripotent stem cells (iPSC) from patients and their differentiation into cardiomyocytes represents a powerful method for the investigation of disease pathogenesis. The aim of this work was to generate iPSCs from peripheral blood of patients with LQTS2 and differentiate these cells into cardiomyocytes to model the pathophysiology of LQTS2 *in vitro*. After confirmation of the mutation in the KCNH2 gene, mononuclear peripheral blood cells were isolated and cultured in erythroblast enrichment medium. Erythroblast isolation was confirmed by coexpression of CD36 and CD71. Cells were transduced using Sendai Virus and after 20-25 days the colonies were selected, expanded, and genotype and karyotype analyses were performed. iPSCs were characterized by RT-PCR, flow cytometry, immunofluorescence and spontaneous differentiation. iPSC differentiated into cardiac lineage following 30 days of induction. On day 0, cells were cultured with RPMI+B27 minus insulin (RB-) and CHIR99021 (9 μM). On days 1-3, cells were cultured with RB-. For the differentiation into cardiac mesoderm (days 3-4), cells were cultured with RB- and XAV939 (10 μM and 5 μM respectively). On days 8-30, cells were cultured with RPMI/B27. Electrophysiology, field potential duration (FPD) by multielectrode-array (MEA) and immunofluorescence were performed. Our results demonstrated that the enrichment of erythroid population was efficient, with coexpression of over 90% of CD36 and CD71. iPSC emerged on days 15-20 and were selected manually for expansion. iPSC had a normal karyotype and the point mutation (c.1600C-T) was reconfirmed after reprogramming. Cells expressed pluripotency markers by RT-PCR. We observed expression of OCT4, SOX2, NANOG, SSEA4, TRA1-60, TRA1-81 in more than 90% of the cells, using flow cytometry and immunofluorescence. iPSC showed spontaneous differentiation into all three germ layers (positive staining for Nestin, Brachyury and Alpha-fetoprotein). Our cardiac differentiation protocol generated cells with positive staining for troponin T and the following distribution: 70.9% ventricular-like, 22.5% atrial-like and 6.4% nodal-like cardiomyocyte based on electrophysiological recordings (n=31). Electrophysiology demonstrated that the action potential duration of LQT2-cardiomyocytes was significantly longer than that of control cardiomyocytes (APD90 LQTS2-iPSC 434.5±87.2 msec (n=16) vs control-iPSC 194.5±49.11 msec (n=11)) as well as FPD (LQTS2-iPSC 1157±164.9 msec (n=9) vs control-iPSC 220±12.25 msec (n=4)) We efficiently generated iPSC from peripheral blood and differentiated them into cardiomyocytes with LQTS2 characteristics. Thus, LQTS2-iPSC derived cardiomyocytes constitute a promising platform to study the pathophysiological mechanisms and drug sensitivity in LQTS2.

Keywords: LQTS2, iPSC, cardiomyocytes, modelling

O-017

Cell Therapy

Effects of Polyunsaturated fatty acid (PUFA)-stimulated Mesenchymal Stromal Cells in Acute Respiratory Distress Syndrome induced by Sepsis

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INTRODUCTION: Cell therapy is a promising strategy that has been reported to reduce inflammation in experimental ARDS; however, to date, clinical studies have reported no significant beneficial effects. Therefore, strategies to potentiate mesenchymal stromal cell (MSC) activity may lead to better results. We hypothesized that metabolites derived from polyunsaturated fatty acids (PUFA) appear to stimulate MSCs, enhancing their anti-inflammatory and antifibrogenic properties, thus improving their therapeutic effects in the management of ARDS. We aimed to investigate the effects of MSCs stimulated with PUFA on inflammatory and remodeling processes in experimental ARDS induced by sepsis. METHODS: Twenty-four C57BL/6 mice were randomly allocated to two groups: sham surgery or ARDS induced by cecal ligation and puncture (CLP). Twenty-four hours after CLP, animals were further randomized to intravenous saline solution (50 uL, SAL, n=6/each), adipose tissue-derived MSCs (105, AD-MSCs, n=6/each), or adipose tissue-derived MSCs stimulated with PUFA for 6 h (105, AD-MSC-PUFA, n=6/each). Twenty-four hours after treatment, survival rate, lung mechanics and histology were analyzed. Additionally, to characterize sepsis severity, a clinical score was developed using the following parameters: fur aspect, activity, posture, behavior, respiration, chest sounds, eyes, and body weight. The higher the number of signs present, the higher the severity of sepsis. RESULTS: 24 hours after the CLP, animals had moderate ARDS characterized by functional and morphological lung alterations. There were no deaths in the sham group. After SAL treatment, ARDS animals showed 30% mortality rate, increased static elastance and viscoelastic pressure (60% and 45%, respectively), alveolar collapse (25%), interstitial edema (12%), and inflammatory cells in the lung parenchyma (22%). AD-MSCs reduced mortality (19%), clinical score, and alterations in lung mechanics (static elastance and viscoelastic pressure) and histology when compared with ARDS-SAL. When animals were treated with ARDS-MSCs-PUFA, these benefits were even more marked. CONCLUSIONS: In this model of sepsis-induced ARDS, MSCs effectively reduced clinical sepsis score, mortality rate, and changes in lung mechanics and histology. Treatment with PUFA-stimulated MSCs further increased therapy effectiveness. These results provide a basis for subsequent cell therapy investigations.

Keywords: Cell therapy, mesenchymal stromal cell, polyunsaturated fatty acids, acute respiratory distress syndrome

0-018

Cell Therapy

Safety Study: Bone-marrow Derived Mesenchymal Stromal Cells Associated with One-way Endobronchial Valves in Patients with Pulmonary Emphysema.

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RATIONALE: Chronic obstructive pulmonary disease (COPD) is a devastating disease that affects millions of individuals worldwide and therapeutic options are limited. The insertion of one-way endobronchial valves (EBV) to reduce pulmonary air trapping has been used as therapy for COPD with good results. However, local inflammation may result and can contribute to worsening of clinical status in these patients. We hypothesized that combined EBV insertion and intrabronchial administration of mesenchymal stromal cells (MSCs) at the EBV site would decrease the inflammatory process, thus mitigating EBV complications in patients with severe COPD. This initial study sought to investigate the safety of this approach. METHODS: A phase I, prospective, patient-blinded, randomized, placebo-controlled design was used. Participants with heterogeneous advanced emphysema (GOLD III or IV) were recruited from Hospital de Clínicas de Porto Alegre, Brazil. Ten patients were randomly selected to receive allogeneic bone marrow-derived MSCs (108 cells/30 mL saline, 2·0 × 106 cells/min) (EBV+MSC) or saline (30 mL) (EBV+SAL) (n=5/group), delivered bronchoscopically just before insertion of one-way EBVs. Patients were evaluated 1, 7, 30, and 90 days after therapy. Outcome assessments included a comprehensive standardized safety evaluation, blood tests, spirometry, lung scintigraphy, quality-of-life questionnaires, 6-min walk test (6MWT), and measurement of systemic inflammation markers. RESULTS: All patients completed the study protocol and 90-day follow-up. MSC delivery did not result in acute administration-related toxicity, serious adverse events, or death. No significant between-group differences were observed in overall number of adverse events (p=0.53), frequency of COPD exacerbations (p=1), or worsening of disease (p=0.23). Additionally, there were no significant differences in blood tests (p=0.63), lung function (p=0.56), or radiological outcomes (p=0.89). However, quality-of-life indicators were higher in EBV+MSC compared to EBV+SAL (p=0.01). EBV+MSC patients had decreased levels of circulating C-reactive protein at 30 and 90 days (p<0.0001, p=0.0009, respectively), as well as BODE and MMRC scores. CONCLUSIONS: Combined use of EBV and MSCs appears to be safe in patients with severe COPD, providing a basis for subsequent investigations using MSCs as concomitant therapy.

Keywords: mesenchymal stromal cells, COPD, lung volume reduction, quality of life, inflammation

O-019

Cell Therapy
Extracellular Matrix: an alternative to hepatic transplant

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Liver transplantation is the only effective treatment for severe hepatic lesion; however, this procedure is limited by organ shortage. In this context, the production of a bioartificial liver can reduce this problem. Although decellularized porcine livers have a wide range of applications in regenerative medicine, previously existing protocols for organ decellularization still need to be adjusted to a full size porcine liver. For this purpose, it is necessary to obtain an extracellular matrix that maintains its integrity and populate it with functional hepatocytes within a short period (3 days). A first step is to establish an efficient decellularization protocol that allows cellular repopulation. Objective: produce a 3D porcine liver bioartificial matrix that enables effective decellularization of the entire porcine liver within a short period with intact extracellular matrix components (ECM) and vascular system and repopulate it with HEPG2 cells. Method: Livers (n=3) were perfused through the portal vein at 50 mL /min for 12 hours with water. On the following day, they were perfused at 100 mL/min for 2 hours with PBS, followed by a 0.2% trypsin solution (at 130 mL/min for 4h 30 min and Triton X-100 for 12 hours. Then, 1% sodium deoxycholate was perfused for an additional 12 hours. All perfusions were carried out at 37 °C. To analyze the integrity of the ECM, we performed histology and electron microscopy after the process. The matrix was sectioned in 300µm slices and kept in culture in DMEM Low Glucose with 15% FBS and 1% penicillin and streptomycin. To evaluate the presence of residual cells we used fluorescent nuclear stain (DAPI) and DNA quantification by spectrophotometry. The presence of type IV collagen was detected by immunohistochemistry. HEPG2 cells (1 mL) were cultured over the matrix in the same DMEM Low Glucose at a concentration of 106/mL. The presence of cells in the recellularized matrix was visualized by DAPI nuclear stain. The presence of albumin was detected by immunofluorescence and the secretion of this protein was analyzed by ELISA after 15 days in culture. Results: After 3 days of decellularization, electronic microscopy showed the presence of collagen in ECM and cells could not be detected. DAPI staining did not indicate the presence of cell nuclei in the matrix. DNA quantification indicated that 97% of cells were removed. After 15 days in culture, HEPG2 cells were able to repopulate the matrix. This was confirmed by the presence of DAPI stained nuclei and by immunofluorescence and ELISA, showing the presence of albumin in the recellularized matrix and in culture supernatant, respectively. Conclusion: Our decellularization method was efficient in removing resident cells and preserving the liver's ECM and vascular system. After 15 days, HEPG2 cells were able to adhere to the matrix and produce and secrete albumin.

Keywords: Decellularization, porcine, recellularization, transplant

0-020

Hematology – Benign Diseases

Haploidentical transplantation with post-transplantation Cyclophosphamide(PT-CY) for the treatment of Bone Marrow Failures (BMF): Analysis of 39 children and adolescents transplanted in Curitiba, Brazil

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The availability of matched unrelated donors, as well as time to find a donor and the costs related to the acquisition of international grafts are limited in countries with ethnical minorities and fewer resources. Herein we describe the experience of 39 pts with BMF submitted to haploidentical BMT with PT-CY between 2008 and 2015. The median age was 9 years (range: 1-16), 74% were males and 95% were CMV positive. Diagnosis: Fanconi Anemia (FA, N=30), severe aplastic anemia (SAA, N= 5), dyskeratosis congenita (DC, N=2) or other inherited bone marrow failure (N=2). Thirty-five pts were transplanted upfront, while 4 pts with FA received this treatment after a primary or secondary graft failure. All pts had failed prior therapies and most were transfused before transplantation. Bone marrow was the only graft source used and all pts received GVHD prophylaxis that included PT-CY on D+3 and D+4, followed by cyclosporine, mycophenolate mofetil and G-CSF. FA pts received PT-CY at 25 mg/kg/day (total dose: 50 mg/kg) and pts with other BMF received PT-CY at 50 mg/kg/day (total dose: 100 mg/kg). Pts with FA received fludarabine(FLU) 150 mg/m2 + TBI 200-300cGy +/- CY 10 mg/kg without (N=14) or with rabbit ATG 4-5 mg/kg (N=16). Pts with SAA, DC or other congenital BMF received CY 30-50 mg/kg, FLU 150 mg/m^2 and TBI 200-400cGy. Results: FA: In the subgroup of pts who did not receive r-ATG (N=14), all pts engrafted, despite the presence of donor specific antibodies (DSA) in 2 pts. Three pts had AML and 2 are in remission 1 and 3 years after transplant. The incidence of acute and chronic GVHD was very high. Six pts died due to GVHD (N=4); toxoplasmosis/CMV pneumonia (N=1) and relapse (N=1). Eight pts are alive with a median follow-up of 44 months after transplant including 2 pts rescued after graft failures. In the subgroup of pts receiving r-ATG (N=16), 2 pts had graft failure and both died, despite a 2nd transplant with different donors. One pt had MDS and is in remission one year after transplant. The incidence of acute and chronic GVHD decreased in severity but was still observed. Three pts died, 2 from graft failure and one due to late acute GVHD. 13 pts are alive with a median follow up of 22 months after transplant, including the other 2 pts rescued after graft failure. All transplanted patients with a diagnosis of SAA, DC or other BMF are alive and engrafted. In this group, no pt developed acute or chronic GVHD. Graft failure was observed in one pt with DC who had DSA. This patient is alive and well after a 2nd BMT from a different haploidentical donor. Altogether, CMV reactivation occurred in 65% of pts at risk, regardless of the primary diagnosis. Conclusion: Haploidentical BMT using PT-CY may be an option for patients with acquired or inherited BMF who need an immediate transplant, but lack a matched related or unrelated donor. New approaches to GVHD prophylaxis and treatment are needed in order to improve quality of life and overall survival of FA pts.

Keywords: Haploidentical, Post-transplantation Cyclophosphamide, Bone Marrow Failures

0-021

Allogeneic Transplantation

Comparison of haploidentical transplant using post-transplant cyclophosphamide with allogeneic 10x10 HLA compatible transplant

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Introduction: Finding an HLA compatible donor is still a limitation for certain patients, especially those of ethnic minorities or in populations with a high degree of miscegenation, as in Brazil. The indication of haploidentical transplant, using post-transplant cyclophosphamide without T cell depletion in patients without identical HLA donor has increased in the last 10 years. The strategy of using cyclophosphamide in the post-transplant period to eliminate alloreactive cells and preserve regulatory T cells has been increasing, due to the low cost and technical facility. Objective: To compare the results of haploidentical transplant (Haplo BMT) with related 10x10 HLA compatible transplant (Rel BMT) and unrelated 10x10 compatible HLA transplant (Unrel BMT) regarding overall survival, recurrence rate, mortality and incidence of acute graft-versus-host disease (aGVHD). Methods: Retrospective analysis of adult and pediatric patients submitted to the first transplant of hematopoietic stem cells with a diagnosis of acute leukemia, myelodysplastic syndrome and myeloproliferative neoplasms from 2010 to 2015. Results: We analyzed 18 patients undergoing Haplo BMT, 26 patients with Rel BMT and 38 patients undergoing Unrel BMT. The 3 groups were comparable in age and underlying pathology. The median follow-up was 35 months. Overall survival at 3 years was 45.2% for Haplo BMT, 52.8% for Rel BMT and 43.3% for Unrel BMT ($p = 0.37$). The cumulative incidence of recurrence at 1 year was 33.2% for Haplo BMT, 23.9% for Rel BMT and 27.8% for Unrel BMT, with $p = 0.65$. Recurrence-free survival at 3 years was 40.4% for Haplo BMT, 41.4% for Rel BMT and 34.8% for Unrel BMT ($p = 0.77$). The mortality unrelated to recurrence within 1 year was similar for the 3 groups: 26.4% for Haplo BMT, 16.2% for Rel BMT and 27.5% for Unrel BMT, $p = 0.40$. The incidence of grade III-IV aGVHD up to D+180 showed a trend to be lower in the Haplo BMT group (5.6%) when compared to Rel BMT (21%) and Unrel BMT (33%), $p = 0.06$. Conclusion: This small group of Brazilian patients reproduces the recent literature data suggesting that haploidentical BMT with post-transplant cyclophosphamide shows results that are comparable to HLA compatible 10x10 transplant for some malignancies. The use of cyclophosphamide in the post-BMT period can decrease the effect of HLA mismatch, as shown by the low incidence of severe aGVHD in the studied group; however, this was not converted into a higher overall survival, probably due to infections in this group with triple immunosuppression.

Keywords: haploidentical transplant, allogeneic transplant, related, unrelated, mortality

0-022

Allogeneic Transplantation

Epidemiological analysis of allogeneic hematopoietic stem cell transplantations in Brazil.

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantations is a very important alternative in many hematological diseases. Therefore, it is important to know the epidemiological profile of these performed procedures, in order to achieve a better groundwork by the health services and a better redirection of public funds. OBJECTIVE: To describe the epidemiological profile of allogeneic hematopoietic stem cell transplantations performed in Brazil between January 2008 and March 2016. MATERIALS AND METHODS: This is a descriptive quantitative study using secondary data available at the database of the Hospital Information System of SUS (SIH/SUS) and Brazilian Institute of Geography and Statistics (IBGE). Data on the number of allogeneic transplantations of hematopoietic stem cells from bone marrow, allogeneic hematopoietic stem cells from umbilical cord blood and allogeneic hematopoietic stem cells from peripheral blood, were analyzed from January 2008 to March 2016, according to all Brazilian states and Brazilian regions that perform this type of procedure. The variables were: total number of procedures performed, related or unrelated donors and receptors and type of health care system (public and private). RESULTS: A total of 5043 procedures were performed from January 2008 to March 2016. The Southeast region had the highest prevalence of allogeneic hematopoietic stem cell transplantation from related (30.1%) and unrelated donors (9.4%). The state of São Paulo showed the highest percentage of peripheral blood stem cell transplantation (16.5%). Umbilical cord stem cell transplantation from unrelated donors represented approximately 3.3% and from related donors, only 0.3% of the total transplantations performed. The private sector showed a higher prevalence of the total procedures performed (49.1%). DISCUSSION: The bone marrow is the traditional source of hematopoietic stem cells, but it is being replaced by hematopoietic progenitor cells, also found in peripheral blood, especially in autologous transplants. Another source is the umbilical cord blood (CURCIOLE, 2010). Regarding the degree of kinship in allogeneic transplantation, which had a higher percentage in this study, in another study performed at the University of Sao Paulo, most of the related donors were siblings, while the others were parents. CONCLUSION: The study shows a higher prevalence of allogeneic hematopoietic stem cell transplantation in the most populous regions, with higher socioeconomic status. Therefore, a higher investment from the public health system is necessary to reduce morbidity and mortality from diseases that can be treated by transplantation.

Keywords: Epidemiology, Hematology, Brazil

0-023

Hematology/Transplantation Pediatric

Use of post-transplant cyclophosphamide for primary immunodeficiencies: experience of 20 patients in three bone marrow transplant centers in Curitiba-PR.

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is still the main treatment for most primary Immunodeficiencies (PIDs). However, many patients (pts) have no compatible donors and the delay in finding donors can lead to death. It has been shown that the use of post-HSCT cyclophosphamide (PT-CY) is effective in preventing rejection and graft-versus-host disease (GVHD) in transplantations for non-malignant diseases. Objectives: To describe the results of HSCT with PT-CY for patients with PID. Materials and Methods: A retrospective, descriptive study of 20 transplanted pts using PT-CY, in three transplant centers in Curitiba. Results: During the period from February 12 to December 15, 15 pts underwent HSCT with PT-CY, while other 5 pts received this treatment as a rescue strategy for grafting failure of the first transplant. Eighteen pts were males and 2 were females. The median age at transplantation was 16 months (2.7 months to 10 years). PID type: Severe Combined Immunodeficiency (SCID), 8 pts, Wiskott-Aldrich Syndrome (WAS) 6 pts, Chronic Granulomatous Disease (CGD) 2pts, Chediak Higashi Syndrome (CHS) 1pt, Hemophagocytic Lymphohistiocytosis (HLH) 2pts. Most patients underwent conditioning with cyclophosphamide (CY) 29-50 mg/kg + Fludarabine 150 mg/m^2 +/- TBI200-400rads +/- ATG5 mg/kg and prophylaxis for graft-versus-host disease (GVHD) with PT-CY 100 mg/kg + mycophenolate mofetil + cyclosporine. All patients received bone marrow (BM). Nineteen patients used related donors, 16 with mismatches (5/10: 15pts, 9/10: 1pt). One patient received BM from a compatible unrelated donor. The median infused TNC (total nucleated cells) was 6.86 x 108/kg (2.8 to 14.4 x 108/kg). All patients were evaluable for the engraftment. All transplanted patients for graft failure rescue showed transplant engraftment and are alive. The median days for neutrophilic engraftment was 15 and for platelet engraftment, 18. Three patients had primary graft failure (1 SCID, 1 HLH, 1 CGD) while secondary failure occurred in 1pt with WAS. Two patients underwent retransplantation and one patient died at 29 months after the second transplant due to disease progression. Of the evaluable patients, 2 pts had acute GVHD grade 3 and 2 pts chronic GVHD grades 3-4. Sixteen pts are alive between 5.3 months and 4.3 years after HSCT (median follow-up: 16 m). Among the pts with SCID, only three did not achieve complete immune recovery and received IGIV replacement. Four patients died between 1.4 and 9.3 months after the HSCT due to bacterial/fungal sepsis (n = 3) or disease progression (n = 1). The overall survival was 80%. Conclusion: The use of PT-CY showed low toxicity and was effective in promoting engraftment and preventing GVHD occurrence. In this study, the use of PT-CY was a promising strategy for the rapid treatment of patients who do not have compatible donors.

Keywords: Immunodeficiency, Transplant.

0-024

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services

Quality of life in patients with sickle-cell anemia undergoing HSCT: a longitudinal study

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The hematopoietic stem cell transplantation (HSCT) can be considered as the only curative treatment for patients with sickle-cell disease. It is indicated in cases where the benefit of the transplant is greater than the risk of the procedure, regarding quality of life maintenance. Therefore, this is a key variable to be assessed in this context. Data from studies carried out in the same unit of this study indicated that, six months after the BMT, there is a decrease in the Social Aspects and Mental Health scores, whereas General Health was the only domain with an increase considered to be significant. Considering that the change in quality of life is an important factor to confirm HSCT effectiveness, we aimed to compare the QoL scores of patients with sickle-cell disease submitted to HSCT before and one year after the procedure, assuming that the time can be decisive to consolidate the gains in the several aspects of the patient´s life. The tool used was the questionnaire Generic Quality of Life Assessment - Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), applied individually, face-to-face. This questionnaire evaluates the physical components: functional capacity (FC); physical aspects (PA); pain intensity (PI); general health (GH); social aspects (SA); vitality (VIT); emotional aspects (EA) and mental health (MH). After it was applied, each question was given a score, which was later transformed into a scale of 0-100, in which zero corresponds to the worst health status and 100 to the best one. The sample consisted of 18 patients, ten males, ranging in age from 18 to 36. The results showed an improvement in all components of patient QoL, when we compared the values of one year post-HSCT with the pre-HSCT period. The results of the physical components were: FC: pre = 66.7, SD = 21.7, post = 82.4, SD = 17.1; PA: pre = 45.0, SD = 40.2, post = 62.8, SD = 40.5; PI: pre = 57.3, SD = 32.0, post = 79.4, SD = 27.6; GH: pre = 59.8, SD = 19.9, post = 78.1, SD = 14.4. As for the emotional components we had: VIT: pre = 64.8, SD = 18.9, post = 78.5, SD = 12.3; SA: pre = 69.1, SD = 25.4, post = 82.5, SD = 25.3; EA: pre = 56.4, SD = 47.9, post = 70.2, SD = 45.3; MH: pre = 75.2, SD = 11.2, post = 78.9, SD = 16.1. This increase in QoL was considered statistically significant in five components: FC ($p = 0.001$), PI ($p = 0.004$), GHv ($p = 0.009$), VIT ($p = 0.003$) and SA ($p = 0.031$). In three of them the improvement was not significant: PA ($p = 0.147$), EA ($p = 0.073$) and MH ($p = 0.212$), which may be related to the presence of immunosuppression still found in these patients. Compared to the aforementioned study of six months post-HSCT, there is a gradual improvement in patient QoL, so that one year after the transplant all components seem preserved, most with a statistically proven gain, reinforcing the importance of this therapy for these patients.

Keywords: quality of life, sickle-cell anemia, Hematopoietic Stem Cell Transplantation

P-001

Hematology - Basic Area

Main indicative diagnoses and types of hematopoietic stem cell transplantations in a reference service

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) has been used as an alternative and effective therapy for patients with oncologic, immunological or hematological diseases, either malignant or not, inherited or acquired. The HSCT may be an autologous transplantation, in which the Hematopoietic Progenitor Cells (HPC) are collected from peripheral blood or from the patient's bone marrow; an allogeneic transplantation, in which the donor is related or not, with compatible human leukocyte antigen (HLA) and the HPC from peripheral blood, bone marrow, umbilical cord or placenta; or syngeneic, when the donor is an identical twin. Objective: To characterize the diagnoses that indicate HSCT in patients treated at a reference center in the state of Rio Grande do Norte (RN), Brazil, in 2014. Methods: This descriptive study was carried out considering the total consolidated number of annual HSCT performed in a transplant service between January and December 2014. This is a temporal extract of data from the Master's Degree Dissertation entitled "Hematopoietic stem cell transplantation in a reference service in Rio Grande do Norte state: clinical and epidemiological aspects", of which research protocol was approved on July 1, 2015, according to Edict 1,132,720 and CAAE: 46202715.7.0000.5537. Results and Discussion: Based on the data analysis, it was observed that of the 60 HSCT performed during the period, Multiple Myeloma (MM) was the diagnosis that led to the highest number of HSCT (38.34%), followed by Acute Myeloid Leukemia (15%), Chronic Myeloid Leukemia (13.34%), Acute Lymphoid Leukemia (11.67%) and Non-Hodgkin's lymphoma (11.67%). Other diagnoses totaled 9.98%. Regarding gender, males predominated with 51.67% of cases and the types of HSCT more often performed were the autologous type (51.67%), followed by related allogeneic (26.66%) and unrelated allogeneic (21.67%). The most commonly used HPC for grafting were collected from peripheral blood (69.5%) followed by the cells collected from the bone marrow (30.5%). The diagnosis of MM was the most prevalent due to its significant occurrence, corresponding to 1% of all cancers, with a higher frequency in males, and because it has as the first choice of treatment the autologous HSCT from peripheral blood, which has a lower risk of contamination by cancer cells. The autologous HSCT shows better results regarding rates of remission and overall survival, when compared to allogeneic transplant. Conclusion: The observed data showed the clinical profile of patients treated with autologous and allogeneic HSCT in a reference institution in the Northeast region of Brazil. Therefore, it is important to consider further studies on the subject aiming to establish the different demographic and clinical profiles from different Brazilian regions regarding HSCT as a therapeutic option.

Keywords: Bone Marrow Transplantation; Multiple myeloma; Myeloid leukemia; Lymphoid leukemia.

P-002

Hematology - Basic Area

Therapies that favor the overall survival of patients submitted to hematopoietic stem cells transplantation

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Introduction: Although the Hematopoietic Stem Cell Transplantation (HSCT) is currently used with a high success rate, HSCT-related morbidity and mortality cases are observed in its several phases. Objective: To identify in the literature therapies that favor the overall survival of patients submitted to HSCT. Method: This is a systematic review carried out through the following electronic databases: SCOPUS, National Library of Medicine (PubMed); Web of Science; Cumulative Index to Nursing and Allied Health Literature (CINAHL); Medical Literature Analysis and Retrieval System Online (MEDLINE); and Science Direct, using descriptors indexed in the Medical Subject Headings and their respective synonymies. The inclusion criteria were: controlled and non-controlled Randomized Clinical Trials (RCTs); published in any language; carried out with patients submitted to HSCT that were tested for any therapy that resulted in improved overall survival. Results: Of the 19.543 retrieved articles, 16 were selected to be part of the final sample, two of which were indexed in the Web of Science and 14 in PubMed. Regarding the Level of Evidence (LOE), 15 of the studies had LOE equal to II, which means evidence derived from at least one controlled and well-designed RCT, with a strong degree of recommendation, and one was assessed with an LOE equal to III, that is, well-designed clinical trial without randomization, with a moderate degree of recommendation. The therapies that showed better results for overall survival were Cyclophosphamide, Doxorubicin, Vincristine and Prednisone with addition of Rituximab (R-CHVP); R-CHVP with further addition of Interferon α-2a; Melphalan at high doses, followed by autologous HSCT; lenalidomide; cytarabine; and umbilical cord blood HSCT. The treatments were adapted according to the diagnosis and clinical status of patients. Overall, survival ranged from 4% to 95% according to the established treatment. Conclusion: There was no agreement on the best therapy type to improve the overall survival of patients with indication for HSCT. It is noteworthy that the choice of treatment will depend exclusively on the clinical characteristics and the HSCT phase wherein the patient is. Therefore, it is necessary to perform further clinical trials to compare the different types of treatments, clinical benefits, costs and patient safety in relation to the cost-effectiveness of the chosen therapies in different groups of patients.

Keywords: Chemotherapy, Review, Survival, Bone Marrow Transplantation.

P-003

Hematology - Basic Area

Hematopoietic stem cell transplantations performed in Brazil between 2010 and 2015: an ecological study

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a therapy used in the treatment of hematological, oncological and immunological diseases, congenital or acquired, such as leukemia, lymphomas and severe anemia. The HSCT can be autologous when the donor is his/her own recipient; syngeneic when the donor is the recipient's identical twin; or allogeneic, when the donor has histocompatibility with the recipient, preferably a relative. Objective: To describe the main types of HSCT performed in Brazil from 2010 to 2015. Method: Ecological, descriptive, retrospective study, carried out on secondary data, for which the analysis units were 13 Brazilian states, plus the Federal District. Data were collected from the website of the Brazilian Association of Organ Transplantation (Associação Brasileira de Transplante de Órgãos - ABTO), during the month of May 2016 and the temporal frame used comprised the years from 2010 to 2015, divided into quarters. The analyzed variables were: state of the federation, allogeneic and autologous transplantation; they were treated as absolute and relative values, organized in a Microsoft Excel® 2016 MSO spreadsheet. Results: Based on the analyzed data, a total of 10,977 hematopoietic stem cell transplantations were recorded by ABTO. Of these, 4,203 were allogeneic and 6,831 were autologous, with an annual mean of 1,829 transplants. The data denoted the transplants performed in the following states: São Paulo, with a total of 5,717 performed HSCT, of which 2,364 were allogeneic and 3,353 autologous, with an annual mean of 953.83; Parana (1,020; 680 allogeneic and 340 autologous, with a mean of 170); Pernambuco (997; 376 allogeneic and 621 autologous, and a mean of 155); Rio de Janeiro (940; 266 allogeneic and 674 autologous) and a mean of 156.67; Rio Grande do Sul (550; with 229 allogeneic and 321 autologous), with a mean was 91.67; Minas Gerais (526; 130 allogeneic and 396 autologous), with a mean of 87.67; Santa Catarina (416 autologous and a mean of 69.33); Ceará (233; 16 allogeneic and 217 autologous, with a mean of 38.83); Bahia (162; 14 allogeneic and 148 autologous, with a mean of 27); Rio Grande do Norte (157, 86 allogeneic and 61 autologous, with a mean of 26.17); Federal District (149, 13 allogeneic and 136 autologous, with a mean of 25.83); Espírito Santo (88 autologous and a mean of 14.67); Goiás (85; 29 allogeneic and 56 autologous, with a mean of 14.17); and Mato Grosso (4 autologous and a mean of 0.67). Conclusion: There was a significant increase in transplantation numbers over the years in Brazil. The results of this study demonstrate that the Brazilian situation is still underreported and show the need for further works to address epidemiological data on the subject, so that society and health professionals involved in carrying out this procedure can have access to more reliable data on the national scenario.

Keywords: Bone Marrow Transplantation; Temporal Series Studies; Nursing; Brazil.

P-004

Hematology - Basic Area

Nutritional Profile of patients from a Private Hematological Center in Porto Alegre.

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Introduction: Malnutrition can be defined as the state of nutrition in which deficiency, excess or imbalance of energy, protein and other nutrients cause adverse effects to the body, with clinical and functional consequences. Hematological patients require an individualized and periodic nutritional therapy to prevent or minimize nutritional deficiencies resulting from chemotherapy and/or radiation therapy. Objective: To analyze the nutritional assessment of patients admitted to a private hematological center in the southern region of the country. Method: This was a retrospective cross-sectional study that analyzed data from medical records of patients evaluated by the hospital nutritional team. Data collection took place between August 2015 and January 2016. The sample consisted only of patients with a hematological diagnosis and excluded pregnant women and individuals younger than 18 years. Results: The study comprised 39 patients, of which 43.5% (n = 17) were females and 56,5% (n=22) males. The mean age was 55 years, ranging from 21 to 89 years. It was observed that 48.7% of them were older than 60 years. The mean BMI was 24.2 kg/m², ranging from 17.96 to 37.03. The nutritional assessment disclosed that 02 patients had severe malnutrition (5%), 24 (61.5%) had some risk of malnutrition/moderate malnutrition and 13 (33.5%) were well-nourished, according to the results of the overall subjective nutritional assessment. Of the 39 assessed patients, 59% were re-evaluated (global n = 23) and 91% (n = 21) maintained their nutritional status, 4.5% (n = 01) improved their nutritional status and 4.5% (n = 01) worsened their nutritional status. Discussion: Despite the observed high prevalence of patients with moderate malnutrition or at risk of malnutrition, nutritional diagnosis was made through the overall subjective assessment, which, despite being a validated method for nutritional assessment, does not use anthropometric data. When the body mass index results were assessed, they showed normal weight and their range did not show malnutrition. The interpretation of the B diagnosis is related to the risk of malnutrition and to the fact that some degree of malnutrition is already established. The re-evaluations were carried out every 07 days, and the found results reflect an adequate nutritional support, as more than 90% of the patients maintained their nutritional status. Conclusions: The maintenance of a good nutritional status is especially important during the entire process of the BMT, with the adequate nutrient supply being a frequent object of studies and apparently crucial for a successful procedure. There is a relevant percentage of patients at nutritional risk in the Hematology Unit; even though patients were more likely to lose weight, more than 90% maintained their nutritional status in relation to the initial nutritional assessment.

Keywords: Nutritional Assessment, Hematology, Nutritional Aspects, BMT.

P-005

Hematology - Basic Area

Febrile neutropenia: clinical management in the bone marrow transplant unit, Fortaleza-Ceará

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INTRODUCTION: Fever in neutropenic patients is considered a medical emergency and the administration of broad-spectrum antibiotics drastically reduces mortality. Severe neutropenia is characterized as if it is lower than 500/mm³, requiring intensive care. Empirical antimicrobial therapy should be compulsorily started after collection of samples to allow identification of the causative agent. Until the mid-80s, bacterial infections were caused predominantly by Gram-negative agents. Since then, Gram-positive bacteria have become responsible for most infections in neutropenic individuals. There are three important reasons for the changes in this pattern: the use of a more aggressive antineoplastic agent associated with severe oral mucositis and, consequently, infection with Gram-positive bacteria of the oral flora; 2) the use of intravenous catheters, resulting in infections by Staphylococcus; and antibacterial prophylaxis with fluoroquinolones (e.g., levofloxacin), resulting in an increase in the esophagus and stomach colonization by Streptococcus oral flora (SERGIO, 2006). OBJECTIVES: To describe the clinical management of febrile neutropenia in a hospital unit specialized in bone marrow transplantation of a university hospital in Fortaleza. MATERIALS AND METHODS: This is a cross-sectional descriptive study, considering that it evaluates the care protocol used in the institution that standardizes conducts and highlights relevant aspects of the topic, aiming to prioritize the quality of care and reduce the damage to critically-ill neutropenic patients. RESULTS: In our care protocol, fever in neutropenic patients is defined as isolated axillary temperature (single measure) of 37.8 degrees, after ruling out environmental causes. The protocol consists in the monitoring of vital signs, as well as the evaluation of associated symptoms and likely infection sites (lung, skin, oral mucosa, etc.). Importantly, patients with non-controlled neoplastic disease, poor performance status (PS) and older age should be considered at high risk in the febrile neutropenia protocol. DISCUSSION: A previous study (Rolston, 2004) confirms the findings of the present study stating that, during the period of neutropenia after chemotherapy, fever may be the only indication of infection, since the signs and symptoms of inflammation are attenuated by the use of corticosteroids or other immunosuppressive agents that block the inflammatory response, thus requiring close monitoring. CONCLUSION: It is understood that the subject is important, as it encourages questions about the clinical management of critically-ill patients, generally triggered by febrile neutropenia. Moreover, the homogeneity and training of the care team contribute to reducing mortality and require a critical view of the adverse conditions and reduced response time.

Keywords: chemotherapy-induced febrile neutropenia. Hematology. Bone marrow transplantation.

P-006

Hematology - Basic Area

Care of children with sickle-cell anemia according to Kolcaba's Theory: an integrative review

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INTRODUCTION: Sickle-cell anemia is a chronic disease that brings much suffering and frequent pain episodes, causing clinical situations of discomfort and malaise for the affected children. This fact requires that nurses have knowledge and seek to provide comfort measures aiming to promote better quality of life for their patients. OBJECTIVES: To describe a therapeutic plan for a child diagnosed with sickle-cell anemia, based on Katharine Kolcaba's comfort theory. MATERIALS AND METHODS: This is a descriptive and integrative review on the clinical care provided by nurses to children with sickle-cell anemia, with a qualitative approach. The study was carried out through the Virtual Health Library (VHL) between March and April 2016, using the following descriptors: nursing care, sickle-cell anemia and child. The search generated 272 references. Articles written in Portuguese and English that addressed, as their main issue, sickle-cell anemia, child health and nursing care were included in the research. Repeated articles, articles not available in full-text and the ones that did not fit the purpose of this study were excluded. A total of 15 articles were obtained. For data analysis, we crossed the NANDA Nursing Process, Katharine Kolcaba's Comfort Theory and care of hospitalized children, described in the identified studies. RESULTS: It was observed that the main symptoms were pain crises, and that complications such as infection, heart disease, kidney disease, growth and development delay, acute chest syndrome, stroke, avascular necrosis of the femoral head and/or humerus and cholelithiasis were frequently seen. NANDA (2015) describes some nursing diagnoses found in children with sickle-cell anemia, including anxiety related to the unknown hospital environment, uncertainty regarding the results and the diagnostic procedures and transfusions; activity intolerance related to weakness; pain related to hypoxia due to the agglutination of sickle cells within the blood vessels; Risk of infection related to immunosuppression, with decreased or absent splenic function. The assessed articles showed that the main goals to be achieved were pain relief, reducing the incidence of crises, increasing the self-esteem and reducing complications. Pain severity and location should be assessed. The swollen joint should be supported until the swelling subsides. Applying moist heat on the site or warm baths help to reduce pain. DISCUSSION AND CONCLUSION: Through the systematization of nursing care based on the Comfort Theory, it was possible to disclose the child's actual needs, which allows us to intervene directly in the care planning. The Nursing Process implementation based on Kolcaba's Theory provides comfort and improves hospitalized children's quality of life.

Keywords: nursing, comfort, diagnosis.

P-007

Hematology - Basic Area

Prevalence of bloodstream infections and characterization of microorganisms isolated from onco-hematological patients with febrile neutropenia in a public hospital in Fortaleza, Ceará, Brazil.

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Bloodstream infections (BSI) represent one of the major complications of onco-hematological patients (OHP). Fever frequently occurs during chemotherapy treatment that induces neutropenia. This study aimed to assess the prevalence of BSI and their etiology, as well as describe the sensitivity profile to antimicrobials of microorganisms isolated from OHP admitted to a reference public hospital in Fortaleza, Brazil. All results of blood cultures requested for hematological patients with febrile neutropenia (FN) from January to December 2015 were retrospectively analyzed. According to the hematology service protocol of this hospital, we considered as neutropenic patients those with a neutrophil count lower than 500/mm^3 and fever, axillary temperature ≥ 38°C or ≥ 37.8°C, sustained for more than one hour. A new FN episode was considered if the fever restarted after a 72-hour afebrile period. The blood culture flasks were incubated in the BacT/ALERT® 3D (BioMérieux, France) automated system. Biochemical and antimicrobial susceptibility tests were performed using the VITEK®2 Compact (BioMérieux, France) equipment. During the study period, 170 episodes of FN in 85 OHP were recorded, totaling 240 requested blood cultures. Of these, 14.17% (34/240) were positive, representing 27 new episodes of FN. The analysis of the isolated microorganisms revealed that the vast majority of infections (28/34; 82.35%) was caused by Gram-negative bacilli (GNB). *Klebsiella pneumoniae* was the most common GNB (14/28; 50,00%), followed by *Escherichia coli* (11/28; 39.29%), *Pseudomonas aeruginosa*, *Proteus mirabilis* and *Stenotrophomonas maltophilia* (1/28, 3.57% each). Two patients had simultaneous infection by two GNB. Gram-positive cocci (GPC) accounted for 17.65% of cases (6/34), with coagulase-negative staphylococci involved in 100% of these cases, suggesting the possibility of potential contaminants. No patient had blood culture showing BSI of fungal origin. The sensitivity of the GNB to different tested antimicrobials was assessed by excluding the *S. maltophilia* strain, which was sensitive to sulfamethoxazole/trimethoprim. Considering the remaining 27 GNB isolates, the highest percentages of sensitivity were observed among the classes of aminoglycosides and polymyxins (26/27, 96.30% each), carbapenems (mean of 19.5/27; 72.22%) and tigecycline (19/27; 70.37%). Seven isolates (25.93%), being one *E. coli* and six *K. pneumoniae*, showed resistance to the three carbapenems tested. Ampicillin (23/27, 85.19%), ciprofloxacin and ampicillin/sulbactam (19/27, 70.37% each) were the antimicrobials with the highest percentage of resistance. Among the GPC, all obtained isolates were sensitive to linezolid, tigecycline and the glycopeptides vancomycin and teicoplanin. The highest resistance rates were observed with erythromycin (5/6; 83.33%), penicillin, quinolones and sulfamethoxazole/trimethoprim.

Keywords: Bloodstream infection; onco-hematological patients; febrile neutropenia; gran-negative bacilli; antimicrobial susceptibility

P-008

Hematology - Basic Area

Characterization of the population submitted to hematopoietic stem cell transplantation performed during a one-year period at a university hospital in southern Brazil

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The hematopoietic stem cell transplantation (HSCT) is a therapeutic procedure that aims to consolidate a favorable response to the chemotherapy treatment or as rescue therapy for recurred or refractory disease. The aim of this work was to describe the HSCT performed during the year 2015 in the Protective Environment (PE) unit of a university hospital in Porto Alegre-RS. This was a retrospective cross-sectional study that analyzed data from all HSCT performed in the PE unit of the institution throughout the year 2015. The data were obtained from the electronic records (Project No. 150011 submitted to the institutional Research Ethics Committee). During the analyzed period 80 transplantations were performed, of which 40 (50%) were autologous, 23 (28.75%), related allogeneic and 17 (21.75%) were unrelated allogeneic. Multiple myeloma was the most prevalent diagnosis in autologous transplantation, present in 22 patients (55%), followed by 6 (15%) non-Hodgkin's lymphomas, 5 (12.5%) patients with myelodysplastic syndrome and the 7 patients (17.5%) with lower prevalence diagnoses. In related allogeneic transplantation, the most prevalent diagnosis was Hodgkin's lymphoma, with 8 (34.78%) cases, followed by acute lymphocytic leukemia, with 5 (21.73%) cases, 4 (17.39%) patients with aplasia and the other 6 (26.08%) with lower prevalence diagnoses. Regarding the unrelated allogeneic transplantation, 11 (64.7%) patients were diagnosed with acute myelogenous leukemia and 6 (35.29%) with acute lymphoblastic leukemia. The median age of the population was 39.5 years (1-66). It was also observed a higher prevalence of the male gender, with 44 (55%) patients, as well as 73 (91.25%) patients who self-reported as white, 4 (5%) as black and 3 (3.75 %) as mixed-race. Regarding the place of origin, 20 (25%) patients were from Porto Alegre-RS, 18 (22.5%), from the metropolitan region, 38 (47.5%), from the countryside of the state of RS, and 4 (5%) from other Brazilian states. Regarding the outcome, the number of deaths among patients submitted to HSCT was 19, with 4 (21.05%) occurring after autologous transplantation, 7 (36.84%) after related allogeneic transplantation and 8 (42.20 %) after unrelated allogeneic transplantation. The present study showed a higher prevalence of males among patients submitted to HSCT, in agreement with the estimates of the National Cancer Institute (INCA), which reported a higher prevalence of hematological cancers in men. According to data from the Brazilian Transplantation Registry (RBT) of 2015, the State of Rio Grande do Sul performed 81 HSCT, which leads us to believe that there is underreporting of data by transplantation centers. This record also shows that the majority of HSCT procedures performed in the country are the autologous type. Therefore, although the findings suggest a similarity to the Brazilian population, it is necessary to carry out further studies and assess the reporting by the transplantation centers.

Keywords: hematological diseases, hematology, transplantation, hematopoietic stem cell transplantation

P-009

Hematology/pediatric transplantation

Evaluation of the manual process of DMSO removal in cryopreserved hematopoietic progenitor cells of pediatric patients in Hospital de Clinicas of Porto Alegre

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Introduction: The maintenance of cryopreserved cell viability depends on its resistance to damage caused by dehydration and by mechanical damage due to the formation of ice crystals inside the cells. One way to prevent this damage is by using cryoprotectants during the freezing process, with dimethyl sulfoxide (DMSO) being the most often used intracellular cryoprotectant in the cryopreservation of hematopoietic progenitor cells (HPC). The use of DMSO is often associated with toxic effects to the patient, such as nausea, vomiting, chills and an unpleasant sensation in the oropharynx. Dyspnea, cardiac dysfunction, anaphylaxis and acute renal failure are rarer effects. It is recommended that the dose of DMSO/kg of patient should not exceed 1g/kg/day. As the toxic effects of DMSO are more common in pediatric patients and the dose of DMSO/kg is associated with the toxicity degree, its removal is indicated for these patients. Objective: To evaluate the DMSO removal process in cryopreserved HPC of pediatric patients from April/2011 to May/2016. Material and Methods: Thirty-nine HPC of pediatric patients were cryopreserved using DMSO, hydroxyethyl starch (HES) and human albumin at final concentrations of 5%, 6% and 3% respectively. After defrosting the HPC at 37 ° C, the manual process of DMSO removal was performed, consisting in adding a wash solution at the proportion of 1: 1 at final concentrations of 2.25% of HES and 2.5% of human albumin, centrifuging at 400g for 20 minutes and removing the supernatant. Cell counts were performed in a hematologic counter. The analyzed parameters were: patients' age and weight, duration of DMSO removal procedure, volume and total nucleated cells (TNC) pre- (pre) and post-removal (post) of DMSO, cell recovery and dose of DMSO/kg. The Shapiro-Wilk's and the Spearman's correlation tests were used. Data are presented as median and interquartile range. Results: Age (years) and weight (kg) of patients were 4 (2-8) and 16.5 (13-24), respectively. Regarding HPC, the results were: time of processing (hours), 1:30 (1:15-2:01); volume pre (mL) 219.5 (161-407); volume post-removal (mL) 81.4 (61.2 to 143.7); TNC pre (x108) 400.0 (236.3 to 663.0); TNC post-removal (x108) 359.4 (201.8 to 548.5); cell recovery (%) 88 (80-94); dose of DMSO (g DMSO/kg patient) 0.82 (0.67 to 0.92). No correlation was found between the analyzed parameters. Discussion: The dose of pre-removal DMSO/Kg was high, although lower than the recommended maximum of 1g/kg/day, with the removal being indicated for pediatric patients. The obtained results demonstrate that manual removal of DMSO was efficient in relation to the TNC recovery and adequate regarding the time of processing. Conclusion: Manual removal of DMSO is a feasible procedure in laboratory practice and is recommended for pediatric patients due to the reduction of adverse effects during the infusion of cryopreserved HPC.

Keywords: cryopreservation, DMSO, pediatric transplantation

P-010

Hematology/pediatric transplantation

Analysis of the first five years of hematopoietic stem cell transplantation (HSCT) in a reference pediatric hospital in southern Brazil.

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Introduction: In Brazil 78 hospitals offer autologous hematopoietic stem cell transplantation (HSCT), with 27 units being accredited for allogeneic HSCT, whereas for this modality, there were only 4 available services in 2003. Despite this increase, there is still a lack of beds, and few units are specialized in the treatment of high-risk pediatric patients. In 2011 a bone marrow transplantation service was implemented in one of the largest, exclusively pediatric hospitals in southern Brazil. Initially, autologous transplants were performed and, after 2013, when a specialized multidisciplinary team was hired, they also started performing related allogeneic transplantations. The unit, which initially had 3 beds, will be have 10 beds available after completion of the expansion project later this year. Objective: To describe the epidemiology profile and evolution of children and adolescents submitted to HSCT in a Pediatric Transplantation Service. Results: From August 2011 to May 2016, 71 transplants were performed in 68 patients, with 64 (91% of transplants) being carried out after 2013. The median age was 9 years (3 months to 16 years); 63% were males. Approximately half of the patients (pts) were from the state of Paraná. In total, there were 23 children with bone marrow failure (7 case of Fanconi anemia), 9 primary immunodeficiencies (6 SCID), 2 adrenoleukodystrophy cases, 34 malignancies (among these, 13 cases of acute lymphoid leukemia, 2 acute myeloid leukemia, 5 Hodgkin's lymphoma, 1 Burkitt's lymphoma, 4 neuroblastomas and 1 multiple myeloma). Fifteen autologous and 56 allogeneic HSCT (6 haploidentical) were performed, with three children undergoing more than one transplantation. In the allogeneic transplantations the cell source used was peripheral blood in 3 patients, umbilical cord for 1 and bone marrow for the others. Thirty-nine allogeneic transplantations were performed with myeloablative conditioning, with 15 being performed with total body radiation therapy. Sixty-one of 68 pts are alive between 6 months and 5 years of follow-up, with an overall survival of 89% at 2 years. Patients with non-malignant diseases had a survival rate of 97%, whereas patients with malignancies had an 82% survival rate. The most common complications were graft-versus-host disease (GVHD) (acute: 5 pts grade I to II and 2 pts grade III to IV, chronic: 1 severe) and recurrence (N = 9). Seven patients died between 1 to 6 months after transplantation with a median of 4 months. The causes of death were disease progression (N = 5), rejection (N = 1) and veno-occlusive disease (N = 1). Conclusion: Implemented in 2011, the transplantation service had a significant increase in its activities after 2013, when a multidisciplinary team specialized in pediatric hematopoietic stem cell transplantations was hired, demonstrating the importance of having qualified professionals working with this high-risk population.

Keywords: transplantation, bone marrow, childhood cancer, stem cells, multidisciplinary team

P-011

Hemotherapy

Transfusion needs of patients submitted to autologous hematopoietic stem cell transplantation

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Introduction: Transfusion of blood products is an essential therapy in hematopoietic stem cell transplantation (HSCT), as the main adverse effect of myeloablative conditioning regimen is hematological toxicity, leading to severe anemia and thrombocytopenia. The aim of this study was to carry out a survey of the transfusion profile of patients submitted to HSCT in a university hospital in Fortaleza, Ceará. Methodology: A retrospective review was performed on data from the Bone Marrow Transplantation service from September 2008 to May 2016. The transfusion history was researched in the Hemoce (Blood Center) based on reports generated by the computerized blood bank system. Transfusions performed from day -5 to +30 were analyzed separately, according to the blood product. Results: A total of 221 autologous transplantations were performed in the described period and 184 patients were evaluated for transfusion need. Regarding the patients' gender, 112 were men, with a mean age of all patients of 46 years. The main diagnoses were Multiple Myeloma (106), Hodgkin's Lymphoma (42) and Non-Hodgkin's lymphoma (29). The other diagnoses were amyloidosis, germ cell tumor and POEMS syndrome. The time of neutrophil engraftment was evaluated in 112 patients, with a mean of 10 days and a mean hospital length of stay of 22 days. A total of 45 patients (24.4%) received transfusion of packed red blood cells (pRBC) during the study period, with a median of 1 pRBC per transfused patient (1-6 units). The most often transfused blood component, as expected, was the platelet concentrate, transfused in 100% of patients, with a median of 3 units per patient (pool of buffy-coat or apheresis, 1 to 18 units). The use of fresh frozen plasma (FFP) appears less frequently, only five patients received seven FFP units and two patients received cryo. Conclusions: Transfusion of blood products in the autologous transplantation is a critical adjuvant therapy, especially platelet transfusion. Transfusion of red blood cells, according to the survey, can be prevented in most patients undergoing autologous HSCT, with the use of a restrictive transfusion protocol, since only a quarter of the patients were transfused, with many receiving only one pRBC unit.

Keywords: Transfusion, Autologous transplantation, restrictive protocol

P-012

Hemotherapy

Immuno-hematological follow-up of patients submitted to bone marrow transplantation in the State of Ceará

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Introduction: Transfusion of blood products is an essential therapy for the support of hematological patients before and after hematopoietic stem cell transplantation (HSCT). However, exposure to foreign erythrocyte antigens can lead to the development of alloantibodies and, occasionally, stimulate an autoimmune response, an expected phenomenon in several onco-hematological diseases. Objective: To assess the immuno-hematological profile of patients undergoing HSCT in Ceará. Material and Methods: This is a documentary and retrospective study. Data were collected from the Blood Bank System Software (Sistema de Banco de Sangue - SBS) and from the manual records of the Blood Center immuno-hematology laboratory. All HSCT performed from September 2008 to March 2016 were included in the study, which contained the results of ABO/RhD, direct antiglobulin test (DAT) and/or irregular antibody screening (IAS). Results: A total of 240 transplantations were assessed, of which 23 were allogeneic. Of the autologous HSCT, the main diagnoses were multiple myeloma (122, 56.2%), followed by Hodgkin's lymphoma (52, 24%) and non-Hodgkin's lymphoma (36, 16.6%). Of the allogeneic HSCT, the main diagnoses were acute leukemia (11, 47.8%), Myelodysplastic Syndromes (MDS, 5, 21.7%) and aplastic anemia (AA, 4, 17.4%). The mean age in the autologous transplantation was 45 years and in the allogeneic, the median age was 47 years. A total of 149 patients (62%) were males. Regarding the patients' ABO type, 103 were O+, 9 O-, 60 A+, 4 A-, 17 B+, 1 B-, 4 AB+ and 1 AB-. DAT records of 23 patients were found, with only two positive cases, in two patients at the post-allogeneic HSCT period, one with AML and other with AA. All patients were screened for IAS, with a positive result in 3.35% (8 patients), with clinically significant antibodies found in only three patients (1.25%), all before 2013. Among the alloantibodies, anti-E, -c, -Jka, -S and -Dia were detected. Discussion: the ABO frequency of the patients is consistent with donors' data from the State of Ceará. Regarding the DAT, the low frequency found is probably related to the fact that it is not a routine examination, being used only before extended phenotyping, when the examination is not recorded in the system, and to evaluate pre- and post-HSCT hemolysis. The Ceará Blood Center regularly performs the erythrocyte phenotyping of onco-hematological patients without recent transfusion and of all patients undergoing HSCT, justifying the small alloimmunization rate found in the study. Additionally, the low occurrence of red blood cell transfusion in autologous HSCT seems to contribute to the low occurrence of this complication. Conclusion: The use of a policy that takes into account the Rh and Kell phenotyping of hematological patients is essential to prevent erythrocyte alloimmunization in this highly transfused population, which allows performing the HSCT without major complications.

Keywords: Hematopoietic stem cell transplantation, Direct antiglobulin test, irregular antibody screening, ABO typing and erythrocyte phenotyping

P-013

Hemotherapy

Blood donation and bone marrow registry: donor profile analysis during a blood drive

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INTRODUCTION: Brazil needs 5,500 units of blood on a daily basis, but only 1.7% of the population donates blood, whereas the WHO recommendation is 3 to 5%. The strategies used to attract blood and bone marrow donors originate from drives at the national level or through the organization of health services and care practices to the population. OBJECTIVE: To describe the profile of blood donors and registered individuals in the bone marrow registry during a blood drive carried out by medical students. MATERIALS AND METHODS: Medical students from the Academic League of Hematology and Hemotherapy of a private university carried out a drive to attract blood donors and carry out a bone marrow registry, in partnership with the Blood Bank. This is a descriptive and qualitative study, using as tool a questionnaire developed by students of the academic league, applied during an interview with volunteers through an individual approach. The study was carried out from May 18 to June 3, 2016 and the study population comprised volunteers for blood donation and registration at the time of action. A total of 158 candidates were enrolled, resulting in 102 blood donations, 39 unfit candidates, 17 dropouts and 201 bone marrow registries. After the collection, data were tabulated and analyzed. RESULTS: 86 individuals were interviewed, 23 men and 63 women, with a prevalence of young individuals aged 16 to 24 years. Of the total that answered the questionnaire, 56 reported previous blood donations, of 27 had done it only once and only 17 declared doing it often. Among the donors, 38 reported they had made their first donation between 16 and 24 years old, and most of them reported donating sporadically. The prevalence of voluntary donation, 46 donors, was higher than the directed donation, 16 donors. Of the respondents, 58 intended to donate in the future. Among the 86 interviewees, 66 were registered in the bone marrow bank, but only one had previously donated. Also in this group, only 39 reported knowing about the bone marrow transplantation procedure, and 43 reported being afraid of this procedure. It was also found that 57 individuals knew someone who needed that type of transplant. DISCUSSION: The questionnaires disclosed that there are a lot of young individuals that had already donated at least once, with most of them being voluntary donors, raising the question of why these individuals do not do more often. Although there are many entries in the bone marrow bank, most people declared they did not know how the procedure is performed and they are afraid to do it, showing a low level of knowledge about the bone marrow transplantation. CONCLUSION: The study showed that the donors' profile was predominantly female gender, of young age, with irregular blood donations and low level of knowledge about the bone marrow transplantation procedures, requiring further educational interventions to increase the frequency of donation.

Keywords: Donation, Blood Drive, Bone Marrow

P-014

Hemotherapy

Patient safety in transfusion therapy: strategies for safe administration of blood and blood products

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Introduction: Transfusion therapy is a complex process that depends on several professionals to safely perform it, and it depends not only on their own knowledge and skills, but also on the entire team and system efficiency. The Collegiate Board Resolution (RDC) 153 of the National Health Surveillance Agency (Anvisa) of 06/14/04, which regulates hemotherapy activities in Brazil, establishes rules and procedures that should be known and followed by professionals working with transfusions. Objective: To verify in the literature the scientific production on transfusion therapy and discuss strategies for safe administration of blood and blood products. Materials and Methods: This is a systematic review of the literature, through a survey of academic literature on the subject, in addition to search for articles in the databases that integrate the VHL (Virtual Health Library), emphasizing the scientific works published in the last ten years. Results: Studies show that transfusion of blood and blood products is an essential support for many treatments and can save lives. It is a valuable therapeutic resource, but the high cost and the risk of adverse events, such as errors, transfusion reactions and infection transmission, require that its use should be cautiously performed and reduced to a minimum, adopting strategies such as: preventing conditions that may result in the need for transfusion, adequate diagnosis and treatment, good surgical and anesthetic techniques and the use of alternative treatments to blood transfusion. Discussion: The World Health Organization (WHO) recommends the rational use of the procedure, based on clinical and/or laboratory assessment, because there are immediate or late risks, even when high quality standards are followed at all stages of the transfusion process. Wherever possible, only the blood product that will meet the specific need of the patient should be transfused, as it is a safer procedure and prevents the waste of products not needed by the patient. Blood transfusion is characterized as a complex process with many interconnected and repetitive stages, with the participation of different professionals and services. Conclusion: The nursing staff should perceive their own importance and autonomy in transfusion therapy, as the implementation and monitoring of the entire process fall under their responsibility, as they not only carry out the transfusion, but should also know its indications, check the important data to prevent errors, inform the patients on transfusion procedures, detect, report and act on the occurrence of reactions, recording the entire process. The performance of these professionals can significantly minimize the risks for the patient receiving transfusion and prevent damage, if the process management occurs safely and with the necessary effectiveness.

Keywords: Safety in transfusion therapy, blood, blood components.

P-015

Infections

Complication after Autologous Hematopoietic Cell Transplantation: infection by Varicella Zoster Virus

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Introduction: The immunosuppression secondary to the autologous hematopoietic stem cell transplantation (autologous HSCT) increases the risk of infection by Herpes Varicella zoster (HVZ), which may occur in approximately 20 to 30% of patients during the first year after autologous HSCT. Different prevention protocols are proposed, varying the dose and time of administration of acyclovir, which is generally initiated on the first day of conditioning and maintained for 30 to 100 days. Objective: This study aims to assess the incidence of HVZ infection in patients undergoing autologous HSCT and early cessation of acyclovir prophylaxis. Materials and Methods: A retrospective analysis of 230 medical records of patients undergoing autologous HSCT between the years 2004 and 2014 was carried out. Prophylaxis for HVZ, with intravenous acyclovir at a mean dose of 500 mg/day, was performed from the first day of chemotherapy and discontinued at the grafting (neutrophils > 500 cells/mm^3). The main clinical characteristics and the risk of infection by HVZ were associated using the statistical software SPSS, using Chi-square and Student's *t* tests. Results: In the assessed population, the mean age was 48.73 years. Most patients were males (58.7%) and the most common diagnosis was multiple myeloma (52.2%). The mean length of hospital stay was 20.78 days. Fourteen (6.1%) patients had HVZ infection, with a mean time of onset of six months after autologous HSCT. Patients with multiple myeloma (64.3%) were the most affected. When the patients' age was associated with HVZ infection, the mean age was 57.14 years for those who developed HVZ *versus* 48.12 for those who did not develop it (p = 0.002). There were no significant differences for other variables. Discussion/Conclusion: Studies suggest that the use of 400 mg/day of acyclovir until the end of the immunosuppressive therapy might not suppress the reactivation of the HVZ virus. The use of anti-viral prophylaxis for a shorter period of time allows a reduction in costs, toxicity and the risk of drug resistance. In this study, the frequency of infection by HVZ (6.1%) indicates that the discontinuation of acyclovir in neutrophil engraftment can be considered in patients undergoing autologous HSCT, reserving the extended prophylaxis for high-risk groups, such as elderly patients and patients with multiple myeloma.

Keywords: Prevention and control, Autologous Transplantation, Herpes Zoster, Immunosuppression

P-016

Infections

Sepsis associated with central venous catheter in patients submitted to hematopoietic stem cell transplantation

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Introduction: Infection is a major complication in hematopoietic stem cell transplantation (HSCT), and is associated with high rates of morbidity and mortality. Although essential for patients submitted to HSCT, the central venous catheter (CVC) is associated with increased risk for infections in this population. Objectives: To determine the incidence and risk factors for sepsis associated with CVC (CRBSI, catheter-related bloodstream infection) in HSCT. Methods: This was a prospective cohort study that included patients submitted to HSCT from 01/01/2013 to 12/31/2015 in a university hospital. The population was defined by the type of HSCT: allogeneic (aloHSCT) and autologous (autoHSCT). We defined "long-term indwelling catheters" (LTIC) as the semi-implanted CVCs and "temporary CVC" the double-lumen CVCs (DLC). We monitored the occurrence of CRBSI during 28 days of HSCT. Analyzed variables were age; gender; site of catheter insertion (internal jugular vein [JV] or subclavian); neutropenia prior to the implantation of CVC and duration of neutropenia (DN). The univariate and multivariate analysis of the CRBSI used, respectively, the X^2 test or Fisher's exact test and the logistic regression model. Gray's test was used to calculate the cumulative incidence of CRBSI (CRBSI-CI). Results: The study comprised 84 HSCT, 51 (61%) aloHSCT (related = 43 [83%]) and 33 (39%), autoHSCT. All aloHSCT received LTIC, while autoHSCT used DLC in 32/33 (97%) cases. The mean age was 43 years, being older in autoHSCT (50 vs. 39, p = 0.002). the JV site predominated in aloHSCT (41/51 cases), with a mean duration of CVC of 25 days (SD = 13 days) and 44 (86%) patients showing DN >7 days, with 14/51 (27%) patients being already neutropenic at the CVC insertion. The JV was used in 28/33 (84%) patients in autoHSCT, with a mean duration of CVC use of 17 days (SD = 6 days) and 10 (30%) patients showed DN >7 days. The overall CRBSI-CI was 50%, being higher in aloHSCT (51% vs. 46%, p 0.89). The incidence density (ID) for LTIC and DLC were, respectively, 16 per 1,000 CVC-day and 18 per 1,000 CVC-day. None of the variables was associated with CRBSI. The main microorganisms in the CRBSI cases were coagulase-negative *Staphylococcus* (13 cultures) and *E. coli* (7 cultures). In the LTIC cases, there was a predominance of Gram-negative bacteria (GNB), while in the DLC cases Gram-positive bacteria predominated. The in-hospital mortality within 28 days of HSCT was 23%, being higher in patients with CRBSI (OR 2.2; p =0.18). Discussion/conclusion: The ID of CRBSI observed in this study was >90th percentile of the CDC publication. No variable was associated with the occurrence of this infection. There was a predominance of GNB in LTIC cultures, which is in agreement with the study by Brown et al. (2011), although with different microorganisms, with *E. coli* (21%) in our study and *Stenotrophomonas maltophilia* (25%) in their study. Although not statistically significant, the occurrence of CRBSI contributed to the high early mortality observed in our study. Further studies with larger samples are necessary to better define the risk factors associated with it.

Keywords: healthcare-associated infection, Central venous catheter, Sepsis, Hematopoietic stem cell transplantation

P-017

Infections

Study of the dynamics of cytomegalovirus (CMV) reactivation in patients submitted to Allogeneic Bone Marrow Transplantation

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Introduction: The allogeneic bone marrow transplantation (allo-BMT) is a curative treatment for acute leukemia. The immunosuppression of the procedure leads to several complications and, among them, to CMV infection. CMV reactivation is a common event and may be associated with severe clinical pictures and death. Methods with high diagnostic sensitivity (such as the use of quantitative PCR test) have been proposed for pre-clinical screening, but to date there is no standardization and validation of cutoff points for this population. Objectives: To describe the frequency of CMV infection reactivation, the dynamics of viral load (VL) quantification and the time until the episode is resolved in a population of patients submitted to allogeneic BMT. Methods: Cohort of patients submitted to allogeneic BMT (AloBMT) in a single institution between 2013 and January 2016. CMV screening is carried out by quantitative PCR (CMVPCR) using a commercial platform (System Taqmanartus CMV Qia-gen). The VL in plasma was used, with the unit copies/mL. The variables analyzed were: age, gender, disease that required the BMT, type of stem cell source, donor and recipient serology for CMV, report of reactivation, time for reactivation in relation to the BMT, initial viral load (VL), maximum VL, time until negative result, antiviral therapy used and outcome (hospital stay for treatment and death). The used statistical analysis were: chi-square test, Mann Whitney test, and overall survival analysis through Kaplan-Meir, considering statistical significance of $p <= 0.05$. Results: 47 patients were followed. Of these, in 2 there was no collection of CMVPCR (1 patient died early, and one patient was only screened for PP55 antigenemia). The remaining 45 subjects had sequential PCR (as a single technique in 33, and associated with antigenemia in 12). Most of them were submitted to BMT due to acute leukemia (n = 33; 73%) and were males (n = 31; 67%). The median follow-up was 240 days (8 months). The median of the collection day of the first CMVPCR was D+16 (ranging from D-13 - +164). In 21 patients (47%) there was at least one positive test. Reactivation occurred on D+45 (ranging from D+8 - +398). The initial and maximum median VL at the first episode were 480 copies/mL (112-116540) and 5820 (239-959643), respectively. The VL peak occurred at a median of 7 days (0-26) after the initial VL. The median time to a negative test was 27 days (13-70). In 2 patients there was a report of more than one reactivation episode. The outcome analysis is ongoing. Conclusion: Reactivation of CMV infection is frequent and occurred in most patients before D+50. There is great variation between the initial and the peak viral load, as well as the time until a negative result was obtained. The standardization of cutoffs for therapy indication is required.

Keywords: cytomegalovirus, reactivation, diagnosis, screening, allogeneic transplantation

P-018

Infections

Bone marrow transplantation in pediatrics and profile of Healthcare-associated Infections

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INTRODUCTION: Patients with onco-hematological diseases are more vulnerable to the development of healthcare-associated infections (HAIs) and when these patients undergo bone marrow transplantation (BMT) this risk tends to significantly increase due to the severe bone marrow suppression, use of long-term indwelling catheters and invasive devices. OBJECTIVE: The aim of this study was to evaluate the epidemiological profile of HAIs in post-BMT patients in a pediatric quaternary care hospital. METHODS: A retrospective study using data from the Epidemiology and Hospital Infection Control Service (SECIH). All hospitalized patients submitted to BMT since the implementation of BMT service, from April 2011 to December 2015, diagnosed with HAIs were included. RESULTS: In this historical four-year series, 62 transplantations were performed, 63% of males and 37% females. Of these 62 transplanted patients, 30 patients (42%) had at least one episode of HAI, totaling 39 cases, and the mean time after the BMT was performed, when patients were diagnosed with HAI, was 11 days. The most prevalent topographies were: 28% (11) clinical primary bloodstream infection (BSI); 21% (8) BSI confirmed by laboratory tests; 15% (6) catheter-related bloodstream infection (CRBSI); 13% (5) Pneumonia; 23% (9) other topographies (mouth, gastrointestinal tract, flu syndrome, urinary tract infection). Of the 8 episodes of BSI confirmed by laboratory tests, the following etiological agents were identified: 25% (2) *Staphylococcus epidermidis*; 25% (02) *Staphylococcus sp*; 13% (1) *Serratia marcescens*; 13% (1) *Candida albicans*; 13% (1) Candida parapsilosis; and 13% (1) *Candida kefyr*. Negative Culture, 49% (19). CONCLUSION: During these four years, we observed that the main topography was the BSI, consistent with the literature. Regarding the etiology, there are still difficulties in isolating the agents, due to the prophylactic antimicrobial regimens routinely used in clinical protocols, resulting in a significant number of negative blood cultures. More studies are needed to increase the understanding of the epidemiology in this group of patients and search for the better preventive measures.

Keywords: BSI, HAIs, BMT, topographies, infection

P-019

Infections

Analysis of surveillance cultures in pediatric patients pre-Hematopoietic Stem Cell Transplantation

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Introduction: Hematopoietic stem cell transplantation (HSCT) is a complex treatment modality and the immunosuppression associated with this therapy predisposes patients to infectious complications, at any stage of transplantation. One way to identify patients colonized by resistant organisms at an early stage and guide the initial empiric therapy of febrile neutropenia is to collect surveillance cultures. Objective: To analyze the colonization profile of pediatric patients in the pre-HSCT stage. Material and Methods: A retrospective cohort study of all surveillance cultures, collected from pre-HSCT patients, was performed from 11/17/14 to 11/19/15 in a single center. Positive results of surveillance cultures pre-HSCT were investigated, confirmed through the analysis of nasal swab, skin swab, anal swab, catheter blood culture and urine culture. Data were obtained through medical record review. Results: The assessed patients included individuals submitted to the following types of HSCT: autologous, related allogeneic, unrelated allogeneic, haploidentical and unrelated allogeneic with umbilical cord blood. The diagnoses were wide-ranging, and the most prevalent one was leukemia. 34 patients were assessed, of which 17 (50%) were submitted to autologous HSCT, 8 (23.5%) to unrelated allogeneic HSCT, 7 (20.5%) to related allogeneic HSCT, 1 (2.9%) to unrelated allogeneic umbilical cord blood HSCT, and 1 (2.9%) to haploidentical HSCT. Within the sample, 29 (85.3%) patients had a positive result in one or more cultures. The main agents were: 10 (29.4%) *Escherichia Coli* in Anal Swab, 9 (26.5%) multidrug-resistant coagulase-negative *Staphylococcus* in Skin Swab, 7 (20.6%) oxacillin-resistant coagulase-negative *Staphylococcus* in Nasal Swab, 2 (5.9%) *Staphylococcus epidermidis* in blood culture and 1 (3%) *Escherichia coli* and 1 (3%) in *E. coli* ESBL in Urine culture. Among the identified agents, there was also the presence of 1 case of (3%) *Klebsiella pneumoniae* ESBL and 2 cases (5.9%) of *Pseudomonas aeruginosa* of the CSP Group in Anal Swab, 1 (3%) *Streptococcus viridans* and 1 (3%) *Staphylococcus aureus* in Nasal Swab and 1 (3%) Candida in Skin Swab. Conclusion: It was verified that 17 (50%) patients had positive cultures pre-HSCT. Of these, 2 (2.9%) developed infections, one with positive blood culture for *Pseudomonas Aeruginosa* of the CSP Group and the other with a positive urine culture for *Klebsiella pneumoniae* ESBL, and both had positive anal swabs pre-HSCT for the same agent that caused the infection during the HSCT. The surveillance culture pre-HSCT in these cases allowed the initial empiric therapy in febrile neutropenia and allowed the contact isolation, reducing the risk of infection to other patients.

Keywords: transplantation, bone marrow, pediatrics, surveillance, infection

P-020

Infections

Hemorrhagic Cystitis: Experience of the Bone Marrow Transplantation Unit of Hospital das Clínicas of the School of Medicine of Ribeirão Preto, Universidade de São Paulo

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INTRODUCTION The most severe form of cystitis in patients with cancer is hemorrhagic cystitis (HC), characterized by inflammation and diffuse bleeding of the bladder mucosa. The intensity can range from the minimum (from 5 to 50 red blood cells per high power field) to the maximum intensity, requiring blood transfusions to maintain stable hemoglobin levels. Despite preventive measures, a mortality rate of 2 to 4% has been reported. It may be caused by radiation, chemotherapy, and infections. MATERIALS AND METHODS: In order to determine the frequency of HC, we reviewed the medical records of transplanted patients in the Bone Marrow Transplantation Unit of Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto (USP), treated from June 2014 to June 2016. RESULTS: Seven cases of HC were found, all in patients who had undergone related allogeneic hematopoietic stem cell transplantation (HSCT). Five patients were males and two were females, with a mean age of 38.14 years (range 21-58 years). Only five patients had ABO compatibility. The following were indications for transplantation: Acute Lymphoblastic Leukemia (ALL, n=3), Acute Myeloid Leukemia secondary to Myelodysplastic Syndrome (n=1), and secondary to treatment of uterine cancer (n=1), Chronic Myeloid Leukemia (n =1) and Severe Aplastic Anemia (n = 1). All patients had positive polyomavirus in urine during the cystitis episode. Six of the seven cases were treated with hyperbaric oxygen therapy, with an average of 12 sessions per patient, in addition to clinical support, such as overhydration, oral estrogens (ES) and ciprofloxacin (CIPRO). Five patients received ganciclovir (GAN), and one received cidofovir. Two of the seven patients died during the period due to infectious complications. CONCLUSIONS: In this series of cases, we found that the viral etiology of hemorrhagic cystitis prevailed, developing in a severe immunosuppression scenario. Most cases showed clinical response to treatment, with the association of antivirals, estrogens and hyperbaric chamber.

Keywords: Hemorrhagic Cystitis

P-021

Infections

Invasive aspergillosis after Hematopoietic Stem Cell Transplantation in Pediatric Patients

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Invasive fungal disease (IFD) is a severe complication in patients submitted to Hematopoietic Stem Cell Transplantation (HSCT), with high morbidity and mortality and high costs of prolonged treatment. Although *Candida spp* is the most common etiological agent, the incidence of filamentous fungi has increased and, among them, the main agent is *Aspergillus spp*. Since 2009 a positive serum galactomannan result has helped to classify patients with suggestive radiological image as having probable invasive aspergillosis, without the need to perform a biopsy (EORTC 2008). Data published on aspergillosis in pediatric patients in Brazil and around the world are extremely scarce. Objective: To evaluate the incidence of invasive aspergillosis (IA), according to the EORTC 2008 criteria, in children submitted to HSCT. Methods: A retrospective cohort study was performed in patients undergoing HSCT from January 2009 to December 2015. During the medical file review, the following were assessed: age, gender, donor, underlying disease, infection site, galactomannan levels, chest tomography, cultures and anatomopathological results. The EORTC-2008 criteria were used for the IA classification, as possible, probable and proved. Patients who were classified as having possible IA were excluded from analysis. Results: During a 7-year period, 300 transplantations were performed in 274 patients, of which 153 (51%) were allogeneic: 81 related and 72 unrelated. 38 patients were identified with invasive fungal infection, 13% of all transplantations or 25% of allogeneic HSCT. No patient had been submitted to autologous HSCT. Of the 38, 17 had DFI possible, i.e., a suggestive image but negative galactomannan result and 4 had infections by non-filamentous fungi and were excluded from the analysis. Seventeen children (6%) were diagnosed with IA, 9 probable (positive galactomannan) and 8 proven (positive culture) cases, with *Aspergillus fumigatus* being isolated in 5. One patient had co-infection with *Aspergillus fumigatus* and Zygomycota. The 17 patients had a mean age of 11 years; 11 were males and most (70%) had acute leukemia: myelogenous (6), lymphoid (5), biphenotypic (1), myelodysplasia (1), aplasia (2) CGD (1) and HLH (1). Ten of the 17 patients underwent unrelated HSCT and among the 7 related ones, 2 were haploidentical HSCT and 3 were submitted to the second HSCT. The affected sites were lung (15), facial sinuses (1) and jaw (1). The death rate was 70%, but 4/12 patients also had recurrence of the underlying disease. Four patients are alive between 1 and 3 years after HSCT. Conclusion: IA was the most common IFD among patients undergoing allogeneic HSCT, with an incidence of 11% (6% in all HSCT), with the highest risk group being: unrelated, haploidentical or second HSCT, suggesting that prophylaxis against filamentous fungi and serial and thorough investigation must be performed in this population, especially considering the lethality of 70% when infections occur.

Keywords: invasive fungal infection, transplantation, pediatrics, incidence, mortality

P-022

Infections

Case report: dyskeratosis congenita and community-acquired pneumonia with suppurative complications.

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Introduction: Dyskeratosis congenita (DKC) is a hereditary chromosomal instability syndrome with multiple inheritance patterns, which manifests with mucocutaneous abnormalities, bone marrow failure, predisposition to cancers and immunological alterations, with consequent susceptibility to infections. It is important to emphasize that the diagnosis is mainly clinical and the triad reticulated skin hyperpigmentation, nail dystrophy and mucosal leukokeratosis is a prominent one. Given the unusual occurrence of this syndrome, this study describes case of a patient admitted in a tertiary pediatric hospital in Fortaleza-CE, previously diagnosed with DKC, who had community-acquired lobar pneumonia, parapneumonic effusion and pulmonary abscess. Materials and methods: case report carried out through medical record evaluation, after the free and informed consent was signed by the patient. Results: we report the case of 16-year-old male patient, with a family history of DKC in two brothers, previously diagnosed with DKC at 7 years, who had community-acquired pneumonia, parapneumonic effusion and pulmonary abscess. He had reticulated skin hyperpigmentation in the cervical, thoracic and dorsal regions, nail dystrophy in fingers and toes and adermatoglyphia, but had no mucosal leukokeratosis, developmental disorders or malformations. Whole blood count showed normocytic and normochromic anemia and thrombocytopenia. The chest computed tomography showed abscess in resolution in the lingular region, accompanied by small homolateral pleural effusion. The patient responded well to antibiotics and was discharged from the hospital and monitored at the Dermatology Outpatient Clinic. Discussion: This report shows immunological changes in patients with DKC, with possible impairment of cellular and humoral immunity, predisposing to more severe infections as it occurred with our patient. Immunological changes have been described in patients with X-linked DKC, such as hypogammaglobulinemia, B and T cell lymphopenia, increased apoptosis rate and decreased cell proliferation of lymphocytes, in addition to combined T, B and NK cell immunodeficiencies. Conclusion: one must consider the importance of disseminating medical knowledge about DKC, as it is a cause of inherited bone marrow aplasia with high morbidity, as well as Fanconi anemia and Shwachman-Diamond syndrome, demonstrating the possibility of treating these patients with bone marrow transplantation. Despite the few cases described in the literature, it is necessary to emphasize its association with solid and hematological malignancies, several immunological abnormalities and complications caused by peripheral cytopenia secondary to bone marrow aplasia.

Keywords: Dyskeratosis congenita, pneumonia

P-023

Infections

Healthcare-associated infections in patients submitted to bone marrow transplantation in a public hospital

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Introduction: Hematopoietic stem-cell transplantation is a procedure in which stem cells capable of reconstituting bone marrow function are infused into a patient. Due to the degree of immunosuppression complexity to which they are submitted, infections in patients undergoing bone marrow transplantation is an important cause of morbidity and mortality and Healthcare-Associated Infections (HAIs) occur in the first post-transplant period. Therefore, this study aimed to identify the main HAIs and microorganisms in a Bone Marrow Transplantation Unit of a Public Hospital in Ceara, Brazil. Material and Methods: This was a retrospective and quantitative study carried out in a Public Hospital in Ceará, from January to December 2015, through notification records of the Hospital Infection Control Commission on patients whose hospital length of stay was >48 hours in the Bone Marrow Transplantation ward. Results: Of the 63 patients transplanted in this period, whether autologous or allogeneic, 32 had HAIs. Of these, 18 (56.2%) were Blood Stream Infections (BSI) and 14 (43.7%) were Clinical Sepsis cases. The main microorganisms were found in the BSI were *S. epidermidis,* 7 cases (21.8%), *E. coli,* 4 cases (12.5%); *K. pneumoniae*, 2 cases (6.25%); *S. warneri*, 2 cases (6.25%), and three microorganisms of different species were found once, 1 (3.1%) *S. aureus*, *E. cloacae* and *S. haemolyticus*. In clinical sepsis-related HAIs, it was not possible to identify microorganisms through cultures and they diagnosed according to clinical criteria, such as: at least 2 systemic inflammatory response syndrome criteria: fever or hypothermia (Temp >38.3 °C or <36 °C), shaking chills, tachycardia (HR >90 bpm), tachypnea (RR > 20ipm), SAP <90 or MAP <65 mmHg, leukocytes >12,000 cells/ mm^3, or <4,000 cells/mm^3 or >10% of young forms. Discussion and Conclusion: The HAI with the highest prevalence was the BSI. Among the microorganisms, gram-positive bacteria are more often present, with *S. epidermidis* being the most frequent one. It is clear the need for prevention and control of hospital infection, directed at patient safety, reducing the length of hospital stay, hospital costs and the unreasonable use of antimicrobials, avoiding preventable diseases and improving the quality of assistance and care offered to these individuals.

Keywords: Nosocomial infection. Bone marrow transplantation.

P-024

Infections

Oral mucositis by Mycoplasma salivarium three years after HSCT mimicking drug inflammatory or autoimmune condition: A case report.

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Introduction: *Mycoplasma salivarium* (Ms) belongs to the class of the smallest Tenericutes replicants. Its smaller size than the that of other bacteria and the absence of cell wall are responsible for their difficult identification in cultures and visualization at microscopy, their poor response to antibiotics and their scarce identification in clinical practice. Although considered a commensal pathogen of the oral cavity, it has been associated with infectious processes, squamous cell carcinoma and as a possible stimulating factor for inflammatory conditions in immunosuppressed individuals. Objective: The objective of this study is to present a case of ulcerative oral mucositis in a patient submitted to hematopoietic stem cell transplantation (HSCT) caused by Ms. Case report: MABS, female, 47 years, three years after related allogeneic HSCT due to Myelodysplastic Syndrome; had grade II Chronic Graft-versus-Host Disease (cGVHD) in the mouth, eyes and skin; was using Prednisone, Methotrexate and prophylaxis with acyclovir, Bactrim and Itraconazole, came to the dental appointment reporting important burning of the oral mucosa in the past 5 days. The oroscopy disclosed erythematous oral mucosa with multiple shallow and bleeding ulcers. The hypotheses were acute GVHD (overlapping) and infection. Although possible, drug reactions were not considered at first, since the patient had been taking the drugs for over 6 months. Results: The AP identified acute mucositis and no criteria for GVHD, with no fungal or viral structures. The mycology and viral PCR were negative. The bacterial culture identified *S. aureus* sensitive to erythromycin, which was prescribed for 15 days without response. We chose to screen for the presence of Mycoplasma, through amplification of the 16S rDNA gene by real-time PCR. The samples analyzed were positive in all triplicates. The mean cycle amplification threshold was 26.95 (Ct≅27), which corresponds to 103 copies of genome/µL. The sequencing of the samples (ABI 3500xL Genetic Analyzer) showed 99% genetic identity with *Mycoplasma salivarium* (n. of access NR_113661.1). Based on the results, the patient was treated with doxycycline, with resolution of the acute picture. Repeat PCR for Mycoplasma 10 days after antibiotic treatment was negative. Final Considerations: Ms infections should be taken into account in acute inflammatory processes after HSCT, as well as its importance in the development and maintenance of the discussed GVHD.

Keywords: Allogeneic hematopoietic stem cell transplantation; Oral Mucositis, Mycoplasma salivarium, Graft-versus-Host Disease

P-025

Histocompatibility

TLR9 gene polymorphism (rs5743836) as a susceptibility factor in patients with Spondyloarthritis

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Introduction: Spondyloarthritis (SpA) is a group of chronic inflammatory rheumatic diseases that share clinical and genetic characteristics, but its etiology is unknown; its clinical manifestations generate a poor quality of life for patients, and annual public costs per patient exceed US $4,000. Toll-like receptors (TLR) are important in the activation and homeostasis of the immune system. The TLR-9 plays a previously reported important role in diseases mediated by the immune system and it is known that the C allele of this SNP is a mutation in the promoter region of the TLR9 gene, which can induce the production of a new IL-6-dependent transcription factor. Carriers of the T/C genotype have an increased expression of the TLR9 molecule and also of IL-6. The aim of this study was to analyze the genetic association of SNP rs5743836 of TLR9 in patients with SpA. Material and Methods: We analyzed 100 patients with SpA and 152 controls without SpA or family history of autoimmune diseases; the diagnosis in the group of patients was performed by a rheumatologist using the ASAS criterion; the genotyping was performed by PCR-RFLP and statistical analysis were performed using SNPStats software, with significant values of $p < 0.05$. The chi-square test and logistic regression were performed. The analyzed groups were matched for gender, age and ethnicity, and were in Hardy-Weinberg equilibrium. Results: The T allele was the most frequent in the control group (78%) and the C allele was the most frequent among patients (35%); genotypic frequencies were different between the two groups, with patients having the T/C genotype as the most frequent one (55%), while in the control group, the T/T genotype (58%) was the most frequent. The genotypes T/C (OR = 1.9, CI= 1.0 to 3.4) and C/C (OR = 5.6, CI = 1.3 to 23) were statistically significant; at the logistic regression analysis, significance was obtained for genotypes T/C (OR = 2.7, CI = 1.2 to 5.9) and C/C (OR = 18.2, CI = 2 to 164.3) for the female gender. Discussion: Based on previous studies one can infer that in the study population, the presence of the C allele confers susceptibility to spondyloarthritis, regardless of gender, age and ethnicity and that the C/C genotype increases this susceptibility by five-fold; female patients carrying the C allele have a greater chance of developing the disease; when we analyze the C/C genotype among patients, we observed this susceptibility showed an 18-fold increase. Conclusion: we observed that C allele was shown to be a factor of susceptibility in this population, resulting in increased susceptibility among female patients.

Keywords: Spondylarthropathies, Toll-Like Receptors, Genetic Polymorphism, Case-Control Study, Genetic Predisposition to Disease.

P-026

Histocompatibility

Interleukin-17: a description of polymorphisms in a Brazilian population.

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Introduction: Interleukin-17 is a newly described cytokine that links the adaptive and innate immune systems. Polymorphisms in gene promoter sequences can modulate its expression rate. This cytokine family induces multiple proinflammatory mediators including chemokines, cytokines, and metalloproteinases from epithelial and fibroblast cells. Polymorphisms of several cytokine genes located within the promoter or other regulatory regions can affect gene transcription, conferring flexibility to the immune response. Moreover, the presence of certain alleles may influence the outcome of both viral and bacterial infections. The genetic constitution of the Brazilian population has peculiarities that vary according the region and the investigation of specific alleles and genotypes of IL17 polymorphism provides insight in the study of genetic composition and the origin of different populations. Objective: the aim of this study was to verify the frequency of IL17A G197A (rs2275913) and 17F T7488C (rs763780) in a mixed Brazilian population from Southern Parana. Material and Methods: A total of 473 healthy subjects were analyzed, which included a mixed group consisting of White, Mixed-race and Black individuals, categorized by self-reporting. DNA samples from patients were genotyped for single nucleotide polymorphisms (SNPs) of IL17A and IL17F by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP). Frequencies of alleles and genotypes of IL17A and IL17F were obtained by direct counting, and these analyses were calculated by the SNPStats. Results: The polymorphisms in the IL17A and IL17F alleles were analyzed in 473 and 456 normal population subjects, respectively. Most participants were females (61%) and Caucasians (71%), with a mean age of 49.14 (range of 20-88) years. Genotype and allele distribution of IL17A and IL17F were consistent with the Hardy-Weinberg equilibrium. IL17A GG genotype and G allele were more frequent in the studied population (0.573 and 0.7674, respectively), as well as the IL17F TT genotype and T allele (0.8838 and 0.9386, respectively). The distribution of IL17A genotype frequencies in our group was 3.8%, 38.9% and 57.3% for IL17A-AA, IL17A-AG and IL17A GG, and 0.6%, 11.0% and 88.4% for IL17F-CC, IL17F-TC and IL17F-TT, respectively. Discussion: These data were similar to those of another previously reported Brazilian population. In contrast, significant differences were observed when comparing mixed-race Brazilian populations with Chinese, Japanese and Tunisian populations. With regard to ethnic background, the distribution of Brazilians and other populations was different. Conclusion: Cytokine polymorphism frequency studies in specific populations may contribute to a better understanding of genetic background and its role in the development of a variety of diseases.

Keywords: IL-17, proinflammatory cytokines, SNP

P-027

Histocompatibility

IL17A and IL17F are associated with Polycystic Ovary Syndrome

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Introduction: Polycystic Ovary Syndrome (PCOS) is a genetically complex endocrine disorder of uncertain etiology, of which major consequence is infertility. Low levels of classical markers of inflammation have been found in this disease, such as tumor necrosis factor and other cytokines. Interleukin-17 (IL-17) is a proinflammatory cytokine that is responsible for the activation and attraction of neutrophils to the infection site, as well as stimulating the production of other cytokines. IL-17 levels were altered in the serum of non-obese women with PCOS; however, IL-17 polymorphisms have not been reported up to this moment in PCOS patients. Objective: The aim of this study was to investigate the influence of polymorphisms of L17A G197A (rs2275913) and IL17F T7488C (His161Arg, rs763780) in the immunopathogenesis of PCOS. Materials and Methods: A case-control study was carried out in women from the same region and ethnic group. Women with PCOS (N=89) were diagnosed according to Rotterdam criteria for the presence of at least two of the following clinical and laboratory signs: anovulation, hyperandrogenism and the presence of polycystic ovaries, whereas healthy women (N=133) were selected for the control group. Women under 18 years old and Asian descendants were not included. The IL17A and IL17F polymorphisms were evaluated by PCR-RFLP (Polymerase Chain Reaction – Restriction Fragment Length Polymorphism). Linear and logistic regression was used to analyze the association using SNPStats software. Results: The distribution of alleles and genotype frequencies of IL17A and IL17F was consistent with the Hardy-Weinberg equilibrium (P>0.05). No significant differences in allelic and genotypic frequencies of IL17A and IL17F SNPs were found between patients and controls in the dominant, recessive or codominant models. However, IL17A A/G genotype (OR=0.15; CI 95%=0.03-0.90) and IL17F T/T and T/C genotypes (OR=0.20; 95%CI =0.05-0.79 and OR=0.15; 95%CI =0.03-0.81, respectively) were associated to protection in the non-obese women when the covariate body mass index (BMI) was analyzed. Discussion: The IL17 polymorphism is related to higher (alleles A and T for IL17A and IL17F, respectively) or lower cytokine production and may influence the risk of a particular disease. Increase in the IL-17 production can cause damage to the ovaries and lead to infertility. In this study, a slightly lower frequency of the IL17F C allele (4% and 7%) and the T/C genotype (8% and 14%) was found in PCOS women when compared to the control group. These results may indicate the protective role of the C allele in the pathogenesis of the disease. According to the literature, the majority of women with PCOS are obese; therefore, a reduced production of IL-17 may protect non-obese women against disease pathogenesis. Conclusion: A possible protective role of IL17A A/G and IL17F T/C and T/T genotypes was associated to non-obese women with PCOS. Additional studies are needed to further elucidate the role of IL17 in PCOS.

Keywords: Polymorphism, proinflammatory cytokines, case-control

P-028

Histocompatibility

HLA Polymorphism and Risk of HPV Infection and Cervical Cancer

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Cervical cancer (CC) is the fourth most commonly diagnosed cancer and the fourth leading cause of female cancer mortality worldwide. Although persistent infection with high-risk human Papillomavirus (HR-HPV) genotypes is required for cervical epithelial cell transformation and cervical carcinogenesis, HPV infection alone is not sufficient to induce tumorigenesis. The genetic variability of the host also plays a role in the risk of developing cervical cancer, especially the variability of genes that control the immune response. The purpose of this study was to investigate the influence of HLA class I and II genes on the risk of HPV infection and cervical lesions/cancer in a Brazilian population. Cervical and blood samples were collected from 124 women referred for colposcopy in União da Vitória city/Parana State. Cervical samples were analyzed for cervical lesions/cancer through Papanicolaou smears (Pap) and for HPV by polymerase chain reaction (PCR). DNA was extracted from peripheral blood cells and HLA class I (A, B, C) and class II (DRB1, DQA1, DQB1) were determined by PCR-SSO methodology using Luminex® (One-Lambda CA, USA). Statistical analysis was performed using the Arlequin 3.0 software. The study sample consisted of 124 women, of which 48 (38.71%) had normal Pap (NILM), whereas 42 (33.87%) had high-grade squamous intraepithelial lesion (HSIL), 27 (21.77%) low-grade SIL (LSIL) and 7 (5.65%) CC. As for HPV, 78 (62.9%) samples were positive, of which 48 (61.54%) had HR-HPV. Intrinsically, the analyses showed that the HLA-DQB1*03 allele was associated with increased risk of cervical lesions (p=0.0219; OR= 2.03; CI: 1.12 - 3.69), HPV infection (p=0.0444; OR= 1.85; CI: 1.02 - 3.36) and with HSIL/CC in comparison to NILM (p= 0.0258; OR= 2.11; CI: 1.11 - 4.02). The HLA-B*07 allele was associated with increased risk of HPV infection (p= 0.0316; OR= 3.87; CI: 1.11 - 13.52) and HR-HPV infection (p= 0.0402; OR= 2.80; CI: 1.05 - 7.49). Both HLA-B*14 and HLA- C*08 were associated with decreased risk of HR-HPV infection (p= 0.0359; OR= 0.12; CI: 0.02 - 0.98) and of HSIL/CC in comparison to both NILM (p= 0.0135) and LSIL (p= 0.0432). Our results showed association of some HLA alleles in the HR-HPV and HSIL/CC susceptibility or protection in Brazilian women. These findings suggest that HLA polymorphisms play a role in the natural history of HPV infection and may contribute to genetic susceptibility to cervical cancer. Further studies with a larger number of cases are expected to confirm our results.

Keywords: Human Papillomavirus, Uterine Cervical Neoplasms, Major Histocompatibility Complex, Genetic Susceptibility

P-029

Histocompatibility

Identification of a new HLA-B*35 alelle and its family distribution in a population from Northeastern Brazil

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Introduction: The major histocompatibility complex (MHC) in humans is known as the human leukocyte antigen (HLA). The genes encoding the Class I HLA (A, B and C) and class II (DR, DP and DQ) are highly polymorphic and there are currently over 14,000 alleles described in this genomic region. Due to its important functional role in antigen presentation for activation of adaptive immunity, the precise HLA typing and identification of new allelic variants is essential when assessing compatibility between recipient and donor of solid organs and bone marrow. Objective: To describe a new HLA allele and its distribution in a family from the state of Maranhao, Brazil. Materials and Methods: DNA was extracted from peripheral blood in a separation column. The PCR was performed with locus-specific primers and hybridization was performed using the RSSO-LABType technique (One Lambda). Analyses of typing were performed with the help of the HLA Fusion 3.4.18 program, which provided results at low and medium resolution. In the presence of inconclusive results, the sample was sent to the Laboratory of Immunogenetics and Molecular Biology of UFPI for sequencing using the SBT (sequence-based typing) technique. Results: Analysis of typing using the RSSO-LABType technique, the HLA-A and HLA-DR loci showed the following results for the index case: HLA-A*24: AECEB and HLA-A*31: AECUZ and HLA-DR*04: AEUNE and HLA-DR*04:11. However, the result of typing for HLA-B locus showed to be inconclusive for both the index case and for the father and two siblings. For this locus, the analyzed sample showed false-negative (FN) reactions for beads 63 and 67, which recognize sequences 148 - ARV-153 and [150ARV-153+161--L(-/Z)164], respectively. False-positive (FP) reactions were also observed in beads 29, 87 and 90, which recognize sequences 20-----26, 112-HD-S---119 and 102-L----107. The sequencing analysis indicated the presence of a new allele, HLA-B*35. This new variant showed two point mutations when compared with the HLA-B*35: 01. One of these changes was detected in codon 67 (TTC → TCC) and the other was observed at codon 152 (GTG → GAG). This variation, in addition to being identified in the index case, it was also observed in the father, in a sister and in a brother. Discussion: The point mutations observed in the new allele HLA-B*35 leads the substitution of amino acids in the peptide (missense mutations), which can change its structure and antigenic properties. Thus, HLA typing laboratories should be able to perform an accurate allelic discrimination, identifying, whenever possible, the presence of new variants. Conclusion: HLA typing results that are inconclusive when using the RSSO-LABType technique may be indicative of a new allele. Thus, performing the sequencing technique associated with parental HLA typing should be used for HLA haplotype definition.

Keywords: HLA, genetic variability, transplant, RSSO and SBT.

P-030

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Evaluation of quality of care to unrelated allogeneic bone marrow donors in the public service in the State of Ceará.

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INTRODUCTION: The hematopoietic precursor cell transplantation (HPCT) consists in the replacement of the patient's deficient or diseased bone marrow (BM) by normal cells from a donor, with the purpose of reestablishing a new bone marrow and ensuring a healthy life to the recipient. The Hematology Center of Ceará (HEMOCE), in the last 15 years, has enrolled 161,837,000 potential BM donors in the National Bone Marrow Donor Registry (REDOME). The HEMOCE BM Center is the link between donors and patients during the donation/bone marrow transplantation process. Considering the REDOME recommendations for Collection Centers and noting the importance of qualified and humanized care, HEMOCE and Walter Cantídio University Hospital (HUWC) carried out an evaluation questionnaire on the care given to fit and unfit unrelated allogeneic donors in the selection for BM collection. OBJECTIVE: To evaluate the care during the bone marrow donation process in HEMOCE/HUWC. MATERIALS AND METHODS: This is a quantitative and descriptive study, carried out by collecting information on care at HEMOCE/ HUWC through a questionnaire. This collection was based on the theoretical references of REDOME recommendations to the collection centers. The service multidisciplinary team evaluated the care provided to BM donors at HEMOCE by telephone contact: Phase I (contact, reception and guidance processes) and Phase III (BM collection) and at HUWC: Phase II (Consultation, exams and mobilization). RESULTS: From June 2012 to June 2016, a total of 32 candidates underwent work up (phases I and II). Of these candidates, 21 were eligible for BM donation (65.6%), of which 18 were men (85.7%) and 3 were women (14.3%). Of the samples taken, 13 were sent to national transplant centers (62%) and 8 to international ones (38%). DISCUSSION: Of the recommendations considered by REDOME, it was observed (Table 1), that the services performed by the HEMOCE in Phases I (98.1%) and III (100%) were approved when considered the excellent/ good criteria. In phase II, there was 80% of excellent/ good approval, even with 20% of regular/ bad criteria related to imaging assessment. We observed that the HUWC staff was not trained to meet the BM necessities in a differentiated manner. Although the questions/answers were not inductive, considering the excellent, good, fair and poor classifications, the study shows that we need other interventions and actions through qualified assessment during the care cycle in BM donation. CONCLUSION: The questionnaire was an important method to evaluate the care provided at HEMOCE/ HUWC collection center, by measuring significant and unknown results in the state of Ceará, which have become indispensable for improving the care provided to the donor.

Keywords: Bone Marrow Center, REDOME, Public Service Evaluation

P-031

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

The importance of the nursing consultation in the evaluation Pre-hematopoietic stem cell transplantation and the impact on nursing care: use of information leaflets

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The hematopoietic stem cell transplantation (HSCT) is a treatment in which chemotherapy protocols are performed at high doses and, therefore, pre-HSCT information is necessary. The patient submitted to HSCT requires careful evaluations by the multidisciplinary team and the nurse. The nursing consultation seeks to offer better guidance to patients and their families and a safer and more efficient care, thus identifying the problems and peculiarities at this stage of treatment and thus prepare the decisions to be made and a specific care plan for each patient. Communication during the nursing consultation improves the understanding not only of the disease but also of the treatment proposed by the medical team and provide patients and families with information on the service routines, such as the use of masks, type of transplantation and its particularities, the intravenous device to be used, applied precautions and the need for transfusions, among other issues of great importance. Objective: This study aims to inform and guide patients and their families about the HSCT treatment through a nursing consultation and deliver illustrative leaflets with information related to HSCT phases for the development of a care plan. Methods: During the nursing consultation, an interview with patients and families was performed and tools were applied, which help nurses to assess social and psychological issues; after the interview, explanatory and illustrative leaflets were delivered, created by the staff of an HSCT outpatient clinic and hospital infection control committee for better clarification. Results: After applying these tools during the nursing consultation, it was observed that the results were positive regarding the instructions given to patients and their families and that they understood the treatment more easily and created a bond of trust with the nurse, in addition to keeping the illustrative leaflets for any further questions. Discussion: The nursing consultation is one of the phases of the nursing process, where the patient is assessed for the creation of a care plan. During this consultation, illustrative leaflets were provided, which are tools used for better visual explanation of their treatment and describe the stages of pre-HSCT and how to proceed. The leaflets also provide nursing guidelines regarding the care that patients and families must have throughout the treatment and addresses questions to be clarified with the nurse, doctor or the multidisciplinary team. Conclusion: We conclude that the nursing consultation and delivery of explanatory and illustrative leaflets prior to treatment contribute to better communication, understanding and adherence to treatment by patients and families, minimizing the onset of complications related to HSCT.

Keywords: hematopoietic stem cell transplantation, nurse, nursing, patient.

P-032

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Myeloid sarcoma in submandibular gland: a rare manifestation of early recurrence of AML after HSCT: a case report.

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Introduction: Myeloid sarcoma (MS) is a rare extramedullary tumor consisting of immature or mature myeloid blast cells and occurs in approximately 2% to 8% of individuals diagnosed with Acute Myeloid Leukemia (AML). The involvement of the salivary glands is extremely rare. Objective: To report a case of MS in the submandibular gland of a patient submitted to allogeneic hematopoietic stem cell transplantation (HSCT) due to LMA with no signs of disease recurrence in other sites. Case report: 38-year-old male patient diagnosed with AML - M3, refractory to four remission inductions with Daunorubicin + Ara-C, submitted to rescue treatment with FLAG-IDA, followed by allogeneic related HSCT. He was referred to the Dental and Stomatology outpatient clinic of a university hospital on D+110 after HSCT due to a picture of painless submandibular volume increase for the last 10 days. At the time he had normal blood count, myelogram showing disease remission and the minimal residual disease screening was negative. Physical examination showed swelling in the submandibular region to the right, fixed, painless and of firm consistency at palpation. The ultrasound showed an increased submandibular gland and heterogeneous aspect. The cytology, performed by ultrasound-guided aspiration, showed moderate cellularity with intermediate-sized cells, high nucleus/cytoplasm ratio, oval nuclei, fine chromatin and visible nucleoli, with positive immunohistochemistry for CD34. For diagnostic confirmation and expansion of the immunohistochemical panel, it was decided to perform a biopsy of the gland. To identify the collection area, an MRI was performed, which showed an expansive formation in the right submandibular gland topography. The biopsy showed signs compatible with Myeloid Sarcoma: submandibular gland tissue diffusely infiltrated by neoplastic cells of intermediate size, scarce eosinophilic cytoplasm, oval vesicular nucleus, marginated chromatin, prominent eosinophilic nucleoli and frequent mitosis; the immunohistochemical analysis was positive for CD117, CD34 (focal), myeloperoxidase and negative for CD20. The CD3 showed a small population of reactive T-lymphocytes. The patient was submitted to another chemotherapy round with Ara-C and radiation therapy on the site, but during treatment he progressed with disease recurrence, infiltration of the central nervous system and mediastinum and died on D +128 after HSCT. Final considerations: Although rare, the dental team must be aware of changes involving the salivary glands in patients with onco-hematological diseases, since the diagnosis of infiltration in the area may precede the medullary recurrence of the disease, allowing its identification and early treatment.

Keywords: Myeloid Sarcoma, Acute Myeloid Leukemia, Hematopoietic stem cell transplantation

P-033

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Envelope of care: a post-hematopoietic stem cell transplantation guidance program for hospital discharge

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Introduction: The patient submitted to Hematopoietic Stem Cell Transplantation will have to face a new daily routine. There are many precautions that should be taken in the post-transplant period, requiring patients and families to acquire new knowledge to be used after hospital discharge. Objectives: Development of a systematic program of care post-Hematopoietic Stem Cell Transplantation (HSCT), for patients and families in the period prior to hospital discharge. Material and Methods: This study followed the action-research method, proposed by Michel Thiollent. Three phases were followed for its development: 1) identification of essential care to patients after the HSCT; 2) Development of a guidance program of post-HSCT care; 3) Creation of teaching materials for the guidelines. For the preparation of the guideline program, initially the essential care actions aimed at patients undergoing HSCT were listed, through literature review and experience of nurses working in a HSCT unit of a university hospital. The literature review was carried out from December 2015 to March 2016 using the following descriptors: nursing; guidelines; care; bone marrow transplantation. The databases were used were LILACS and VHL and the inclusion criteria were: full-text articles available in the databases; the first author was a nurse; published between the years 2010 to 2016. Results and Discussion: Of the analyzed studies and based on the experience of nurses who work in the service, the field of this study, it was concluded that of the care to be explored regarding patients submitted to HSCT and their families, the following should be emphasized: body, oral and hand hygiene; care of Hickman® catheter; temperature control and exposure to the sun; care of clothing and the environment; care of domestic animals; care of visits, leisure and recreation; care of physical and sexual activity; care of sleep and rest; care of vaccination and medical routine. For this purpose, we created a "Guidance program for post-transplantation care", which included providing material such as the "Care envelope". Considering the number of necessary guidelines for better assimilation by patients and families, the program starts on D+12 post-transplantation, with one or two themes being addressed every day. After each presentation, the patient will receive a guidance page, which will comprise the "Care Envelope". Conclusion: by implementing the guidelines at an early stage, we can provide better understanding of patients and their families about the care required after discharge, encouraging them to seek solutions for simple complications, and reducing the number of unnecessary patient returns to the clinic.

Keywords: Nursing, Guidelines, Care, Bone Marrow Transplantation.

P-034

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Psychology and Bone Marrow Transplantation: Review from the BVS-Psi database

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Introduction: The Bone Marrow Transplantation (BMT) has been widely used in neoplastic, hematological and onco-hematological diseases, when conventional therapies do not offer a good prognosis. The method involves infusion of stem cell suspensions aiming to reverse the pathological bone marrow function. Although effective, the BMT is an aggressive procedure that can either cure the recipients or lead them to death. Therefore, the treatment is viewed with ambivalence by the patient and family and may lead to the onset of varying degrees of anxiety, depression and expectations. After the 1990s, the studies related to BMT started to be interested in a better understanding of the influence of psychological factors on the survival of patients undergoing BMT. This study aimed to understand what is being produced in Psychology, from 1999 to 2016, related specifically to the BMT. Material and Methods: The study use a qualitative approach and documental research as a research tool. Aiming at the proposed objectives, a search for scientific publications was carried out in the BVS-Psi electronic database using the following keywords: "psychology" and "transplant". Publications specifically related to BMT were identified and the most significant ones were selected. The material was read and charted and the data analysis and discussion of the results were carried out. Results: The material comprised only scientific articles (8). Of the authors of the publications, 19 had an academic degree in Psychology, 4 in Medicine, 1 in Education and 1 in Music, which may suggest that although the studies were in the Psychology area, considering its predominance, other professionals have produced studies in the area. It was observed that the studies portrayed more specifically the reality of the following Brazilian states: Sao Paulo (n = 6), Minas Gerais (n = 1) and Paraná (n = 1). Discussion: The authors of the selected studies used qualitative approaches, many with psychoanalytic theory references and aimed basically at the evaluation of the psychological state of BMT candidates, using tools such as the Thematic Apperception Test and the factorial personality inventory; to report group intervention experiences with caregivers of patients undergoing BMT; to systematically review the scientific studies dedicated to research the association between the patient personality and post-BMT survival; to investigate the meaning of death for doctors who work with critically-ill patients in the context of BMT. Conclusion: The scientific production in psychology related to BMT is scarce in the searched database and the selected articles provide interesting contributions to the understanding of the psychological manifestations related to BMT, as well as possibilities of intervention with patients and families in this context.

Keywords: Psychology; Transplant

P-035

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Evaluation of oral health status and dental care in patients undergoing allogeneic hematopoietic stem cell transplantation: a retrospective assessment.

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Introduction: Although not available in all transplant centers, the evaluation and adaptation of the oral environment prior to hematopoietic stem cell transplantation (HSCT) is recognized as part of good preventive practices for infectious complications of the treatment. The knowledge of the oral status and dental needs at this stage of treatment is an important factor for understanding the necessity for such care. Objective: To assess the oral health status and dental treatments performed in patients candidates to HSCT in a university hospital. Patients and Methods: We performed a retrospective review of dental records and panoramic radiographies of patients referred for pre-HSCT assessment during the year 2015. To assess the health status, the following data were obtained: 1. decayed, missing and filled teeth index (DMF-T). 2. Quality of oral hygiene, as satisfactory (absence of visible biofilm) and Unsatisfactory (presence of visible biofilm); 3. Infectious, periodontal (active gingivitis and/ or periodontitis) and endodontic foci. To evaluate the performed treatments, all procedures carried out after the initial assessment were reviewed. Results: All 33 patients undergoing allogeneic transplantation during the study period, 20 males and 13 females, were evaluated by the dental team. The underlying diseases were acute leukemia (15); Sickle-Cell Anemia (7); Myelodysplastic Syndrome (4); Severe aplastic anemia (2); Sickle-Cell Anemia (2); Chronic Myeloid leukemia (1); Lymphoma (1). The oral health assessment showed a DMF-T of 10.31, compatible with the Brazilian population; 40% of patients (13) had poor oral hygiene, 40% had some infectious focus, with 33% showing a periodontal focus and 15% an endodontic focus. In total, 17 patients (51%) had to be submitted to dental intervention: 5 (Extraction + Periodontal Treatment + Restoration); 2 (Restoration + Periodontal Treatment); 6 (Periodontal Treatment); 1 (only restoration); 1 (removal of braces); 1 (removal of gingival hood); 1 (endodontic dressing). Altogether, 44 procedures were performed: 18 restorations; 12 Periodontal scraping procedures; 9 extractions; 3 prophylactic procedures; 1 removal of gingival hood and 1 brace removal. Final considerations: The study population showed a significant incidence of oral disease and infectious conditions that could bring complications throughout the HSCT. These data, coupled with the number and variety of performed procedures suggest the importance of pre-HSCT dental evaluation and an integrated multidisciplinary team. Studies assessing the impact of dental care performed pre-HSCT on the outcome of transplantation with emphasis on infectious complications, hospital length of stay and survival are necessary.

Keywords: Allogeneic Hematopoietic Stem Cell Transplnatation; Oral Health; pre-HSCT dental care.

P-036

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Quality of life of children after HSCT: comparison between self-assessment and the mothers' evaluation

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Several authors have dedicated themselves to understanding the quality of life (QoL) of children after treatment, but few analyze the agreement between the HR-QoL measured by the child and that evaluated by parents. In this context, the objective of this study was to evaluate the health-related quality of life of children immediately after the HSCT, and compare the results of the self-assessment made by the children with the evaluation performed by mothers. We used the Pediatric Quality of Life Inventory (PedsQL ™ - child's report and the parental report on the child (8-12 years), applied individually, face-to-face. The mothers answered the same questions as their children, but referring to children (For example: "My son/ My daughter has pain ...). This questionnaire evaluates the level of difficulties with: a) pain and bruises; b) nausea; c) anxiety with procedures (injections and tests); d) anxiety with treatment (medical consultations and hospital); e) post-treatment concerns; f) Cognitive difficulties; g) perception of physical appearance; h) communication (staff and other people). After the questionnaire was applied, a score was given to each question, which was later transformed into a scale of 0-100, where zero corresponded to the worst health status and 100 to the best. The sample consisted of 14 participants, seven mothers and their children. The age of patients ranged from 8 to 10 years. The results (means) of the assessments were: a) pain: mothers = 97.9 (SD = 4.6), children = 70.4 (SD = 22.1); b) nausea: mothers = 79.1 (SD = 21.8), children = 70.8 (SD = 22.61); c) anxiety with procedures: mothers = 48.5 (SD = 32.0), children = 72.0 (SD = 23.3); d) anxiety with treatment: mothers = 84.6 (SD = 15.4), children = 76.0 (SD = 28.5); e) post-treatment concerns: mothers = 82.0 (SD = 11.5), children = 64.3 (SD = 30.7); f) cognitive difficulties: mothers = 70.8 (SD = 28.1), children = 66.6 (SD = 30.7); g) appearance: mothers = 84.7 (SD = 13.11), children = 66.6 (SD = 28.3) and h) communication: mothers = 67.9 (SD = 24.2), children = 68, 0 (SD = 45.2). Differences were observed between the assessments of mothers and children, especially the pain components, which showed a statistically significant difference in the scores (p = 0.03), with mothers overestimating the absence of pain and anxiety with procedures that appear as one of the most often preserved in the children's evaluation and the least preserved from the point of view of mothers. The level of agreement in these responses was 0% in four aspects (b, c, e, h), 16% in three (a, f, g) and 33% in one (d). This level is low compared to another study in the Portuguese context, which found a minimum of 34% and a maximum of 50% agreement. These data indicate that mothers tend to minimize the difficulties that children experience, believing that their QoL is higher than the level that they evaluate. This is an important indicator of the need for interventions with both parents and children, to facilitate the dialogue and broaden the understanding of the emotional experiences of children by their mothers.

Keywords: Hematopoietic Stem Cell Transplantation, quality of life, mothers, children

P-037

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The operationalization of out of home treatment (OHT) in the State of Ceará

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Introduction: The principle of universality states that health is a citizenship right for all individuals and the state must ensure it, since the principle of integrality requires the conjoining of health and other public policies to ensure an intersectoral action between the different areas that have an impact on health and quality of life of individuals. Objectives: This study aimed to understand the operationalization of the Out-of-Home Treatment (OHT) Program in the state of Ceará, to identify how many public health users from the state of Ceará participated in this program to undergo Bone Marrow Transplantation (BMT) or follow-up in other states of Brazil in 2014, as well as draw a profile of these users by assessing gender, age, city of origin and city of destination. Methods: This is in quantitative study consisting of two phases, literature survey and field research. Tables related to the months of January to December 2014 that included data on patients referred to other states of Brazil were analyzed. Results and Discussion: Of the analyzed tables, it was found that 228 patients were referred from the State of Ceará to other states in Brazil to undergo BMT or to any relevant procedure for patient follow-up. Among the 228 patients, 107 were females and 121 were males. Regarding age, approximately half of the program's beneficiaries were adults, i.e., between 30 and 59 years. Regarding the origin of these patients, the majority comes from the city of Fortaleza, 52%, followed by the municipalities of Redenção, Juazeiro and Itapipoca, each with 4% and Senador Pompeu and Granja, with 3% each. As for the final destination to undergo the bone marrow transplantation or follow-up, the patients that were beneficiaries of the program were sent to five states: São Paulo, Rio Grande do Norte, Paraná, Pernambuco and Rio de Janeiro. The State of São Paulo was the main city of destination for the performance and follow-up of BMT with 74% of cases, followed by the states of Rio Grande do Norte 13%, Paraná with 10%, Pernambuco 2% and Rio de Janeiro with 1% cases. Conclusion: According to the analysis, this study discloses health actions and provides information about a little-known program of relevant significance for the treatment of patients and users of public health policies. The study highlighted the importance of OHT as an effective right regarding the principle of universality of public health policy in the state of Ceará, since all patients who aimed to be sent to other states of the federation to undergo hematological treatment and had bone marrow transplantation indication in 2014 were assisted by the program.

Keywords: Public Health; Out-of-Home Treatment; Bone marrow transplant.

P-038

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Music therapy changes the mood of patients submitted to hematopoietic stem cell transplantation (Controlled Randomized Study)

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Introduction: The allogeneic hematopoietic stem cell transplantation (Alo-HSCT) is a therapeutic medical treatment carried out against several neoplastic hematological disorders, congenital, genetic or acquired. In this procedure, which combines high doses of chemotherapy and/ or radiation therapy and has a high degree of toxicity, the patient goes through a social isolation regimen that causes psychological changes, such as emotional disorders, anxiety, mood disorders, dulled affectivity and altered cognition, which can lead to depression. Objectives: To investigate the impact of live music by applying the techniques of music therapy, and quantify, through the Distress Thermometer, the results of interventions in hospitalized patients undergoing Alo-HSCT. Moreover, to verify whether music therapy can reduce patient anxiety, relieve pain and improve the mood. Methods: Controlled Randomized Experimental Study; n = 50 were randomized to the music therapy experimental group (MEG) and n = 50 for the control group (CG). Live music was applied using the music therapy techniques in (MEG) and the levels of mood, anxiety and pain were evaluated by the tool Distress Thermometer Cancer Patients (Jacobsen et al. 2005) after the end of the music therapy session. In (CG), which did not receive the music therapy intervention, the levels of mood, anxiety and pain were also assessed using the Distress Thermometer. The materials used were musical instruments: the guitar, voice, percussion instruments such as Bongo, Tambourine, caxixi shaker, triangle, egg shaker (rattles shaped like little eggs), and tambourine. Results: To compare the groups (MEG) and (CG) in relation to quantitative variables, the Student's *t* test and Mann-Whitney nonparametric test were used for independent samples. To evaluate the homogeneity of the groups in relation to the distribution of qualitative variable classifications, the chi-square test was used. P values <0.05 were considered statistically significant. Discussion: The patient with a neoplastic hematological disease goes through a great deal of emotional, physical, psychological and social distress. It was observed that the patients feel a lot of anxiety, pain, mood disorders, nausea, insomnia, and the constant fear of death. Using the assessment tool Distress Thermometer, data were statistically analyzed and showed statistical significance in the reduction of anxiety, pain relief and improved mood. With the interactive participation of the patient through musical action, the rhythm provides a psychomotor body movement when playing a percussion instrument and it is believed that this movement can contribute to the bone marrow engraftment, a matter to be investigated. Conclusion: Music therapy has proven to be effective; it improved mood, reduced anxiety and provided pain relief with statistical significance, resulting in biopsychosocial well-being.

Keywords: Distress, Anxiety, Mood

P-039

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Impact of hematopoietic stem cell transplantation on functional capacity and quality of life of patients with systemic sclerosis

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Introduction: Systemic sclerosis (SSc) is an autoimmune chronic disease, which is associated with decreased physical capacity, limitation in the performance of activities of daily living and impaired quality of life of patients. Autologous hematopoietic stem cell transplantation (AHSCT) has been studied as a therapeutic alternative for patients with SSc, resulting in improved skin condition and at least stabilization of pulmonary symptoms. Objective: To evaluate the impact of AHSCT on skin involvement, functional capacity and quality of life in patients with SSc, and compare these results with SSc patients undergoing conventional immunosuppressive therapy. Methods: This is a longitudinal, prospective study carried out at a university hospital in Brazil. SSc patients undergoing AHSCT (transplant group) or conventional treatment (control group) were evaluated initially and re-evaluated 6 and 12 months after the treatment. The evaluation comprised the following items: skin involvement using the modified Rodnan score (mRSS), respiratory muscle strength (maximal inspiratory pressure - MIP and maximal expiratory pressure - MEP), six-minute walk test (6MWT), functional evaluation of hands (hand grip strengthtest, finger-to-palm-FTP, COCHIN questionnaire) and quality of life questionnaire (SF-36). Results: We evaluated 11 patients in the transplant group and 9 in the control group. After treatment, patients in the transplant group showed significant improvement in mRSS variables ($p < 0.0001$), MIP ($p < 0.001$), MEP ($p = 0.0076$), 6MWD ($p = 0.0166$), hand grip strength of the dominant ($p = 0.0001$) and nondominant hand ($p < 0.0001$), FTP in the dominant ($p = 0.0045$) and non-dominant hand ($p = 0.0203$), COCHIN ($p < 0.0001$) and physical component score (PCS) of the SF-36 ($p = 0.0053$). The control group showed no significant change in any of the assessed variables. When the groups were compared after treatment, transplant patients showed significantly better results in mRSS variables ($P = 0.0080$), MIP ($p = 0.0055$), MEP ($p = 0.0329$), distance walked at the 6MWD ($p = 0.0315$), hand grip strength of the dominant ($p = 0.0110$) and non-dominant hand ($p = 0.0020$), COCHIN ($p = 0.0035$) and PCS in the SF-36 ($p = 0, 0438$). There was a significant correlation between the mRSS and distance measurements in the 6MWT ($p = 0.0026$; $R = -0.50$), hand grip strength of the dominant ($p = 0.0002$; $R = -0.59$) and nondominant hand ($p = 0.0007$, $R = -0.55$), FTP in the dominant hand ($p = 0.0014$; $r = 0.53$), COCHIN ($p < 0.0001$, $r = 0.62$) and PCS of the SF-36 ($p= 0.0003$; $R= -0.59$). Conclusion: AHSCT promotes an improvement of skin involvement, functional capacity and quality of life of patients with SSc. The results were significantly better in transplanted patients when compared to patients undergoing conventional treatment.

Keywords: systemic sclerosis, bone marrow transplantation, functional evaluation, physical capacity.

P-040

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Effect of milk protein concentrate on oral mucositis in patients submitted to Hematopoietic Stem Cell Transplantation

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Introduction: Patients undergoing the conditioning regimen for hematopoietic stem cell transplantation have a high incidence of the most severe forms of oral mucositis. The whey protein concentrate is constituted of a series of cell growth factors, including beta transforming growth factors, which comprise a family of milk peptides that contribute to tissue repair. Material and Methods: Based on the hypothesis that dietary supplementation with whey protein concentrate would have the potential to reduce oral mucositis, a prospective study of patients undergoing autologous and allogeneic hematopoietic stem cell transplantation was developed. Patients were supplemented with a daily dose of whey protein concentrate containing 50% of the daily protein requirements according to the Dietary Reference Intakes and later classified regarding the amount of supplement ingested up the median onset of oral mucositis. The National Cancer Institute criteria, version 4.0, was used to classify the occurrence of adverse events and to evaluate oral mucositis, based on the oral toxicity level of the World Health Organization. Results: Of a total of 73 patients submitted to hematopoietic stem cell transplantation were evaluated. Of these, 43 were part of the historical control and 30 were supplemented with whey protein concentrate. Oral mucositis had a mean duration of 5.3 days (SD: 4.5), ranging from the day of the infusion of stem cells until the 17^{th} day after the infusion and median on day 5 after the infusion. The duration of oral mucositis was influenced by the conditioning protocol ($p < 0.01$) and whey protein concentrate ($p = 0.01$). Patients who consumed the whey protein concentrate at an amount equal to or greater than 40% of the daily protein requirements showed a 35% reduction in the duration of oral mucositis ($p = 0.007$) and an 11-fold decrease in the incidence of oral mucositis grades 3 and 4 ($p = 0.004$). The nutritional status and adverse reactions such as diarrhea, nausea and vomiting, dysphagia, xerostomia and sialorrhea showed no statistically significant differences. Conclusion: Therefore, we can evaluate that whey protein concentrate intake greater than or equal to 80% of the period measurements (40% of the daily protein requirement), contributed to reducing the severity and duration of oral mucositis. Further studies in this population are needed in order to assess the supplement action and its real effectiveness.

Keywords: Mucositis, whey protein concentrate, conditioning protocol

P-041

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
It is about time for a hematopoietic stem cell transplantation multidisciplinary team

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The Hematopoietic Stem Cell Transplantation (HSCT) is a highly-complexity procedure whose target audience are patients that have been submitted to previous treatments without success and with intense physical and emotional suffering. The Protected Environment Unit (PEU), where patients stay during hospitalization for treatment, need to constitute a setting that must support anxieties, sorrows, sufferings, real fears of death and uncertainty regarding the outcome of the transplant. Thus, it requires from the multidisciplinary care team a high level of technical development and emotional investment. This report aims to describe an experience of working with a multidisciplinary team of PEU. The intervention was requested by the team itself, through the head of the department, who identified moments of anguish in the presence of suffering of patients, families and occurrence of deaths. It was coordinated by a work psychologist linked to the Occupational Medicine Service, whose goal is to promote the health of employees of the institution. The objectives were to provide a space to listen to the team's experiences while working with HSCT patients, to help recognize feelings that appear in the care relationship and build collective strategies to better face this reality. It comprised a diagnostic phase (3 months), during which preliminary individual interviews were carried out with the medical management and team members; monitoring of the multiprofessional round and subsequent return of the observations and the first reading of the scenario, generating an intervention contract with the team. The diagnosis showed intense cognitive and affective investment by the team; modifications in the teamwork with the addition of new professionals; discussion of cases focused on medical issues; high-demand patients and families; deaths of patients; limits versus high hopes; permanent tension; "race against time"; decision-making; weight of responsibility. The intervention itself, lasted 12 months, with sporadic reflective evaluations, and consisted in encouraging the staff to think about their work process, observing the inclusion of different knowledge and listening to each other; the search for greater cohesion in managements carried out by the team; ongoing experimentation of deeper and more integrated discussion of cases; the psychological dimension of mourning. At the end of the contracted period, the team was able to participate in case discussions more spontaneously and effectively; there was a change in the modes of communication, with a deeper and more integrated understanding of the patient; development of a shared treatment plan and a test to include the experience of patients' death in the round. It is understood that the investment of the PEU team is strongly linked to each professional's motivation and desire to articulate collective and specific actions of care with the patient and their families.

Keywords: multiprofessional team; healthcare team; staff and HSCT

P-042

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The nurse's role at the bone marrow aplasia stage in patients submitted to hematopoietic stem cell transplantation

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Introduction: The hematopoietic stem cell transplantation (HSCT) is the intravenous infusion of hematopoietic progenitor cells aimed to restore bone marrow and immune function in patients with several malignant and nonmalignant disorders, inherited or acquired. During HSCT, diseased stem cells are treated with high-dose chemotherapy associated or not with total body irradiation (conditioning), aimed to reduce or eradicate the patient's underlying disease; to have more physical space within the bone marrow so that engraftment of donor cells (allogeneic), which may be related (family member) or unrelated (another individual) or the recipient's own progenitor cells (autologous) can occur, and cause severe immunosuppression in the recipient to prevent graft rejection. Objective: To describe the nurse's role at the bone marrow aplasia stage in patients after hematopoietic stem cell transplantation. Methodology: This is a report of a nurse's experience working at the protected environment unit in a public hospital in the South of the country, with patients submitted to Hematopoietic Stem Cell Transplantation. Results: The conditioning regimen that results in bone marrow aplasia is the most critical stage, as the patient is subject to hematological toxicities (anemia, neutropenia and thrombocytopenia) and, thus nursing care becomes extremely important for the detection of these complications. Conclusion: Consequently, nurses play an important role, because through their knowledge and careful evaluation, they lead the nursing staff and determine the best interventions for the patient at this critical time of bone marrow aplasia, aiming to prevent risks and minimize damage caused by bleeding and infections.

Keywords: transplantation, stem cell aplasia, nursing

P-043

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Aspects of nursing care for onco-hematological thrombocytopenic patients

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Introduction: The treatment modalities for the onco-hematological patient include chemotherapy, radiation therapy and bone marrow transplantation, which have thrombocytopenia as one of the adverse effects of treatment or the underlying disease. Platelets are cells without nuclei, originating from megakaryocytes and their main function is the platelet plug formation, preventing the individual from dying of hemorrhage and their number varies from 150,000 to 450,000/mm^3. Thrombocytopenia is a decrease in the absolute number of circulating platelets in peripheral blood, characterized as below 150,000/ mm^3. When the platelet count reaches values <50,000/mm^3, it is considered that the patient has a risk of hemorrhage with invasive procedures. Upon reaching values <15,000/ mm^3, the patient is considered at risk of spontaneous bleeding. Objective: To warn about the importance of recognizing the presence of thrombocytopenia, identify the signs and symptoms and recommend the best nursing interventions to be used when treating onco-hematological thrombocytopenic patients. Methods: This is a descriptive study with a qualitative approach based on the review of relevant literature. Results: It was observed that thrombocytopenia may be accompanied by several signs and symptoms, with the most common ones being prolonged bleeding from minor cuts and scrapes or after surgeries, tooth extraction or other invasive procedures; epistaxis; bleeding from the mouth or gums; heavy menstrual bleeding; hematuria; skin petechiae of which emergence is inexplicable; extensive conjunctival bleeding and severe bleeding, such as the digestive (hematemesis, rectal bleeding or melena) and intracranial hemorrhage. Nurses must monitor laboratory tests and thoroughly evaluate the patient regarding alterations that would require interventions to be carried out by the nursing staff. The latter must be able to recognize the main signs of bleeding, as these data can assist in decision-making for the nursing care. Conclusion: Based on this study we conclude that the nursing staff plays an important role in the care of onco-hematologic thrombocytopenic patients because, most often, they are the first to identify early signs and symptoms that may have an impact on the treatment and also reaffirm the importance of nurses in thoroughly and systematically assess the patient to prevent or minimize damage from bleeding.

Keywords: Thrombocytopenia, Nursing, Onco-hematology, Bleeding

P-044

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Clinical and epidemiological aspects related to catheter infection in bone marrow transplantation in a teaching hospital

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Introduction: A central venous catheter (CVC) is essential to perform the hematopoietic stem cell transplantation (HSCT), as the entire treatment is carried out through it. However, the presence of this device is associated with several complications including infectious ones, which can be fatal in HSCT patients due to their weakened defenses. The nurse as an agent that can minimize risks is a key professional to maintain the quality of care and thus, should seek and evaluate evidence on CVC-related complications, as well as the early detection of complications and know the type of microorganism involved in case of infections Objective: To evaluate clinical and epidemiological characteristics related to catheter infection in HSCT in a teaching hospital from 2010 to 2014, describe key factors predisposing to catheter infection in HSCT patients and define the main infectious agents related to CVC infection in transplanted patients. Method: this was a retrospective, exploratory, descriptive study, with a quantitative approach. Data were collected through medical records and information from the Clinical Analyses laboratory records of all inpatients submitted to HSCT in HU-UFJF from 2010-2014 Results: A total of 125 patients underwent HSCT at HU-UFJF in the analyzed period. Most of the assessed patients (93.6%) underwent autologous transplantation. Regarding catheter-related infection, we observed that personal characteristics such as gender, age, diagnosis, comorbidities and social history were not related to the occurrence of catheter-related infections, or those related to treatment, such as duration of neutropenia, type of chemotherapy protocol used and type of catheter (long or short term). However, an association was found between the duration of CVC use, patient hospital length of stay and the occurrence of catheter infection. The catheter-related infection was present in 12% of the analyzed patients. The main causative agent was the gram-positive cocci coagulase-negative *Staphylococcus*. High resistance to penicillin and ampicillin was observed, both in gram-positive cocci, as in Gram-negative rods. Final considerations: The rate of catheter-related infection was lower to that found in other institutions, perhaps associated with the most common type of transplantation performed – the autologous type. The continuity of this study is essential to determine guidelines that will guide the nursing staff in the prevention of CVC-related complications.

Keywords: Hematopoietic stem cells, Nosocomial Infection, Nursing, Bone Marrow Transplantation

P-045

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Importance of nursing care for the patient candidate for hematopoietic stem cell transplantation in a reference center in Ceará.

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Introduction: Hematologic Stem Cell Transplantation (HSCT) is performed to replace a diseased or suppressed bone marrow by another with normal function or to help the patient's recovery after very high-dose chemotherapy. The bone marrow is located within the bones of the central skeleton (skull, vertebrae, ribs, sternum and iliac bones) and the body of the vertebrae, being the place where blood cells originate. Outpatient follow-up is required for a long period after hospital discharge, during which there is the possibility of complications caused by the treatment, in addition to the potential recurrence of the underlying disease. The nursing attention in pre-HSCT period becomes important to increase users' access to the service, to humanize care and to function as a device for the reorganization of the working process and to promote adequate and effective communication with other services and institutions. Objectives: To reorganize nursing attention to patients who are candidates to HSCT, treated at the outpatient clinic. Material and Methods: This is a descriptive, qualitative study of experience report type, carried out during the reception of patients during pre-transplantation consultations in the Hematology Outpatient Clinic located in a Hematology Center, linked to a University Hospital in state of Ceará, Brazil. Results: Currently, the hematology outpatient clinic receives patients from all over the state of Ceará, both through the public and the private health care network. Candidates to transplantation come after being referred from other units or general hematology outpatient clinic, being welcomed by the service nurse. At the first consultation, the following actions are performed: the first appointment is scheduled after checking the medical referral, information is given on the necessary documents, the opening of a medical record is requested and a CBC is scheduled to be collected on the day before the medical consultation. Discussion: The attention provided by the nursing staff on the first contact with the patient radically changes the working process, as the service organization starts to include individualized and good quality care to the users. This scenario opens up the possibility for the professional having the first contact with patient to use basic technology to welcome, listen and solve health problems brought on by the users. Conclusion: The nurse should be able to perform an overall assessment of the patient at the time of the first contact, answer questions regarding the procedure, expectations and give all the necessary guidelines for this process. With a reorganization of the welcoming provided by the nursing service to patients eligible to HSCT, the health service will provide better access at the several stages of clinical treatment in order to keep patients confident and make them feel welcome by the staff and cooperate with treatment.

Keywords: health care, bone marrow transplantation, nursing care.

P-046

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Effective communication strategy in promoting patient's safety post-hematopoietic stem cell transplantation at an outpatient basis.

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Introduction: The hematopoietic stem cell transplantation, HSCT, is a therapeutic alternative for patients with hematological and oncological diseases, which consists in the intravenous infusion of hematopoietic stem cells, aiming at restoring bone marrow function. It is important for the nurse of the HSCT service to provide guidance to the patient and family throughout the entire process, pre, trans and post-transplantation and about the complexity of their treatment. Objectives: To adopt safety measures for the post-HSCT patient during outpatient follow-up, using an effective communication strategy. Material and Methods: This is a descriptive, qualitative, experience report-type study, carried out during the post-transplantation consultations, at the hematology outpatient clinic located in the Hematology Center, linked to a university hospital in the state of Ceará. Results: Nurses from the hematology outpatient clinic adopted some measures during the performed routines aimed at the safety of patients submitted to hematopoietic stem cell transplantation, as follows: checking vital signs, patients' physical integrity condition and general health status, as well as checking adherence to the prescribed drug therapy, whether the guidelines on self-care for patients and their families were being followed, emphasizing the importance of all the steps that favor this type of care, among others. Discussion: Patient safety, defined as "reducing the risk of healthcare-associated unnecessary harm to an acceptable minimum," is a fundamental responsibility of health institutions. Since then, Brazil has used a number of initiatives to increase patient safety and, more recently, in 2013, the country established the National Program for Patient Safety, which determined, among their strategies, the promotion of safety culture through learning and organizational improvement, involving professionals and patients in the prevention of incidents, with emphasis on the creation of safety systems in order to avoid individual accountability. Conclusion: through these measures, we can highlight the importance of the nurse in promoting patient safety in HSCT in order to increase the effectiveness of this procedure and ensure good-quality care for these patients.

Keywords: patient safety, hematopoietic stem cell transplantation, nursing care.

P-047

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing care in the detection of transfusion reactions

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Introduction: Nursing assistance directed at patients after transfusion of blood products aims to prevent and identify reactions and provide greater safety to patients. It is important to mention that this assistance should not only be present in the early and late periods; the monitoring of these patients should be continuous, as reactions can be diagnosed even several years after the transfusion. In situations in which the health care professional suspects a possible reaction, the transfusion should be stopped immediately, venous access should be maintained and a blood sample should be collected for analysis. After confirmation of a transfusion reaction, the National Health Surveillance Agency (ANVISA) provides the notification to the National Hemosurveillance System through NOTIVISA. The nursing staff should be alert to any alteration in the health status of patients, such as fever (defined as an increase of 1 °C); chills; nausea with or without vomiting; chest pain; tachycardia; hypersensitivity or hypotension; dyspnea or tachypnea; skin rash, hives, edema, anaphylaxis and urine color alteration. The appearance of any of these signs or symptoms should be reported immediately by the section nurse to the attending physician. The care provided by the nursing team has great importance for early detection of these reactions, as these professionals are the ones in direct contact with patients during all periods of the procedure. Objective: To demonstrate the importance of nursing care regarding the detection of transfusion reactions. Methods: This is a descriptive study, of the literature review type, carried out by searching the website of the National Health Surveillance Agency, Ministry of Health (Guide to transfusion reactions) in addition to databases (Scielo, Lilacs and VHL), using the following descriptors: “Transfusion reactions” and “health Promotion”, in August 2015. Results and Discussion: Nursing care must be present in all instances of the health service, as it allows the nursing professionals to provide a service that aims to improve the quality of care, focusing on health promotion and aiming to reduce the risks of potential transfusion reactions. It is the nurses’ responsibility to suspect possible reactions, being aware of the signs and symptoms that patients are likely to show. Conclusion: The entire process of transfusion of blood components must be monitored by the nursing staff, as these are the professionals who provide more direct care to patients. It is their responsibility to prevent reactions and monitor these patients to confirm these reactions. As it is a high-complexity process, the consequences caused by the reactions mean high risk of death in these patients.

Keywords: Transfusion reactions, Health promotion

P-048

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services) Graft-versus-host disease - Importance of Rehabilitation

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Summary: The incidence of GVHD and cases of scleroderma in the pediatric population treated with HSCT point to an increasing necessity for early approach of professionals working in the rehabilitation field. The participation of the occupational therapist in the multidisciplinary care team since the pre-transplantation period guarantees the necessary bond to monitor the occupational potential of these patients in order to treat them in the possible occurrence of GVHD in the post-transplant phase. Methods: Based on a brief literature review, questions were raised associated with the rehabilitation of patients with chronic GVHD, which identifies the team's performance with emphasis on the description of the occupational therapist's (OT) role in this area. With the organization of these data, some topics emerge to be studied and reflected upon: how do the OT professionals direct their rehabilitation practices in GVHD; how have the HSCT services incorporated these OT rehabilitation practices; and what are the established researches that have been identified in the rehabilitation area. Discussion: With the study and tabulation of these data regarding the three topics for reflection, there is enough material to describe the approaches used by the OT in GVHD rehabilitation in pediatric patients, as well as the possible interaction with other approaches, such as partnerships with physical therapy, always present in the described protocols. The way these services are being created and how HSCT teams are integrating these actions in the daily life of a transplant unit, are also discussed in this brief review, showing that GVHD assistance in both adults and in children does not lack rehabilitation actions. Finally, many aspects of GVHD rehabilitation must be disclosed in long-term studies with this population, aiming to demonstrate the clinical efficacy of therapeutic actions, especially in the area of OT. Conclusion: After studying and reflecting on the realities of Rehabilitation and Occupational Therapy services described in the reviewed articles, our services are encouraged to walk in this direction, increasingly integrating rehabilitation professionals into transplant units, favoring the integration of essential care required by patients with chronic GVHD, identifying and knowing the role of OT and its importance in the quality of life of these individuals, and giving opportunity for further research to be carried out in this area.

Keywords: GVHD, Occupational Therapy, Rehabilitation

P-049

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing actions supporting the care of individuals with coagulopathies in health services

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Introduction: Inherited coagulopathies are bleeding disorders resulting from quantitative and/or qualitative deficiency of one or more plasma proteins (factors) of coagulation. They have in common the reduction in thrombin formation, an essential factor for blood clotting. General data presented by the Ministry of Health (2011- 2014) on the profile of inherited coagulopathies in Brazil report that currently the total number of individuals with some type of coagulopathy was 17,370, of which 8,848 (50.94%) correspond to hemophilia A; 1.723 (9.92%), to hemophilia B; 4,934 (28.41%), to Von Willebrand disease; and 1,865 (10.74%), to other inherited coagulopathies and other undiagnosed bleeding disorders. This means that health professionals must be trained to treat these patients and the health services should provide good-quality care , seeking to improve the health of these individuals. Objective: To report the relevance of nursing actions, to promote the care of patients with hereditary coagulopathies in the several health services. Methods: This is a literature review carried out at SciELO and VHL databases with the help of the Health Ministry's website, as well as other literature publications relevant to the topic, in July 2015. The following were used as search descriptors: "Nursing Care", "Hemophilia A", "Hemophilia B", "Von Willebrand disease." Results and Discussion: Over the years, the records of individuals with inherited coagulopathies have increased significantly. Although not considered as commonly reported diseases, the health services, mainly in the primary network, as it is considered the gateway to the system, must be prepared to meet this demand. The training of professionals promotes better care, thus being able to meet the individual's actual health needs, while minimizing the risk of sequelae caused by bleeding episodes. Conclusion: The provision of assistance directed to the needs of patients, requires previous knowledge of health demands. Health professionals should always be updated and readily prepared to treat patients with inherited coagulopathies. It is the health professionals' responsibility to provide care from the holistic point of view, where the patient is not seen only as a sick individual, but as a whole. It is important that all health services be prepared to treat individuals with inherited coagulopathies, so they do not depend solely and exclusively on a specialized service.

Keywords: Nursing care, disorders of blood coagulation

P-050

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Experience report: patient health education in physical therapy care in Hematopoietic Stem Cells Transplantation (HSCT)

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INTRODUCTION: The hematopoietic stem cell transplantation (HSCT) is a procedure with a high degree of mortality and comorbidity that requires the attention of a multidisciplinary team. Chemotherapy, radiation therapy and HSCT can lead to some limitations such as bone pain, muscle retraction, shortening and weakness, decreased range of motion (ROM), respiratory disorders and physical deconditioning. In this context, physical therapy monitoring aims to preserve and restore patient functional integrity and to prevent disorders caused by the disease treatment. Health education directed to patients and family members performed during the course of physical therapy care aims at helping to promote health and quality of life during treatment. OBJECTIVES: To describe the importance of patient health education in physical therapy activities for better evolution and prevention of respiratory and motor complications, favoring patient recovery during HSCT. METHODS: A retrospective review of medical records of a public hospital. RESULTS: A 34-year-old patient, diagnosed with ALL, was submitted to syngeneic HSCT. At the late postoperative period, he had left (L) patellar tendon injury with decreased muscle strength, ROM and proprioceptive deficit. He reported frequent falls due to L knee instability and required the use of Canadian crutches. During hospitalization for HSCT, proprioception and balance training were performed, with progression from bilateral to unilateral support, global active, isometrics and self-stretching exercises and gait training. Pulmonary re-expansion breathing exercises, associated with active elevation of the upper limbs were performed. The patient was instructed to perform these exercises daily, to be continued after discharge. The patient showed good adherence to the exercises proposed by the physical therapist. 45 days after the HSCT, the patient was walking 40 minutes, 3 times a week. He had L quadriceps atrophy and L knee flexion limitation; however, without the help of Canadian crutches and no history of falls. DISCUSSION and CONCLUSION: Although the physical therapy goal during HSCT is not the recovery of an orthopedic injury, we believe that in the case of an individual who will undergo a period of severe thrombocytopenia and risk of falls due to joint instability, education becomes essential. We can observe in clinical practice that the patient who becomes the protagonist of his treatment has a better performance and recovery. Monitoring by a physical therapist can provide improvement or even the cure of problems, through light physical exercises, stretching and respiratory exercises and other techniques.

Keywords: physical therapy, education, HSCT

P-051

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Checklist implementation as a safety tool when checking the care routine in hematopoietic stem cell transplantation unit for autoimmune diseases

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Introduction: The implementation of new strategies to improve nursing care and promote team integration with the service to be developed at the unit may lead to a favorable overall outcome of patients with autoimmune diseases undergoing autologous hematopoietic stem cell transplantation. The systematization of the routines and the evaluation of the team's activities through checklists identifies situations that can affect patient safety during the particularities of treatment. Objective: To implement a new strategy to improve nursing care (checklist). Method: Work carried out in three stages, the first being a narrative literature review on the subject in the Lilacs electronic database; the second was the preparation and implementation of the checklist in the form of printed sheet with 71 items, which was bound for the review of the general routine of the unit and the third, the assessment of its impact on care. The study period was from December 1, 2015 to May 31, 2016. The tool was filled out by the nurse on duty in the afternoon shift by verifying the performance of each routine item daily, according to the previously established schedule and known by the collaborators. Results: We identified positive results after implementing the checklist: increase in the so-called preventive maintenance and decrease in the corrective maintenance in equipment; decrease in medication requests outside the standard time; immediate corrections and adjustments of medical prescriptions; decrease in episodes of incomplete or inadequate filling out of medical records and greater integration between the team members. As negative points, we have: initial resistance by some team members to collaborate in filling out; failure to understand between "checking" and "performing" the routine. Discussion: During the check-list implementation assessment, we realized the need for the nurse's insertion into the routine, following the "how" and "when" to do a certain task, in an active and participatory manner, allowing their continuous and ongoing evaluation. The assessment was largely empirical, based on direct observation and through staff reports, as many items have not been previously quantified. The filling out of the 71 items initially required some time to be accomplished; however, as the nurses got more acquainted with the tool, this issue was seen as positive because it enabled them to address important items of the unit. After the adjustment period, the team members disclosed their feelings of belonging, as they had their small day-to-day actions acknowledged as capable of significantly impacting the overall outcome of assistance. Conclusion: We consider valid the implementation of the checklist at the unit aimed to preserve and ensure the continuous improvement of safe patient care.

Keywords: patient safety, transplantation nurse, health management

P-052

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing consultation in the hematopoietic stem cell transplantation service

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Introduction: The Hematopoietic Stem Cell Transplantation – HSCT, is a type of treatment for hematological, oncological, hereditary and autoimmune diseases, which consists in the intravenous infusion of hematopoietic stem cells aimed to restore the patient's bone marrow function and immunity. This type of treatment is, in many cases, the only chance of cure for oncological-hematological patients, with satisfactory results. The HSCT process is quite delicate and complex, requiring the candidate to be evaluated regarding the need for other treatments, increasing the waiting time, which could result in several health risks. The nursing consultation is systematized and includes from the initial contact with the patient to the overall assessment of the service provided, as it is the nurse's responsibility: to collect information, observe, examine, understand and explain the health and disease status before deciding on the nursing diagnosis and nurse therapy. Thus, throughout the process, the nurse is the professional that carries out an extensive work on behalf of the patient follow-up and a close relationship with the candidates and their families, guiding them on the necessary care. Considering the paucity of nursing studies in HSCT, we decided to carry out an experience report supported by the limited available literature, considering that the HSCT Outpatient Unit where we work is a reference in the North and Northeast regions. Objective: To propose nursing consultation and guidance actions on self-care to the HSCT candidates and their family members of a large general hospital in Fortaleza/Ceará. Material and Methods: This is a qualitative, descriptive study, of the experience report type, carried out during the post-transplant consultations, the hematology outpatient clinic located in the Hematology Center, linked to a university hospital in the state of Ceará. Discussion: During the nursing consultation, the anamnesis and physical examination are carried out the candidates and their family members receive information on laboratory tests, radiological examinations, respiratory tests, cardiological evaluation and others according to clinical needs. Conclusion: Due to the critical and unstable status of these patients the nurse who works in the HSCT area should have specific knowledge to develop an appropriate treatment plan, as nurses act decisively at all stages of treatment. Therefore, the nurse's evaluation, in addition to establishing the risk factors related to the assessment, seeks to provide emotional support to the candidates and their family members, valuing and improving the assistance, favoring learning and the development of self-care, consolidating the patient's self-esteem, which is one of the key factors for a successful treatment.

Keywords: nursing consultation, hematopoietic stem cell transplantation

P-053

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Patient Safety: Zero Tolerance for Adverse Events Related to Patient approval process for Hematopoietic Stem Cell Transplantation

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There is a growing concern by health institutions with the implementation of systemic processes to manage risk and improve the safety and quality of patient care. The Hematopoietic Stem Cell Transplantation (HSCT) is a highly complex procedure, associated with substantial morbidity and mortality risks. The approval of the patient for transplantation is a multifactorial and interdisciplinary process that must be carefully analyzed by the multi-professional team, constituting an important action in patient safety. The objective of this study is to demonstrate the use of a continuous improvement method: the PDCA (Plan/Do/ Check/ Act) and its impact on patient safety using the experience report method at a HSCT center in São Paulo, aiming to reduce adverse events related to the approval of the patient for transplantation. The reporting of adverse events subsidizes the process improvement management. In the first half of 2014 5 events were reported within a total of 32 transplants; these events were discussed at a meeting of the quarterly critical analysis of the quality committee. Using the Ishikawa diagram, it was possible to identify the possible causes of events and then propose a plan of action with the aid of 5W2H tool, to be completed by January 2015, of which goal was to reduce 50% of events related to patient approval for the transplantation within 6 months. During the implementation of the action plan, it was possible to observe a significant reduction in adverse events, with an 81% decrease in the number of events in the first half of 2015. Once the first goal is achieved and because it is a continuous improvement, a new and challenging target was proposed: zero tolerance for these events. The last event was reported in January/ 2015, totaling to date 16 months with zero rate of events related to the approval of the patient for transplantation. Among the reported events, 2 were related to hospitalization of patients with infectious focus, 2 admissions with pending pre-HSCT exams, 2 missing notifications for radiation therapy evaluation, 1 missing signed free and informed consent form for the research project and 1 missing immune assessment. The actions performed included: update of the HSCT program operational manual, unit hospitalization and care procedures flowchart, creation of a check-list and table of minimum requirements for conditioning approval. Concomitantly, the care team was trained to implement the process. It is necessary to create systems and backups to prevent or detect faults before they occur, in the areas that constitute the transplantation process: clinical, collection and processing. The creating of robust actions such as the flow chart, checklist and tables were essential to the effectiveness of the actions, providing a safe, effective and centralized assistance to the patient.

Keywords: Quality Management, Patient Safety, Bone Marrow Transplantation

P-054

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Emotional and social vulnerabilities of patients and their families immediately after the Allogeneic Hematopoietic Stem Cell Transplantation

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Introduction: Hospitalization for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) has as characteristics the need for intensive care and a prolonged length of stay in a protected environment unit (PEU). During this period, patients and family members have to live with a series of procedures, interventions and approaches, often invasive and highly technical ones. After discharge from the PEU, at immediate post-HSCT period, patients and their family members must deal with the care management and develop greater autonomy regarding the treatment. At this moment, the team has to face the vulnerabilities expressed by patients and their families, which have an impact on the adherence to the proposed therapy. Objective: This study aims to report the main emotional and social vulnerabilities of patients and their families, identified during the care monitoring period in the immediate post-HSCT period. Materials and Methods: As work methodology, we implemented the weekly multidisciplinary round to discuss cases, identify care demands and develop shared treatment plans. Data from the social and psychological interviews carried out with the patient and family, as well information shared during the rounds are used to identify psychosocial vulnerabilities. These data are recorded in a single electronic medical record, allowing the access of all the members involved in the care process. Results: The main emotional and social vulnerabilities identified were: exacerbation of psychiatric disorders; fragile support network (previously nonexistent or worn out by the illness/treatment process); cognitive difficulties for treatment management; difficulties in patient co-responsibility regarding self-care; difficulty in recovering autonomy; difficulty to have access to essential resources for treatment maintenance such as medications, individual transportation and accommodations close to the hospital; lack of social protection related to work/ income; disruption or deterioration of social and community ties due to the need to move to place far from the city of origin; difficulty to have access to Out-of-Home Treatment (OHT) resources. Discussion: In this context of intense vulnerability, patients and their families need to engage emotional and social resources that will enable them to face the demands of the moment. A vigilant team, attentive to these vulnerabilities, makes it possible to think of guidance and multidisciplinary assistance/educational conducts that will encourage patient co-responsibility and autonomy, aiming to recover their capabilities to manage the self-care process. Additionally, the identification of psychosocial vulnerabilities allows articulating family and social assistance network resources, minimizing adherence difficulties found in post-HSCT monitoring.

Keywords: hematopoietic stem cell transplantation; vulnerability and health; interdisciplinary care team

P-055

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing care in the family context of patients submitted to hematopoietic stem cell transplantation

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Introduction: The Hematopoietic Stem Cell Transplantation (HSCT) is a therapeutic modality used for the treatment of hematological, oncological and immunological diseases, benign or malignant, inherited or acquired. Although the HSCT is performed with high success rates morbidity and mortality cases are perceived in relation to the procedure in its several stages. During the steps that follow the HSCT, patients and families experience moments of anxiety, anguish and uncertainties that can cause stress and interfere with their daily lives. In this context, the nursing staff of the HSCT service plays an important role regarding the planning of actions to guide and train the family members/caregivers in patient-centered care, in addition to the implementation of interventions, always from a perspective that helps or improves their quality of life, as it considers the context in which the patient is placed. Objective: To identify in the literature the nursing care offered to patients undergoing Hematopoietic Stem Cell Transplantation and their families. Method: This is an integrative review, carried out in June 2015, in the SCOPUS, National Library of Medicine (PubMed), Web of Science, Cumulative Index to Nursing and Allied Heath Literature (CINAHL) and Latin American and Caribbean Health Sciences (LILACS) databases, using the descriptors "hematopoietic stem cell transplantation."

Keywords: Nursing Care, Nursing, Family, bone marrow transplantation.

P-056

Cell therapy

Effects of mesenchymal stromal cells on lung vascular function and remodeling in experimental pulmonary arterial hypertension

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Introduction: Although pharmacological therapies can reduce right ventricular pressure in pulmonary arterial hypertension (PAH), they are unable to reduce the remodeling process. We hypothesized that mesenchymal stromal cell (MSC) therapy would lead to beneficial effects on hemodynamics, endothelial dysfunction and remodeling process through growth factor modulation in an animal model of monocrotaline-induced PAH. Methods: 28 Wistar rats were divided into two groups: 1) Control (CTRL) group (n=14) which received saline solution; 2) Monocrotaline (MCT)-induced PAH group, of which animals received 60 mg/kg of MCT intraperitoneally. On day 14, both groups were randomized to receive 105 adipose-derived MSc intravenously (i.v.) (CTRL-MSC and MCT-MSC groups) or saline (i.v.) (CTRL-SAL and MCT-SAL groups), (n=7/group). On day 28, hemodynamics, endothelial dysfunction of the pulmonary artery, lung fibroblast expression of pro-fibrotic mediators, histology of pulmonary parenchyma and arteries, immunohistochemistry for vascular endothelial growth factor (VEGF) and histochemistry for smooth muscle cell proliferation were evaluated. Results: After MSC therapy, right ventricle systolic pressure (38.8±1.8 mmHg, MCT-Sal vs. 28.8±0.7 mmHg MCT-MSC, p=0.0005), lung tissue collagen (36.3±2.2µg, MCT-Sal vs. 26.8±2.6µg, MCT-MSC, p=0.0169, and the histopathological score mainly related to medial hypertrophy [4(4-4), MCT--Sal vs. 2(1-3) MCT-MSC, p=0.0083)] were decreased compared to MCT-Sal. In addition, both smooth muscle cell proliferation and VEGF expression in lung tissue were more reduced in MCT-MSC than in MCT-Sal. Conclusion: In the current model of PAH, MSC therapy not only improved the hemodynamic parameters, but also prevented the lung vascular remodeling process, probably due to reduced expression of VEGF.

Keywords: Pulmonary Artery Hypertension, Mesenchymal Stromal Cells, Cell Therapy, Lung Vascular Remodeling, Hemodynamics, Vascular Endothelial Growth Factor, Monocrotaline

P-057

Cell therapy

Transplantation of bone marrow mesenchymal stem cells inhibits apoptosis and induces cell proliferation and homeostasis between MMP 2 and 9 TIMPs 1 and 2 in the kidney of rats with renovascular hypertension

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Renovascular hypertension (RVH) is caused by renal artery stenosis with subsequent activation of the renin-angiotensin-aldosterone system, and is considered a starting point for systemic arterial hypertension onset. RVH is a progressive disease and, if left untreated, it leads to the establishment of chronic kidney disease (CKD). A picture of fibrosis is commonly found and associated with the presence of inflammatory infiltrate, activation of fibroblasts/ myofibroblasts, tubular atrophy and extracellular matrix deposition. The matrix metalloproteinases (MMPs) have the potential to fragment the deposited extracellular matrix, but also to cleave other substrates, such as growth factors, which paradoxically promote renal fibrogenesis. Recent studies have shown that MMP-2 and MMP-9 can degrade the tubular basal membrane, consisting primarily of laminin and type IV collagen, and damage the integrity of the renal parenchyma, thus promoting CKD progression. Considering the limited number of strategies that can effectively control or delay CKD progression, the use of mesenchymal stem cells (MSCs) became an attractive alternative in cell therapy. In this study, we analyzed the transplantation of bone marrow MSCs in the renal subcapsular region, in an experimental model of renovascular hypertension (clipping of the left renal artery, two kidneys, one clip – 2R1C). Our aim was to evaluate the expression of MMP-2 and MMP-9, as well as the tissue inhibitors of MMPs (TIMPs) types -1 and -2. Wistar rats (n = 18) were divided into 3 groups: Sham, 2R1C and 2R1C + CTM (received transplant after 4 weeks of clipping). Euthanasia occurred 2 weeks after transplantation (week 6), when the kidneys were collected and processed for microscopic assessment and Western blotting. The expression of MMP-2, MMP-9, TIMP-1, TIMP-2, Bcl2 and Bax were analyzed by western blotting, together with the analysis of the proliferating cell nuclear antigen (PCNA) and type IV collagen by immunohistochemistry. Our results showed a significant reduction in type IV collagen in the clipped kidney and increased cell proliferation in both the cortical and medullary regions, after transplantation of the MSCs. We also observed a decrease in the expression of MMP-2, MMP-9 and bax proapoptotic protein, associated with an increase in TIMP-1, -2 and Bcl2 anti-apoptotic protein. Thus, we conclude that a single transplantation of MSCs in the subcapsular region of the kidney, using a 2R1C model, was able to improve the renal parenchyma architecture by reducing fibrosis, decreasing the expression of MMP-2 and -9, together with an increase in TIMP-1 and -2. We also observed an increase in cell proliferation associated with a decrease in apoptosis.

Keywords: Renovascular hypertension, 2R1C, mesenchymal stem cell, metalloproteinases

P-058

Cell therapy

Oxysterols in adipose tissue-derived mesenchymal stem cell proliferation and death

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Oxysterols in adipose tissue-derived mesenchymal stem cell proliferation and death Introduction: Mesenchymal stem cells (MSCs) are multipotent cells characterized by self-renewal and cell-differentiation capabilities. Oxysterols comprise a very heterogeneous group derived from cholesterol through enzymatic and non-enzymatic oxidation. Potent effects on cell death processes, including cytoxicity and apoptosis induction have been described in several cell lines. Very little is known about the effects of oxysterols on MSCs. 7-keto- cholesterol (7-KC), one of the most important oxysterols, has been shown to be cytotoxic to human adipose tissue-derived MSCs. Objective: we describe the short-term (24 h) cytotoxic effects of cholestan-3α-5β-6α-triol, 3,5 cholestan-7-one, (3α-5β-6α)-cholestane-3,6-diol,7-oxocholest-5-en-3-beta-yl acetate, and 5β-6β epoxy-cholesterol on MSCs derived from human adipose tissue. Methods: Human adipose tissue-derived MSCs were obtained from three different donors (n=3) from LIM31 pattern inventory. Several concentrations of oxysterols were added, followed by incubation for another 24 h. The Annexin V: FITC Apoptosis Detection Kit 1 was used to determine the percentages of apoptotic cells and cell viability. Caspase-3/7 activity was measured using the NucView 488 Caspase-3 Assay kit for live cells. TRME was used to evaluate the transmembrane mitochondrial potential. Cell cycle evaluation with Hoechst 33342 and changes in actin organization were investigated using Alexa Fluor 488 phalloidin. Autophagy was studied through LC3B antibody. KI67 antibody was used to perform proliferation assay. Results: 3,5 cholestan-7-one and 7-oxocholest-5-en-3-beta-yl acetate did not promote cell death or affected cell proliferation. The other oxysterols led to a complex cell death mode that could include apoptosis, necrosis and autophagy, depending on the type and concentration of oxysterol. Cholestan-3α-5β-6α-triol was the most effective one. Proliferation inhibition was also promoted by these oxysterols, but no changes in cell cycle were observed. Conclusion: The effects observed depend on the type of oxysterol and the concentration used.

Keywords: oxysterol, mesenchymal stem cell, apoptosis, cell death

P-059

Cell therapy

Polyunsaturated Fatty Acids Potentiate the Beneficial Effects of Mesenchymal Stromal Cells in Experimental Asthma

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RATIONALE: Asthma is a chronic inflammatory disease characterized by inflammatory and remodeling processes that leads to a progressive deficit of lung function. So far, no therapy has been able to revert the remodeling process in asthma patients. In this context, the use of mesenchymal stromal cells (MSCs) is a promising strategy that has shown reduction of airway inflammation and remodeling in experimental asthma. However, MSCs are unable to revert airway fibrosis in asthma models. Therefore, stimulation of MSCs may be regarded as a potential strategy to repair lung damage. We hypothesized that metabolites derived from polyunsaturated fatty acids (PUFAs) stimulate MSCs and potentiate their therapeutic effects in experimental allergic asthma, thus enhancing their anti-inflammatory and antifibrogenic properties. METHODS: Asthma was induced in twenty-four C57BL/6 mice by intranasal challenges of house dust mite extract (HDM; 25 µg in 25 µL) three times a week for three weeks. Control groups received only saline solution (25 µL) using the same protocol. Twenty-four hours after the last challenge, the HDM group were further randomized to intravenously receive saline solution (50 µL, SAL, n=6/each), bone marrow-derived MSCs (10 5, BM-MSCs, n=6/each), or bone marrow-derived MSCs stimulated with PUFA for 6h (10 5, BM-MSC- PUFA, n=6/each). Three days after treatment the following parameters were evaluated: 1) morphometry and collagen fiber content in airways and lung parenchyma, 2) levels of interleukin (IL)-4, IL-13 and vascular endothelial growth factor (VEGF) expression in lung tissue and bronchoalveolar lavage fluid (BALF), 3) total and differential cell count in lung tissue, BALF, mediastinal lymph nodes (mLN), thymus, and bone marrow, 4) airway resistance, viscoelastic pressure and static lung elastance and 5) airway mucus secretion. RESULTS: Both cell therapies, in comparison to HDM-SAL, led to a reduction in static lung elastance, alveolar collapse, bronchoconstriction index, mucus secretion, inflammatory cell infiltration in lung tissue, BALF, mediastinal lymph nodes (mLN), thymus and bone marrow, collagen fiber content in lung parenchyma (but not in the airways) and levels of IL-4, IL-13, and VEGF. All these parameters were significantly more reduced in BM-MSCs-PUFA when compared to BM-MSCs CONCLUSION: In the present model of asthma, even though BM-MSCs reduced lung inflammation and remodeling, BM-MSCs associated with PUFA led to further reduction. These results provide a basis for subsequent cell therapy investigations.

Keywords: Asthma, cellular therapy, mesenchymal stromal cell, polyunsaturated fatty acid

P-060

Cell therapy

Embryonic stem cell-derived cardiomyocytes improve cardiac function in a mouse model of doxorubicin-induced cardiomyopathy

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Background: Doxorubicin (Dox) is a chemotherapy drug with limited use due to cardiotoxicity that may progress to heart failure. Objective: This study aims to evaluate the role of cardiomyocytes derived from mouse embryonic stem cells (CM-mESC) in the treatment of Dox-induced cardiomyopathy (DIC). Methods: Mouse embryonic stem cells (mESC) line E14TG2A was characterized by karyotype analysis and expression of pluripotency genes by RT-PCR and Immunofluorescence. Cells were transduced with luciferase 2 (luc2) and submitted to cardiac differentiation. For the establishment of DIC in CD1 mice, different doses of Dox (4.0 or 7.5 mg/kg) and routes of administration - intraperitoneal or intracavitary (left ventricular cavity) were tested. Dox was delivered once a week for 3 weeks. In the 4th week, a group of animals was injected with CM-mESC (8x105 cells, intramyocardially) and cells were tracked by bioluminescence assay and body weight, ECHO and ECG were recorded. Results: mESC showed normal karyotype and expressed pluripotent markers. CM-mESC had action potentials with prevalence of ventricular cells. Mice that received 4.0 mg/kg Dox through both routes did not develop heart failure. Mice that received 7.5 mg/kg Dox intraperitonally did not survive. However, mice that received 7.5 mg/kg Dox through an intracavitary injection developed heart failure 3 weeks after Dox injection, showing significant reductions in body weight, ejection fraction (EF), stroke volume (SV) and heart rate (HR), and significant increases in end-systolic volume (ESV) and QT and corrected QT (cQT) intervals. Dox-group treated with CM-mESC showed significant increases in EF and SV and significant reductions in QT and cQT intervals 30 days after treatment. Cells were detected up to 11 days after injection. Conclusion: CM-mESC transplantation contributes to cardiac improvement in DIC.

Keywords: Dox-induced cardiomyopathy, heart failure, cardiomyocytes derived from mouse embryonic stem cells, cell therapy

P-061

Cell therapy

Bone marrow, adipose and lung tissue-derived mesenchymal stromal cells yield diverse effects on lung inflammation and remodeling in experimental allergic asthma.

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Rationale: Different sources of mesenchymal stromal cells (MSCs) generally meet accepted criteria for MSCs definition, but MSCs can be distinguished by cytokine production and gene expression and therefore may promote different effects on asthma. Aim: The aim of this study is to investigate the effects of MSC from bone marrow, adipose and lung tissues on inflammatory and remodeling processes in experimental chronic allergic inflammation. Methods: 48 female C57BL/6 mice were randomly assigned into eight groups. In the OVA group, mice were sensitized and challenged with ovalbumin, while the control group (C) received saline using the same protocol. C and OVA groups were further randomized into four subgroups receiving saline (50 μL, SAL, n=6/each), bone marrow-derived mesenchymal stem cell (105, BM-MSC, n=6/each), adipose tissue-derived mesenchymal stem cell (105, AD-MSC, n=6/each) and lung tissue-derived mesenchymal stem cell (105, L-MSC, n=6/each), intratracheally, 24 hours after the last challenge. Airway and lung parenchyma remodeling were evaluated by quantitative analysis of collagen fibers. Additionally, total and differential cellularity in the bronchoalveolar lavage fluid (BALF) and in the tissue were measured. Furthermore, the levels of interleukin (IL)-4, IL-13, transforming growth factor (TGF)-β and vascular endothelial growth factor (VEGF) in lung tissue, as well as static elastance, viscoelastic pressure and airway resistance and hyperresponsiveness were analyzed. Finally, *in vitro* experiments were performed to evaluated macrophage polarization, basal levels of different growth factors [VEGF, insulin-like growth factor (IGF) and platelet-derived growth factor (PDGF) and cytokines (IL-4 and eotaxin) produced by each cell type, as well as after stimulation with serum obtained from asthmatic mice. Results: MSC therapies led to a reduction in resistive and viscoelastic pressures, airway hyperresponsiveness, alveolar collapse, bronchoconstriction index, inflammatory cell infiltration, collagen fiber content in lung parenchyma (but not in the airways) and levels of IL-4, IL-13, TGF-β and VEGF compared to OVA-SAL. However, these decrements were more pronounced after BM-MSC, when compared to AD- MSC and L-MSC therapies. In addition, L-MSC showed higher basal levels of cytokines and growth factors when comparing BM-MSC and AD-MSC, whereas stimulation with asthmatic serum promotes a higher reduction of these parameters in the BM-MSC compared to other cell types. Conclusion: In the present model of chronic allergic asthma, MSC therapies were effective at modulating the inflammatory and fibrogenic processes; however, lung mechanics and the remodeling process showed greater improvement after BM-MSC, when compared to AD-MSC and L-MSC therapies, probably due to higher immunomodulatory response shown by the BM-MSCs.

Keywords: mesenchymal stromal cells, allergic asthma

P-062

Cell therapy

Effects of Two Doses of Bone Marrow-Derived Mesenchymal Stromal Cells in a Model of Elastase-Induced Severe Emphysema

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Rationale: Emphysema is characterized by airspace enlargement, parenchymal destruction and impaired pulmonary regeneration. Preclinical studies have shown that a single dose of bone marrow (BM)-derived mesenchymal stromal cells (MSCs) decreases inflammation and apoptosis in experimental emphysema, with controversial findings regarding effects on the remodeling process. We hypothesized that two doses of MSCs would be more effective than a single dose in reducing inflammation, elastolysis, and fibrogenesis, thus improving lung mechanics in a model of severe emphysema. Methods: Forty-eight female C57BL/6 mice were randomly assigned to two groups. In the emphysema (E) group, mice received 0.2 IU of porcine pancreatic elastase once a week for 4 weeks, whereas controls (C) received saline solution, intratracheally, following the same protocol. One day after the last administration of saline or elastase, C and E groups received SAL or MSCs (2x106) intratracheally once or twice, with a one-week interval between doses. One week after the last administration of SAL or MSC, the animals were anesthetized and cardiopulmonary morphofunction was evaluated. Total and differential cell counts were performed in bronchoalveolar lavage fluid (BALF), thymus, and bone marrow samples. Results: One week after the last treatment, MSCs resulted in no beneficial effects concerning reduction in static lung elastance induced by emphysema. However, MSCs reduced the mean linear intercept [E-SAL: 50.3±6.7μm, MSC-1 dose: 33.4±2.8μm, MSC-2 doses: 21.8±7.2μm ($p<0.05$)] and collagen deposition in the small airways (MSC-1 dose: 39.3%, MSC-2 doses: 67.8%), while increasing elastic fiber content (MSC-1 dose: 191.4%, MSC-2 doses: 267.2%), compared to E-SAL group. Differences between doses were also observed in hyperinflated areas, with a 25.9% reduction in MSC-1 dose group vs. 89.4% in MSC-2 doses. Echocardiography revealed increased right diastolic ventricular area in the E group compared to C. Only two doses of MSCs reduced right diastolic ventricular area compared to E-SAL. In the bronchoalveolar lavage fluid, MSCs significantly decreased total cell counts in MSC-1 group without significant differences in macrophages, neutrophils and lymphocytes. Animals in the E group exhibited increased thymus weight (58.6% compared to C), an effect mitigated only in MSC-2 doses. No differences in total or differential bone marrow cell counts were observed between groups. Conclusion: In this elastase-induced model of severe emphysema, MSC therapy did not significantly improve pulmonary mechanics, but mitigated lung inflammation, fibrosis and elastolysis. The number of MSC doses led to significant beneficial effects on cardiac function, decreasing fibrogenesis and increasing elastogenesis. Our study suggested that repeated doses of MSC therapy were required to improve cor pulmonale associated with emphysema.

Keywords: Stem cells, emphysema, mesenchymal cells

P-063

Cell therapy

Induced pluripotent stem cells improve experimental chronic kidney disease, but give rise to Wilms tumors.

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Introduction: Although being the treatment of choice, renal transplantation has organ shortage as the most important impediment and moreover, the long-term adverse effects of maintenance immunosuppression. Dialysis is an expensive treatment and provides inferior quality of life than transplantation. It has been previously shown that rats with CKD treated with bone marrow-derived mesenchymal stem cells (MSC) injected into the renal parenchyma showed disease progression stabilization. Although MSC have the capacity for site-specific differentiation into several tissue types, they are limited by the low number of cells available at the injured site and therefore, the perspective of utilizing other stem cells has attracted substantial interest. Recently, it was demonstrated that pluripotent cells could be produced from cultured somatic cells preserving all the properties of ES cells. The development of the iPS technology circumvented some ESC hurdles and opened new promising therapeutic possibilities to produce cells suitable for use in regenerative therapy. But until now, the therapeutic effect of induced pluripotent stem cells (iPS) on the progression of experimental chronic kidney disease (CKD) has not been demonstrated yet. The objective of the present study was to evaluate iPS efficacy to stop the progression of chronic kidney disease when compared with mesenchymal stem cells (MSC). Material and Methods: Untreated 5/6 nephrectomized female rats were compared with CKD animals receiving the same amounts of MSC or iPS cells. Renal function, histology, immunohistochemistry and gene expression were studied in the remnant kidney. Implanted iPS cell were tracked by the SRY gene expression analysis. Results: Both treatments minimized increase in serum creatinine, significantly improved clearance and slowed down progression of disease on day 60 after surgery. The proteinuria was significantly reduced only in the iPS group. Both treatments reduced glomerulosclerosis, iPS decreased macrophages CD68+ and TGF-β was significantly reduced in rats from the MSC group. Both types of treatments increased VEGF gene expression, TGF-β was upregulated only in the iPS group and IL-10 had low expression in both groups. The SRY gene was found in 5/8 rats treated with iPS. These 5 animals showed tumors with histology and cells staining highly positive for PCNA and WT-1 antibody, characteristics of Wilms' tumor. Conclusions: We concluded that iPS cells may be efficient in ameliorating CKD, but still carries the risk of Wilms' tumor development.

Keywords: CKD, iPSCs, MSC, Wilms tumor, Cell Therapy

P-064

Cell therapy

Magnetic targeting increases lung retention of mesenchymal stromal cells in a murine model of silicosis

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Magnetic targeting technique (MT) has been shown to increase mesenchymal stromal cells (MSCs) engraftment in target organs, promoting their long-term retention and optimizing cell therapy effects. Despite its potential, to date MT has not been explored in pulmonary diseases. Thus, this study aimed to evaluate the effects of MT of MSCs in a murine model of silicosis. For this purpose, twelve C57Bl/6 mice were intratracheally instilled with saline solution (Ctrl) or silica particles re-suspended in saline (Sil). After 15 days, Sil mice were treated intravenously with saline (Sil-SAL) or 105 MSCs (Sil-CELL). These MSCs were previously incubated with iron oxide nanoparticles (IO-NPs), diluted to 80 μg/mL, for 24 hours, becoming magnetically responsive. Immediately after MSCs injection, some animals received external neodymium magnets around the thorax (Sil-CELL-Mag). Forty-eight hours after MSCs instillation, pulmonary mechanics were evaluated and lungs removed for histological analysis and iron quantification. Sil-CELL and Sil-CELL-Mag mice had higher amounts of iron in the lungs; however, more in the Sil-CELL-Mag group when compared to Sil-CELL, as demonstrated by the iron measurement (Ctrl:34.3±5.1; Sil-SAL: 30.3±6.7; Sil-CELL: 64.5±5.4; Sil-CELL-Mag: 81.4±1.5 μg of iron per gram of lung tissue) and histological analyses with Prussian blue staining. Concomitantly, we observed a qualitative reduction in alveolar thickening in Sil-CELL-Mag group compared to the Sil-SAL group. Additionally, Sil-CELL-Mag group showed a significant reduction in static lung elastance (Ctrl: 27.9±1.5; Sil-SAL: 37.9±10.6; Sil-CELL: 33.6±2.7; Sil-CELL-Mag: 28.5±5.1cmH2O. mL-1) when compared to Sil-SAL group. Viscoelastic pressure was reduced in CELL groups regardless of Mag (Ctrl: 0.69±0.14; Sil-SAL:1.23±0.15; Sil-CELL: 0.70±0.11; Sil-CELL-Mag: 0.71±0.08 cmH2O). These data suggest a greater MSC retention in Sil-CELL-Mag group; however, this increased retention provided no enhancement in lung function, when compared to the Sil-CELL group. MSCs improved lung mechanics regardless of the use of MT, due to the fact that the analysis was performed after 48 hours (early in the course of therapy), during which MSC paracrine effects are still present. Our study warrants long-term analysis in order to better assess the possible beneficial effects associated to MSC retention.

Keywords: Silicosis, cell therapy, iron oxide nanoparticles, magnetic targeting.

P-065

Cell therapy

Viability evaluation of bone marrow-derived mesenchymal stromal cells after exposure to 0.3 Tesla static magnetic fields

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Magnetic targeting technique (MT) has been increasingly explored in stem cell-based therapies, as it increases cell retention in target organs. However, static magnetic fields (SMF) used in MT cause effects on the viability of several cell types. Thus, this study aimed to evaluate the viability of mesenchymal stromal cells (MSCs), labeled or not with iron oxide nanoparticles (IO-NPs), after exposure to SMF. For this purpose, MSCs isolated from bone marrow of C57BL/6 mice were initially divided into two groups: control (ctrl) and magnetized (mag). MSCs of the mag group were incubated with IO-NPs diluted to 80 μg/mL for 24 hours, thereby becoming magnetically responsive. Subsequently, 4x104 mag and ctrl MSCs were seeded in 12-well plates with or without a pair of 0.3 Tesla circular neodymium magnets in each well. After 24, 48, 72, and 96 hours, MSCs were assessed for viability by methylthiazol tetrazolium (MTT) assay, trypan blue exclusion assay and using optical microscopy to analyze morphology. According to MTT assay, mag MSCs had a significant viability loss after exposure to the magnets' SMF, during all exposure times (from 75-80%, compared to unexposed ctrl cells). No changes were observed in the other experimental groups. However, trypan blue assay data showed that at least 97% of mag MSCs remained alive after exposure to the SMF, at all time points, whereas similar values were observed in other experimental groups. In addition, there were no qualitative changes in shape and size of mag MSCs after exposure to SMF, regardless of time point analysis. These results suggest that exposure of magnetized MSCs to SMF affected their mitochondria, even though not enough to induce apoptosis. Future tests should be performed to better evaluate different markers of cell death, as well as other effects of MT on MSCs.

Keywords: Magnetic targeting, Mesenchymal stromal cells, Iron oxide nanoparticles, biocompatibility

P-066

Cell therapy

In vitro comparative study of human mesenchymal stem cells from adipose and dermal tissues for application in cutaneous wound healing

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INTRODUCTION: Mesenchymal stem cells (MSC) participate in the homeostasis and repair of adult tissues. Due to their potential, they are broadly studied for their application in regenerative medicine. Therefore, the source of MSC influences the achieved efficiency, as well as *in vitro* characteristics and therapeutic properties. Adipose tissue is a well-known source of MSC, having been used in some clinical studies of wound healing. However, dermis represents a promising alternative source of these cells, which has been poorly described in literature. OBJETIVES: The aim of this study was to comparatively investigate the *in vitro* characteristics of MSC derived from human adipose (ASC) and dermal (DSC) tissues from the same donors and evaluate their possible application in cutaneous wound healing. METHOD: ASC and DSC were obtained from skin samples discarded from abdominoplasties at the University Hospital of Santa Catarina Federal University (Florianópolis, Brazil). Cells were evaluated regarding the achieved efficiency, cell morphology, proliferation, phenotypic profile, differentiation potential, nuclear stability, biocompatibility to the dermal regeneration template Integra® and *in vitro* wound healing capacity. RESULTS: 16-fold more ASC were obtained per skin fragment than DSC. Both ASC and DSC displayed fibroblastic morphology, plastic adherence, and colony forming ability *in vitro*. In addition, both cell types showed similar population doubling time (48 hours), were positive to mesenchymal markers CD73 and CD90 and negative to the hematopoietic markers CD34 and CD45. Moreover, they were able to differentiate into adipocytes, osteocytes and chondrocytes. Less than 4% of both MSC proliferating cells showed nuclear alterations. ASC and MSC were able to adhere to and proliferate in the commercial dermal regeneration template (Integra®) in 3D culture system. The *in vitro* wound healing potential was verified by cell scratching assay after 24 hours, in which DSC closed 77% of the wound, while ASC closed 55%. DISCUSSION: The results showed that the isolation of MSC from adipose tissue is more efficient than from the dermis. However, when ASC and DSC were compared *in vitro*, they displayed similar morphology, proliferation, phenotypic profile and differentiation potential. Both cell populations showed nuclear stability *in vitro*, suggesting that they are safe for transplantation. In addition, the ASC and DSC can be effectively cultured in a 3D substrate for future therapeutic uses. Nevertheless, DSC were more efficient in closing the *in vitro* wound than the ASC. CONCLUSION: Despite the higher efficiency of isolation protocol for ASC when compared to DSC, both of them display mesenchymal stem cell characteristics and are equivalently biocompatible to the dermal template Integra®. The higher efficiency in *in vitro* wound healing of DSC in comparison to ASC might indicate that the dermis could be a better source of MSC in future cutaneous wound healing applications. CEP/UFSC: 1.076.62

Keywords: MSC, characterization, cell scratch, source.

P-067

Cell therapy

Evaluation of the healing process and immunomodulatory action of mesenchymal stromal cells from adipose tissue when adhered to suture strands and used in the treatment of enterocutaneous fistulas

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Enterocutaneous fistulas are difficult to heal and bring a lot of inconvenience to patients, making their treatment difficult. The surgical treatment is often flawed, causing the fistula to recur. The healing process occurs in a coordinated manner through cell, molecular and biochemical events, which act jointly to reconstitute the damaged tissue. Therefore, mesenchymal stromal cells (MSCs) may be a new treatment in the healing of fistulas. MSCs are capable of self-generation and have a high proliferative capacity and can differentiate into several cell lineages; besides having immunomodulatory capacity providing a paracrine effect and being easily obtained from adipose tissue (AT). This study aims to evaluate the mechanisms by which a better and faster healing of fistulas occurred when the sutures with AT-MSCs adhered to them were used in a murine model of enterocutaneous fistula. The AT-MSCs were obtained from liposuction procedures. After the characterization according to the International Society for Cell Therapy (ISCT "Mesenchymal and Tissue Stem Cell Committee") the cells, 1x10e6 AT-MSCs were adhered to polyglactin sutures (4-0 Vicryl Poly/ Polyglactin 910) with the help of a special formulation fibrin glue. The animal experiment was carried out in Wistar male rats, which were divided into 3 groups of 5 animals each, and one group was euthanized on day 7, the other on day 14 and the last on day 21. In all groups, the suture used to "construct" the fistula contained AT-MSCs adhered to it. After euthanizing the animals, histological slides were made. Histological sections were stained with H.E for analysis of cell morphology. Immunohistochemical tests were performed with markers for VEGF, COL1, COL3, MMP9, IL-6 and TNF-alpha proteins. The results and analysis of slides stained with HE showed that on day 7, many neutrophils were present in the lesion, with the connective and muscular tissue trying to organize, presence of blood vessels and the formation, at the site of the lesion, of a tissue similar to AT, which is not found in this region of the intestine. On day 14, we observed the formation of more specialized epithelium, a reduced neutrophil count, with organized conjunctive tissue and basal lamina formation. On day 21 we observed the presence of many blood vessels, a very specialized epithelium with goblet cell formation and a region with morphological characteristics very close to normal.

Keywords: mesenchymal cells, enterocutaneous fistula, suture, cell therapy, stem cells

P-068

Cell therapy

Assessment of the viability of bone marrow stem cells of obese Swiss mice treated with IGF-1

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Obesity is associated with several changes in organs and tissues and has recently been associated with bone marrow alterations. The ongoing process of blood cell production, hematopoiesis, occurs in the bone marrow. For that, hematopoietic stem cells are regulated by microenvironmental factors important for cell survival, proliferation and differentiation. Bone marrow cells (BMCs) of obese mice are in a niche with limited angiogenesis and low levels of oxygen, which leads to the release of inflammatory cytokines by adipose tissue, interfering with the proliferative capacity and leading to increased cell death. The insulin-like growth factor 1 (IGF-1) is involved with a decrease in apoptosis and increased cell proliferation. Our group has demonstrated a reduced viability of BMCs of Swiss mice submitted to the Western diet. Therefore, treatment with IGF-1 would be capable of stimulating the reduction in apoptosis of BMCs from obese individuals and, thus, restore cell viability. Therefore, the objective of this study is to evaluate the viability and amount of stem cells from the bone marrow of obese mice induced by the Western diet and treated with IGF-1, through flow cytometry. After weaning, Swiss mice (n = 32) were divided into 4 groups: CG, OG, CG treated with IGF-1 and OG treated with IGF-1. The suspensions of cells isolated from bone marrow were incubated with Annexin V to detect apoptosis. For the quantification of stem cells, hematopoietic stem cells were labeled with the c-kit antibody and mesenchymal stem cells with the CD105 antibody. Fluorescence data were collected from a flow cytometer (BD-Accuri, BD Biosciences). The results were expressed as mean ± SEM, and differences between groups were analyzed by One-Way followed by Tukey's test, with $P < 0.05$ being considered as statistically significant. The results demonstrated that the proportion of Annexin V + (positive) of BMCs (4,429 ± 1,236) and of the sub-population of stem cells (SC) (0.3843 ± 0.1686) found in the bone marrow of obese mice treated with IGF -1 was significantly lower compared to the untreated OG (26.74 ± 2.851, 7.614 ± 1.273), respectively; and that the animals from the OG (25.39 ± 4,553) and OG + IGF (27.56 ± 5,969) showed a significantly higher percentage of hematopoietic cells compared to the CG (9.865 ± 1.303) and CG + IGF (7,468 ± 1,303). No difference was observed in the percentage of mesenchymal stem cells between the groups. IGF-1 reduces cell death, confirming the benefit of recovering cell viability and ensuring the preservation of the number of BMCs; and obesity leads to the stimulation of hematopoietic stem cell production, suggesting a need for a higher supply of blood cells in obesity.

Keywords: Obesity, cell viability, insulin-like growth factor 1

P-069

Cell therapy

VEGF electrospun scaffolds maintain the immaturity of endothelial progenitor cells

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In severe cases of peripheral arterial diseases, tissue loss can occur. In these situations, implantation of a vascular graft may be required. Electrospun scaffolds functionalized with biomolecules, such as heparin and vascular endothelial growth factor (VEGF), exhibited adequate properties for vascular use and improved vessel regeneration, preventing graft failure. Endothelial progenitor cells (EPCs) have a critical role in endothelium homeostasis, showing a high vessel-forming ability. VEGF increases the adhesion and proliferation of EPCs on the scaffold surface. However, to date, the effects of VEGF scaffolds on gene expression of EPCs have not been reported. Thus, the aim of this study was to evaluate the effects of scaffolds containing VEGF on EPCs gene expression. Materials and methods: Scaffolds were produced by electrospinning using poly(caprolactone) (PCL). The scaffolds were then hydrolyzed and immersed in 1% heparin solution. Subsequently, they were immersed in 1 μg/mL VEGF solution. Four groups of scaffolds were evaluated: (I) PCL, (II) hydrolyzed PCL, (III) hydrolyzed PCL, functionalized with heparin and (IV) hydrolyzed PCL, functionalized with heparin and VEGF. EPCs isolated from umbilical cord blood were seeded onto the scaffolds at a density of 5 x 10^5 cells/sample and cultivated at 37ºC in 5% CO_2. After 15 days of cultivation, total RNA from each sample was extracted using Trizol reagent. Complementary DNA was synthesized from 2 μg of total RNA using reverse transcriptase M-MLV kit. RT-PCT was performed using Platinum sybr green supermix kit. The expression of the genes CD31, CD34, von Willebrand factor (vWf) and VE-cadherin was analyzed. The genes were normalized to the house-keeping gene β-actin and the relative quantification of mRNA was determined by ΔΔCT. Results: The EPCs exhibited a reduction of fvW expression in all of the scaffold groups. All four groups caused an increase in VE-cadherin expression. This shows that the tridimensional cultivation, using scaffolds, favors contact between the cells. When the CD31 was analyzed, it was possible to observe that groups I, II and III exhibited an increase in their expression, while the cultivation on scaffolds II and III caused a reduction in CD34 expression. The cells cultivated in the group functionalized with VEGF did not show significant changes in the expression of these two genes, compared to the control (culture plate). These results suggest that the cultivation of EPCs on scaffolds results in their differentiation into mature endothelial cells, as demonstrated by the increased expression of the mature cell marker (CD31) and reduction of the progenitor cell marker (CD34). Group IV maintained the immaturity of the EPCs. Conclusion: VEGF presence on the scaffold surface was able to maintain the profile of EPC gene expression. The association of VEGF with electrospun scaffolds maintains the ability of EPCs to form the endothelial layer and regenerate damage vessels.

Keywords: vascular scaffolds, endothelial progenitor cells, electrospun substitutes

P-070

Hematology – malignant diseases

How nursing care to the individual with sickle-cell anemia has been discussed in the literature: an Integrative Review

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Introduction: Sickle-cell disease is a generic term that encompasses a group of hereditary hemolytic anemias characterized by the structural alteration in the beta-globin chain leading to the production of an abnormal hemoglobin, called HbS (hemoglobin S). This sickling of red blood cells is one of the main mechanisms responsible for the entire pathophysiological picture of the disease, which translates as chronic hemolytic anemia, vaso-occlusive phenomena, painful crises, immunological alterations and multisystem involvement. The nursing staff, during the direct care to individuals with sickle-cell anemia, aims to relieve pain based on a comprehensive evaluation of these individuals. Objective: To characterize the scientific production in online articles about the nursing care provided to individuals with sickle-cell disease. Material and Methods: This is an integrative literature review. The search for the references was carried out in the Virtual Health Library (VHL), and used the following descriptors: nursing care, pain, sickle-cell disease, with the following inclusion criteria: full text, in English, Spanish, French and Portuguese, published from 2009 to 2013. A toal of 19 articles were selected. Results: For the analysis, a summary table was prepared with the selected articles and, subsequently, a summary of these articles and a survey of the themes was performed. The selected articles were organized based on the database, journals, professional category of authors, the country of origin and year of publication. Discussion: After grouping the themes identified by similarities, the categories were created: Knowledge, Education and Nursing Care. In the Knowledge theme, it was found that newborn screening is a concern in many countries and the nurse has a political and social transformative role, being responsible for the understanding of the pathological process of pain and triggering factors in sickle-cell disease. In the theme Education: the education of the family and client with sickle-cell disease is essential in relation to pain and it is the nurse's duty to assess the precipitating causes, as well as to help family members to participate in the treatment. In the topic Nursing Care: the care of a patient with sickle-cell anemia should be directed to the prevention of disease complications, as well as to promote improved quality of life. Conclusion: This study showed nursing publications related to the care of individuals with sickle-cell disease are still incipient. Thus, the prospects of investigations and discussions in the nursing knowledge area addressing the individual with sickle-cell anemia should be expanded. Therefore, nursing professionals must seek to build a body of specific knowledge that must be used to guide and support their practice and, consequently, to improve the quality of their care to individuals with sickle-cell disease.

Keywords: Nursing care, sickle-cell disease, pain

P-071

Hematology – malignant diseases

Palliative care and quality of life in leukemia: an integrative review

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Introduction: Leukemia is a type of hematologic tumor that affects the bone marrow, and differs according to the affected cell type; it is a chronic disease that affects mainly children and young adults. As in any chronic disease, it requires long-term treatment, often only to prolong life, and the cases of cure are still very scarce. In order to provide a better quality of life to these individuals, currently palliative care is given in parallel to the "curative" treatment. Palliative care is provided to relieve pain and other symptoms, as well as to give psychological, social and spiritual support and its main objective is to ensure the best possible quality of life for the patient and his family, through an affirmation of life and by accepting death as a normal evolution of existence. Objective: To characterize the scientific production in online articles about the quality of life offered by palliative care in leukemia patients. Material and Methods: This is an integrative literature review. The search for the references was carried out in the Virtual Health Library (VHL), and used the following descriptors: leukemia, palliative care, quality of life and nursing care, with the following inclusion criteria: full text, in English, Spanish, and Portuguese, published between 2010 and 2015. A total of 11 articles were selected. Results: the 11 selected articles were organized according to the database, language, and year of publication. Discussion: After separating the articles into three categories, we observed in the theme: leukemia, palliative care and quality of life that the authors reported the importance of palliative care being started together with the treatment itself at the time of the leukemia diagnosis, also emphasizing the aging population and the lack of study and resources to treat them effectively in relation to young individuals. As for the theme: leukemia, palliative care and nursing care, we observed an emphasis on professionals and their watchful eyes in order to have an early palliative intervention, again emphasizing the elderly population. As for the theme: leukemia, quality of life and nursing care, the focus of the research was on the quality of life of caregivers and patients undergoing chemotherapy. Conclusion: We observed in this study that palliative care is still being used mostly for the so-called terminally-ill leukemia patients; more than a few studies have emphasized the need for an early start, so that patients can go through treatment while maintaining a better quality of life and that there is much emphasis on the elderly, but none on the pediatric population. Therefore, further studies should be developed covering new age groups and nursing care, to provide support for their practice and, consequently, to improve the quality of assistance to the patient with leukemia.

Keywords: leukemia, Palliative Care, Quality of Life, Nursing Care

P-072

Hematology – malignant diseases

Anthropometric Assessment of Onco-Hematological Patients: comparison between different methods.

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INTRODUCTION: There are several types of hematological cancers, named according to the affected cell type and how fast it progresses. Nutritional status impairment is associated to increased morbidity and mortality in cancer patients, with the sporadic nutritional assessment being essential in patient treatment. Several anthropometric methods have been used and studied to assess the nutritional changes and through these measures one can verify the amount of muscle and fat reserves and predict malnutrition, overweight or obesity. OBJECTIVES: To compare different methods of anthropometric measurements to determine the nutritional diagnosis in onco-hematological patients. METHODS: This was an analytical cross-sectional study. The sample consisted of onco-hematological patients attending a specialized outpatient clinic located in Fortaleza-CE. The methods employed for the anthropometric measurements were: Body Mass Index (BMI), triceps skinfold (TSF), Brachial Circumference (BC), Arm muscle circumference (AMC) and thumb adductor muscle thickness (TAMT). RESULTS: The study included 100 individuals, with a mean age of 52.4 ± 14 years, of which 44% were men and 56% were women. The most common etiologies of oncological malignancies were: chronic myeloid leukemia (23%), Hodgkin's Lymphoma (19%) and Multiple Myeloma (MM) (19%). Of the patients studied, 27% were undergoing chemotherapy and 3%, radiation therapy. The nutritional assessment method that identified the highest number of patients with malnutrition and, therefore, resulted in a poor nutritional diagnosis was the Arm Muscle Circumference (56%), followed by the thumb adductor muscle thickness (44%), Brachial Circumference (41%), triceps skinfold (22%) and body mass index (12%). DISCUSSION: This study showed a high prevalence of malnourished individuals (56%) according to the AMC, corroborating literature findings that cancer and nutritional status are closely related. According to the study by Freitas et al. (2010), when they assessed the nutritional status of cancer patients according to different indicators, they found an incidence of malnutrition of 56% according to AMC, 41% for BC and 13 ± 3.2 mm for TAMT, similar results to those of the present study. Differently from Sommacal et al. (2010), who assessed leukemia patients undergoing bone marrow transplantation (BMT) and found that the BC was the most sensitive of all measures. CONCLUSION: The anthropometric assessment in onco-hematological patients showed great variation between the different methods, in which the AMC was the method that best identified malnutrition. We suggest that the nutritional assessment be performed using different parameters, such as biochemical evaluation, food history, physical examination and anthropometrics, to better predict the diagnosis of onco-hematological patients.

Keywords: Anthropometric assessment, hematological cancer, Nutritional diagnosis

P-073

Hematology – malignant diseases

Use of Brentuximab Vedotin in patients with relapsed Hodgkin's lymphoma after Autologous Bone Marrow Transplantation - experience report in a Hospital in Fortaleza, Ceará.

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Introduction: The classical Hodgkin's lymphoma is a lymphoproliferative disease originating from B cells, consisting in mononuclear Hodgkin's cells and Reed-Sternberg cells residing in an infiltrate containing several non-neoplastic cells, such as lymphocytes, eosinophils, neutrophils, histiocytes and fibroblasts. The disease has a bimodal character, with peaks of incidence in patients between 15 and 30 years old and at 55 years old. In our service, we observed a predominance of younger patients, with a median age of 20 years. In patients with relapsed disease, rescue therapy should be performed, followed by high-dose chemotherapy and autologous bone marrow transplantation (BMT). In patients with relapsed disease after autologous transplantation, the therapy of choice is the use of brentuximab vedotin, followed by allogeneic bone marrow transplantation. Brentuximab vedotin is an antibody-drug conjugate, which acts selectively on CD30 + cells. Objective: To report the experience of the Hematology Service in a Hospital in the city of Fortaleza, Ceará, regarding the use of brentuximab vedotin in patients with Hodgkin's lymphoma relapse after autologous BMT. Material and Methods: Retrospective study, consisting in the review of medical records of patients with relapsed Hodgkin's lymphoma after autologous BMT in the years 2015 and 2016. Results: During this period, 6 patients with Hodgkin's lymphoma showed disease recurrence after being submitted to autologous BMT. The median age of the patients was 22.5 years. Of the 6 patients, 2 were females and 4 were males and 66.67% of patients had advanced disease at the diagnosis. The median time to the first recurrence was 6.5 months after the end of the first treatment. The protocol used for the conditioning of the autologous BMT was NEAM. The median time to recurrence after BMT was 5 months (ranging from 2 to 8 months). Brentuximab vedotin was the chosen treatment for these patients after the recurrence diagnosis post-autologous BMT. Two patients showed toxicity, one neurological and the other severe bronchospasm, requiring treatment discontinuation. Four patients were reevaluated, on average after 6 cycles of brentuximab vedotin, three with complete remission and one with partial remission by conventional computed tomography with contrast or PET-CT. A patient has yet to be reevaluated as, so far, only 2 medication cycles have been performed. We had only one death due to complications of the underlying disease. Patients with available donor are undergoing pre-allogeneic BMT examinations. Conclusion: brentuximab vedotin is a good option for patients with recurrence after autologous BMT and should be a good option as a bridge to allogeneic BMT.

Keywords: Hodgkin's lymphoma; Autologous transplantation, brentuximab vedotin

P-074

Hematology – malignant diseases

Acute myeloid congenital leukemia - case report

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INTRODUCTION - Congenital Acute Myeloid Leukemia is a rare disease, which is not associated with gender or ethnicity, but when well-documented, it can be diagnosed during the first 30 days of life. Diagnosis in a newborn involves findings such as hepatosplenomegaly, DHF or infiltrative skin lesions, together with parameters obtained from complete blood count, bone marrow aspirate and immunophenotypic profile. OBJECTIVE: To report the case of a rare form of leukemia: congenital AML. METHODS: We report the case of a female newborn, CR, who was born in a Reference Teaching Hospital of Macror, North region of Ceara, on 02/05/2016 and died at the age of 1 month and 9 days (03/14/2016). He showed all the classic clinical signs considered for congenital leukemia since birth. He had respiratory distress, sepsis and was preterm. Blood counts were performed, showing a significant increase in the number of total leukocytes, which increased from 67,000/mm^3, on 02/06/2016 to 281,000/mm^3 on 03/02/2016, leukocytosis at the expense of 88% blasts, macrocytic anemia and thrombocytopenia. The myelogram disclosed a hypercellular bone marrow, infiltrated by 72.25% medium-to-large myeloid blasts, with cytoplasmic granules, marked nucleoli and the presence of Auer rods. The Sudan-Black cytochemical staining was positive in blasts. It was not possible to perform the immunophenotypic tests. The patient developed extreme disease severity, making it impossible to transfer her to the reference hospital and she died due to severe hemorrhagic complications. CONCLUSION: The high number of blasts in the peripheral blood, plus the clinical signs and massive bone marrow infiltration by myeloblast elements in a newborn patient, allow us to support the diagnosis of congenital Acute Myeloid Leukemia. The literature was reviewed and the rarity of the disease in newborns was verified.

Keywords: Acute Myeloid Leukemia, congenital, Myelogram, hemorrhage.

P-075

Hematology – malignant diseases

Lymphoproliferative disorder after allogeneic bone marrow transplantation in a patient with aplastic anemia: a case report

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Introduction: Immunosuppression, necessary to prevent rejection in allogeneic bone marrow and solid organ transplantation, can predispose to post-transplant lymphoproliferative disease (PTLD). It is believed that this complication is associated with Epstein-Barr virus infection (EBV), which is able to penetrate B cells and induce their proliferation. Pediatric patients are more likely to develop PTLD, as the majority has not been exposed to EBV. The incidence of PTLD is higher in allogeneic bone marrow, heart and lung transplant, occurring in up to 20% of patients. Approximately 33-48% of cases, however, have no association with the EBV virus. The mechanism in these cases is not well understood and may be related to other infectious agents or autoimmune response triggered by the graft. However, it is possible to differentiate the clinical characteristic, which is usually faster (months) in case of EBV+ and more insidious (years) in EBV- patients. The association of this disorder with older age with no reported EBV virus infections after immunosuppression is still not well understood and requires further studies. Objective: To report the case of a patient diagnosed with lymphoproliferative disease after related allogeneic bone marrow transplantation. Material and Methods: We reviewed the patient's medical record, analyzing his diagnosis, laboratory and imaging tests and medical history. Patient identification was preserved in this study, considering ethical and moral criteria. Results and Discussion: MANS, 43 years old, farm worker, was diagnosed with aplastic anemia. He was submitted to related allogeneic bone marrow transplantation 12 months before admission. He arrived at the Reference Center reporting abdominal pain lasting 5 days, with intensity 8, located in the periumbilical region, without irradiation, worsening after meals and decreased intensity after dipyrone use; gripping, continuous pain type, with nocturnal waking and exacerbation peaks. He denied fever, nausea, vomiting, diarrhea or constipation. He reported decreased appetite and weight loss of 3 kg (67 KG to 64 kg). On admission, he was submitted to an abdominal CT scan, which disclosed the presence of a necrotic mesenteric lymph node, measuring 5x6 cm. On the following day he underwent an exploratory laparotomy and right colectomy, terminal ileectomy and removal of lymph nodes were performed. The histopathological analysis described non-Hodgkin's lymphoma, supporting the diagnosis of post-transplant lymphoproliferative disease. Conclusion: The diagnosis of post-transplant lymphoproliferative diseases is difficult due to their rarity, their heterogeneous morphological aspects, their lack of prospective studies and the number of differential diagnosis, leading to disease underdiagnosis. Therefore, it is important to use case reports for broader dissemination and study of this disease, which, if not treated rapidly, has a poor prognosis.

Keywords: hematology, EBV, lymphoma

P-076

Hematology – malignant diseases

Perception of families when facing the diagnosis of childhood leukemia

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Introduction: Leukemia is considered a treatable chronic disease and, for the most part, it can even be cured, especially when there is an early diagnosis. Childhood leukemia presents as devastating news, with the capacity to produce changes, disorders, and manifestations never before experienced, not only in the child's life but also in the lives of their families. Objective: To assess scientific publications on the perceptions of families when facing the diagnosis of childhood leukemia in their children. Material and Methods: This is an integrative literature review, carried out by searching the LILACS, BDENF and CAPES database. The keywords "child", "leukemia", "psychology" "parents" and "family" were used in the article search, with the following inclusion criteria: articles only in Portuguese, full texts published between 2008 and 2013, which allowed the identification of 73 articles. Results: The abstracts were read and 16 articles were selected. After the analytical reading of the selected articles, data were systematized and shown based on the assessed variables: by number order, descriptors, author, title, results, study type, journal, year and database. Discussion: After grouping the topics identified by similarities, the following categories were established: the need for changes in daily life routine, seeking support in religion and fear at the prospect of death. In the axis: need for changes in daily life routine, the discovery of the disease is very often experienced with much surprise by the family, which threatens their normal daily function and the family is forced to develop new roles for which they are not prepared most of the time; seeking support in religion, when they relinquish their troubles, sorrows and hopes to God, is a situation often experienced by the family, for religion helps to cope with the situation, comforts and alleviates the suffering of family members who accompany their children on a daily basis; and fear at the prospect of death, the stress experienced together with the child throughout treatment is accumulated and displayed in the form of fear of death. The anguish caused by the uncertainty regarding the disease evolution makes everyone to proceed cautiously, concerned with the final outcome of treatment. Conclusion: being the parent of a child with leukemia is to genuinely experience several changes that alter the family dynamics, and thus the initial contact with the nurse provides comfort for parents during the child's stay at the hospital. It is important to carry out more studies focused on pediatric cancer, as it is a chronic condition of which incidence has been increasing among children.

Keywords: Child, leukemia, psychology, family.

P-077

Hematology – malignant diseases

Case Report: Non-Hodgkin's lymphoma in a patient with ataxia-telangiectasia

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Ataxia-telangiectasia (AT) is a rare, autosomal recessive, hereditary disease (incidence of 1: 40000). The clinical presentation gives the disease its name: cerebellar ataxia (mixed type and with axial predominance) and telangiectasia (located mainly in the bulbar conjunctiva and skin exposed to the sun). There are also recurrent infections (in the facial sinuses, lungs, skin and gastrointestinal tract) due to poor immunity. The diagnosis is made by cytogenetic analysis of lymphocytes. AT is a progressive disease (usually resulting in dependence on a wheelchair at 10 years of age) and a high risk of lymphoma, leukemia and cancer development. In this context, non-Hodgkin's lymphomas (NHL) represent a group of different B and T cell malignancies that affect lymphoid organs, extranodal sites. The clinical presentation ranges from a generalized painless lymphadenopathy to weight loss, fever, painful lymphadenopathy, ascites and superior vena cava syndrome. Given the rarity of ataxia-telangiectasia and its association with malignant neoplasms, this study aims to report the case of a patient with AT who developed non-Hodgkin's lymphoma of large B cells. The data were obtained based on the analysis of the patient's medical records in a public hospital in Fortaleza, Ceará. A male patient, diagnosed with ataxia-telangiectasia since 2012, was admitted at pediatric neurology service with ambulation difficulties, frequent falls, delayed speech, poor school performance and episodes of tearfulness. At the time, the examination revealed global cerebellar syndrome with appendicular predominance, lower-limb areflexia, absent Babinski, oculomotor apraxia, cavus feet, grade 4 global muscle strength, unsteady gait, horizontal positional nystagmus, conjunctival and pinna telangiectasia. In 2013, he developed B symptoms and acute renal failure, enlarged kidney with slightly heterogeneous echotexture and a slight reduction of the corticomedullary differentiation at the ultrasound. Renal biopsy was performed, disclosing poorly differentiated neoplastic infiltration, with strongly positive staining for CD45 and CD20, in addition to vimentin, with positive Ki67 in approximately 90% of cells. The myelogram showed normocellular marrow with discreet erythroid hypoplasia and discrete dyserythropoiesis. The aforementioned findings led to the diagnosis of Diffuse Large B Cell Lymphoma still in 2013. The chest computed tomography revealed thyroid nodules and grouped supraclavicular lymphadenopathy. The abdominal CT scan showed enlarged kidneys and spleen. He started to be followed by the Oncology service and underwent chemotherapy and hemodialysis. It is concluded that ataxia-telangiectasia is a risk factor for malignancies and, therefore, these cases should be assessed and reported in the literature for better management of these patients.

Keywords: ataxia-telangiectasia, lymphoma, renal failure

P-078

Hematology – malignant diseases

Cutaneous Kaposi's sarcoma in HIV-negative patient with aplastic anemia: a case report

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Introduction: Kaposi's sarcoma (KS) is a vascular neoplasm of slow progression, associated with the Human Herpes Virus 8 (HHV-8), which usually affects the skin and subcutaneous tissue, but it can affect viscera. A more aggressive form of the disease has been reported in patients with acquired immunodeficiency syndrome (AIDS) and a faster form has been described in immunocompromised patients on immunosuppressive drug therapy. In the latter form, the mean time of KS development is 16 months after the immunosuppressive therapy has been implemented, with frequent mucocutaneous manifestations and in 25% of cases, visceral ones. Ganglia involvement is rare. In most cases, the discontinuation of the immunosuppressive therapy is sufficient for tumor involution. Objective: To report a rare case of cutaneous Kaposi's Sarcoma in an HIV-negative patient after treatment for Aplastic Anemia. Case report: Male patient, 59 years old, from Pentecostes, states of Ceará, had hypertension and diabetes with asthenia, adynamia and dizziness for three months, associated with loss of appetite and skin and mucosal pallor. He showed symptom worsening 15 days prior to going the emergency room, where pancytopenia was detected and he was sent to a Reference Center, where he received the diagnosis of Aplastic Anemia. The patient was treated with cyclosporine, prednisone and immunoglobulin. Nine months later, in one of the return consultations, the patient showed skin erythematous, violaceous, macular lesions measuring 1 to 2 cm in diameter on the neck, chest, back, upper limbs and groin. Groin skin biopsies were performed and showed proliferation of spindle cells and endothelial cells, extravasation of red blood cells, macrophages filled with hemosiderin and inflammatory cell infiltration. A immunohistochemical study was performed, which disclosed Kaposi's sarcoma. The patient improved with vincristine, but developed severe recurrence of aplastic anemia, continuing with hematologic monitoring and expectant management for KS. Discussion/ Conclusion: KS in an HIV-negative patient is a rare finding and when it occurs in patients with aplastic anemia, there is no treatment option. The presence of KS in HIV-negative patients represents a diagnostic and therapeutic challenge. It is important to consider this differential diagnosis in the presence of erythematous, violaceous, macular lesions in cases of immunosuppression. More studies and options should be tested in negative-HIV patients with KS.

Keywords: immunosuppressed, herpes virus, hematology

P-079

Hematology – malignant diseases

ATP induces differentiation of human hematopoietic and leukemic stem cells

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Acute myeloid leukemia (AML) is a malignant disease, characterized by the overproduction of leukocytes and cells with different characteristics in the morphology, immunophenotype and genetic alterations. Leukemic stem cells (LSCs) have been described as a population present in leukemia, in which self-renovation abilities are enhanced and proliferative rates are reduced. These cells are commonly resistant to most often used chemotherapy drugs. In addition, ATP induces differentiation of murine hematopoietic stem cells. The aim of this study was to investigate the ATP ability to induce cell differentiation in human hematopoietic and leukemic stem cells. For this purpose, human hematopoietic cells were obtained from AML samples and volunteer donors in accordance to ethical guidelines. Peripheral blood was isolated by ficoll-histopaque gradient and maintained in a co-culture system with stromal cells (MS-5). The immunophenotype analyses (Lin-CD38- CD34+) were verified by flow cytometer after treatment with ATP (300, 700 and 1000 μM) for 72 h. For the clonogenic assays, cells were mixed with methylcellulose-based medium with cytokines (Methocult H4434 Classic, Stem Cell Technologies, USA). The mixture was placed in 35-mm dishes and cultured in a humidified incubator for 21 days. At the end of this period, colonies consisting of more than 50 cells were counted using an inverted microscope at 40x magnification. The results showed an increase in the percentage of Lin-CD38-CD34+ population in a concentration-dependent manner, mainly after 72 h and low concentration. In clonogenic assays, ATP increased the clonogenic capacity after treatment, which supports the flow cytometry analysis. Therefore, our results indicate that ATP was able to differentiate human and leukemic stem cells. Acknowledgements to FAPESP and CAPES.

Keywords: ATP, Acute myeloid leukemia, Leukemic stem cells, flow cytometry.

P-080

Allogeneic Transplantation

Hepatic veno-occlusive disease as complication of bone marrow transplantation: an integrative review of the literature

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Introduction: Bone marrow transplantation (BMT) consists in the intravenous infusion of hematopoietic stem cells, of which goal is to restore bone marrow function. This procedure can result in several complications and among them, the hepatic veno-occlusive disease (HVOD) stands out, also known as sinusoidal obstruction syndrome (SOS), as the third most common complication in transplanted patients, especially in allogeneic transplantation. Objective: To characterize the scientific production in online articles on hepatic veno-occlusive disease. Material and Methods: This is an integrative literature review, carried out by searching the LILACS, MEDLINE, BDENF, IBCS and Coleciona SUS databases, using as descriptors: bone marrow transplantation, sinusoidal obstruction syndrome, complications, nursing care and the following inclusion criteria: Articles in Portuguese, English and Spanish, full texts published between 2006 and 2016, which allowed the identification of 74 articles. Results: the abstracts were read and subsequently 18 articles were selected, as they met the proposed inclusion criteria, thus allowing a more accurate data selection. To organize the obtained content after the data collection, a demonstrative table was created with information on each study, which included the assessed variables: authors, year, title, database, methodology and journals. Discussion: The data analysis showed that hepatic veno-occlusive disease is a potentially fatal complication of hematopoietic stem cell transplantation (HSCT), having a high incidence of 10% to 60%. Its implications are severe and can lead to multiple organ failure, being directly related to the HSCT conditioning regimen. Its main risk factors are previous history of viral hepatitis or other liver diseases; abnormal liver function before HSCT; liver metastases; intensity of chemotherapy and radiation therapy (Total Body Irradiation); positive serology for cytomegalovirus; advanced age; Hepatotoxic medications; HSCT with unrelated donors and second transplant, among other factors. It is observed that there is scarce material in the literature on daily nursing care in the post-transplant follow-up of this type of client. Nursing care directed to the early prevention of HVOD complications would thereby prevent tragic outcomes. Conclusion: The articles assessed in the study superficially address HVOD; therefore, it is necessary to pay more attention to this topic, considering its importance not only for the medical but also for the nursing field, because it is still incipient in terms of numerical productivity and level of knowledge.

Keywords: bone marrow transplant, nursing care, complications, sinusoidal obstruction syndrome

P-081

Allogeneic Transplantation

The experience of the Bone Marrow Transplantation Service in Fundação Amaral Carvalho - Jau, to decrease post-transplant loss to follow-up in patients whose data were reported to CIBMTR

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INTRODUCTION: The service, located in São Paulo, started its operations in August 1996, performing 2,538 transplants up to March 2016 and in January 2009, it became a data reporter to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR collaborates with the global scientific community to promote advances in hematopoietic stem cell transplantation (HSCT) and cell therapy research. In the period from January 01 2009 to March 30 2016 1,355 patients were included in the International Register. We received patients referred from several Brazilian states (24 of the 27 states). Of patients registered in CIBMTR, 55.1% are referred from other states and, therefore, not all continue the post-transplant follow-up in our service, which hinders the completion of follow-up forms. With the commitment to direct the follow-up to CIBMTR, which requests the completion of forms at 100 days, 6 months, and annually after the 1st post-transplant year and, in an attempt to overcome the obstacle of the distance regarding patients, the data collection team created a routine aiming to avoid the loss of follow-up. OBJECTIVE - To demonstrate the effectiveness of the contact routine of the data collection team. METHOD - We follow a routine of contact attempts: (1) sending an e-mail and telephone contact with the attending physician who referred the patient; (2) sending e-mail and telephone contact with the social worker at the service of origin; (3) contact with the patient or family members; (4) search in social networks; (5) telephone contact/ sending e-mails to hospitals, health secretariats, health basic units and/or city hall of origin of the patient; (6) loss to follow-up. RESULTS - The loss to follow-up form becomes available for filling out at 6 months, post-transplant. Following this routine monitoring, of the 1,355 patients included in the CIBMTR until March 2016, 1,072 were evaluable for follow-up filling out at 6 months. Of these 1072 patients, 12 (1.12%) showed loss to follow-up; however, we resumed contact with 7 (58.33%) of them in the following update. Currently, only 5 patients are in the loss to follow-up status (0.46%) in the CIBMTR system. CONCLUSION - Considering the large number of transplants performed in our service, the varied origin of patients and by adopting an active search routine of contact with those who are monitored in the city of origin, we obtained satisfactory results in sending information to CIBMTR and we maintain a reliable update in our database.

Keywords: Bone Marrow Transplant, Collection of data, loss to follow-up

P-082

Allogeneic Transplantation

Survival outcomes of pediatric patients submitted to allogeneic transplantation for the treatment of acute leukemias

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Introduction: Data on the overall survival (OS) and disease-free survival (DFS) in patients undergoing allogeneic transplantation (BMT) in Brazil are heterogeneous. Thus, most of the data used for comparison of results comes from international literature, being of the utmost importance the analysis and dissemination of data from national centers. Objective: To describe the evolution of children and adolescents submitted to BMT for the treatment of acute leukemias in a single institution. Methods: Retrospective analysis of patients undergoing allogeneic bone marrow transplantation for the treatment of acute leukemias. Data were obtained by reviewing medical records. Results: from May 1999 to May 2016, 160 patients underwent allogeneic bone marrow transplantation for the treatment of acute leukemias in our service. Eighty-nine patients (56%) patients had acute lymphoblastic leukemia (ALL), 65 (40%) acute myeloid leukemias (AML) and six (3.7%) biphenotypic leukemias (ABL). Thirty-eight patients were in their first clinical remission (CR), 85 in the second CR and 26 were in the third CR or more and 11 had refractory disease. Related donors were used in 111 transplants, including eight haploidentical transplantations. The most used source of cells was the bone marrow (131), umbilical cord blood (22) and peripheral stem cells (7). A myeloablative conditioning regimen was used in almost all cases, based on the total body irradiation or busulfan. Twenty-nine (44.6%) of AML patients are alive after a median of 1355 days (103-4946); 29 (32.6%) of ALL patients are alive after a median of 1339 days (26-5911); and four (66.7%) of patients with ABL are alive after a median of 3361 days (1420-4148). Disease recurrence was the cause of death in 54% of cases. The OS was 38% for the entire group, 47% for those transplanted in the early stage of leukemia, 40% for patients submitted to BMT at the intermediate phase and 17% for those with advanced disease at the time of BMT. When we evaluated patients transplanted in the last five years, OS was 49% (53% for patients transplanted at an early stage, 49% for patients transplanted at intermediate stages and no patients transplanted with advanced disease), which shows a tendency to improved OS in non-refractory patients in recent years. The causes of death were recurrence in 54%, transplant-related mortality (TRM) in 26% and extensive graft-versus-host disease in 9%. Conclusion: The results obtained are lower than those described by the Center for International Blood and Marrow Transplant Research (CIBMTR). However, one has to consider that more than 76% of patients undergo BMT at the intermediate and advanced stages of acute leukemias. A broader and multicentric data analysis is necessary so we can assess the real picture of the transplant outcomes in Brazil and define action plans.

Keywords: transplantation, leukemia, child

P-083

Allogeneic Transplantation

Allogeneic bone marrow transplantation in elderly patients with onco-hematological diseases: are there any differences in age-related clinical outcomes?

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Introduction: Little is known about the toxicity profile and clinical results of allogeneic bone marrow transplantation (allo-BMT) in elderly patients, especially in the group aged ≥70 years. Objective: To evaluate results of allo-BMT in elderly patients and compare clinical outcomes between different age groups. Method: A retrospective analysis of consecutive elderly patients with onco-hematological diseases submitted to allo-BMT in our institution from January 2010 to April 2016 was performed. Results: 16 patients aged ≥70 years and 44 between 55 and 69 years were studied. The overall median follow-up (MF) was 174 days. For transplanted patients aged ≥ 70 years, the majority (n = 9) had a diagnosis of AML, followed by MDS (4), CLL (1) and myelofibrosis (1). Regarding the donor, 7 were related, 5 unrelated 10x10 and 4-haploidentical identical. Only 2 patients received myeloablative conditioning and the others received low intensity. Among those <70 years, 13 had AML, followed by MDS (12), Non-Hodgkin's Lymphoma (7), CMML (4), myelofibrosis (3), ALL (2), biphenotypic leukemia (1), CML (1) and fungoid mycosis (1). Twelve had a related donor, 25 unrelated and 7 had a haploidentical donor, being 18 with myeloablative conditioning, 9 non-myeloablative and 17 with reduced intensity. Regarding the source of cells, among those aged ≥ 70 years, 8 received cells from peripheral source and 8 from bone marrow (BM) and among those aged <70 years, 26 received BM cells, 15 from peripheral source and three from cord blood or double cord blood. In all patients, prophylaxis against GVHD was based on calcineurin inhibitors. Among the 16 patients ≥70 years, none died before grafting, but 11 died after (4 due to disease progression and 7 due to TRM) with MF of 117 days. The overall survival (OS) was 93.8%, 60.3% and 35.2%, whereas the recurrence rate was 6.2%, 21.9% and 33% and event-free survival (EFS) was 87.5%, 60.6% and 45.4% at 30, 100 and 180 days, respectively. Among the 44 patients aged 55 to 69 years, 26 died (7 due to disease progression and 19 due to TRM) with MF of 203 days. OS was 93.1%, 71.7% and 67%, with a recurrence rate of 2.5%, 17.3%, 24% and EFS of 90.7%, 62.2%, 57.1% at 30, 60 and 100 days, respectively. When comparing the two groups, we found no difference regarding mortality, recurrence and EFS (P = 0.20, 0.92 and 0.44, respectively). We also found no factors related to higher mortality in the 2 groups (pre-transplant disease status, P = 0.75; type of transplant conditioning, P = 0.68, presence of GVHD, P = 0.80). Conclusion: Despite the sample size limitation, in our institution, allo-BMT in elderly patients is feasible, even in patients aged ≥ 70 years and shows no difference in clinical outcomes between groups.

Keywords: allogeneic transplantation, elderly, clinical outcomes, onco-hematological diseases

P-084

Allogeneic Transplantation

Influence of ABO mismatch on allogeneic hematopoietic stem cell transplantation outcome

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Introduction: Receptor-donor ABO blood type mismatch (ABOi) is not considered an obstacle to allogeneic hematopoietic stem cell transplantation (allo-HSCT), even though it may be associated with several immunohematological complications. However, there are still conflicting data regarding the influence of ABOi on survival (OS) transplant-related mortality (TRM) and the incidence of graft-versus-host disease (GVHD). Objective: To evaluate the influence of the presence of ABOi on allo-HSCT outcome. Methods: A prospective cohort study including onco-hematological patients undergoing the first allo-HSCT from 01/01/2008 to 12/31/2014 in a university hospital was carried out. We evaluated the overall survival (OS) in two years and TRM incidence in the first year, acute GVHD II-IV (aGVHD) in 100 days and neutrophil recovery (NR) in 30 days. The analyzed variables were: ABOi, gender, age, source of cells (bone marrow and peripheral stem cells [PST]), CD34/kg cell count, number of nucleated cells/kg [NNC], primary disease, conditioning regimen (myeloablative [MA] and reduced intensity) and type of donor. Kaplan-Meier method and Cox regression were used for the OS analysis. Regarding the incidence rates of TRM, aGVHD and NR, Gray's test and regression testing were used for competitive events. Results: 130 patients were included, of which 55 (42%) were males, with a mean age of 35 years (SD = 16); 44 (34%) had ABOi, 75 (58%) had acute leukemias, 111 (85%) had related allo-HSCT, 100 (77%) used PST as the source of cells and 99 (76%) patients used the MA regimen. The mean number of CD34 and NNC infused were respectively 2,9x106 and 5,3x108. Mean follow-up was 1.6 years (SD = 1.9 years). The OS, TRM, aGVHD and NR were respectively 34%, 39%, 34% and 85%. The presence of ABOi did not influence the OS, TRM, aGVHD and NR. The other variables did not influence the OS, aGVHD and NR, either. Only CD34+ count/kg was statistically significant for TRM [HR 0.55; CI (0.32 to 0.92); p =0.02]. Discussion/ Conclusion: In this study, the presence of ABOi did not influence the incidence of OS and TRM, NR and aGVHD II-IV. A retrospective cohort study of 153 patients undergoing allo-BMT, carried out by J. Goldman et al. (2003) found no statistically significant differences in OS between allogeneic transplants with ABO isogroup and those with ABO mismatch. There have been no studies to date, demonstrating the influence of ABO mismatch on neutrophil recovery and transplant-related mortality. On the other hand, some authors, such as Kim J. G. et al. (2005) and Stussi G et al. (2002) showed an increased risk of acute graft-versus-host disease among those submitted to allo-BMT with ABO mismatch. We therefore conclude that a prospective study with a larger and more homogeneous population, and with longer follow-up is needed to elucidate these issues.

Keywords: ABO blood group, hematopoietic stem cell transplantation, overall survival, transplant-related mortality

P-085

Allogeneic Transplantation

Lymphoproliferative disorder Post-Allogeneic Hematopoietic Stem Cell Transplantation: a Case Report

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Introduction: Post-transplant lymphoproliferative disease (PTLD) are lymphoid and/or plasmacytic proliferations occurring after solid organ transplantation or after allogeneic hematopoietic stem cell transplantation (HSCT) as a result of the immunosuppression regimen that patients undergo. We report on a 43-year-old male patient, diagnosed with aplastic anemia in September 2015. He was admitted at Hospital Universitário Walter Cantídeo for pre-transplant assessment (HLA-compatible sibling). He underwent immunosuppressive therapy with ATG, prednisone and received cyclosporine until the conditioning regimen with fludarabine, ATG and cyclophosphamide. He underwent the allogeneic HSCT, with a related male donor, with bone marrow source and major ABO mismatch on February 12, 2016. The patient developed febrile neutropenia, used meropenem and vancomycin. Neutrophilic grafting occurred on D+19. 100% Chimerism was seen on D+31. He was discharged with CBC showing anemia, neutrophil count between 1,000 and 1,500, reticulocytopenia and thrombocytopenia. A new hospital admission occurred in April 2016, with abdominal epigastric pain of high intensity, without improvement with powerful painkillers. Abdominal CT scan showed an expansive lesion of necrotic appearance in the mesentery of the mesogastric region, likely of nodal nature. He underwent laparotomy on May 12 with complete resection of the lesion and the histopathological analysis showed a poorly differentiated tumor suggestive of non-Hodgkin's lymphoma. Objective: To report the case of a patient who underwent allogeneic HSCT and developed PTLD, diagnosed after removal of abdominal mass. Methods: Study carried out by reviewing medical records and literature on Pubmed database. Results: Rituximab was started on May 18. At the moment, the patient is clinically stable, using meropenem for recurrent fever, with hematological worsening and new chimerism with mixed results. Discussion: There are several risk factors associated with PTLD, such as previous use of ATG and post-transplant time, with greater risk during the first year. The clinical presentation and course of PTLD vary according to the type of lymphoproliferative disease and the affected area. The diagnosis of PTLD should be suspected in all patients undergoing allogeneic HSCT showing B symptoms, lymphadenomegaly, unexplained hematological and biochemical abnormalities and any symptom that can be attributed to infiltration of non-lymphoid tissues. Radiological evidence of a mass and positive PET are strongly suggestive of PTLD. The types of PTLD are differentiated by histopathology, immunophenotyping and cytogenetics, with specific treatment for each specific type. Conclusion: PTLD should be suspected in all post-allogeneic HSCT patient. A major challenge is related to the immunosuppression management of the patient in order to prevent PTLD progression with increased immunosuppression and, on the other hand, prevent loss of the graft with its reduction.

Keywords: hematopoietic stem cell transplantation; post-transplant proliferative disorder, immunosuppression.

P-086

Allogeneic Transplant

Acute Kidney Injury in Allogeneic Hematopoietic Stem Cell Transplantation - the AKIN Criteria Predict Overall Survival

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Introduction: Acute kidney injury (AKI) is a well-known complication of allogeneic hematopoietic stem cell transplantation (Allo-HSCT), increasing morbidity and mortality. In this study, we described AKI incidence, its classification through the Acute Kidney Injury Network (AKIN) criteria and its impact on overall survival. Methods: Cohort study of 120 patients submitted to an Allo-HSCT between 2000 and 2006. Fifteen patients were excluded (CKD prior to transplantation). AKI was diagnosed and graded through the AKIN criteria (AKIN 1, AKIN 2 or AKIN 3). Patients' characteristics (gender, baseline disease, stem cell source, conditioning regimen and GVHD) and outcomes (hemodialysis, multiple-organ dysfunction syndrome, and death) were recorded. Statistical analyses were performed by Chi-square, Fisher`s exact test, Kaplan-Meier, and Cox model (Overall survival). A p value < 0.05 was considered statistically significant. Results: Of the 105 reviewed patients, one patient was excluded (not eligible for assessment due to early death on D+3) and 10 did not develop AKI after a median follow-up of 599 days (60-2319 days). A total of 94 (89.5%) developed AKI. The median time for AKI diagnosis was D+28 (D0 – D+407). The median age was 41 years and 55 individuals (58.5%) were men. Chronic myeloid leukemia (42.6%) and acute myeloid leukemia (18.1%) were the most frequent baseline disease. GVHD was present in 73 (77.7%). Drug nephrotoxicity (n=47; 50%) and sepsis (n=35; 37%) were the two leading causes of AKI. More than one AKI etiology was observed in 16 (17%) patients. Overall survival at 20 months was 80%, 65% and 45% in patients with AKIN 1, AKIN 2 and AKIN 3 stages, respectively (p=0.047). At the multivariate analysis, low serum albumin (HR 0.38; p<0,001) and high ALT (HR 1.01; p=0.004) were associated with overall survival. Conclusion: AKI was a frequent event in Allo-HSCT patients and it was multifactorial in almost 20% of cases. There was a significant correlation with AKIN stage and overall survival. A close monitoring of renal function and a better understanding of the injury mechanism are major recommendations in the HSCT setting.

Keywords: transplant, acute kidney injury, kidney injury, incidence, survival

P-087

Allogeneic Transplantation

Experience in collecting hematopoietic cells from volunteer donors from a single center

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Introduction: The allogeneic hematopoietic stem cell transplantation (HSCT) is a therapeutic option with real chances of cure for patients with several diseases. However, in Brazil, the possibility of having a related donor is only 25%, requiring the search for volunteer donors in most cases. Currently, there are 4,017,142 donors registered in the National Bank (REDOME) and the possibility of identifying a compatible donor is 1: 100,000. Thus, it is the important to capacitate collection centers to meet the demands and reduce the waiting time for HSCT. Objective: To describe the profile of volunteer donors and characteristics of hematopoietic stem cell (HSC) collection at a single center. Material and Methods: A retrospective cohort study on HSC collection from voluntary donors in registered REDOME was carried out from January 2014 to May 2016. Data were obtained through review of medical records, and the assessed variables were age, gender, race, transplant center, recipient's underlying disease, the source of cells, obtained cellularity and side effects related to the procedure. Results: a total of 29 collections from volunteer donors were computed, averaging one collection per month. The donors were predominantly males (55.2%), Caucasians (72.4%) with a mean age of 31 (+6.8) years. 37.9% of the collections were carried out for international transplant centers. As for the recipient's underlying disease, there was a higher frequency of acute leukemia (51.7%). It was found that 55.2% of donors were submitted to the collection of peripheral stem cells (PSC), but a donor from this group showed mobilization failure; 34.5% were submitted to bone marrow (BM) collection and 10.3% to lymphocyte collection (DLI). In the PSC collections, the average cellularity was 10.2 x 10 (6) CD34/kg, whereas in the BM collections, the average was 6.9 x 10 (8) CNT/kg, and DLI was 25.2x10 (7) CD3/kg. Regarding side effects, 81.3% of donors submitted to PSC collection reported low back pain and headache and 37.5% had paresthesia. BM donors had as major side effects local pain (90%), pallor (50%) and nausea and vomiting (40%). Conclusion: Donors from this sample are young, which is related to the fact ours is a pediatric center and the service limits donor age up to 45 years. It was observed that 37.9% of the collections were performed for international centers, which is related to the miscegenation of the Brazilian population. The quality of the collected product met the requests of 100% of transplant centers, regarding graft cellularity. As for the side effects, all were transient and easy to manage, ensuring greater safety and comfort to the donors.

Keywords: Tissue donors, Bone Marrow Transplantation, Side Effects

P-088

Allogeneic Transplantation

Resolution of c-ANCA positive neutrophilic vasculitis secondary to rheumatoid arthritis post-hematopoietic stem cell transplantation for the treatment of sickle-cell disease: a case report

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Introduction: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) is a curative option for patients with hemoglobinopathies, including sickle-cell disease (SCD). Systemic vasculitis comprises a heterogeneous group of autoimmune diseases, with good response to immunosuppressive treatments, depending on the organ involved and its subtype. Case report: A 29-year-old female patient, diagnosed with Sβ-thalassemia, was referred to our service for related allogeneic HSCT due to recurrent painful crises and alloimmunization. During pre-HSCT evaluation, painful purpuric lesions and several ulcers were observed, with the two largest ones being approximately 10 cm in diameter, in the gluteal and lower-limb regions. The patient also had arthralgia and morning stiffness, imaging assessment compatible with rheumatoid arthritis and positive rheumatoid factor (RF). After skin biopsy, she was diagnosed with c-ANCA positive neutrophilic vasculitis of small vessels, secondary to vasculitis. Treatment was started with methotrexate (15 mg) and prednisone 20 mg/day with gradual reduction to 5 mg/day, with symptom improvement. A month later, the patient was admitted for related allogeneic HSCT, with sister donor with sickle-cell trait, HLA compatible (6X6) with minor ABO mismatch (donor O and patient B), under myeloablative protocol with FLUBU (12) + ATG (5.5 mg/kg), peripheral blood source, with 8.8X106/kg CD34 cells, prophylaxis for GVHD with MTX and CSA. Before the HSCT, the patient developed acute transfusion reaction compatible with hyperhemolysis. Pre-transfusion blood count: Hb = 6.5 g/ dL, hematocrit = 20%, positive direct Coombs test, IAS showing auto and alloantibodies association. Post-transfusion tests: HMG: Hb = 3.7 g/dL, hematocrit = 12%. The following alloantibodies were identified: anti-E, anti-Fy (a) anti-Jk (b), anti-S, anti-K. Immediately before the HSCT, the patient received Rituximab (375 mg/m^2, in 3 weekly doses), plasmapheresis (5 sessions), cyclophosphamide 100 mg/day, Immunoglobulin (2g/kg) and methylprednisolone (1 g/kg/day). There was clinical and laboratory improvement, with stable Hb levels, which allowed the transplantation to be performed uneventfully. Currently, two years after the HSCT, the patient shows absence of auto and alloantibodies, negative FR and c-ANCA, inflammatory markers without alterations, with only a residual perimalleolar ulcer measuring approximately 1.5 cm secondary to vasculitis and not to SCD. She has sickle cell trait, with Hb = 12 g/dL, Ht = 38%, negative hemolysis, indeterminate ABO typing (direct test O and reverse B) and mixed chimera (evaluated by VNTR). Conclusion: We presented a case of resolution of neutrophilic vasculitis of small vessels/ rheumatoid arthritis, as well as alloimmunization after related allogeneic HSCT, indicated for treatment of SCD. The results demonstrate the therapeutic potential of intensive immunosuppression followed by allogeneic immune reconstitution for the treatment of these pathologies.

Keywords: bone marrow transplantation, neutrophilic vasculitis, sickle-cell disease, alloimmunization

P-089

Allogeneic Transplantation

Vasculitis resolution neutrophilic c-ANCA secondary positive post-transplantation of hematopoietic stem cells rheumatoid arthritis for the treatment of sickle cell disease: a case report

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Introduction: Allogeneic hematopoietic Stem Cell Transplantation (HSCT) is a curative option for patients with hemoglobinopathies, including sickle cell disease (SCD). Systemic vasculitis are a heterogeneous group of autoimmune diseases, with good response to immunosuppressive treatments, depending on the organ involved and its subtype. Case report: A female patient, 29 years old, diagnosed with Sβ-thalassemia, referred to our service for allogeneic HSCT related due to recurrent painful crises and alloimmunization. During evaluation before HSCT painful purpuric lesions and several ulcers occurred, the two largest of about 10 cm in diameter, in the gluteal and lower limb region. The patient also had arthralgia and morning stiffness, imaging compatible with rheumatoid arthritis and rheumatoid factor (RF) positive. After skin biopsy, diagnosed with neutrophilic vasculitis of small vessels c-ANCA positive secondary to vasculitis. Made methotrexate (15 mg) and prednisone 20 mg/ day with gradual reduction to 5 mg/ day, with improvement in symptoms. A month later, the patient was admitted for allogeneic HSCT, Akin, donor sister with sickle cell trait, HLA compatible (6X6) with minor ABO mismatch (donor O and patient B), myeloablative protocol FLUBU (12) + ATG (5, 5 mg/ kg), peripheral blood supply with 8,8X106/ kg CD34, prophylaxis for GVHD with MTX and CSA. Before HSCT period, the patient developed acute transfusion reactions compatible with hiperhemólise. pre-transfusion blood count: Hb = 6.5 g/ dL, hematocrit = 20%, Coombs positive, PAI self and alloantibodies association. post-transfusion tests: HMG: Hb = 3.7 g/ dL, hematocrit = 12%. Alloantibodies identified the following: anti-E, anti-Fy (a) anti-Jk (b) anti - S, anti-K. Immediately before HSCT conducted Rituximab (375 mg/ m2 weekly doses 3) Plasmapheresis (5 sessions), Cyclophosphamide 100 mg/ day, noglobulina Immunization (2g/ kg) and methylprednisolone (1 g/ kg/ day). There was clinical and laboratory improvement, maintaining stable Hb levels, thus allowing the transplantation was performed uneventfully. Currently, two years after HSCT, keep absence of self and alloantibodies, FR and c-ANCA negative, inflammatory evidence unchanged, with only a residual perimalleolar ulcer approximately 1.5 cm secondary to vasculitis and not to DF. Presents sickle cell trait Hb = 12 g/ dl, Ht = 38%, evidence of hemolysis negative, indeterminate ABO typing (direct Tasting and reverse B) and mixed chimera (evaluated by VNTR). Conclusion neutrophilic demonstrated resolution of a small vessel vasculitis/ rheumatoid arthritis, as well as alloimmunization after allogeneic HSCT Akin, indicated for treating PD. The results demonstrate the therapeutic potential of intensive immunosuppression followed by allogeneic immune reconstitution for the treatment of these pathologies.

Keywords: bone marrow transplantation, neutrophilic vasculitis, sickle-cell disease, alloimmunization

P-090

Allogeneic Transplant

Engraftment data in haploidentical Hematopoietic Stem Cell Transplantation - Experience of a Center

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Introduction: The lack of compatible HLA (human leukocyte antigen) donors is a major limitation for performing hematopoietic stem cell transplantations (HSCT). Less than one third of patients find 100% compatible related donors and even a smaller percentage finds alternative donors. However, most patients have a potential haploidentical donor. The recent T-lymphocyte depletion technique *in vivo*, with post HSCT cyclophosphamide, seems to prevent severe forms of graft-versus-host disease (GVHD) and reduce grafting failure, allowing the performance of transplants with haploidentical donors, giving patients the opportunity of undergoing a potentially curative treatment. Objective: To evaluate the engraftment data of patients submitted to haploidentical HSCT. Patients and Methods: A retrospective observational study based on the review of medical records. All patients submitted to haploidentical HSCT at the institution were included. The criteria for undergoing haploidentical HSCT were the unavailability of a 100% compatible related donor, unavailability of donor from the Bone Marrow Donor Registry (REDOME) after 4 months of searching and the urgency in transplanting the patient. Results: Data from 12 patients who underwent haploidentical HSCT were analyzed from February 2013 to May 2016. Most patients were males (7 patients), and one of these, with bone marrow aplasia, underwent 2 haploidentical HSCTs. There were 4 cases of aplasia, 3 cases of acute myeloid leukemia, 1 acute lymphoblastic leukemia, 2 Hodgkin's disease (HD) and 2 congenital immunodeficiencies. Eleven patients received fludarabine/cyclophosphamide and TBI 2 Gy in the conditioning regimen and the source was the bone marrow in 100% of cases. The median age of patients at the transplant was 13.31 years, ranging from 6 months to 26 years. The median follow-up was 11.3 months (1.6 to 37.6). The engraftment occurred on average at 15.5 days (15-20), and only one patient had engraftment failure. The median amount of infused CD34/kg cells was 4x106. At the control monitoring 30 days after the HSCT, only 2 patients did not have complete chimerism. One patient had a recurrence of HD and 3 patients died, two of them due to complications related to the procedure, one due to late graft rejection. Overall survival was 75%, whereas the event-free survival rate was 66.66%. Discussion: The literature shows that haploidentical HSCT is a viable alternative for patients without compatible related donors, with resulting morbidity and mortality rates similar to procedures with a related donor and, in some studies, better than unrelated HSCT. The results described above corroborate the impression that haploidentical HSCT promotes early engraftment and complete chimerism. However, there are still questions regarding recurrence rates and immune reconstitution which, due to the small number of patients and duration of follow-up in this sample could not be assessed.

Keywords: Haploidentical, Stem Cell Transplantation

P-091

Allogeneic Transplant

Analysis of the number of Brazilian centers that perform hematopoietic stem cell transplantation (HSCT) and actively report data to CIBMTR (Center for International Blood &Marrow Transplant Research)

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INTRODUCTION: Evidence-based medicine is directly associated with exposure of hospital data, being of clinical, economic and administrative importance the analysis of results and national and international benchmarking. In some countries there has been the development of centers to collect, manage and potentiate data, with scientific production development. One can have as a reference the United States of America through the CIBMTR (Center for International Blood and Marrow Transplant Research), a center created with the aim to contribute to scientific production, the creation of specific forms as data collection tools, enabling multicentric studies. Therefore, currently, there is a movement started in the Hematopoietic Stem Cell Transplantation reference centers in Brazil, in partnership with the CIBMTR to raise awareness on the importance of inclusion of Brazilian data into both national and international available databases. OBJECTIVE: To evaluate the number of centers performing HSCT in Brazil and that actively reported data to CIBMTR during the years 2010 to 2015. METHODS: We analyzed the CIBMTR Annual Report, available on the CIBMTR website, searching for Brazilian centers that reported data to CIBMTR in recent years, comparing transplants performed by these centers, according to the data sent to the Brazilian Association of Organ transplantation (ABTO) and data reported to CIBMTR. In 2015, ABTO was the bank with the highest volume of transplants reported in Brazil, 2,137 in 48 centers (SUS/Private Health Network). The DataSUS database reported in the same period, 1,711 transplants in 45 centers (SUS). RESULTS: From 2010 to 2015, we observed a decrease in the number of Brazilian centers that report data to CIBMTR. Comparing the total number of transplants performed in centers actively reporting to CIBMTR year per year, the total number performed in the country according to ABTO was: In 2010, 18 centers reported data to CIBMTR, corresponding to 64.96% of the total performed in Brazil; 18 centers in 2011 (57.23%); 8 centers in 2012 (30.23%); 7 centers in 2013 (23.66%); 7 centers in 2014 (21.96%), 8 centers in 2015 (25.31%). When we analyze only the allogeneic transplants with the percentage of data being reported we have: 79.25% in 2010, 71.19% in 2011, 52.38% in 2012, 41.55% in 2013, 37.63% in 2014 and 41.10% in 2015. CONCLUSION: As the ABTO is a solid organ database, with only basic information about HSCT without outcome update and considering the lack of a national registry where we can receive and evaluate the outcome of transplants performed in the country, the decrease in the number of centers that report data to CIBMTR becomes a problem to be discussed, as we do not have control on the exact number of transplants performed in Brazil or how to evaluate the outcomes of these transplantations.

Keywords: Data collection, Bone Marrow Transplantation, Epidemiology

P-092

Allogeneic Transplant

Intestinal pneumatosis in the context of Hematopoietic Stem Cell Transplantation (HSCT): a case series

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Pneumatosis intestinalis (PI) is a rare disorder characterized by extensive gas collections in the intestinal submucosa that can develop into abdominal rupture. The diagnosis is established based on imaging studies such as computed tomography (CT). In post-HSCT patients, their origin can be multifactorial, such as conditioning, infections, graft-versus-host disease (GVHD) and prolonged use of steroidal anti-inflammatory drugs (SAIDs). Objective: To report 4 cases of PI and discuss the presentation and management in the context of HSCT. Case 1: 23-year-old female patient, with Myelodysplastic Syndrome, submitted to related 10x10 allogeneic HSCT. After 6 months, the patient developed watery diarrhea and weight loss, with acute GVHD in the GIT being confirmed by duodenal biopsy. She received methylprednisolone 2 mg/ kg/ day and oral budesonide, with no improvement. He received 2 infusions of basiliximab, with partial improvement. After 30 days, she suddenly developed painful abdominal distension and dyspnea. CT scan showed PI with pneumoperitoneum and pneumomediastinum. She developed septic shock (SS) and started receiving broad antimicrobial therapy (AMT), zero diet by mouth (NPO) and parenteral nutrition (TPN). After 15 days, she partially reabsorbed the pneumatosis, but died due to candidemia by *C. tropicalis*. Case 2: 8-year-old male patient old, with Wiskott-Aldrich syndrome, submitted to the 2nd 10x10 unrelated (UNR) allogeneic HSCT due to loss of the previous graft. He developed acute skin and GIT GVHD with good response to SAIDs. After two years, he developed abdominal pain and fever, and the CT scan showed PI. He required AMT, NPO and TPN for prolonged periods. He showed complete resolution of the condition. Case 3: One-year-old female patient, submitted to UNR 10x10 HSCT due to Combined Immunodeficiency Syndrome. After 90 days she started with diarrhea, bloating and weight loss. She was diagnosed with GIT GVHD, treated with SAIDs, with partial improvement. However, she developed SS and the CT showed PI. She received AMT, NPO and TPN, with clinical picture resolution in three weeks. After one month she had a new episode of SS and died. Case 4: A 12-year-old female patient was submitted to UNR 9x10 HSCT for acute lymphoblastic leukemia. After the engraftment she had acute skin GVHD with good response to SAIDs. On D+164, she started to have fever and malaise. CT showed extensive PI and pneumoperitoneum. The patient remained stable, treated with AMT and NPO. She did not need TPN. She progressed well and was discharged after 4 weeks. Discussion: Pl is a rare late complication of HSCT with high morbidity and mortality. We demonstrated 4 cases of PI, of which onset occurred after the first 100 days with concomitant diagnosis of GVHD of TGI and use of SAIDs. Conclusion: Treatment of PI remains controversial and conservative or surgical management can be performed. Our patients showed good evolution with GIT rest, TPN and broad spectrum AMT. Nevertheless 3 of them died, but only during the first episode of PI, which may represent mortality that is not directly related, but a marker of severity in HSCT.

Keywords: Transplantation, Stem Cells, Pneumatosis, GVHD, Antimicrobials

P-093

Allogeneic Transplant

Unrelated allogeneic transplant in hematological malignancies: analysis of prognostic factors in two Brazilian institutions

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Introduction: The allogeneic transplantation with unrelated donor is an option for patients with no compatible family donor. With the decrease in fertility rates in Brazil, the importance of transplantation with alternative donors increases. Objectives: To evaluate prognostic factors in unrelated transplantation in two heterogeneous institutions. Material and Methods: We selected all patients with malignancies submitted to the first unrelated allogeneic transplantation between 2010 and 2015 in two heterogeneous institutions. Baseline characteristics were compared according to the degree of HLA compatibility. The assessed outcome measures were death, recurrence and death in remission. Results: During the study period 103 patients were included. The median time of follow-up was 32 months. The median age was 36 years; 60% had acute leukemia and 33% had high or very high Disease Risk Index (DRI). The source was the bone marrow in 60% of the transplants, myeloablative conditioning was carried out in 81%, and HLA compatibility at high-resolution was 8x8 and 10x10 in 77% and 67%, respectively. Overall survival at 3 years was 41% for HLA 8x8 and 26% for HLA 7x8 (p = NS). Factors associated with poor survival in the multivariate analysis were age (HR = 1.4 for every 10 years; p <0.001) and high/very high DRI (HR = 2.5; p = 0.01). HLA compatibility was not significant (HR = 1.4 for HLA 7x8, p = NS). Stratification by compatibility in 8 loci was better adjusted to data than the compatibility in 6 or 10 loci. The DRI effect is apparently lower in transplants with donors with HLA mismatch (interaction test, p = 0.09). The cumulative incidence of Transplant Related Mortality (TRM) at 1 year was 33%. In the multivariate analysis, the only factor associated with TRM was age (HR = 1.3; p = 0.01). The cumulative incidence of recurrence at 3 years was 31%. In the multivariate analysis, high/very high DRI associated with bone marrow source was associated with increased risk of recurrence (HR = 5.4; p = 0.002); when the source was mobilized peripheral blood, the effect of high/very high DRI was lower (HR = 2.7, positive interaction; p = 0.04). Discussion: This is a retrospective study of two heterogeneous Brazilian institutions covering a recent period. An HLA mismatch in A, B, C or DR did not correlate significantly with any outcome studied. We found a nonsignificant HR = 1.4, consistent with a recent meta-analysis by Kekre et al, which showed a slightly higher risk of death for unrelated transplant with mismatch (HR = 1.27). The biological age was the main factor associated with TRM. In malignancies with high/very high DRI, the use of mobilized peripheral blood may be advantageous, with lower risk of recurrence. Conclusion: This study shows that when an unrelated donor HLA 8x8 is unavailable, a 7x8 donor is an option, especially in diseases with high/ very high DRI. In these, it may be advantageous to choose mobilized peripheral blood.

Keywords: Unrelated Transplant, HLA, Source of Hematopoietic Stem Cells

P-094

Allogeneic Transplant

Hematopoietic Stem Cell Transplantation in Myelodysplastic Syndrome – Experience of the Hematology Service Transplant Unit of Hospital Universitário do Ceará

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INTRODUCTION: The Myelodysplastic Syndrome (MDS) is a clonal hematopoietic stem cell disease characterized by dysplasia and ineffective hematopoiesis, with a variable risk of transformation to acute leukemia. MDS patients have a decreased production of red blood cells, platelets and mature granulocytes. Moreover, these formed elements can have qualitative functional defects. These quantitative and qualitative changes often result in a variety of systemic manifestations, including anemia, hemorrhage and increased risk of infection. Objective: To report the experience of the Bone Marrow Transplant Unit of the Hematology Service UFC HUWC in relation to outcomes and prognostic factors. Materials and Methods: Observational study describing the findings of MDS patients submitted to Allogeneic HSCT from February 2015 to June 2016. Results: A total of 8 patients, 4 men and 4 women, aged between 37 and 65 years and a median of 55 years were submitted to HSCT. Two patients had hypocellular MDS, 2 patients had Refractory Anemia with Excess Blasts II (RAEB-II), 3 patients had refractory cytopenia with multilineage dysplasia and 1 patient had unclassifiable MDS/MPS. The mean number of days from diagnosis to transplantation was 282 days (154-570) and all patients underwent transplantation with a related donor, with the source of stem cells being peripheral blood in 100% of cases, one patient with greater mismatch and 1 with minor mismatch, the others with the same blood group. 100% of conditioning regimens were carried out with fludarabine and melphalan, with 2 patients being submitted to HSCT with reduced intensity due to age; the mean neutrophil engraftment was 17 days. Two patients died on D+5 and D+18, respectively, both due to severe infection. Another patient died on D+70, was discharged and after new hospital admission died from complications related to dengue encephalitis. As post-transplant complications, 2 patients had skin GVHD, 1 patient developed GVHD in the mouth, 3 patients liver GVHD and 2 patients had lung GVHD. There was no recurrence of the underlying disease in any patient. Conclusion: HSCT is currently the only curative therapeutic modality for MDS and performing the transplant with reduced intensity allows the inclusion of the elderly population, an age group in which the prevalence of MDS is higher. The initial results of allogeneic transplantation in MDS at HUWC have shown that factors related to the time of diagnosis until transplantation, age range and risk classification can interfere with mortality rates and that it is still early to carry out the overall survival and disease-free survival analysis.

Keywords: Allogeneic Transplantation, Myelodysplastic Syndrome, Prognosis

P-095

Allogeneic Transplant

Impact of monoclonal antibody antiCD25 in the scenario of acute graft-versus-host disease refractory to corticoids.

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The acute graft-versus-host disease (aGVHD) is still the leading cause of morbidity and mortality after Hematopoietic Stem Cell Transplantation (HSCT). Approximately 50% of patients who undergo related or unrelated allogeneic transplant develop aGVHD. Of these, approximately 30% are corticoid-resistant, requiring a second-line treatment. To date, there is no literature consensus on what is the best therapeutic strategy for this severe complication of HSCT and different therapeutic strategies have been used, including monoclonal antibodies (Anti CD25 or Anti-tumor necrosis factor). Objective: To evaluate the response to monoclonal antibody antiCD25 in patients who are refractory to steroids in our center. Methods: We retrospectively evaluated the records of patients submitted to related and unrelated allogeneic HSCT from 2004 to 2010. Thirty-seven patients with aGVHD were refractory to corticosteroids and were assessed regarding the response rate to antiCD25 taking into account the frequency and degree of GVHD, overall survival (OS) and underlying disease variables, gender and age of the donor, type of conditioning, ABO mismatch, gender and age of the recipient. Results: A total of 149 patients were included in the analysis, 81 patients (54.3%) developed aGVHD and 37 patients (45.7%) were refractory to steroids and 97.3% (36 patients) used antiDC25 as second-line treatment. The complete response rate to AntiCD25 was 24.3% in 28 days. The overall survival (OS) of patients without aGVHD at 5 years was 66.6%; in patients with aGVHD grade I-II was 50.0% and grade III-IV, 12.5%. For patients who were refractory to steroids and received antiCD25 as a second-line treatment, overall survival at 5 years was 22.2%. At the multivariate analysis, the age of the donor and of the recipient were risk factors for the development of aGVHD grade IV. The causes of death were sepsis (97%) and hemorrhagic stroke (3%). Conclusion: In our population the overall survival at 5 years in corticoid-resistant patients who received therapy with antiCD25 was 22%. These results are equivalent to those found in the literature, demonstrating an extremely high mortality rate for patients who develop corticoid-resistant aGVHD. The main cause of mortality in our patients was sepsis, most probably demonstrating a poor immune reconstitution associated with the use of antiCD25. Further investigations of new strategies for early detection of aGVHD as biomarkers or therapeutic innovations are necessary to effectively improve survival in these patients.

Keywords: GVHD, antiCD25, Corticoid resistance, Hematopoietic Stem Cell Transplantation.

P-096

Allogeneic Transplant

Mucormycosis in a patient post-Hematopoietic Stem Cells transplantation: successful therapy with amphotericin and posaconazole as consolidation

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Mucormycosis is a severe opportunistic infection caused by Mucorales fungi. It is more common in patients with poorly controlled diabetes, chemotherapy, undergoing corticosteroid therapy, solid organ and bone marrow post-transplant and large burns. The rhinocerebral form starts with the infection of the sinuses and progresses locally with up to central nervous system infiltration. It has a 40% mortality that can reach 65% in patients after hematopoietic stem cell transplantation (HSCT). Objective: To describe the case of a patient diagnosed with mucormycosis post-HSCT, with successful treatment with amphotericin lipid complex. Case: 18-year-old male patient, with a diagnosis of monocytic AML with central nervous system infiltration was submitted to Hematopoietic Stem Cell Transplantation (HSCT), haploidentical with the mother, on second complete remission on 08/28/2014. Conditioning was performed with fludarabine and TBI; GVHD prophylaxis included tacrolimus, mycophenolate and cyclophosphamide post-infusion. He received 3.96 x 10^6 CD34 cells/kg from bone marrow source, isogroup, and engraftment occurred on day +20. The patient developed skin and liver GVHD Grade II refractory to corticosteroids, requiring two infusions of antiCD25. Seven months after HSCT, he had a perianal infection, treated with vancomycin and meropenem. When assessing the infectious foci, he underwent facial sinus CT that showed mucosal thickening and positive serum galactomannan. He required nasal secretion drainage and fungal screening showed hyaline hyphae and growth of *Aspergillus flavus*, configuring a diagnosis of fungal rhinosinusitis by Aspergillus. He started treatment with voriconazole. Thirty days after the use of voriconazole, he had fever and CT scan showed lingular opacity measuring 1.5 cm. He underwent a bronchoalveolar lavage (BAL) that showed the presence of galactomannan antigen 5.03 and positive culture for *Cunninghamella spp*. (mucormycosis). We then chose to change the antifungal agent to Amphotericin lipid complex. Sensitivity testing was performed, showing MIC 1 for amphotericin and MIC for voriconazole above 16. He received amphotericin B lipid complex for 40 days and after that, switched to posaconazole as secondary prophylaxis, as well as gradual reduction in corticosteroids. The control CT scan showed complete resolution of the infection. The patient is currently receiving prophylactic posaconazole, as well as high-dose methylprednisolone for GVHD in the GIT. There was no fungal infection reactivation to date. Conclusion: Mucormycosis is a severe infection in HSCT, associated with high mortality and usually it does not show positive galactomannan; however, the case described above had high galactomannan in BAL and yet the culture was positive for *Cunninghamella*. The patient was receiving voriconazole and had good response to induction treatment with amphotericin lipid complex and consolidation with posaconazole.

Keywords: Transplantation, Stem Cells, Mucormycosis, Galactomannan, Amphotericin

P-097

Allogeneic Transplant

Risk factors and early mortality causes in allogeneic bone marrow transplantation

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Introduction: Allogeneic hematopoietic stem cell transplantation (HSTC) is associated with the risk of treatment-related mortality (TRM) and mortality associated with recurrence. To determine the risk factors for early mortality, up to 100 days after transplantation (D+100), as well as the causes, are important to select the highest risk group and to develop preventive strategies. Objective: To determine the highest risk group for mortality up to D+100 in HSCT and the causes of mortality in this group. Material and Methods: Review of medical records of all patients undergoing HSCT, from January 2010 to January 2016 in a single hospital. Overall survival (OS) was calculated by the Kaplan-Meier method. Risk factors related to mortality up to D+100 were assessed by bivariate Cox regression methods, log-rank test and multivariate Cox regression. Results: Of 235 patients who underwent bone marrow transplantation, 42 patients died up to D+100, with overall survival of 81.1%. In mortality group up to D+100, 47.6% had AML, high-risk MDS or MPS, 21.4% had ALL, 19% had benign diseases, including immune deficiencies and 12% had multiple myeloma or lymphoma. Regarding the type of transplant, 12% were submitted to related HSCT (REL HSCT), 38% to unrelated HSCT (UNR HSCT) 10x10, 19% to haploidentical transplantation (Haplo HSCT), 8% to UNR HSCT with mismatch and 23% to umbilical cord blood transplant. In relation to the performance status, 83% showed Karnofsky-Lansky ≥ 80. Most of the conditioning regimens (64%) was the myeloablative type, reduced intensity in 24% and 12% non-myeloablative. aGVHD grade II-IV was identified in 30% of patients. In the multivariate analysis evaluating gender, age, diagnosis, type of transplant, Karnofsky-Lansky, disease status and conditioning, older age (HR 1.016, 95% CI: 1.01- 01.03, p = 0.025), HSCT post 2nd recurrence (HR 7.18, 95% CI: 2.81-18.34, P <0.001), myeloablative conditioning (HR 7.17, 95%CI: 2:52 to 20:43, P <0.001) reduced intensity (HR 5.61, 95%CI: 1.77-17.34, P = 0.003) were associated with higher risk of mortality up to D+100. Karnofsky Lansky ≥80% was associated with lower mortality risk (HR 0.031, 95%CI: 0.00-0.23, P = 0.001). When comparing the types of transplant (REL HSCT, UNR HSCT, haploidentical HSCT, cord blood and UNR HSCT with mismatch), there was no difference in relation to the risk of mortality (P = 0.095). Regarding the causes of mortality, 79% had TRM and 21% had recurrence. In the TRM group, 24% had aGVHD grade III-IV as the cause of death. Of these, 77% underwent UNR HSCT, 28% with mismatch. Mortality from septic shock corresponded to 34% of cases, with only 4 cases of multidrug-resistant bacteria. Mortality from viral infection corresponded to 7% and fungal to 10%, with 25% being related to other causes. Conclusion: Age, HSCT post-2nd recurrence and conditioning were associated with increased risk factors for mortality up to D+100. The greater the intensity of conditioning, the higher the risk of mortality. The main cause of death was bacterial infection followed by aGVHD.

Keywords: Early Mortality, Allogeneic Bone Marrow Transplant, Risk Factors

P-098

Allogeneic Transplant

The experience of a bone marrow transplant unit in the State of Ceará in allogeneic transplant

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Introduction: Until 2014, patients in the State of Ceará that required allogeneic bone marrow transplantation were sent to other states. With the experience acquired in autologous transplants, the Allogeneic Transplantation Service was implanted in the state, initially with related donors and, in 2016, with unrelated ones. These advances have ensured improved access to treatment and quality of life of referred patients. Objectives: To disclose the data on allogeneic bone marrow transplantation in a public hospital in the state of Ceará. Methods: Patients underwent myeloablative or reduced intensity protocol, depending on the previous status and underlying pathology. The source of hematopoietic stem cells was peripheral blood or bone marrow. As prophylaxis against GVHD (graft-versus-host disease), patients received methotrexate and cyclosporine. Results: 26 allogeneic transplants were carried out between September 2014 and May 2016, 2 of these unrelated. In 19.23% (5), the source of cells was the bone marrow; 57.69% (15) of the patients were male. The median age was 42 years. The underlying diseases were: acute (7) and chronic myeloid leukemia (2), myelofibrosis (1), acute lymphoblastic leukemia (4), aplastic anemia (5) and myelodysplastic syndrome (7). In 26.92% (7) of the transplants there was major ABO mismatch, one of them requiring erythrocyte removal from the blood unit and 11.53% (3) had minor ABO mismatch. 73.07% (19) of the patients underwent the myeloablative protocol. The median neutrophil engraftment was 16 days and for platelets, 17 days. 80.76% (21) of the patients had febrile neutropenia. Two patients had aGVHD, one responsive to corticosteroid therapy and another refractory to second-line therapy with basiliximab. 30.76% (8) had chronic GVHD. Skin, liver, lungs and oropharynx were affected. To date, 26.92% (7) patients reactivated CMV. One patient is being treated for post-transplantation lymphoproliferative disease. The treatment-related mortality rate was 11.53% (3). One patient died of chronic lung GVHD and another of aGVHD. One patient is receiving post-transplantation hypomethylation due to positive minimal residual disease. One patient with early recurrence is receiving palliative treatment. Conclusion: The initial results of allogeneic transplantation in Ceará demonstrated a low transplantation-related mortality rate and that it is still early to perform the analysis of overall survival and disease-free survival.

Keywords: Allogeneic transplantation

P-099

Allogeneic Transplant

Study of HLA haplotypes in patients candidates to hematopoietic stem cell transplantation

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HLA genes encoded on chromosome 6 are highly polymorphic and HLA allelic and haplotype diversity is a major barrier to find ideal donors (8x8 allelic considering the loci HLA-A, B, C, -DRB1) for hematopoietic stem cell transplantation (HSCT). The large number of available donors in international banks of voluntary bone marrow donors and REDOME increased the probability, but patients with non-Caucasian haplotypes are less likely to find donors, especially those of mixed heritage. The National Marrow Donor Program (NMDP) provides a database that contains the haplotype frequencies estimated using EM (expectation-maximization) algorithms, called Haplostats. Frequency data are shown at the base of 4 predominant ethnic groups: African, Asian, Caucasian and Hispanic. Objective: To determine the number of Brazilian patients in our service that found an unrelated donor in the registries and evaluate their haplotypes. Method: 251 searches for donors for unrelated HSCT were analyzed, registered from period December 2009 to March 2016. The mean age of patients was 38.6 years. Of these, 60.2% (151) were males and 39.8% (100) were females. All patients had HLA-A, -B, -C, -DRB1 and DQB1 typing at high resolution. We presumed the HLA haplotypes and their respective ethnicity using the tool Haplostats and national publications that characterized national haplotypes. Results and Discussion: donors were found by REDOME or at international banks for 84 patients (33.5%) and unrelated transplants with 8x8 compatibility were performed in 54 (21.5%), with 35 donors from the National Bank (64.8%). Donors were found for 30 (11.2%) patients, but they did not undergo transplantation due to death or transfer or because the need for transplantation was dismissed. All patients that found a donor had at least 1 common haplotype among the 100 most common in Caucasoid individuals. Thirty-one (12.3%) of patients who found no donor had at least one black or Amerindian haplotype. Alternative transplants were performed in patients without an 8x8 donor, in 7 (2.8%) with unrelated donor with mismatch (7x8), in 13 (5.1%) using cord blood and in 40 (15.9%) with haploidentical donor. In 5 (1.9%) haploidentical transplant was performed due to the patient's emergency status, although a potential 8x8 donor was located. In twenty patients (8%), no donors were found and alternative transplants were not performed. In the others the analyses were not carried out due to the lack of search completion. Conclusion: The frequency of 33.5% of patients that found donors in the registries is in accordance with the expected. Recruitment directed to haplotypes representative of ethnic minorities is the key to increase the finding of compatible donors.

Keywords: Hematopoietic Stem-Cell Transplantation, HLA Haplotypes

P-100

Allogeneic Transplant

Extramedullary recurrence after allogeneic bone marrow transplantation for primarily chemorefractory AML

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Introduction: Bone Marrow Transplantation (BMT) is one of the few curative options for Acute leukemias (AL), due to both the chemotherapy (CMT) used, as the graft-versus-tumor effect. Recurrence remains the leading cause of death in this context, with isolated extramedullary relapse (EMR) being rare, but more frequent in the context after BMT than post-CMT, probably due to the protective action of the graft-versus-tumor effect in BM than in EM sites. Case Report: 38-year-old male, with a diagnosis of AML in May/ 2015. He received 4 Remission Inductions at an external service, without response and was referred to BMT due chemorefractory disease. The donor was young, male, 33 years old, 10x10 HLA-compatible sibling. TANDEM conditioning protocol was initiated on 10.02.2015 and infusion of 8.8x10 (6) of CD34+ cells/kg harvested from peripheral blood stimulated with G-CSF, by apheresis, on 10.16.2015. Neutrophil engraftment occurred on D+20. Early withdrawal of prophylactic cyclosporine was started and finished on D+116, without GVHD. BM is now in remission, with negative MRD, VNTR full chimera donor. The patient developed right submandibular nodule and poor general status prior to initiating preemptive donor lymphocyte infusion (DLI). Total excision biopsy disclosed submandibular gland diffusely infiltrated by intermediate-sized cells, scarce cytoplasm, marginated chromatin and prominent nucleoli, in addition to positive IH for CD34 and CD117, compatible with Myeloid sarcoma. Myelogram and MRD were performed and ruled out bone marrow relapse. Subcutaneous ARA-C cycles were programmed followed by DLI and local radiation therapy. After 1 ARA-C/ DLI cycle, the BM showed marrow relapse (8% blasts). A new of ARA-C/DLI cycle was performed and he started radiation therapy with 2.25 Gy, fractionated in 14 sessions. At the end of radiation therapy, he started to have dry cough, refractory headache, poor general status and circulating blasts in peripheral blood. CT scans showed a new mass in the anterior mediastinum and CNS. Palliative Care was started and he died on 05.24.2016. Discussion: The EMR rate ranges from 6 to 20% of cases and late recurrences are more common, with concomitant marrow relapse, usually involving soft tissues of the head and neck, bones, skin and CNS/breast, with overall survival at 2 years ranging from 11 to 38%. The main risk factors described are age <18 years, AML M4/5 subtype, cytogenetic abnormalities, disease status, leukocytosis at diagnosis and history of previous extramedullary disease. The therapeutic management remains a challenge, with different local and systemic strategies being observed, such as surgical excision, radiation therapy, high-intensity chemotherapy, hypomethylating agents, DLI, monoclonal antibodies and a new BMT. Conclusion: EMR has a reserved prognosis and no effective therapies, requiring further studies on the real incidence, biological factors involved and appropriate therapies.

Keywords: AML, BMT, Extramedullary relapse

P-101

Allogeneic Transplant

Allogeneic Transplantation in Patients with Acute Lymphoid Leukemia in a Public Hospital Hematology Service in the State of Ceará

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Introduction: Acute Lymphoid Leukemia (ALL) is a lymphoproliferative disease that has excellent response to therapy when it affects children. In adults aged <60, however, the 5 five-year disease-free survival remains about 30%. Thus, bone marrow transplantation is shown as an alternative to patients stratified as high-risk disease. Patients younger than 40 have indication for total body irradiation (TBI) as conditioning regimen; as this treatment is not available in Ceara, these patients are referred to other states. Objectives: To disclose the data on patients diagnosed with ALL from 2011 to 2015 in the Hematology Service of a public hospital in Ceará submitted to allogeneic bone marrow transplantation. Methods: Patients undergoing transplantation in Ceará were submitted to the myeloablative protocol with fludarabine 120 mg/ mm^2 and melphalan 180 mg/ mm^2 without TBI in the conditioning regimen, while those submitted to the transplantation in another state used TBI in the conditioning. The source of hematopoietic stem cells was peripheral blood in all cases. Results: Of the 45 patients who started treatment for ALL from 2011 to 2015, 8 (17.7%) were submitted to transplants, 4 in the state of Ceará and 4 in other states. 75% (6) of the patients were males. Among those performed in other states, 75% (3) was due to the fact they had TBI indication for conditioning and 1 because, at the time, there was no allogeneic transplant service in Ceará. These patients returned to the service in the post-transplant period to be followed together with the transplant center of origin. Among those carried out in Ceará, 50% (2) were older than 40 years, while the others had contraindication to TBI, one due to fungal infection and isolation of multidrug-resistant bacteria at the induction and the other for having undergone CNS prophylaxis with radiation therapy in the induction according to the protocol used. Considering all transplanted patients, 50% (4) had chronic GVHD (graft-versus-host disease), with skin, oropharynx, liver and lung being the affected organs. So far there has been no record of death or disease recurrence. Conclusion: The data show, although there are a few cases, good results in allogeneic transplantation in patients with ALL; however, it is not possible to assess overall and disease-free survival yet. Another relevant factor is that the unavailability of TBI in the state of Ceará is an obstacle to the growth of the Bone Marrow Transplant Service for ALL patients.

Keywords: Transplantation, Allogeneic, Acute Lymphoblastic Leukemia

P-102

Allogeneic Transplant

Study of Natural Killer alloreactivity in hematopoietic stem cell transplantation with haploidentical donor.

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INTRODUCTION: The factors to be considered when choosing the best haploidentical donor in hematopoietic stem cell transplantation (HSCT) are still the subject of research. A potential study target is the presence of alloreactive NK (Natural Killer) cells in the graft. These cells represent a favorable factor for patient recovery, as they decrease the recurrence rate of the disease due to their capacity to eliminate residual tumor cells without inducing GVHD (graft-versus-host disease). NK alloreactivity occurs due to the presence of KIR (Killer-Cell Immunoglobulin-like receptors) present in the donor's NK cells that perceive reduced or no expression of HLA (Human Leucocyte Antigen) class I molecules in the patient's altered cells. The KIR genes are organized into haplotypes, of which two are well characterized and known as A and B. Haplotype A is very common in several populations and has an important characteristic to the presence of only one activator gene (KIR2DS4). Type B has variable numbers of genes and combinations and may have up to six activator genes. Despite the promising results with NK alloreactivity in haploidentical transplants, studies are still scarce, especially in Brazilian patients. OBJECTIVE: In this context, the aim of this study was to describe the KIR genetic diversity and KIR/HLA interactions to predict NK alloreactivity in HSCT with haploidentical donor, using cyclophosphamide after infusion, in malignant diseases, with Brazilian patients and donors. MATERIAL AND METHODS: In this phase of the study, 14 patients were retrospectively assessed at the HSCT service and their respective donors. The rSSO Luminex® technique (polymerase chain reaction-sequence specific oligonucleotides) (Thermo Fisher, USA) was used in HLA and KIR typification. The reactions were read in a LABScan flow cytometer and analyzed using the programs Fusion and Fusion Research, respectively. RESULTS: AA haplotype was identified in 13 individuals (46.42%), 7 receptors and 6 donors; haplotype AB in 6 (28.5%), 2 patients and 4 donors and haplotype BB in 9 (32.14%), 5 patients and 4 donors. Eight patients (57%) were homozygous for KIR ligands from group C1 and two (14%) were homozygous for the C2 group. DISCUSSION and CONCLUSION: The study is still at an early stage; therefore, the small number of samples is insufficient to draw conclusions about the impact of NK alloreactivity in haploidentical transplantation. Interestingly, 50% of patients are carriers of the AA haplotype and could benefit from a haplotype B donor, whereas 71% were homozygous for KIR ligand and opening up the possibilities of donors with NK alloreactivity. The study with larger samples will be needed to assess the impact of NK alloreactivity on transplant outcome.

Keywords: Haploidentical transplantation, Natural Killer Cells, KIR, HLA.

P-103

Allogeneic Transplant

Neutrophil engraftment in elderly patients submitted to Hematopoietic Stem Cell Transplantation (HSCT): importance of geriatric and body composition assessment

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Introduction: Loss of muscle mass is the biggest change that occurs with aging, which may lead to decline in muscle strength and functionality. In 1989, Rosenberg proposed the term "sarcopenia" to describe this age-related decline in muscle mass. Patients with hematological malignancies are usually well-nourished before undergoing HSCT; however, changes in body composition after HSCT have been the subject of studies. Complications post-HSCT, such as infections and graft-versus-host disease (GVHD) can affect body weight and composition. The immunosuppressive therapy and corticosteroid use post-HSCT also alter skeletal muscle metabolism. Thus, treatment and complications post-HSCT have significant negative effects on lean muscle mass, especially in elderly patients. Objectives: To determine whether body composition measures have an impact on outcomes of elderly patients submitted to HSCT. Methods: Retrospective longitudinal study carried out through the review of medical records of 48 patients aged ≥ 60 years submitted to HSCT at Hospital Israelita Albert Einstein, from 2013 to 2015, with chest Computed Tomography (CT) scans being performed during clinical evolution in up to 60 days before HSCT or 15 days after transplantation. Body composition data were analyzed in chest CT scans at T4 level using the Sliceomatic® program. The SSPS x program was used to calculate descriptive statistics for age, body mass index, hand grip strength and body composition parameters. Results: Of the 48 patients assessed, 24 were males. The median age was 67 years (± 4.2). In relation to the underlying disease, it was observed that 35.4% were diagnosed with multiple myeloma, 18.8% had myelodysplastic syndrome, 14.6% had lymphoma and 10.4% had acute myeloid leukemia, whereas 10.8% had other diagnoses at a lower proportion, such as amyloidosis, cutaneous lymphoma and lymphocytic lymphoma. Regarding the type of HSCT, 50% were autologous, 45.8% were allogeneic and 4.2% were haploidentical. In relation to body mass index (BMI), 45.8% of the patients were within the normal range, 21% were overweight and 5% were considered underweight. The median Hand Grip strength was 29 kgf (± 9.2). Of the 48 assessed patients, neutrophil engraftment showed a median of 13 days (± 4.3); 17 patients had acute GVHD, with 9 being Grade I-II and 8 Grade III-IV. 60.4% of patients are alive; of the 19 deaths, 10 were not related to recurrence. Evaluation of the chest CT found a mean muscle area of 151 cm^2 (± 41) and subcutaneous adipose tissue of 230.5 cm^2 (± 78). The only positive correlation was found between neutrophil engraftment and subcutaneous adipose tissue ($r = 0.8$, $p < 0.05$). Conclusion: Our elderly patients submitted to HSCT showed a strong correlation between neutrophil engraftment and subcutaneous adipose tissue. The assessment of body composition in this group of patients may provide data associated with prognosis, thus changing nutritional and geriatric conducts in HSCT.

Keywords: Body Composition, Sarcopenia, Oncogeriatrics, Hematopoietic Stem Cell Transplantation

P-104

Allogeneic Transplant

Bone marrow stimulated with Granulocyte-colony stimulating factor (G-CSF): are there any benefits in allogeneic transplantations?

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Introduction: the use of allogeneic hematopoietic stem cell transplantation (HSCT) for the treatment of several malignant and non-malignant diseases has increased over the last 50 years. Currently, the most commonly used source of hematopoietic stem cells (HSC) in transplantation is mobilized peripheral blood (MPB), which contains greater numbers of CD34+ cells when compared to bone marrow (BM). However, the larger number of lymphocytes in the MPB seems to be associated with increased incidence of graft-versus-host disease (GVHD). A third alternative is the use of BM stimulated with G-CSF (SBM), which can lead to a larger number of HSC, without concomitant increase in GVHD. Objectives: To compare the cellular product obtained from BM, SBM and MPB and its impact on allogeneic transplants performed in a hospital in Sao Paulo. Material and Methods: study of allogeneic HLA-matched HSCT, related or not, and haploidentical transplants performed from January 2011 to December 2014. The donor received 10mg/kg/day of filgrastim for 4 days for SBM collection and 5 days for MPB. The BM target volume collected was 10-20 mL/kg of the recipient to obtain a minimum of 2.0 x10E8 nucleated cells and a target of 5x106 CD34+ cells/kg of the recipient for MPB. The characteristics of the collected products and clinical outcomes were compared depending on the source used. Results: A total of 35 BM transplants, 43 with SBM and 35 with MPB were assessed. The clinical and demographic characteristics were similar, except the mean age of the recipient and donor and the recipient's mean weight, which were higher in the SBM group when compared to BM. The median volume collected/kg of recipient was 25.96 mL (BM), and 20.08 (SBM) ($p < 0.001$). The mean cellularity/kg of the recipient was 5.13x108 (BM) and 5.58x108 (SBM) ($p < 0.999$). The total number of CD34+ cells/ kg of the recipient was 5.20x106 (BM) and 3.67x106 (EOM) ($p < 0.999$). The median neutrophil engraftment was lower with SBM (15 days) compared to BM (19 days) ($p = 0.046$). Platelet engraftment was similar (median 21 and 28 days, respectively; $p = 0.097$). The incidence of acute and chronic GVHD was 33.3% and 0% with BM, 52.9% and 35.3% in the SBM and 62.5% and 12.5% in MPB, with no significant difference ($p = 0.429$ and $p = 0.063$, respectively). The hemoglobin variation in the donors of SBM and BM pre and post-collection was, respectively, 2.50 g/ dL and 3.71 g/ dL ($p = 0.034$), and the hematocrit was 7.07% and 10 57% ($p = 0.035$), with no more need for transfusion. Conclusion: The use of G-CSF did not significantly alter the composition of the collected product, but allowed reaching the target cell with a smaller volume of marrow aspirate, which could have an impact on donor safety. HSCT with SBM resulted in faster neutrophil engraftment, and in this short follow-up, it showed no increase in the incidence of acute and chronic GVHD.

Keywords: Bone Marrow Transplantation. Hematopoietic Stem Cell Transplantation, Stimulated Bone Marrow

P-105

Allogeneic Transplant

Validation of the Disease Risk Index refined for allogeneic transplantation in two Brazilian institutions and analysis of risk factors related to transplantation and the recipient

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Introduction: The hematopoietic stem cell transplantation (HSCT) is a potentially curative therapy for several hematological malignancies. The pre-transplant risk assessment is crucial and, currently, some algorithms are used in clinical practice. The Disease Risk Index (DRI), updated in 2014, was developed as a tool to compare different populations. Objective: To validate the DRI in two heterogeneous Brazilian institutions and identify risk factors for death. Material and Methods: This is a multicenter retrospective study that included patients with hematological malignancies who received the first HSCT between 2010 and 2014. The DRI was defined retrospectively. Overall survival was estimated by the Kaplan-Meier method. Risk factors for death were estimated by the stratified Cox model. Results: 275 patients were included. The median follow-up was 37 months. The median age was 37 years, 26% younger than 18 and 25% over 50 years. The diagnoses were very wide-ranging, including 178 acute leukemias, 35 lymphomas, 24 myelodysplasias and 17 myeloproliferative diseases, among others. The source was bone marrow (BM) in 169 transplants, peripheral blood (PB) in 75 and umbilical cord blood (UCB) in 31. 145 donors were related and 110 were unrelated, with 20 haploidentical ones. The DRI was low in 6%, intermediate in 60%, high in 26% and very high in 8%. The mortality at 100 days was 26%. The estimated survival at 1 and 3 years was, respectively, 54% and 40%. The median survival was not reached in the low risk DRI, was 22 months in the intermediate risk and 7 months in high and very high risk DRI ($p = 0.002$). In the multivariate analysis, the following risk factors were identified: age (<18 years, compared to age 18-50 years, HR = 0.5; $p = 0.006$), transplant with unrelated donor (HR = 2.0, $p < 0.001$) and haploidentical (HR = 2.5; $p = 0.008$) and high/very high DRI (compared to intermediate risk, HR = 1.8; $p < 0.001$). Conditioning regimen and source of stem cells were not significant in the multivariate analysis. Specifically regarding the UCPB source, not controlling by DRI in the multivariate analysis made this source marginally associated to a higher risk of death (HR = 1.7; $p = 0.06$ against HR = 1.3; $p = 0$, 31 controlled by the DRI analysis). Discussion: This study validates the Disease Risk Index, in a heterogeneous Brazilian sample, as an important tool to control different diseases at different stages. More importantly, not controlling by DRI in this sample could have led to incorrect inferences, especially in relation to umbilical cord blood use. The use of alternative donors (unrelated and haploidentical) was associated with higher risk of death. Taking into account that the study took place in a recent period (between 2010 and 2014), this result was somewhat unexpected. Conclusion: The DRI can be used by Brazilian institutions to compare their results with international institutions.

Keywords: Disease Risk Index, Allogeneic Transplantation, Unrelated Transplantation, Haploidentical Transplantation

P-106

Allogeneic Transplant

Strategies for managing patients with long survival after hematopoietic stem cell transplantation

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Introduction: long-term medical follow-up post-hematopoietic stem cell transplantation (HSCT) is essential to detect complications related to the procedure and to prevent the incidence of morbidity and mortality. Data management of long-term transplantation survival in Brazil is a difficult task, because in addition to the economic problems of the country, some transplant centers have a large number of live post-transplant patients and few human and financial resources to keep updated data. Objective: To improve the quality of information of patients with long survival after HSCT. Material and Methods: Between 10/1979 and 05/2016, 2,600 transplants were performed and of the living patients, 1,006 had more than 5 years of survival. The experience of the analysis of 2,172 patients submitted to allogeneic transplantation showed that 9% of patients rejected or relapsed one year after transplantation; 14% of 555 developed chronic graft-versus-host disease (GVHD) after the first year of transplantation. The incidence of malignant neoplasms, especially in patients with Fanconi anemia (FA) is also relevant. Data analysis showed that of 17 patients with AF who died after 5 years of transplantation, 9 died due to cancer. To identify, locate and monitor patients with long survival, our group developed a flowchart to recover patients that had not had a consultation for more than five years, with the exception of constitutional anemias, where monitoring should be more frequent. If the date of last contact in the database (DB) was more than 2 years in constitutional anemias and 5 for the others, we checked the Hospital Information System (HIS) for recent consultations. We created and shared a list of patients that needed new follow-up in Google Drive™ with the Medical Social Service (MSS), medical service and the "data managers". Any patient information is updated in this list and an alert email is sent to the "data managers". Patients who live far from the transplant center are contacted through the MSS, which verifies whether the patient is being followed and undergoes examinations. We contact the medical professional at the origin, who is instructed to send a report of follow-up with all the necessary information and test results by email. Results: Using the flow chart we were able to maintain the DB updated for 125 patients with FA with longer survival than 5 years, and despite the many difficulties, only 5 patients were lost to follow-up. Discussion: The implementation of the work is not fully consolidated; for that purpose, we must apply it to other diagnoses, which requires at least a year of assessment. Conclusion: After this flowchart was implemented, there was significant improvement in data collection for FA, ensuring its accuracy as well as identifying complications such as chronic GVHD and secondary malignancies, in order to improve long-term results.

Keywords: Follow-Up, Follow-Up Loss, Allogeneic

P-107

Allogeneic Transplant

Survival analysis of acute lymphoblastic leukemia patients submitted to myeloablative allogeneic stem cell transplantation, according to minimal residual disease status

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Introduction: Evaluation of Minimal Residual Disease (MRD) before and after allogeneic Stem Cell Transplantation (alloSCT) is an important predictor of relapse in the post-transplant period in Acute Lymphoblastic Leukemia (ALL). The early detection of MRD after transplantation allows therapeutic intervention in an attempt to prevent overt disease. Focusing on patients who underwent alloSCT with myeloablative conditioning, survival was assessed according to MRD levels and other parameters that influence patient survival. Objective: The evaluation of overall survival (OS), relapse-free survival (RFS) and relapse incidence (RI) in ALL patients with a sensitivity of 10-4 and 10-5 leukemic cells, assessed by flow cytometry (FC), before alloSCT and at days +100, D+200 and above. Material and Methods: MRD results of 161 ALL patients were reviewed, who were submitted to myeloablative alloSCT between February 2005 and December 2015. Not all MRD assessments were performed in the same patients at the 2 moments in time. The median age was 20 years (1-47), and the median follow-up was 13.9 months (0.5 – 96.89). Four or eight color panels of monoclonal antibodies were used for FC, based respectively on BFM panels and Euroflow panels for MRD in ALL. 500.000 to 5.000.000 events were acquired respectively in flow cytometers of 4 and 8 colors. Statistical analysis was performed using SPSS software (IBM)®. Parameters evaluated for statistical purposes were: MRD level (>0.01% or <0.01%), age (≤18 or > 18 years old), clinical remission status (CR1 or ≥CR2), donor (related or unrelated), stem cell source (BM, PBSC, UCB), acute or chronic GVHD. Results: MRD level > 0.01% and < 0.01% before alloSCT (n=126) had an impact on the probability of RFS (6% versus 42%) (p<0,001) and on RI (81% versus 44%) (p < 0,001), respectively. There was no statistical significance for OS (p=0,08). MRD evaluation (level > 0.01% or < 0.01%) on D+100 (n=107) after SCT showed significance on the probability of OS (21% *versus* 52%)(p<0,002), RFS (0 *versus* 38%)(p<0.001) and RI (100% *versus* 53%) (p< 0,001). On D+200 or above (n=84), the probability of OS was 8% *versus* 60% (p < 0.001), of RFS was 17% *versus* 35% (p<0.001) and of RI, 83% *versus* 54% (p< 0.001), respectively, for MRD higher or lower than 0.01%. In the multivariate analysis of parameters evaluated before alloSCT, the factors that influenced RFS and RI were: MRD status (p<0,001), donor gender (p= 0,04) and related or unrelated donor (p=0,01). Only MRD status had an impact on RFS and RI after alloSCT (p<0.007). There was no impact of MDR status post- alloSCT on OS (p=0,662). Discussion: The best moments in time for MRD assessment aiming at relapse prediction were before SCT and above D+100 after that. However, at these moments in time, MRD flow assessment cannot effectively identify all individuals that will relapse after SCT, requiring the association of a more sensitive approach or methods, such as PCR, for this purpose.

Keywords: Minimal Residual Disease, Acute Lymphoblastic Leukemia, Allogeneic Stem Cell Transplantation

P-108

Allogeneic Transplant

Impact of lymphocyte infusion after allogeneic of hematopoietic stem-cell transplantation

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Introduction: The allogeneic hematopoietic stem-cell transplantation (BMT) is a treatment option for patients with hematological malignancies, as it provides increased survival and cure. The major concern is disease recurrence after BMT. Therefore, techniques have been developed in an attempt to increase the graft-versus-leukemia (GVL) effect, such as lymphocyte infusion, known as DLI (donor lymphocyte infusion), which has the disadvantage of triggering GVHD and aplasia. Objectives: The objective of the study is to describe the indication of lymphocyte infusion post-BMT and the response. Material and Methods: Analysis of patients who underwent BMT and hat underwent lymphocyte infusion from 2010 to 2016 in a single hospital. The analyzed variables were age, gender, diagnosis, date of BMT, BMT type, indication of DLI, number of infused cells, presence or absence of GVHD, response to DLI and survival. Results: The total number of assessed patients was 14, with male gender prevalence (64.3%). The mean age was 46 years (11-70 years). Among the diseases found, 43% had AML diagnosis, 22% HL, 14% NHL, 14% MDS and 7% ALL. Regarding the type of BMT, 64.3% were related and 35.7% unrelated. The main indication of DLI was disease recurrence (86%), followed by loss of chimerism (7%) and part of the conditioning protocol (7%). The number of infused CD3 cells was on average 3.91 X 10 7/ kg (0.5 to 17.63 x 107/kg). The mean time between the lymphocyte infusion and the BMT date was 152.5 days (11-2616 days). Only 25% of patients had GVHD after DLI. Of the 35% who developed it, the manifestations occurred in the GIT and skin, clinical grade 2, and only 1 patient developed clinical grade 3 in the skin. Chronic GVHD was observed in 2 patients. Regarding the response to treatment with DLI, 71.4% responded to treatment and overall survival was 47.6%. There was no significant difference when compared to the type of transplantation (p = 0:48) and underlying diagnosis (p = 0:37). Discussion: The DLI indication, the ideal time and the number of cells are controversial subjects in the literature. It is a rescue treatment option in case of disease recurrence or loss of chimerism. According to Luznik et al., it is not known whether induction chemotherapy at the time of relapse followed by DLI increases disease-free survival. Regarding GVHD after DLI, our incidence resembles that of literature. Flowers et al studied 225 cases of BMT and 39% had GVHD after DLI and the main risk factor was CD3 cell infusion greater than 10 x 107/kg. In our series, the only patient who developed severe GVHD was the one that received the highest number of lymphocytes (17.63 x 10 7/ kg). There were no cases of post-DLI aplasia. Conclusion: Despite the small number of patients analyzed, we conclude that lymphocyte infusion is an important tool when dealing with the underlying disease.

Keywords: BMT, DLI, GVHD

P-109

Allogeneic Transplant

Influence of KIR-HLA genotype combined with cytomegalovirus reactivation on the outcome of allogeneic HSCT, HLA compatible, related and without T-lymphocyte depletion

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Many studies have shown that KIR-HLA interaction can influence the outcome of allogeneic hematopoietic stem-cell transplantation (HSCT). In addition to this interaction, other factors such as the post-transplant reactivation of cytomegalovirus (CMV) infection may also have an effect on HSCT outcome. The aim of the study was to evaluate the possible interaction of KIR and HLA genes, combined with the post-transplant CMV reactivation on the clinical outcome of HSCT, HLA compatible, related and without T-lymphocyte depletion in patients with hematological diseases. This was a prospective study carried out at the Universidade de Campinas Hematology Center and 50 patients with their donors were included and followed from 2008 to 2014. The KIR and HLA class I genes were genotyped by polymerase chain reaction using the protocol with Sequence-Specific Oligonucleotide (SSO) utilizing a commercial KIR and HLA genotyping kit (One Lambda Inc R, Canoga Park, CA, USA). Patients were grouped based on the presence of the HLA-Bw4 and/ or Cw ligands, combined with the KIR genotype of the respective donors. CMV reactivation was detected using antigenemia tests and nested PCR performed with specific primers described by Demmler et al. The analysis performed before transplantation in relation to immunization against CMV showed that 47 donor/patient pairs had positive/ positive IgG, 2 pairs had negative/ positive IgG and 1 pair had negative/ negative IgG. After the transplant, CMV reactivation occurred in 66% (33/50) of patients, demonstrating a beneficial effect on overall survival ($p = 0.015$) and event-free survival ($p = 0.001$). The impact of CMV reactivation after transplantation was evaluated for patients with myeloid diseases ($n = 18$), showing that among patients that had CMV reactivated, those with one or more missing ligands for the inhibitory KIR receptors ($n = 12$) had better overall survival ($p = 0.085$) and event-free survival ($p = 0.013$) compared with patients with all the ligands for present inhibitory KIR ($n = 6$). Many studies have shown that CMV reactivation influence the post-transplant outcome, decreasing recurrence rates in patients with acute myeloid leukemia. These studies suggest that the breaking of tolerance to NK cells allows better response in patients with myeloid diseases. Our results indicate that the KIR-HLA interaction, combined with post-transplant CMV reactivation, can have an effect on the outcome of allogeneic, HLA-compatible transplantation, particularly in myeloid diseases.

Keywords: natural killer cells, GVHD, CMV, myeloid leukemia, HLA

P-110

Allogeneic Transplant

Use of brentuximab vedotin followed by related allogeneic hematopoietic stem cell transplantation (HSCT) in the treatment of patient with relapsed Hodgkin's lymphoma – a case report

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INTRODUCTION: Hodgkin's lymphoma (HL) has high cure rates with the first-line treatment; however, 15 to 25% of cases can relapse or be refractory. In these cases, the standard rescue treatment is carried out with high-dose chemotherapy followed by autologous HSCT. Recurrence after autologous transplantation have a poor prognosis and few treatment options. OBJECTIVE: To describe a case of HL that relapsed after autologous transplantation, successfully treated with brentuximab followed by allogeneic HSCT. CASE REPORT: W.S.R., 16-year-old patient, diagnosed with nodular sclerosis HL stage IIB in Jan/2010, treated with 6 cycles of ABVD (Adriblastine, Bleomycin, Vincristine, Dacarbazine) associated with cervical and mediastinal radiation therapy. He showed complete response and remission for a year. He had recurrence with abdominal mass in Oct/2011 and received rescue chemotherapy with 2 cycles of ESHAP (etoposide, methylprednisolone, cisplatin and cytarabine) with partial response and autologous HSCT. The conditioning regimen was BEAM (BCNU, etoposide, Aracytine and Melphalan) and the transplant was performed without severe complications. At the reassessment 6 months after the autologous HSCT, the CT scan showed the presence of a retroperitoneal node and PET-CT activity in the right armpit and abdomen, with recurrence being confirmed by axillary lymph node biopsy. He was submitted to axillary and abdominal radiation therapy followed by chemotherapy with 4 cycles of GDP (Gemcitabine, Cisplatin and Dexamethasone) regimen, followed by 3 doses of Brentuximab, 1.8 mg/kg every 3 weeks. The control PET-CT showed complete remission of the disease. The related compatible HSCT occurred in Apr/2014 with HLA-compatible 10/10 sibling donor (loci A, B, C, DQ and DP). The selected conditioning regimen was reduced intensity with Fludarabine 132 mg/kg and Melphalan 140 mg/kg and prophylaxis against graft-versus-host disease with cyclosporine and methotrexate 10 mg/m^2 on D+1 and 5 mg/m^2 on days +3 and +6. The source of cells was peripheral blood and the number of infused CD34+ cells was 8,25x106/kg. He had hematological toxicity grade IV and mucositis grade III and febrile neutropenia as complication. Platelet engraftment occurred on day +15 and neutrophilic engraftment on day +20 and the patient was discharged 18 days after transplantation. Chimerism analysis on days +30 and +100 showed complete engraftment (100% donor cells). Evaluation through PET-CT 70 days after the HSCT showed no signs of disease activity and biannual control CT scans have been negative. The patient is alive without evidence of disease, with a follow-up of two years after allogeneic HSCT. CONCLUSION: The role of allogeneic HSCT is still controversial in patients with relapsed HL. Reduced -intensity conditioning regimen and infusion of peripheral blood, together with disease control pre-HSCT with Brentuximab seems to be effective in the treatment of recurrences.

Keywords: allogeneic transplantation, Hodgkin's lymphoma, Brentuximab.

P-111

Allogeneic Transplant

Allogeneic Bone Marrow Transplantation in Chronic Myeloid Leukemia - profile of a center in the last 20 years

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Introduction: Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder that results from the neoplastic transformation of hematopoietic stem cells and accounts for 15% of leukemias. It presents a specific cytogenetic abnormality, the Philadelphia (Ph) chromosome, derived from the translocation between chromosomes 9 and 22. The molecular consequence of this alteration is the encoding of a hybrid protein, BCRABL1, with tyrosine kinase activity and autonomous capacity of activation, responsible for the pathogenesis of leukemia. The use of tyrosine kinase inhibitors (TKI) in the last fifteen years has dramatically changed the scenario of the results obtained with the treatment in CML. Objectives: To analyze the profile of allogeneic hematopoietic stem cell transplantation (HSCT) as a treatment modality for patients with CML treated at a referral center. Method: Retrospective evaluation of medical records in patients with CML treated at the Hospital Universitário Walter Cantídio (HUWC) in the last twenty years. Data from medical records were analyzed in 80 patients with CML followed at HUWC between 1996 and 2016. Results: A total of 81 transplants was performed. Only one patient underwent the procedure twice. As for gender, 47 (58%) were men. The mean age range was 34.3 years. Most patients (90%) were in the chronic phase of the disease at the time of the HSCT. Sixty grafts (74%) were performed between 2000 and 2005. The last five years of the study period concentrates six of the eight cases of the disease at the advanced phase (blast crisis after remission with polychemotherapy). Six patients received bone marrow from unrelated donors. Overall treatment-related mortality was 25%. Different centers in Brazil have received our patients for transplantation. In the last two years, with the performance of allogeneic HSCT in our service, our patients have not been referred to other centers. Discussion: The treatment of CML with TKI has changed the natural history of the disease, adding significant improvement to survival. Therefore, the easier oral administration, fast response and excellent tolerability in most patients have changed the CML treatment algorithm, choosing chemotherapy with molecular target as the first-line therapy. The HSCT, introduced in the late 70s, lost its former importance as the "only curative therapy." We observed a significant concentration of transplants in the period between the years 2000 and 2005. This finding demonstrates the evolution of the treatment algorithm in CML. It is noteworthy that, in Brazil, the use of imatinib as first-line treatment occurred after 2008. Conclusion: We can observe a significant decrease in transplantation as the treatment option for CML in the sample. However, a chronological delay in this trend can be observed, when compared with the literature.

Keywords: Chronic Myeloid Leukemia, Allogeneic Transplantation

P-112

Histocompatibility

IL4RA Polymorphism Impact on Chronic Periodontitis Patients from Northwest Paraná

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Chronic Periodontitis (CP) is a complex pathogenesis that involves persistent bacterial infection, immune system activation and bone tissue destruction. The immune system activation includes cytokine production, such as interleukin-4 (IL-4) produced by leukocytes. IL-4 has a central role in the development of a Th2 response. The biological effects of IL-4 occur through binding to IL-4 receptor (IL-4Rα) and they suffer influence of genetic polymorphisms. Until now, there have been few studies that investigated the presence of IL-4RA polymorphisms in association to the chronic state of periodontitis. The aim of this study was to analyze the IL4RA polymorphism (rs1801275) in relation to susceptibility or resistance to CP development. This study included 53 control individuals and 49 cases evaluated in dental clinics of the State University of Maringa and Inga University. Peripheral blood was collected from these individuals and DNA was extracted using the salting-out method. The IL4RA +1902A>G (rs1801275) genotyping was performed by PCR-SSP using the Invitrogen kit Cytokines®, USA. The amplicon was subjected to agarose gel at 3% and was visualized using a UV transilluminator. Allele and genotype frequencies were assessed using SNPStat software. A p value < 5% was considered statistically significant. The allele and genotype frequency distributions were in Hardy-Weinberg equilibrium. When we analyzed the genotype frequencies, the A/G was less frequent in CP than in controls (30.6% vs. 52.8%, P:0.03, OR:0.39, CI:0.17-0.89; co-dominant inherence model). Genotypes with the G allele (A/G+G/G) were also less frequent in the case group (36.7% vs. 58.5%, P:0.02, OR: 0.41, CI:0.19-0.91; dominant model), such as the A/G genotype compared with the homozygous A/A+G/G (30.6% vs. 52.8% P:0.02, OR:0.39, CI:0.17-0.89, overdominant model). The best model according to the Akaike information criterion (AIC) is the overdominant model. When the data were adjusted by ethnic group, the overdominant models were also found to being a protection factor and A/G was significantly lower in mixed-race individuals (OR=0.14, CI=0.02-0.93). When the analyses were stratified by smoking status into groups of smokers, never smoked and stopped smoking, smokers with CP had higher frequency of the A/A genotype (OR=5.16, CI=1.13- 23.3). Our results support the fact that the G allele (+1902) may interfere in IL-4Rα signaling and binding between IL-4Rα and IL-4. This process promoted Th1 response. In contrast, the A/A genotype confers CP susceptibility in smokers. In conclusion, the results suggest that the A/G genotype conferred resistance to CP, in an overdominant model, with smoker mixed-race individuals. Thus, the +1902 A/G SNP of IL4RA seem to be associated with CP development. In order to obtain more substantiated results, our preliminary results should be indicative for prospective studies investigating a larger number of individuals.

Keywords: Chronic periodontitis, IL4RA, polymorphism, cytokine genes

P-113

Histocompatibility

Influence of TNFA polymorphisms on Chronic Periodontitis in Brazilian patients

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Chronic Periodontitis (CP) disease is an oral inflammatory disease manifesting as chronic inflammation, with microbial infection and immune system activation, affecting the gingival tissue and which may lead to the loss of tooth-supporting tissues. Tumor necrosis factor alpha (TNFα) mainly produced by macrophages is a cytokine that plays an important role in the inflammatory response in CP. This study was carried out in order to evaluate possible associations between TNFA (rs1800629, -308G>A, and rs361525, -238 G>A) and CP. A case-control study was carried out with individuals from southern Brazil, patients with CP (n=47) and healthy controls (n=53). Genotypes were determined by sequence-specific primer (SSP) technology using the Invitrogen kit Cytokines®, USA. Statistical analyses were performed using the SNPStats software to determine the association and testing for Hardy-Weinberg equilibrium. Adjustment of genotypic differences for the effect of gender, ethnic, and smoking status was applied. For all patients, TNFA -308 G/A genotypes were associated with protective effect in CP (OR=0.33; CI:0.13-0.86) and when covariate ethnicity was analyzed, it also was observed in Caucasian patients with CP (OR=0.04; CI:0.00-0.45). Interaction analysis with the covariate smoking habits showed that -308 G/G is a risk factor for CP in smoker patients (OR=7.20; CI:1.37- 37.86) and also in ex-smoker patients (OR=3.66; CI:1.22-10.96), but A/G is a risk factor only for smokers (OR=11.25; CI:1.11-114.37). For TNFA-238, the G/G genotype was a risk factor for smoker patients with CP (OR=14.81 CI: 2.88-76.00), as well as for ex-smoker patients (OR=4.79; CI: 1.70-13.48) and Black patients with CP (OR=9.55; CI:1.12-10.43). There were no significant associations between TNFA alleles with CP and when the covariate gender was analyzed. Some studies have reported the contribution of TNFA genotypes on CP susceptibility. TNFα levels in periodontal tissues were associated to endothelial injury and attenuated the osteogenic differentiation capacity of human periodontal ligament stem cells. Our data showed that the TNFA (rs1800629 and rs361525) was associated with smoker CP patients. It highlights the need for more samples to get more reliable results.

Keywords: Chronic Periodontitis, SNP, TNFA, cytokine

P-114

Histocompatibility

IL17 gene polymorphisms and Chagas disease in the south and southeast regions of Brazil

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Introduction: Chagas disease (CD) is a common anthropozoonosis in the Americas, described as the most serious parasitic disease in Latin America. Interleukin-17A (IL-17A) and IL-17F are cytokines that play an essential role in inflammatory processes and probably in CD. The aim of this study was to investigate possible associations between genetic polymorphisms of IL17A G197A (rs2275913) and IL17F C7488T (rs763780) and CD and/or severity of left ventricular dysfunction (LVD) in patients with chronic chagasic cardiomyopathy (CCC). Material and Methods: A controlled study with 260 patients and 92 controls was carried out in the South/Southeast regions of Brazil. The genotyping was performed by PCR-RFLP (Restriction Fragment Length Poly- morphism). Results: The AA genotype and A allele of IL17A were more frequent in patients with CCC and severe LVD, when compared to the control group (13.8 vs. 2.2%, OR 6.96, 95%CI:1.29 - 37.41, P=0.042; 35.3 vs. 23.4%, OR 1.78, 95%CI 1.01 - 3.14 P=0.043, respectively). In male patients with CCC and severe LVD, the frequency of CT genotype of IL17F was higher than in patients with CCC and mild to moderate LVD (34.5 vs. 8.7%, OR 6.02, 95% CI 1.18 -30.78, P=0.034), and in patients without CCC (34.5 vs. 4.2%, OR 6.70, 95%CI 1.19 - 37.53, P=0.022). Conclusion: The results suggest possible involvement of the polymorphism IL17A (AA genotype and A allele) in the development of CCC with severe LVD and IL17F (CT genotype) in male patients with CCC and also severe LVD.

Keywords: Chagas disease, chagasic cardiomyopathy, genetic polymorphisms, IL1

P-115

Histocompatibility

Association of HLA-class I, class II and MICA gene polymorphisms in leprosy patients and their household contacts.

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Introduction: Leprosy is a chronic infectious disease caused by a highly infectious microorganism of low pathogenicity. HLA genes can participate in the host-pathogen interaction process as susceptibility and/or disease resistance factors. Objectives: The aim of this study was to investigate the possible association of MHC class I and II and MICA gene polymorphisms with leprosy patients and their household contacts. Material and Methods: This study was carried out with 183 leprosy patients in the northwest of Paraná and 238 healthy controls that had prolonged contact with patients, but were not relatives. Polymorphisms of genes HLA-A, B, C, MICA, DRB1 and DQA/DQB were investigated by LABType®SSO and genes HLA-A, B, and DRB1 with the LABType® SSO HD kit. Statistical analysis was performed using Chi-square test with Yates correction or Fisher's exact test, with Bonferroni correction (Pc). Results: The sample was in HW equilibrium. Our results for allelic groups of MHC class I showed that HLA-C*07 was higher in the control group than in patients with leprosy by itself (Pc = 0.05) and HLAB*08 was also higher in the control group than in patients with the multibacillary (MB) form (Pc = 0.04), suggesting protection against the disease and its most severe form, respectively. As for the HLAC*17 allele, it indicated susceptibility to the clinical paucibacillary (PC) form when compared with the control group (Pc = 0.05) and HLA-C*03 was higher in MB patients than in PB patients, suggesting a risk for the most severe form (Pc = 0.02). A protective association was observed between the specific allele HLA-C*07: 01 (Pc = 0.001) and leprosy by itself and for the MB form and HLA-B*08: 01 (Pc = 0.04) also showed a protective effect for this clinical form. The specific allele HLA-C*17: 01 showed susceptibility to the PB form (Pc = 0.005). The MICA*008_B*08 Haplotype (Pc = 0.01) was associated with protection against leprosy by itself and its most severe form, MB. As for the MHC allelic groups class II, the frequency of the DRB1*04 allele was higher in the control group than in leprosy patients (Pc = 0.046), respectively. The haplotype DRB1*14-DQA1*01-DQB1*06 was associated with leprosy by itself (Pc = 0.39), but lost statistical significance after Bonferroni correction. Moreover, the DRB1*15:02 and DQB1*06:01 alleles were associated with susceptibility to leprosy by itself and for the MB form, but also lost their statistical significance after correction. On the other hand, DQA1*03:01 (Pc = 0.009) was associated with protection against leprosy by itself and the MB form when compared to controls. Conclusion: The results indicate that the class I and II MHC genes may influence the development of leprosy or protection against it in patients and their household contacts and may also have some influence in the most aggressive forms of the disease.

Keywords: Leprosy, HLA Genes, MICA, *Mycobacterium Leprae*, Genetic Predisposition.

P-116

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Pastoral Services in a hematological therapy center of a hospital in southern Brazil.

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Introduction: The study hospital was founded under the direction of Lutheran deaconesses, providing pastoral care to their patients and treating them through an ecumenical and inter-religious perspective. The specific objective of this service is to offer pastoral, ecumenical, inter-religious and personalized care to hospitalized individuals, their families and collaborators. This assistance to the hematological patient is essential, as the work developed in this unit considers the human being in their entirety. Objectives: To describe the Pastoral Service in a hematological therapy center of a hospital in southern Brazil. Material and Methods: Pastoral Service experience report in a hematological therapy center of a hospital in southern Brazil. Results: Through the integrated information system, the Pastoral Service have access to the name, bed and religion of the patients admitted in this unit. A member of the pastoral team is responsible for assistance to patients, families and collaborators at the hematological therapy center. Assistance is offered to everyone, while respecting their culture, creed, faith or atheism. The visit should always aim at the understanding of the other's way of being, with ecumenical openness, by putting oneself in the other's place and listening. By being a comforting voice, but also how to be a complaint voice (ethical dimension). This service must measure the chances and limits of the pastoral action and attitude at the Hematological therapy center. When fighting the disease, in the cure and treatment processes, the pastoral care has its active space beside the patient and with the care team. The work of the pastoral service goes hand-in-hand with that of psychology. There is a harmony between psychology and pastoral service, which makes it easier to feel and understand the needs in this unit. Both participate in activities such as, weekly during the round, training, pre-BMT interview and discussion with the specialist, which also occurs weekly. Discussion: The verbal report of patients, families and collaborators is that the pastoral work carried out at this admission unit brings tranquility, calmness, confidence and comfort, by being able to talk about their fears and concerns, as well as having their sacramental and spiritual needs met. Conclusion: The Pastoral Service tries to work together with all the assistance sectors at the hematological therapy center, being a proactive and regular work. It is also always willing to help in cases of necessity. The assistance provided by the pastoral service is to support the patient, who is going through a moment of weakness and concern. However, the pastoral service must be better organized to be even more active and care for the patients admitted in this unit.

Keywords: Pastoral, spirituality, religiousness, BMT

P-117

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Participation of a nursing technician in the multidisciplinary round in a hematological therapy center of a hospital in southern Brazil.

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Introduction: The Hematological Therapy Center is characterized by treating patients with hematological diseases and those submitted to autologous and allogeneic hematopoietic stem cells transplantation. The term "round" is used in health centers for scheduled meetings for discussions and case discussion. The round practice is carried out in this center aiming to share all relevant information to the patient care to ensure an improvement strategy in the continuity of care. However, in general, the description of such action in the literature narrates the participation of a multidisciplinary team, but only higher-education professionals. Objectives: To describe the multidisciplinary round that occurs with the participation of a nursing technician in a hematological care unit of a hospital in southern Brazil. Material and Methods: Experience report of the participation of a nursing technician in a multidisciplinary "round" in a hematological therapy center. Results: The rounds at the unit occur weekly and are held twice a day to include the day and night shifts. This practice has been going on for almost two years, with more than 106 rounds performed. All meetings include the participation of doctors, nurses, nursing technicians, physical therapists, nutritionists, pharmacist, psychologists, pastoral worker, social worker, blood bank representative, infection control service, among others. The schedule is recorded in the book of minutes by all participants and the steps taken are recorded in the medical files of the patients discussed. Discussion: Since the beginning of the center implementation, the presence of nursing technician was seen as essential to the practice, as their work contributes to prioritize actions and care, enabling a harmonious, dynamic, productive and better work. Conclusion: Currently, the inclusion of the nursing technician to round is seen as essential, as this professional spends more hours at the patient's bed, warning and pointing out the needs and necessary changes to the rest of the team.

Keywords: Multidisciplinary, Hematology, BMT, Round

P-118

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Lights, camera and hand hygiene

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Introduction: Hematopoietic stem cell transplantation is a highly complex procedure, used in the treatment of several onco-hematological diseases when therapies do not offer a good prognosis. Due to severe and prolonged neutropenia, related to the underlying disease and the treatment, the risk of severe infections rises considerably, increasing the death rate. Therefore, the importance of hand hygiene of the care team, as well as of caregivers and family is essential in patient care, as first barrier of infection. Objectives: To describe the education actions related to hand hygiene and the respective hand washing rate in a Hematopoietic Stem Cell Transplantation unit of a hospital in the South of the country. Material and Methods: The service education actions in this hospital are implemented weekly, with different addressed themes, according to the analysis of improvement opportunities. Associated to that, the hospital encourages an institutional goal of annual improvement entitled the "Challenge Program". In 2015, the central theme of the program was related to adherence to hand hygiene, proposing a target above 88%. Adherence is monitored monthly by the Infection Control Service, which includes observations of the moments and the steps of hand hygiene. Integrated to the annual target, during the same year there were over 8 continuing education activities, where the theme was also hand hygiene encouraging development of free activities for the nursing team. Results: Among the actions performed, lively videos were created giving information on the form of transmission, blocking infections and the steps and moments of hand hygiene through parodies of a song and creation of characters. The videos were released within the hospital, and won the "Oscar" for best hand hygiene video (prize offered by the institution's infection control service). The hand hygiene adherence rate observed in 2014 in the entire hospital was 80.16%, increasing in 2015 to 87.95%. However, at the hematological center, the hand hygiene rate reached 100% in a few months, always remaining above 93.9%. Discussion: According to the results, we observed the improvement of adherence indicators regarding hand hygiene and the absence of crossed infections in the unit. The activities, in addition to stimulating the employees' creativity, make the collaborators research on the theme and educate colleagues, so that the activity is carried out correctly. Conclusion: The analyses show the effectiveness and the need to maintain educational activities, thus resulting in the maintenance of high hand hygiene adherence rates.

Keywords: Educational Actions; Hand hygiene, HSCT, Multidisciplinary

P-119

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Haploidentical Stem Cell Transplantation: Nursing Care Specifics

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The haploidentical hematopoietic stem cell transplantation (HSCT) is an alternative in the absence of a compatible donor and in cases that require urgency, with advantages such as faster donor search and easier donor identification, when a new donation or lymphocyte collection is necessary. Specific care has an impact on morbidity and mortality outcome and should be carefully evaluated, giving subsidies to daily care planning. Between D0 and D+5, high fever and chills are common, especially when cyclophosphamide is used post-cell infusion and myeloablative conditioning, which occurs presumably due to cytokine storm during the period of intense alloreactivity. The nursing staff is very important in the care of these patients. Objective: To demonstrate the specific assistance to patients undergoing haploidentical HSCT. Methodology: This is an experience report of a HSCT center in São Paulo. For the presentation of the data, a survey was carried out on the number of patients undergoing haploidentical HSCT, with analysis of data on antibiotic therapy indicator up to 60 minutes in patients with febrile neutropenia from April 2013 to March 2016. Between 2008 and 2016 61 transplants of this type were carried out. One of the main transplantation procedure complications is febrile neutropenia; in order to reduce morbidity and mortality, the time of antibiotic therapy start is managed at the first temperature elevation and/or clinical alteration in neutropenic patients. During the analysis period, 49 patients underwent haploidentical HSCT and of these, 23 cases were eligible for indicator calculation. Among the assessed patients, 19 had fever/clinical alteration between D0 and D+5, 74% with evidence of fever and 36% with clinical alterations observed as poor overall status, sub-febrile state or other symptoms. Eighteen (95%) patients received antibiotics within 60 minutes, with a mean time of 33 minutes. Fourteen patients (74%) had blood cultures collected prior to the start of antibiotic therapy and 12 (86%) showed no bacterial growth. In addition to the observation of fever, patients receiving post-infusion cyclophosphamide in the immunosuppression period should not use immunosuppressant drugs up to the D+5, including the use of corticosteroids to control nausea, as they may impair the effectiveness of post-transplant cyclophosphamide. Conclusion: The nursing care for patients undergoing haploidentical HSCT should be systematically carried out, reducing complications of therapy and care. Steps should be followed with care to prevent infection, keeping strict temperature control and optimizing the time of start of the empiric treatment for febrile neutropenia. The training of the staff is crucial, with an impact on the reduction of adverse events, increasing the safety and efficacy of treatment.

Keywords: Bone Marrow Transplantation, Febrile Neutropenia, Nursing Care

P-120

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing care systematization (NCS) of a hematopoietic stem cell transplantation inpatient unit

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INTRODUCTION: The hematopoietic stem cell transplantation (HSCT) is a therapeutic procedure consisting in the intravenous infusion of bone marrow, blood, obtained from previously selected donors, into an appropriately conditioned receptor, i.e., submitted to a preparative chemotherapy procedure with or without radiation therapy, with myelo and immunoablative properties. In the first four weeks after the procedure, while still in the hospital, the patients will have as main risk factors for developing infection the presence of a venous catheter, mucositis and neutropenia. The treatment of mucositis, the care of the skin and the central venous catheter and protective isolation procedures are included among the main specific areas of nursing practice in HSCT. MATERIAL AND METHODS: Therefore, this is a descriptive, qualitative experience report study type. OBJECTIVE: To develop the NCS for a bone marrow transplantation inpatient unit. RESULTS: After the introduction of HSCT was decided as an alternative therapy, it was necessary for the nursing staff to proceed with the recognition of the clients' care needs and arrange for their care to be provided. By observing the requirements described in the NANDA's diagnostic taxonomy (2015), the nursing diagnoses that can be found in this situation were listed, as well as their respective prescriptions, considering the information obtained in the researched literature that shows mucositis, neutropenia and central venous catheter infections as the main problems faced by the patient and the HSCT healthcare team. DISCUSSION: This is true in any relationship of care in which the quality of the process and the nursing care product is sought and it is no different when it is related with patients submitted to HSCT. This guide refers mainly to the HSCT hospital stay period, but some of the care procedures are extended to the entire process and, when used, the peculiarities of each period and patient should be observed. It includes the diagnostic enunciation, according to the pattern of human response and the appropriate conduct to be adopted and the expected results according to the Nursing Interventions Classification (NIC 2010) and the Nursing Outcome Classification (NOC 2010). CONCLUSION: The implementation of the NCS in this process is essential for the quality of care provided as basis, the choice of interventions for the identified care needs, minimizing complications, thus aiming to promote, maintain and restore the patient health. It is necessary for nurses to have the knowledge and capacity to implement it, considering the benefits it can bring, offering patients the necessary care to have a complication-free, post-transplant recovery. It is necessary that nurses continue to seek continuous improvement in their practice, effectively developing the NCS.

Keywords: Nursing care systematization, HSCT, Care, Nursing

P-121

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Cure of diabetes mellitus through stem cells: an integrative review

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INTRODUCTION: The pathophysiology of Diabetes Mellitus (DM) involves insulin secretion by the pancreas β-cells, which regulate blood glucose levels. The understanding of the role of stem cells (SC) in the regeneration of pancreatic β cells is of utmost importance, characterizing an important step for the therapeutic progress of DM. The dissemination of study outcomes contributes to the investigation of new researches on the subject. OBJECTIVES: This is an integrative review, which sought to identify which types of stem cells can be used to cure/treat DM and what types of DM are being studied with cell transplantation. MATERIALS AND METHODS: In April 2015, searches were carried out in the Latin American and Caribbean Health Sciences (LILACS) and Scientific Electronic Library Online (SciELO) databases using the keywords (Stem Cells) AND (Diabetes mellitus); (Cell Transplantation for Diabetes Mellitus); (Stem Cell Treatment for Diabetes Mellitus). The included studies were those published in Portuguese and available as full-text; complete or review articles concerning the treatment of Diabetes Mellitus. Studies carried out in animals and repeated studies in the assessed databases were excluded. RESULTS: Voltarelli et al. (2009) and Andrade et al. (2010) show in their studies that there are cells that promote pancreatic differentiation: the SC located in the pancreas itself, in the bone marrow, in the umbilical cord, in the hepatic oval cells, in splenocytes as a source of mature β cells and embryonic stem cells. The most frequently studied cell type for therapeutic purposes in DM is the hematopoietic bone marrow SC (SANTOS, 2012). The autologous Hematopoietic Stem Cell Transplantation (AHSCT) is used in DM1, in which the individual's own bone marrow is removed and preserved until the infusion can be performed. Evidence suggests that the action of immunosuppression together with the infusion prevents the complete destruction of pancreatic β cells, making these cells efficiently resume insulin production (Santos et al, 2012). Studies on SC action in DM2 are scarce. Authors such as Leal, Voltarelli (2010) state that there are some difficulties that hinder the viability of stem cell transplantation in patients with DM2, such as the challenge in understanding the mechanisms that regulate glucose-stimulated insulin secretion and the adaptation of pancreatic β-cells to the constant metabolic variations, as well as the scarce reports in humans on the effectiveness of that treatment on blood glucose level control in DM2. DISCUSSION AND CONCLUSION: it can be observed that the stem cell is a favorable alternative for the treatment and possible cure of diabetes, particularly type 1, although these treatments are still experimental and are not being offered to the population.

Keywords: cell transplantation, diabetes mellitus, nursing

P-122

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The impact of data management on the production of scientific papers

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Introduction: The development and production of scientific papers are of considerable importance to science development. New knowledge, benchmarking between national and international centers and new therapeutic strategies are directly associated to scientific production. During the building process of scientific work, meticulous data compilation and management are necessary to attain results with a level of precision that ensures high accuracy. Objectives: The overall objective is to demonstrate the impact of data management on the multidisciplinary scientific production; the specific objective is to discuss data management implementation in the HSCT unit. Methodology: Experience report of a Hematopoietic Stem Cell Transplant (HSCT) center in São Paulo, after carrying out a survey of the number of updates of data reported to the CIBMTR (Center for International Blood and Marrow Transplant Research), which is a scientific production center of reference, as well as the number of data record requests made by researchers from December 2014 to May 2016. Results: A professional data manager was hired in late 2014, based on the mapping of actions after preparatory diagnostic internal audit for reaccreditation of the Cell Therapy Program. The management and integration of data related to the transplant process was started, enabling the organization and creation of a real-time database, which allowed the follow-up of post-transplant patients, providing subsidies for the analysis of outcomes such as survival, pre- and post-procedure complications and significant variables. The reporting of data to CIBMTR became a routine in the HSCT, which allowed the benchmarking with international centers, upgrade to more elaborate forms, enabling participation in multicenter studies. 471 survival cases have been updated, related to transplants performed between 2007 and 2015. Between the years 2010 to 2015 there were: 100 cases of recurrence, 141 cases of Graft-versus-Host Disease (GVHD). The data availability productivity from the end of 2014 until May 2016 comprised 20 requests, of which 14 (70%) were internal works (multidisciplinary team) and 6 (30%) related to works of external researchers. 75% of the data surveys were related to adult patients and 25% to pediatric ones; there were 3 requests regarding multicenter trials, of which 2 were international. We observed a decrease in the time necessary for data collection, use of standardized information in the developed works and greater availability of time for content development. Conclusion: data management with real-time updates in the HSCT unit had a positive influence on the preparation of scientific papers, resulting in increased productivity, quality and complexity.

Keywords: Bone Marrow Transplantation, Data Collection, Epidemiology

P-123

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Nursing interventions in patients submitted to Allogeneic and Autologous Hematopoietic Stem Cell Transplantation (HSCT) with the Nursing Diagnosis for Bleeding Risk

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Introduction: In the autologous and allogeneic HSCT, the patient goes through a thrombocytopenia phase, which is characterized by platelet counts below 150,000/mm^3. Because this condition causes severe alterations that must be identified and treated quickly, these patients receive the Nursing Diagnoses (ND) for bleeding risk, which leads to the prescription of specific care for this phase. Objective: To describe the nursing care procedures for the patient with the (ND) bleeding risk. Method: This is a descriptive study, based on nursing experience in a Protected Environment Unit. Results: The care procedures consist in: recommend full bed rest if platelet count is <10,000/mm^3; assist in ambulation; evaluate the surgical wound aspect; assess circulatory conditions; evaluate vaginal losses; actively seek signs and symptoms suggestive of bleeding; communicate hematoma formation; ambulate only if accompanied; avoid risk behaviors; avoid punctures; avoid use of sharp materials; recommendations on oral hygiene with a soft bristle toothbrush; advise patients to avoid blowing their noses; explain to the patient the importance of complication prevention; implement care of arterial/venous puncturing of great vessels; implement care of arteriovenous fistula puncture; maintain the bed at the lowermost position; keep the bell within reach of the patient; maintain compressive dressing; maintain elevated bed rails; monitor bleeding; monitor signs of bleeding; advise patients to apply pressure on the spot when sneezing or coughing; advise patients to avoid physical exertion; advise patients and their families about risks and severity of trauma when platelet counts are below 150,000/mm^3; advise patient/ family about the risks and prevention of falls; advise patients and families to avoid trauma; advise patients and families about warning signs that require immediate attention; advise partial bed rest if platelet counts are between 20,000/10,000 mm^3; advise about oral hygiene; perform manual compression after punctures until hemostasis is attained; perform compressive dressings; request the presence of family member or companion; check for the presence of hematuria; check vital signs. Discussion: The nursing prescriptions guide the nursing staff actions and are created based on the care procedures deemed necessary to promote a comprehensive and individualized attention, ensuring the safety of a thrombocytopenic patient. For the choice of care, the nurse employs logical reasoning, taking into account the clinical situation and what stage of treatment the patient is, in addition to the particularities of each one. Conclusions: It was observed that the thrombocytopenic patients receiving specific care related to (ND) bleeding risk have lower complications in this period. The nursing prescription and implementation of a care plan for these patients is essential for their safety and quality of care.

Keywords: Nursing Diagnosis, Nursing Care, Thrombocytopenia

P-124

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Hickman Catheter-related complications in the Hematopoietic Stem Cell Transplantation Service of Hospital Pequeno Príncipe

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The implementation of a central venous catheter is part of the therapeutic support in Hematopoietic Stem Cell Transplantation (HSCT). The Hickman catheter is the most appropriate, as it dispenses with the percutaneous puncture and allows the infusion of large volumes of fluids simultaneously, including the safe infusion of hematopoietic stem cells. Although it has many advantages, some complications can occur with this central venous catheter. The aim of this study was to evaluate the incidence of Hickman-catheter related complications in a HSCT unit. We carried out a retrospective study from 04/2011 to 03/2016, during which a total of 66 catheters were implanted, of which 50 for related allogeneic transplantation and 16 for autologous transplantations. The observed complications were infections, of which 11 were primary clinical bloodstream infections (BSIs), 8 BSIs confirmed by laboratory tests (2 cases of *Staphylococcus epidermidis*, 2 cases of *Staphylococcus sp*; 1 case of *Serratia marcescens*, 1 *Candida albicans*, 1 *Candida parapsilosis*; 1 *Candida kefyr*). In 2 cases it was necessary to remove the catheter and implant a new one. There were 3 mechanical displacements; of these, 1 required new implantation; 2 cases had surgical complications in catheter implantation, resulting in hemothorax; 1 case of fracture requiring a new device and 2 displacements with repositioning. We demonstrate the need for trained, qualified and motivated professionals for an effective and safe approach. The implementation of specific protocols guides the team working in the area; the continuous training contributes to the improvement and valuing of professionals, preventing turnover and absenteeism. The recommendations given to patient companions about catheter care are also of utmost importance, since the family can contribute to the prevention of several complications. This study helps the clinical practice nurse to identify the main reasons for catheter removal and provide data that can support proposed interventions to minimize them.

Keywords: Nursing care, central venous catheters, bone marrow transplantation.

P-125

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Immunosuppressed Patient Submitted to Allogeneic Hematopoietic Stem Cell Transplantation: Contributions to the Nursing Care Protocol Development

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Introduction: Patients submitted to allogeneic hematopoietic stem cell transplantation routinely receive immunoprophylaxis for graft-versus-host disease (GVHD) since the day before the bone marrow infusion and during several months after the procedure. The immunoprophylaxis classically comprises cyclosporine and methotrexate, and there may be some adaptations with the use of other drugs such as tacrolimus, mycophenolate mofetil and corticosteroids. The patient submitted to bone marrow transplantation (BMT) and to the use of these drugs requires skilled nursing care, based on technical and scientific knowledge related to the transplantation and the safe preparation and administration of these drugs. This study reports the experience of a group of nurses from the Inpatient Unit of a Bone Marrow Transplantation Center in a national reference institution located in the city of Rio de Janeiro (RJ) regarding the preparation of the institutional Nursing Patient Care protocol for patients submitted to Hematopoietic Stem Cell Transplantation receiving Immunosuppressive Therapy. Objectives: To establish an institutional nursing care protocol appropriate for the patient undergoing bone marrow transplantation receiving preventive immunosuppressive therapy for GVHD and graft rejection. Material and Methods: Our research was based on articles and institutional books, concomitant with scientific articles published in the past 10 years found in the following databases: LILACS, BIREME, BDENF and MEDLINE using the aforementioned descriptors. The sample consisted of 08 documents used for the creation of this protocol. Results: The care practice has encouraged us to seek an update, which resulted in the preparation of this protocol. The tea development of protocol using teamwork allowed the professionals to express their experiences, resulting in discussions that enabled a consensus on standardized conducts applicable to the reality experienced in the institution and in the light of scientific knowledge. The use of protocols results in a more qualified practice and increasingly effective and humane assistance to the patient. Discussion: After the preparation of the protocol, its implementation phase was initiated. Currently, the entire nursing staff is undergoing the training process. Aiming to evaluate the implementation of this protocol, monthly evaluations are being carried through the monitoring of prescriptions and nursing records. Conclusion: The protocol has attained a positive assessment by the professionals involved with the process and has also resulted in the improvement of the nursing care provided. We believe that striving for nursing care quality should be a constant, continuous process, and one that never ends. We hope this work can help professionals to provide good-quality and humane care.

Keywords: bone marrow transplantation, immunosuppression, nursing care

P-126

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Alteration of membrane potential detected by the standardized phase angle in adult patients submitted to allogeneic hematopoietic stem cells transplantation

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Introduction: The phase angle (PA) is a cell integrity variable and has been considered a nutritional status and outcome indicator in patients submitted to hematopoietic stem cell transplantation (HSCT); however, the association between PA and molecular mechanisms has not been fully elucidated and, therefore, the aim of this study was to assess the PA behavior throughout treatment in this population. Participants and Methods: A prospective study was carried out between February 2015 and March 2016 at a university hospital involving 29 adult patients undergoing allogeneic HSCT and 28 healthy adults who comprised the control group. The data were collected before the start of the conditioning regimen, at 14 (D+14), 30 (D+30) and 90 days (D+90) after HSCT. The control group was evaluated only once. The weight, height, arm circumference and triceps skinfold thickness were obtained and, based on these, body mass index and arm muscle area were estimated. Reactance (Xc) and resistance (R) were obtained through bioelectrical impedance (BIA) and the PA was estimated through the formula arctan(Xc/R) x 180°/π, followed by the calculation of the standardized phase angle (SPA) based on reference values for a healthy population. Results and Discussion: Most patients were males, with a median age of 30 years and 52% had malignant diseases. In the pre-HSCT period, patients had similar characteristics to the healthy group, with no significant difference between the two groups. The SPA was not correlated with any nutritional assessment parameter, only with Xc. Between the first and the third evaluations, there was a significant reduction in the SPA, which was low up to D+90. Xc had the same behavior as SAP, since R showed no significant difference between the four assessments. The low values of SAP and Xc indicate cell physiology alterations, with consequent changes in the electrical properties of tissues and ionic conduction. It is possible that the immune response, strongly affected during treatment, influenced the changes in membrane potential. It seems that the SAP can detect bodily differences before anthropometric and laboratory abnormalities occur, since it was not comparable to the nutritional assessment methods. Conclusion: The SAP detected changes in the electrical properties of tissues in patients submitted to allogeneic HSCT, but further studies are needed to understand what are the causative factors for the changes observed in this population.

Keywords: bioelectrical impedance, phase angle, electrical properties.

P-127

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The impact of muscle mass and strength and visceral fat on neutrophil engraftment in patients submitted to hematopoietic stem-cell transplantation (HSCT)

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Introduction: In the HSCT, muscle mass and visceral fat are associated with comorbidities, mortality, hospital length of stay, duration of immunosuppressive drug use, development of graft-versus-host disease (GVHD) and survival. A recent study in patients undergoing allogeneic HSCT showed an inverse association between areas of visceral and peripheral fat with the disease-free interval. In allogeneic HSCT, decreased muscle mass is associated with a higher prevalence of chronic GVHD and low performance. Objectives: To evaluate the quadriceps femoris muscle thickness (FT) and visceral fat (VF), and grip strength (GS), correlating them with time to neutrophil engraftment (NE). Methods: We studied 14 adult patients (>18 years) on the first day of hospitalization for HSCT at Hospital Israelita Albert Einstein, São Paulo, Brazil. The measurement of the right (RFT) and left (LFT) femoral quadriceps muscle thickness was performed at 6 cm from the top edge of the patella, at the anterior intermediate region of thigh, using ultrasound (US) in B-mode. The VF was measured in the abdominal region, being characterized by the distance between the linea alba and the anterior wall of the aorta. In addition, all patients underwent assessment of the dominant upper limb strength with an adjustable and validated dynamometer (hand grip). Results: Most patients were women (57%) with a mean age of 50 years (± 16 years) and 50% of our patients were elderly (≥60 years). The haploidentical HSCT was the predominant type in the sample, corresponding to 57%, followed by autologous (36%) and allogeneic (7%). Most of our patients were overweight, with body mass index (BMI) of 27 kg/m^2 (± 4 kg/m^2). The mean time of NE was 16 days (± 6 days). RFT was 1.5 cm (± 0.3 cm), VF was 5.3 cm (± 1.4 cm) and HG 31kgf (± 7,0kgf). There was a negative correlation between NE and RFT (rs = 0.8, p <0.05), regardless of the age of the patients and type of HSCT by linear regression. There was no significant correlation between VF and HG with NE. Conclusion: The FT showed a strong correlation with NE; its assessment by US is practical, low cost and has no risks in HSCT.

Keywords: HSCT, Neutrophil engraftment, Ultrasonography, Muscle Mass, Visceral Fat

P-128

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Access to medications after HSCT: the reality of the South of Brazil

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The hematopoietic stem cell transplantation (HSCT) requires a complex and prolonged follow-up that brings emotional, social and economic alterations. The continuing use of some medications after HSCT is essential for a successful treatment, as their correct use can avoid unnecessary and prolonged hospitalizations and/or worsening of clinical symptoms. However, difficulties in having access to these drugs in the public health care network has caused problems for both patients and for the healthcare staff who need to create strategies so that the patient does not go untreated. Therefore, this study aims to describe the main difficulties found by patients regarding access to prescription drugs after discharge of the HSCT. This is a descriptive study, based on the experience report of the multidisciplinary team of a hospital in the south of the country. The difficulties are mainly related to lack of medications in the public network; the obligatory delivery of the drug only at the address registered in the patient's SUS card; the municipal list of drugs (REMUME), variable in each municipality, in many cases, not including the entire implemented treatment and the high cost for the purchase of medications in the private network, considering the amount and frequency of use. According to the Decree 11/15 of the Municipal Health Department, patients who are not residents of the municipality cannot obtain their medications in the capital city. As the vast majority are from the countryside or other states, they end up finding temporary housing near the transplant center for a minimum of 100 days. Seeking to minimize these difficulties, a contract was established between the hospital and pharmaceutical assistance from City Hall. Therefore, a list of post-HSCT patients who remain living near the hospital was created, which is forwarded periodically by Basic Health Unit pharmacist linked to the hospital to the Health Center responsible for the dispensing of medications. This list is prepared, revised and updated as necessary by the social worker and pharmacist of the transplant team. It is concluded that the recognition by the health team of their role in the process of creating and developing strategies, considering the lack of access to medications and consequent inadequate treatment adherence, is essential to ensure the success of transplantation and quality of life of patients. We also observed the importance of multidisciplinary guidelines at hospital discharge and during outpatient follow-up, seeking ways to acquire the medications, so that the patient would not be harmed. It emphasizes the need to consolidate and extend public health policies in order to implement the principles that rule SUS, especially regarding the comprehensiveness of care and universal access.

Keywords: Hematopoietic Stem Cell Transplantation; Patient Care After Discharge; Public Health Policies.

P-129

Multidisciplinary (Nursing, Psychology, Physical therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Neutrophil and platelet engraftment are not affected by nutritional status in patients undergoing hematopoietic stem cell transplant

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The aim of this study was to analyze the association between pre-transplant nutritional status and engraftment time in patients undergoing hematopoietic stem cell transplantation (HSCT). Thirty-three patients were evaluated and stratified by body mass index (BMI). The mid-upper arm circumference, triceps skinfold thickness and the mid-upper arm muscle circumference were also evaluated. The underweight group (BMI<18.5) could not be included because only one patient was classified as underweight. The median time for granulocyte engraftment (>0.5 x 109/L) was 11 days for the obese and 14 days for the overweight and normal weight groups. The median platelet engraftment time (>20 x 109/L) was 15 days for the obese, 19 days for the overweight and 16.5 days for normal weight group. The median time to platelet engraftment was significantly higher in the overweight when compared to the obese group (P=0.009). Nevertheless, there was no significant correlation between BMI or anthropometric parameters and neutrophil or platelet engraftment time. This study demonstrates that neutrophil or platelet engraftment is not affected by nutritional status; however, it is negatively correlated to the number of CD34+ cells and positively correlated with the number of days of adjusted hospital length of stay, graft type (BM or PBSC) and transplant type (autologous or allogeneic).

Keywords: Body mass index; nutritional status; hematopoietic stem cell transplantation; arm anthropometry.

P-130

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Actions to promote drug administration safety in patients submitted to HSCT.

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Introduction: When submitted to Hematopoietic Stem Cell Transplantation (HSCT), the patient requires several medications, which have pharmacokinetic characteristics and may also cause adverse events, from mild to severe, affecting the patient's health. Additionally, the limited number of administration routes, time of infusion and dose administration interval of each drug makes drug prescription a challenge for the nursing staff. In order to promote patient safety in drug administration, the pharmacy, nursing and nutrition staffs are mobilized to jointly develop strategies to avoid drug interactions and their consequences, medication errors and adverse events. Objectives: To describe multiprofessional actions to promote safety in drug administration. Material and Methods: This is a descriptive study based on the experience report. Results: A survey of the most frequently used drugs in a Protected Environment Unit of a university hospital in southern Brazil was performed. Each drug was reviewed regarding the pharmaceutical and drug interactions. A MICROMEDEX solutions V 2.0, Up to Date 2016 database was used to review the tables prepared by the hospital medication Information Center. Based on the collected information, a general spreadsheet was developed on incompatibilities, listing the drugs with continuous infusion solutions most frequently used in the unit. With these data, the clinical pharmacist evaluates the medical prescription, developing individualized guidance according to the stage of treatment and the patient's clinical status, which are recorded in spreadsheet format. The information available in the spreadsheet are: pharmaceutical and drug interactions, maximum and minimum dilutions of each drug, time required for each infusion and observations identified at the time of recommendation. This worksheet is available in the patient's file by the team clinical pharmacist and reviewed daily. When a drug/ food interaction is identified, multiprofessional actions are taken, such as assessment of drug validity, specific diets, dietary restrictions, observing the route of administration in order to minimize risks and optimize drug therapy. Discussion and Conclusions: The pharmacy staff intervention, based on the implementation of the drug interactions table, allowed the nursing staff professionals to perform their activities regarding the preparation and administration of medications safely and accurately during patient care. With the optimization of the time of care, it is possible to identify, monitor and define actions for adverse events that may occur resulting from the administration of drugs at an early stage. This integrated work reinforces the importance of the multidisciplinary team in the care of patients undergoing HSCT, promoting quality and safety in drug administration.

Keywords: Patient Safety, Communication in Health Care, Hematopoietic Stem Cell Transplantation

P-131

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Care in a Hematopoietic Stem Cell Transplantation Outpatient Clinic: readaptation of a Pre-HSCT routine flow

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The hematopoietic stem cell transplantation (HSCT) is a therapeutic modality characterized by the infusion of hematopoietic stem cells after high-dose chemotherapy. This treatment requires the training of the multidisciplinary team, using technical-scientific knowledge for the benefit of patients and providing comprehensive care. The hematology and HSCT services of the institution have characteristics that are not aligned with the routines for referral of pre-HSCT patients, due to different locations. For this communication to be established, it was suggested, by the new board of directors, to readapt to a new flow and alignment of pre-HSCT routines between these services, which involve professionals and referrals of patients to the HSCT. For better restructuring of the service, it was necessary for the entire staff to endeavor to adapt routines and processes in the service, in addition to the achievement of goals and results. Objective: To align routines to establish better communication between professionals of the hematology and HSCT services of the institution. Material and Methods: After the suggestion of the new board of directors, a nurse prepared a flowchart on pre-HSCT service routine, which created a new model for the organization of care routines to pre-HSCT patients and to align the communication between the hematology and the HSCT services of the institution. A tool was used through a diagramming program that utilizes graph vectors for the creation/ visualization of routines. These were presented to the teams as a slide show in clinical meetings and implemented in the service. Additionally, a group was created through the mobile network with nurses at the institution, hematology and HSCT services to discuss cases of central venous catheter (CVC) implants, start of mobilization and date of admission for the HSCT. Case discussions were carried out during clinical meetings about patients referred by the hematology service. During these meetings, CVC implants were discussed, as well as hematopoietic stem cell collection, conditioning, socioeconomic aspects, such as the need for home support, psychological aspects and need for new drugs. The professionals attending these meetings received previously the patient list for discussion through e-mail. Results: After the presentation of this tool, the results were satisfactory. Better communication was observed between services and professionals, in addition to establishing a single routine model in the pre-HSCT. Discussion: These modified routines showed a new alignment of the pre-HSCT service flow and organized processes were started, with better communication. Patients were referred through reports, which were evaluated by the attending physician and then the clinical cases were discussed at meetings. Conclusion: Communication is essential for the effectiveness of the HSCT, establishing patient routines in an organized manner.

Keywords: Hematopoietic stem cell transplantation, flow, routines, organization

P-132

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The Scarf-tying Project: rescue of the self-image in hematopoietic stem cell transplantation through the scarf-tying manual

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Introduction: changes experienced during the Hematopoietic Stem Cell Transplant (HSCT) are reflected in body image, self-esteem and sense of identity of the patient undergoing this therapy. Objective: This study presents an intervention proposal based on the creation of a material developed with a female patient undergoing transplantation. Method: To illustrate the intervention, we used the follow-up report by a patient, based on which we developed a manual on different manners of tying a scarf. The patient, called N., was 29 years old and had been diagnosed with systemic sclerosis and was referred to HSCT. Results and Discussion: Throughout the hospital length of stay, she expressed important emotional mobilization associated with the fall of her hair, signaling concerns with self-image and the changes brought on by the treatment. In order to assist the development of adaptive resources by the patient, meetings were carried out during which different ways of tying head scarves were tested, using photos and videos found on the Internet and brought by the psychologist. During these sessions, the companion (mother) learned to tie the scarves on N., since the patient had reduced mobility due to scleroderma. The companion had concerns about her capacity to offering care to her daughter; however, during the interventions, she started to recognize her capacity to meet the necessities of N., both practical and affective. The exercise on patient autonomy permeated the meetings, and it was N. who chose the scarf to be used and the tying style that would be tested. After each time, the patient had the opportunity to look at herself in the mirror. At this time, questions were raised related to the feeling aroused by the image, and the patient reported an increase in self-esteem and perception of positive aspects in herself. Based on these consultations, it was proposed to the patient to record ways to tie the scarf in photographs, in order to create a manual on how to tie scarves, intended for use in the ward with other patients. Conclusion: The intervention allowed meeting the demands of reassigning the experience of treatment, promoting the perception of capacities and difficulties experienced by the patient. The addressed issues went beyond the concreteness of the loss of hair, making it possible to reflect on other losses, of a symbolic nature, thus tying the feelings attributed to treatment and appropriation of coping resources and adaptive strategies of the patient and her companion. The manual showing ways to tie headscarves has been completed and will be employed in the ward as a trigger to be used during care, providing more tools for the professional to understand the patient's experience and offering patients the possibility of being treated, validated and accepted in their several aspects.

Keywords: Hematopoietic Stem-Cell Transplantation, Systemic Sclerosis, Manual, Self-image.

P-133

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Quality of life, stress, anxiety and depression in patients with systemic sclerosis submitted to hematopoietic stem-cell transplantation.

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Systemic sclerosis (SSc) implies in loss of quality of life (QOL), creating a sense of impotence, especially when conventional treatments do not result in improvements. In these cases, the Autologous Hematopoietic Stem-Cell Transplantation (AHSCT) is considered a therapeutic option to change the course of the disease. This is a prospective study assessing QoL, stress, anxiety and depression in patients with SSc submitted to transplantation, mapping changes in these variables at different times (pre-, 6 months, 12 months post-AHSCT). Sixteen patients participated in the study (20-53 years). The Generic Quality of Life Assessment Questionnaire (SF-36) was used, organized into physical (FC-capacity functional, PA- physical aspects, Donor, overall health status-OHS) and mental components (SA-social aspects, VIT-vitality, EA-emotional aspects, mental health - MH). The score of the questions was transposed to a scale in which 0 corresponds to the worst health status and 100 to the best. We also used the Hospital Anxiety and Depression Scale and Lipp Stress Symptom Inventory, which checks symptoms in the last 24 hours (warning), month (resistance and near-exhaustion) and three months (exhaustion). At the assessment of QoL, the physical components were: FC: pre = 37.2, SD = 21.3, 6 months = 53.8, SD = 25.1, 12 months = 58.2, SD = 20.3; PA: pre = 7.8, SD = 15.1, 6 months = 53.1, SD = 47.3, 12 months = 38.6, SD = 49.2; D: pre = 42.7, SD = 13.1, 6 months = 68.4, SD = 22.0, 12 months = 72.5, SD = 24.2; OHS: pre = 49.7, SD = 20.5, 6 months = 65.0, SD = 17.2, 12 months = 61.6, SD = 23.3. For the emotional components, we had: VIT: pre = 50.9, SD = 18.4, 6 months = 68.1, SD = 19.8, 12 months = 65.9, SD = 19.2; SA: pre = 56.3, SD = 28.9, 6 months = 71.9, SD = 23.5, 12 months = 69.3, SD = 26.4; EA: pre = 58.3, SD = 44.7, 6 months = 62.5, SD = 43.7; 12 months = 60.6, SD = 49.0; MH: pre = 62.0, SD = 16.5, 6 months = 73.9, SD = 23.5; 12 months = 72.7, SD = 14.4. There were improvements in all areas, with the highest increase between pre- and post-6 months. Regarding depression, it was observed that 20% of the sample had significant depressive symptoms before, 15.4% at 6 months and 33.3% at 12 months. A gradual decrease in anxiety was verified, from 60% in the pre- to 11.1% at 12 months, showing a statistically significant difference (p = 0.02). The stress evaluation results indicate that the in warning phase, symptoms increased (0% - pre, 15.4% at 6 months; 33.3% at 12 months), varying in the resistance (46.7% - pre, 7.7 % at 6 months; 44.4%, at 12 months) and exhaustion phase (26.7% - pre; 15.4% at 6 months; and 22.2% at 12 months). It is worth mentioning the increase in near-exhaustion after 6 months (15.4%) indicating exhaustion of adaptive reserves. These results highlight an overall improvement in QoL, reinforcing the importance of treatment and positive impacts on health since the first months. However, it is clear that the symptoms of depression and stress remain high after treatment, increasing the need for psychosocial care after hospital discharge to meet the high demand for adaptive efforts.

Keywords: Systemic sclerosis, Hematopoietic Stem Cells Transplantation; Quality of Life, Stress, Anxiety, Depression

P-134

Cell therapy

Assessment of genetic instability of Induced Pluripotent Stem Cells

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Introduction: Pluripotent stem cells are able to differentiate into any cell of the three germ layers (endoderm, mesoderm and ectoderm) and so, their study is of great scientific interest worldwide in the area of cell therapy and experimental models. The induced pluripotent stem cells (iPSC) are generated from adult cells reprogrammed to a state of pluripotency, that is, they can originate several cell types in the body, which increases their therapeutic potential, and do not pose any ethical problems related to use of embryos. Somatic cells are reprogrammed with the overexpression of the transcription factors OCT4, SOX2, Klf4 and c-MYC. However, in addition to insertion of genes, the fact that they are cultured *in vitro* increases the possibility of the onset of genetic instability, which could explain, at least in part, the tumorigenic potential of these cells. Therefore, maintaining the genetic stability after reprogramming is one target of the researchers for a possible clinical application and studies in experimental models. These instabilities can be characterized by chromosomal abnormalities. Objectives: To standardize a protocol for the cytogenetic study of iPSCs lineages and check the frequency of chromosomal abnormalities. Methods: The iPSCs used in this study were generated in the Cellular and Molecular Cardiology Laboratory of Universidade Federal of Rio de Janeiro. For analysis, we used the conventional cytogenetic test by G-banding, where different times of mitotic interruption and hypotonic solution concentrations were evaluated. Slide analysis was performed using the LUCIA (Laboratory Universal Computer Analysis of LIM - Laboratory imaging s.r.o.) program at Pontifícia Universidade Católica do Paraná, where, whenever possible, twenty karyograms were analyzed for completion of the final karyotype. Results and Discussion: A total of 45 samples of 14 lineages of iPSC were assessed. Most (92.8%) did not show clonal chromosomal aberrations. A total of 147 metaphases were analyzed, which showed the following chromosomal alterations: acentric fragments, chromosomal fusions, premature centromere division, presence of double minutes, image formation and annular chromosome. These signs are frequently reported in tumor cells, although without specificity. Conclusion: It was possible to establish a protocol for conventional cytogenetic by G-banding for iPSCs, with ideal quality for analysis. This technique showed to be an essential tool to detect chromosomal alterations, with important repercussions on possible clinical and experimental applications of iPSC lineages.

Keywords: Cell therapy, iPSC, cytogenetics, karyotype, tumorigenic potential

P-135

Cell therapy

Recruitment to the central nervous system of bone marrow-derived mononuclear cells after allogeneic transplantation in dogs with canine distemper sequelae

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Introduction: Canine distemper is an infectious disease that causes demyelinating encephalitis in dogs, and that can be used as a model for the study of demyelinating diseases in humans. The neurological signs of distemper are variable and progressive and can result in permanent sequelae. There is no specific therapy for dogs that show clinical signs of distemper, therefore, the use of new therapeutic alternatives should be considered. Stem-cell therapy has been studied as an alternative for the treatment of several types of lesions, including neurological ones. Mononuclear cells (MNC) of the bone marrow (BM) can be easily isolated and are widely used as a therapeutic strategy in several clinical and pre-clinical studies. However, one of the challenges associated with this therapeutic procedure is the administration route for the efficient delivery of cells at the action site. Intravenous (IV) administration has been used, as it is a simple and noninvasive method of cell transplantation. The labeling and tracking of cells allow assessing whether the cells transplanted via IV route migrated to the lesion site. The PKH26 is a fluorescent dye molecule, non-cytotoxic and stable for a long period. Due to these characteristics, this dye seems to be ideal for tracking transplanted cells. Objective: To evaluate the migration of cells to the central nervous system (CNS) after allogeneic transplantation of BM MNC in 10 dogs with neurological complications of canine distemper. Methods: The BM was collected from eight healthy donor dogs, through puncture of the iliac crest under general anesthesia. After collection, the MNC were isolated in a density gradient (Histopaque 1.077 g/dL), labeled with PKH26 and intravenously transplanted into the patients. The migration to the cerebrospinal fluid (CSF) was measured at different times post-transplant, being quantitatively evaluated by flow cytometry and qualitatively by fluorescence microscopy. Results and Discussion: On average, 8.84 x 106 (± 2.56 x 106) MNC/mL of collected BM were obtained. The flow cytometry showed labeling of 93% (± 9.9%) of the MNC with PKH26, with an average viability of 87.6% (± 12.8%). The quantitative analysis showed a wide variation in the percentage of labeled cells in the CSF, at different times of collection, with a greater percentage being observed between 4:00 and 5: 30h after the IV infusion, with subsequent decrease. The qualitative analysis showed the presence of MNC labeled with PKH26, recruited by the CNS in the CSF. Conclusion: This study demonstrated that the BM MNC can be efficiently labeled with PKH26 and that these cells can be monitored after IV transplantation in dogs with neurological sequelae of canine distemper.

Keywords: Cell therapy, stem cells, intravenous transplantation

P-136

Cell therapy

Analysis of cardiac progenitor cells in an experimental model of obesity after treatment with IGF-1

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Cardiovascular diseases are the leading cause of mortality in obesity [1]. The presence of progenitor cells in the myocardium, including the resident cardiac stem cells (CSC; c-kit+Lin-) and endothelial progenitor cells (EPC; CD133+), has been suggested as a possible mechanism of cardiac regeneration [2]. However, despite progress in the understanding of these cells, the mechanisms that regulate their survival in pathological conditions are not yet clear. Our group has recently shown that obesity is related to damage to bone marrow stem cells. [3] Moreover, diabetic cardiomyopathy is associated with a decrease in the number and proliferative capacity of CSC [4]. The administration of IGF-1 and HGF in a myocardial infarction model stimulated the CSC regenerative response without the need for cell transplantation, inducing the migration, proliferation and differentiation of CSC cells into cardiac and microvasculature cells [5]. The objective of this study was to evaluate the therapeutic potential of IGF-1 on the CSC in an obesity model induced by the Western diet. Male 21-day-old Swiss mice were divided into control group (CG, N = 16), fed a standard diet, and the obese group (OG, N = 16), fed the Western diet, high in saturated fats and simple carbohydrates, for 12 weeks. Part of the obese animal group (N = 8) received a daily subcutaneous injection of IGF-1 for seven consecutive days (OG + IGF-1). Control animals (N = 8) received saline solution. The following were assessed: body weight, naso-anal and tibial length (TL), adiposity and left ventricle (LV) weight. After the euthanasia, the heart was collected and processed for microscopy, western blotting and flow cytometry. The results were expressed as mean ± SEM and differences between groups were analyzed by ANOVA with Holm-Sidak post-test ($P < 0.05$). The OG + IGF1 showed reduced body weight (CG = 44.7±0.6; OG= 52.4 ± 2.3; OG +IGF-1 = 44.3 ± 0.6), Lee index (CG = 358 ± 7.7; OG = 416 ± 4.7; OG + IGF-1 = 283 ± 11.6) and epididymal (CG=0.30± 0.06, OG=0.91±0.12, OG + IGF-1 = 0.52 ± 0.06) and retroperitoneal fat deposits (CG = 0.82 ± 0.1, OG = 2.24 ± 0.3, OG + IGF-1 = 1.32 ± 0.1) when compared to the OG. The LV weight/TL ratio also showed a reduction in OG + IGF-1 when compared to OG (CG=0.002±0.0002; OG=0.004±0.0005; OG+IGF 1=0.002±0.0006), indicating that IGF-1 reduced cardiac hypertrophy. The OG+IGF-1 showed a quantitative increase in CSC (CG = 1.99 ± 0.4; OG = 0.24 ± 0.06, OG + IGF-1 = 0.4 ± 0.1) and in EPC (CG = 3.25 ± 0.6; OG = 1.57 ± 0.2; OG + IGF-1 = 2.55 ± 0.15) in the heart in relation to the OG, demonstrated by flow cytometry. These data were corroborated by an increase in the content of c-kit+ (CG = 1.16 ± 0.05, OG, 0.78 ± 0.04, OG + IGF-1 = 1.13 ± 0.07) and CD133 (CG = 1.04 ± 0.1, OG = 0.62 ± 0.06; OG + IGF-1 = 0.81 ± 0.06). The results suggest that treatment with IGF-1 has a cardioprotective effect, promoting the preservation of cardiac stem cells and endothelial progenitor cells in obese mice.

Keywords: resident cardiac stem cell, endothelial progenitor cell, Western diet, IGF-1.

P-137

Cell therapy

Evaluation of stem cell response to a biomaterial

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The aim of tissue engineering is to repair tissue lost or damaged through use of cell therapy and biomaterials. With the increasing trend of extended life expectancy and with the severe limitations for the use of allogeneic, autologous or xenogeneic grafts, scientists have been encouraged around the world to search for new alternatives. Therefore, the synthesis of new polymers that may provide better physicochemical and biological properties is a constant target. To achieve this, a new biodegradable and biocompatible polymer has been synthetized, the poly(octylene succinate) (POS) with molecular weight of 67,000 g/mol. Electrospinning was used to transform the polymer into scaffolds on which cells could be cultivated. This technique allows for the construction of biomaterials that mimic the extracellular matrix, due to an applied electrical field. The scaffolds were then constructed using the electrospinning technique after optimization. Morphology and fiber diameter were assessed by scanning electron microscopy (SEM). For cytocompatibility evaluation, mesenchymal stem cells (MSC) were used and the following analyses were performed: 1) adhesion assay after 1 day of seeding; 2) viability assay on days 1, 4 and 7; and, 3) live/dead assay on days 1 and 7. Cell morphology was also analyzed by confocal microscopy. SEM results showed that the best morphology, with well-formed fibers and no beads was achieved using 15% POS in a hexafluoroisopropanol/chloroform solvent mixture (7:3) (w/V). The fiber diameter was 687±259 nm. The preliminary results showed that MSC adhesion was similar in the POS scaffolds (12.23±2.51 cells/region of interest-ROI) and controls, which were cells directly seeded on plastic wells (11.4±1.8 cells/ROI). In relation to cell viability, the metabolic activity was better in the control group on all analyzed days. The absorbance for the POS groups on days 1, 4 and 7 were 0.149±0.059, 0.502±0.290 and 0.623±0.170, respectively. For the control groups, the absorbance was 0.502±0.126, 2.775±0.269 and 1.859±0.026 for days 1, 4 and 7, respectively. The live/dead assay showed an increased number of live cells in the control group. In conclusion, thought it was possible to seed and cultivate cells on the new biomaterial, longer cell experiments and analysis should be performed. Financial support: CNPq, CAPES, FAPERGS and Stem Cell Research Institute.

Keywords: tissue engineering, electrospinning, stem cells, poly(octylene succinate)

P-138

Cell therapy

Effects of different mesenchymal stromal cell sources in experimental acute respiratory distress syndrome

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Effects of different mesenchymal stromal cell sources in experimental acute respiratory distress syndrome Introduction: Even though all mesenchymal stromal cell (MSCs) share similar general properties, cells from different sources can exhibit significant differences in anti-inflammatory or regenerative potency depending on the particular injury. Recent studies have compared the characteristics of adult MSCs from different sources, and have demonstrated distinct effects in different experimental models, even when cells have similar proliferation and differentiation capacities. The relevant mechanisms whereby different MSCs populations have distinct actions in experimental acute respiratory distress syndrome (ARDS) remain unclear. We investigated the effects of bone marrow (BM)-MSC, adipose tissue (AD)-MSC, and lung tissue (L)-MSC on lung mechanics and morphometry, as well as inflammation and remodeling in endotoxin induced-ARDS. Methods: Forty-eight female Wistar rats received *Escherichia coli* lipopolysaccharide (LPS) (100 µg, ARDS) or saline solution (C) intratracheally. At 48 hours, ARDS and C groups were further randomized into subgroups receiving saline (0.05 mL), BM-MSC, AD-MSC, and L-MSC (1x105]) intravenously. Results: All MSC sources were characterized as CD19-/CD34-/CD45-/CD29+/Sca1+ by flow cytometry. LD-MSCs were 10% and 24% larger in size compared to AD-MSCs and BM- MSCs, respectively. All MSC lineages were similarly capable of *in vitro* differentiation into osteoblasts and chondroblasts. On day 7, MSCs from each source led to reduced static lung elastance, resistive and viscoelastic pressures, alveolar collapse, collagen fiber content and number of neutrophils in lung tissue, and pro-inflammatory mediators. However, the beneficial effects of BM-MSC and AD-MSC on lung parenchyma remodeling were greater than those observed with L-MSC. Conclusion: All three MSC sources tested (BM-MSC, AD-MSC and L-MSC) attenuated lung damage in this mouse model of endotoxin-induced ARDS. Nevertheless, MSCs from different sources exhibited distinct effects on the different aspects of lung injury, through mechanisms that remain unclear.

Keywords: mesenchymal stromal cell

P-139

CELL THERAPY

Which is the best therapeutic strategy for experimental emphysema: bone marrow-derived mesenchymal stromal cells or extracellular vesicles?

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INTRODUCTION: The alveolar destruction associated with emphysema cannot be repaired by current clinical practices. Several preclinical studies have shown that mesenchymal stromal cells (MSCs) have therapeutic potential in emphysema because of their immunomodulatory properties. However, clinical use of MSCs has been frustrating, suggesting that MSCs viability and/or function are greatly reduced after infusion. This could be partially explained by the activation of complement of innate immunity induced by MSCs after their contact with serum. The aim of this study was to evaluate and compare the therapeutic impact of MSCs with different doses of MSCs-derived extracellular vesicles (EVs) in a murine model of severe emphysema induced by elastase. METHODS: Emphysema was induced in C57BL/6 mice by intratracheal (it) administration of porcine pancreatic elastase (ELA, 0.2 UI) once a week during 4 weeks. The Control (C) group received saline solution (50 ml, it). After the last instillation of elastase, when lung and cardiovascular pathologically-related emphysema changes had already occurred, ELA groups were intravenously injected with saline (SAL, 50 ml), bone marrow (BM)-MSCs (1x106), low dose of BM-MSCs derived-EVs (proportional volume obtained from 106 BM-MSCs), or high dose of BM-MSCs derived-EVs (proportional volume obtained from 3x106 BM- MSCs). One week after the respective treatment, echocardiographic parameters, as well as lung mechanics and histology were evaluated. RESULTS: Our chronic protocol of experimental emphysema showed several characteristics of clinical emphysema, including: increased right ventricular area, pulmonary arterial hypertension (indirectly inferred by pulmonary artery flow time to pulmonary ejection time ratio), reduced pulmonary static elastance, and increased hyperinflated airspace, mean linear intercept, as well as neutrophil infiltration. After therapy with BM-MSCs or a different amount of BM-MSCs derived-EVs, we observed that both 106 BM-MSCs and proportional dose of EVs obtained from 3x106 BM-MSCs were not effective at restoring lung and cardiovascular dysfunction induced in the present experimental model. Nevertheless, the proportional dose of EVs obtained from 106 BM-MSCs was significantly effective in reducing all these altered parameters. CONCLUSION: In our current model of emphysema, the higher amount of BM-MSCs derived-EVs was unable to revert lung and cardiovascular damages induced by elastase. In contrast, a proportional dose of EVs obtained from 106 BM-MSCs was more effective, thus suggesting a dose-dependent effect in the therapeutic role of EVs, which is likely due to the nature of the target disease.

Keywords: Mesenchymal Stromal Cells, Emphysema, Extracellular Vesicles, Cell Therapy

P-140

Cell therapy

Impact of bone marrow or adipose tissue derived-mesenchymal stromal cell therapy in a murine model of allergic asthma induced by House Dust Mite.

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Background: Prophylactic administration of mesenchymal stromal cells (MSCs) inhibit the development of allergic airway inflammation induced by ovalbumin in a regulatory T (Treg) cell-dependent manner. However, so far, no study has evaluated whether MSCs act through Treg cells in a well-established model of asthma, when inflammatory and remodeling processes were already installed. For this purpose, we sought to test the therapeutic effects of two different sources of MSCs on lung function, inflammation, remodeling, as well as the number of Treg cells in experimental asthma. Methods: Asthma was induced in C57BL/6 mice by intranasal challenges of house dust mite extract (HDM; 25 μL) three times a week for three weeks. Control groups received saline solution (25μL) using the same protocol. Twenty-four hours after the last challenge, animals were randomly divided to receive saline (50 μL), bone marrow-derived MSCs (BM-MSCs, 105) or adipose tissue derived-MSCs (AD-MSCs, 105) intratracheally. Three and seven days after therapy, lung mechanics, inflammation, remodeling, as well as Treg cell count were evaluated. Additionally, *in vitro* analyses were performed using MSCs and lymphocytes co-cultures with and without HDM. Results: BM-MSCs and AD-MSCs reduced inflammation in bronchoalveolar lavage fluid (BALF), but only BM-MSCs reduced eosinophil and B-cell numbers. Nevertheless, both BM-MSC and AD-MSC therapy did not affect airway hyper-responsiveness, mucus secretion and inflammation. Even though no upregulation of Treg cell numbers was observed in the BALF or mediastinal lymph node (mLN) after cell therapy, IL-10 levels were upregulated by BM-MSC administration. In addition, both MSCs reduced Treg cell levels when lymphocytes obtained from mLN were re-stimulated with HDM *in vitro*. In contrast, unprimed lymphocytes derived from inguinal LNs had their Treg cells levels increased in the presence of BM-MSCs or AD-MSCs. Conclusions: In the current model of asthma induced by house dust mite, lymphocytes are unlikely to acquire a Treg cell profile after MSC therapy. Moreover, BM-MSCs seem to be more effective than AD-MSCs and act independently from Treg cells by increasing IL-10 levels, but they do not mitigate lung functional and histological changes.

Keywords: Mesenchymal stromal cell, asthma, Treg, allergic inflammation

P-141

Cell therapy

Therapeutic potential of stem cells in an experimental neural model of epilepsy in Wistar rats

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Introduction: Cell replacement with the use of neural stem cells is a promising alternative for the treatment of neurodegenerative diseases. Epilepsy is a set of neurological disorders that result in a high number of cerebral function disorders that affect the brain, leading to neurodegeneration. Objective: To evaluate the therapeutic potential of neural stem cells in experimental models of epilepsy in promoting neural repair. Methods: Epilepsy was induced by three experimental models (pilocarpine, pentylenetetrazole and picrotoxin). The animals were divided into seven groups (n = 4) containing epileptic animals treated and untreated with neural stem cells. After 1h of epilepsy induction, the treated groups received neural stem cells through the tail vein. After 30 days, the animals were euthanized and their brains submitted to histopathological analysis. Results: A total of 24 animals were treated with PIL, PTZ and PTX. The mortality rate was 8.3% (2/24), with the animals being from the groups treated with picrotoxin. Histopathology showed lesions in the brain tissue of rats with induced epilepsy in the groups of animals treated and untreated with neural stem cells. These lesions consisted of neuronal necrosis, areas of multifocal hemorrhage, edema and loss of myelin except in the control group. Discussion: The pentylenetetrazole and picrotoxin groups treated with neural stem cells showed intracerebral hemorrhage and diffuse areas of liquefaction necrosis. This may be related to the imbalance of the excitation/inhibition state (glutamate/GABA) caused by epilepsy inductors that generate a calcium influx and block chloride channels in brain tissue, thus leading to central nervous system lesions and, consequently, cell death. The pilocarpine group treated with neural stem cells also showed focal intracerebral hemorrhage, which was less intense, with neural stem cells showing cell differentiation similar to astrocyte cells. Conclusion: The neural stem cells showed a promising potential, particularly in the epilepsy model induced by pilocarpine in mice, as it showed a process of neural stem cell differentiation for lesion repair.

Keywords: Induced Epilepsy; Neural Stem Cells; Histopathological assessment; Cell Therapy

P-142

Cell therapy

Isolation and expansion of swine bone marrow mesenchymal stem cells in different culture media

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Introduction: Bone marrow mesenchymal stem cells (BMMSC) constitute a multipotent population with significant clinical potential for cell therapy, considering how easily they can be obtained and their immunosuppressive characteristics, which enable very viable xenograft possibilities. However, there are still doubts regarding the most appropriate culture media for cell viability and kinetics *in vitro*. Objective: To evaluate the *in vitro* confluence kinetics of swine BMMSC maintained in expansion in different culture media. Methods: BM samples were collected through biopsy aspiration from the femur of a healthy pig (UFPI/EAEC n. 097/15), which were divided into three samples, seeded separately in 12.5 cm² flasks, each containing a medium with different types of supplements and maintained in the incubator at 37 °C, 5% CO_2 and 95% humidity. One flask contained Minimum Essential Medium (MEM Alpha + GlutaMAXTM-l) with 20% FBS and two flasks contained Dulbecco's Modified Eagle's High Glucose (DMEM) culture medium for growth with 15% and 20% FBS, respectively. All culture media were further supplemented with 1% antibiotics, 1% L-glutamine and 1% non-essential AA. The culture media were replaced in compliance with their change in color and saturation and the cultures were observed until they reached 80% confluence in P2. Results: The culture maintained in MEM Alpha + GlutaMAXTM-l with 20% FBS showed medium saturation on days 2, 4, 5 and 6, reaching 80% confluence on the 7th day and displaying fibroblastoid morphology. The cultures maintained in DMEM High Glucose with 15% and 20% FBS, respectively, showed saturation of the medium on days 3 and 9, without achieving confluence. After the nine-day period of observation, the DMEM High Glucose 20% FBS was maintained and the DMEM High Glucose 15% FBS was replaced by MEM Alpha + GlutaMAXTM-l 20% FBS and both flasks were maintained incubated for eight more days under the same temperature and humidity conditions. Cell growth resumed only in the flask containing MEM Alpha + GlutaMAXTM-l 20% FBS, which showed medium saturation on the 13th day and reached 80% confluence on the 18th day. Discussion: The results obtained are inconsistent with the scientific literature, in which the DMEM medium is endorsed for BMMSC cultures in different animal species. The data showed no cell expansion using the DMEM, in contrast with the rapid cell growth obtained with MEM Alpha + GlutaMAXTM-l. It is necessary to evaluate the components of DMEM medium to stimulate the expansion of swine BMMSC in kinetics similar to that obtained with MEM Alpha + GlutaMAXTM-l. Conclusion: The MEM Alpha + GlutaMAXTM-I induced expansion and confluence of swine BMMSC in a shorter time interval when compared to DMEM High Glucose medium, while maintaining uniform and fibroblastoid cell morphology.

Keywords: mesenchymal stem cells; swine, culture medium

P-143

Cell therapy

Development of protocols for the production of hepatoblasts (HB) derived from human induced pluripotent stem cells (hiPSCs)

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Introduction: Pluripotent stem cells (PSCs) have great potential in modern Medicine. Among the PSCs, are the induced pluripotent stem cells (iPSCs), which are an abundant source of cells and that can be used for differentiation assays, disease models and cytotoxicity assays. In this context, the differentiation of iPSCs into hepatocytes have great appeal in the biomedical and pharmaceutical fields, for the culture of primary hepatocytes (PHs) from biopsies is difficult to obtain, have high maintenance cost and short time of use. Therefore, the development of protocols for the production of hepatoblasts and hepatocytes from iPSCs is of great interest, especially if this protocol is easy to be implemented and has economic viability. Objectives: To establish a iPSCs differentiation protocol in HB that is highly efficient and economically viable, allowing for the expansion and maintenance of the culture that allows the production of hepatocyte-type cells on a large scale. Material and Methods: Experiments were performed with iPSC clones generated in our laboratory using non-integrative vectors. Cells were grown in media for maintenance of PSCs. Based on methodologies of DUNCAN (2013) and NINOMIYA (2015), we performed the first differentiation stage (definitive endoderm) using CHIR99021 in D1 and Activin A in RPMI+B27 medium or using a differentiation kit for Stem-Diff definitive endoderm. At the next stage (hepatic specification), we used BMP4 and bFGF in D5 - D9 in RPMI + B27 medium. At the third stage (hepatoblasts), we used HGF in RPMI + B27 in D10-D14. At the last stage (hepatic maturation) was used Oncostatin-M in HCM medium in D15- D20. In each differentiation stage, a cell sample was collected to undergo analysis by flow cytometry (FC) using the markers CD184 (CXCR4)-PE-Cy5, CD117 (c-Kit)-PE, SOX17-FITC, CD13-APC, CD133-APC α-fetoprotein (AFP)-PE, albumin (ALB) -APC. Statistical analyses were performed using GraphPad5 program and Student's *t* test. Results: Initially, we established cell density to initiate differentiation at 7.5x10e4/cm^2. The analysis by FC showed that the tested clones differentiated into definitive endoderm cells with 80.2 ± 2.6% efficiency observed through CD184+/CD117+/SOX17+ labeling. Subsequently, cell differentiation into hepatoblasts was observed in 22.3 ± 1.2%, through hi CD13 +/ CD133 + labeling. During the course of experiments, we observed the labeling of cells positive for AFP (31.0 ± 20%) and ALB (26.9 ± 15%). Discussion and Conclusion: We reduced the inputs to achieve differentiation, with no loss in efficiency at the initial stage, with consequent reduction in protocol costs. The protocol still needs improvement to increase its efficiency at the hepatoblast and hepatocyte generation stages and to produce these cells in a large scale.

Keywords: stem cells, iPSCs, differentiation, hepatoblasts, hepatocytes

P-144

Cell therapy

Mesenchymal stem cells derived from Wharton's jelly display different patterns of P53 gene expression

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Introduction: Wharton's Jelly mesenchymal stem cells (WJ-MSC) have been studied extensively due to the variety of potential therapeutic applications. However, the role of p53 in the proliferative capacity, senescence and processes involved in the differentiation potential are poorly understood. The p53 signaling pathways are known to play a central role in the regulation of cellular senescence. There are two important p53 isoforms involved in this process: p53β accelerates and Δ133p53 represses replicative senescence, according to their modes of functional interaction with full-length p53. Additionally, the important role of p53 in cell cycle control, apoptosis, genomic stability and tumor development highlights the importance of studying p53 in the context of the biology of WJ-MSC. In this study, we evaluated the gene expression profile of p53 isoforms and specific p53 pathway controlling genes comparing undifferentiated WJ-MSC with cells undergoing replicative senescence in *in vitro* assays, and after adipogenic differentiation. Methods: MSCs were cultured until replicative senescence was reached. The samples were collected at an early stage (passage 5), at an intermediate stage (passage 15), and in the replicative senescence (generally between passages 20 and 25) (n=4). For adipogenic differentiation, the cells were cultured for 14 days with differentiation media (n=3). After this period, the samples were collected for gene expression profiling by real-time PCR of p53, p53 isoforms (Δ133p53 and p53β), p21, p16, and MDM2. Results and Conclusion: Gene expression of p53 varied among the samples, but did not follow a specific pattern. However, the expression of Δ133p53 isoform was decreased in senescent cells, whereas the p53β isoform was increased. The p21 and p16 genes, which are involved in cell cycle regulation, showed the same expression profile. Moreover, both were increased at the point where WJ-MSC reached replicative senescence. In the adipogenic differentiation, experiment expression of all analyzed genes was decreased when compared to undifferentiated cells, except for the Δ133p53 isoform. Our results show that neonatal WJ-MSC display different patterns of full length p53 mRNA expression in contrast to the p53β isoform, which may be used as an additional marker to detect senescent cells. It remains to be seen if changing p53β isoform levels is able to reverse senescence and increase the expansion potential of WJ-MSC. Financial support: FAPESP (fellowship). We thank Mr. Roberto Ruhman for his support of the IIEPAE-WIS Scientific Cooperation Program.

Keywords: mesenchymal cell, Wharton jelly, p53 isoforms, senescence

P-146 (CORRIGIR P/145!)

Cell therapy

Differentiation of RPE cells from Human Embryonic Stem Cells Aiming to the Treatment of Retinal Degenerative Diseases

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Introduction: The WHO estimates that the number of individuals who lose their vision due to Retinal Degeneration is expected to reach 6 million per year in 2020. The retinal degenerative diseases affect the retinal tissue responsible for both central and detailed vision, the macula. Most of macular degeneration appears in the elderly (AMD); however, there are hereditary diseases that affect young individuals, such as Stargardt's disease. The degeneration begins when there is a loss of retinal pigmented epithelium (RPE) due to formation of drusen (atrophic) or abnormal vessels (exudative). Since its discovery, human embryonic stem cells have been considered a valuable tool for therapeutic purposes. Although intractable, there is evidence that RPE transplantation differentiated from hESCs cells can recover the photoreceptor and prevent vision loss. Therefore, the objective of this project is the establishment of new stem cell therapeutic strategies to treat patients with AMD and Stargardt's disease. Material and Methods: Human embryonic stem cells (H9) were cultured in mTeSR1 medium and subsequently spontaneously differentiated into Retinal Pigmented Epithelial cells under cGMP conditions for 12 weeks. These hESC-RPE cells were cultured and maintained in serum-free medium (XVIVO 10) on Synthemax plates. The pigmented RPE-like cells were enriched by mechanical isolation. RPE cells were characterized by specific mRNA and protein analysis. Results and Discussion: Here we show the directed differentiation of hESCs into RPE cells under defined culture conditions. The hESC-derived pigmented cells exhibit the morphology, function, and marker expression of authentic RPEs. To characterize the developmental stages during RPE differentiation, several assays were used to identify the expression levels of genes key to each stage of development. qPCR was developed to provide a quantitative and relative measurement of the abundance of cell type-specific mRNA transcripts. Differentiated RPE cells were positive for specific RPE antibodies, such as RPE65 and ZO-1. Conclusion: Our results suggest that hESCs could serve as a potentially inexhaustible source of RPEs for the effective treatment of a range of retinal degenerative diseases.

Keywords: hESC, RPE, AMD, Cell Therapy

P-146

Cell therapy

Bone Morphogenetic Proteins (BMP2 and BMP4) expressed in Mammalian Cells aiming at Bone Tissue Engineering and Stem Cell Proliferation and Differentiation

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Bone morphogenetic proteins (BMPs) are glycoproteins secreted and members of the TGF-β superfamily that have been implicated a wide variety of roles. On the other hand, aberrant BMP signaling is associated with several human diseases, such as fibrosis, bone and immune disorders, cancer progression and metastasis. BMP involvement in MSC biology has been explored in Regenerative Medicine, as they are multipotent, having the ability to generate a limited number of specialized cells when stimulated by several trophic signals. These proteins act as a disulfide-linked homodimer, being potent regulators of bone and cartilage formation and repair, cell proliferation in embryonic development and bone homeostasis in the adult individual. BMPs are dimeric molecules displaying sites for N- and O-glycosylation, which increases the stability and half-life of the protein in the body, in addition to determining the specificity of receptor coupling. BMPs currently have an important potential biotechnological and therapeutic approach, to treat physiopathological bone loss, non-union fractures and in oral surgery, and to accelerate and increase osseointegration. BMP2 induces cartilage and bone formation. BMP4 has also been described to play a role in triggering the osteoblastic differentiation of MSCs, through activation of osteoblastic-related genes. The high cost of these recombinants is the major obstacle to their clinical use. In order to ensure proper glycosylation and conformational folding and prevent immunogenicity, we elected a mammalian cell expression system to produce these BMPs, aiming at bone regeneration, stem cell proliferation and differentiation and their application in human and veterinary cell therapy. BMPs cDNAs were amplified from our Human Full-Length cDNA Bank and cloned into pGEM®-T-Easy vector. *E. coli* transformants were screened by colony PCR. Upon DNA sequencing, the BMPs inserts were transferred to a lentiviral expression vector. HEK293 cells were co-transfected with a lentiviral plasmid containing both BMP2 or 4 and eGFP cDNAs, by co-transfection with a Hygr vector for clone selection, at a 40:1 ratio. Cell clones were selected using 100 ug/mL of hygromycin. BMP expression was analyzed by qRT-PCR and Western blot. The biological activity was demonstrated both *in vitro*, by alkaline phosphatase activity in C2C12 cells, and *in vivo* by induction of ectopic bone formation in Rowett rats after 23 days, respectively. BMPs were continuously secreted to the medium even after 120h of serum starvation. rhBMPs were purified using heparin-affinity chromatography (more than 90% purity). To assess the glycosylation status of the rhBMPs produced, PNGaseF treatment was carried out and a reduction in rhBMP molecular mass was detected, indicating that the rhBMPs expressed are glycosylated. The use of these biopharmaceuticals in Bone Tissue Engineering is likely to allow accelerated recovery of both human and animal patients.

Keywords: Bone Tissue Repair, Osteogenesis, Non-Union Fracture, Mammalian cell expression, osseointegration.

P-147

Autologous Transplantation

NEAM protocol at the Walter Cantídeo University Hospital (HUWC): complications related to the transplant

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Introduction: Bone marrow transplantation (BMT) consists in obtaining stem cells (HSC) through a phase called HSC mobilization and a second phase, which is the transplant itself: conditioning regimen, infusion of collected CD34+ cells, bone marrow aplasia and recovery. Among the conditioning protocols used in autologous bone marrow transplantation in patients with Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) at Walter Cantídeo University Hospital (HUWC), BEAC and BEAM were utilized; both used the drug carmustine, an antineoplastic alkylating agent. With the lack of carmustine in Brazil, it became necessary to use another conditioning regimen in BMT. We found in the literature a Korean alternative protocol: NEAM (mitoxantrone, etoposide, cytarabine and melphalan), which was used from April 2014 to February 2015. It is important to analyze the results and compare them with the original Korean protocol. Among the BMT complications, febrile neutropenia and toxicities related to chemotherapy (CT) were common. The degree of CT-related toxicity can be classified according to the common toxicity criteria of the cancer therapy evaluation program revised in 2009. Objectives: To determine the frequency and degree of toxicity related to BMT, as well as the frequency of febrile neutropenia and microorganisms isolated in cultures. To compare the results obtained at HUWC with the results of the Korean study carried out with the NEAM protocol. Method: Retrospective analysis carried out by reviewing the medical charts of patients submitted to NEAM in HUWC, from April 2014 to February 2015 and follow-up until December 31, 2015. Results: 25 transplants were performed using the NEAM protocol, 13 (52%) HL and 12 (48%) NHL cases. In the HL group, 85% had febrile neutropenia, 55% had microorganisms isolated from blood cultures, being 83% *E. coli* and 17% *S. epidermidis*. Regarding oral mucositis, 8% had grade 0; 62%, grade 1; 15% grade 2 and 15% grade 3. As for intestinal mucositis, 31% had grade 1; 31%, grade 2 and 38% grade 3. 31% had grade 0 of hepatotoxicity; 38%, grade 1; 8%, grade 2; 23% grade 3 and no one had toxicity grade 4. In the NHL group, 92% had febrile neutropenia, 36% had microorganisms isolated in blood cultures and rectal swabs, being 14% *E. coli*, 14% *Klebsiella*, 14% *A. baumannii* 14% *E. faecalis*, 30% *S. epidermidis*, and 14% VRE. Regarding oral mucositis, 42% had grade 1 and 5. Conclusion: Patients undergoing conditioning with the NEAM protocol at HUWC had a similar rate of febrile neutropenia when compared with the literature, but with a higher rate of microorganism isolation in cultures, which may correspond to a more stringent infection screening at the HUWC transplant sector. The higher rate of isolation of gram-negative bacteria may be associated with a high rate of intestinal mucositis. Regarding the toxicity associated with chemotherapy, acceptable grades of oral and intestinal mucositis, as well as hepatotoxicity occurred.

Keywords: conditioning, NEAM, BMT, complications

P-148

Autologous Transplantation

Prognostic assessment of patients with classical Hodgkin's lymphoma submitted to Autologous Hematopoietic Stem-Cell Transplantation

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Introduction: The classical Hodgkin's lymphoma (cHL) has an indication for autologous hematopoietic stem cell transplantation (HSCT) when it manifests as refractory or relapsed disease. Its prognosis can be influenced by several factors at diagnosis, such as: bulky mediastinal disease, extranodal disease, nodal involvement, gender, age, stage IV and laboratory levels of hemoglobin, leukocytes, lymphocytes, albumin and VHS. Objective: To evaluate the prognosis of cHL in patients submitted to autologous BMT. Material and Methods: patients submitted to autologous HSCT were analyzed from January 2004 to January 2016. Prognostic factors of the International Prognostic Score (IPS) were evaluated, as well as Epstein-Barr virus (EBV) positivity in tumor by *in situ* hybridization, in relation to overall survival (OS) and event-free survival (EFS). Results: Sixty-two cHL cases were evaluated, most of them females (56.5%), aged <45 years (88.7%). The most common histological subtype was nodular sclerosis (NS) in 74.2% of cases. The OS and EFS in 2 years were, respectively, 74% and 69%. Among the factors assessed at diagnosis, none was able to influence survival rates in the univariate analysis. Discussion/Conclusion: The OS and EFS rates were similar to those in the international literature. Although it was not possible to identify factors, which at diagnosis had the capacity to predict survival in this population, we believe that further studies with a larger number of patients with this objective is important to define the expected response and conduct after autologous HSCT.

Keywords: Hodgkin's Lymphoma, Autologous Bone Marrow Transplantation, Risk Factors

P-149

Autologous Transplantation

Low toxicity, immediate clinical and quality of life impact in patients with severe and refractory Crohn's disease submitted to autologous hematopoietic stem cell transplantation

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In severe and refractory patients with Crohn's disease (CD) without a treatment option, the Hematopoietic Stem Cell Transplantation (HSCT) is an alternative. The goal was to determine HSCT toxicity at mobilization, conditioning, and the immediate clinical and quality of life impact 30 days after the procedure. Fourteen patients selected from 44 patients with CD were submitted to autologous HSCT, evaluated from 2013 to 2105. Inclusion criteria were: diagnosis of CD, disease confirmed by colonoscopy or capsule endoscopy, with CD activity index >150, positive Harvey & Bradshaw and Craig indexes, risk of further surgical resections, implant of definitive stoma or rectal amputation. Mobilization: Cyclophosphamide (Cy) 60 mg/kg/day and G-CSF 10 mcg/kg/day from day 5 until the end of the HSC collection. Conditioning: Cy 200 mg/kg and Thymoglobulin 6.5 mg divided into 4 consecutive days. Toxicity was determined according to the NCI common criteria index, clinical evaluation, CD activity index (CDAI) and quality of life (Short Form 36) prior and 30 days after the procedure. Results: Of the 14 patients (7m/7f) aged 34 years (24-50), CDAI 281.59 (450.20 155-) two patients had mild, 10 had moderate and two had severe disease. The Montreal classification showed sample heterogeneity. The mean time from symptom onset to transplant completion was 11 years. Twelve patients had had previous surgery and six had perianal involvement. Evidence of lesions was positively assessed through colonoscopy assessment indexes (12) and one with capsule endoscopy. The number of infused cells was 13.94 CD34/kg (4.3 to 36.65) and grafting occurred on D+10 (7-12). The number of erythrocyte concentrates occurred in four patients in the mobilization period (6 units), and of 41 units in the conditioning period. The number of platelet concentrates did not occur in any patient in the mobilization period and only nine required the component during conditioning. Febrile neutropenia was observed in a patient during mobilization and four during conditioning, with positive culture in CVC sample only and negativity after antibiotic therapy. The quality of life showed significant improvements, particularly in the domains of pain, overall health perceptions, vitality, social functioning and mental health. The CDAI showed a significant downward trend with an average of 95.81 (45.40 to 177). Toxicity was limited to hematological sector in aplasia. There were no deaths, sepsis or toxicity to drugs, and all showed symptom improvement. The procedure can be considered safe, of low toxicity and a therapeutic option in CD.

Keywords: Intestinal Inflammatory Disease, Cell Therapy, Toxicity

P-150

Autologous Transplantation

Gynecological health profile in patients post-BMT: Principles, Proposal of Care Protocol and Peculiarities.

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Introduction: Some gynecological symptoms are often neglected in post-BMT patients. Problems such as premature ovarian failure associated with the use of alkylating agents, coagulation disorders, risks to the use of oral contraceptives and menopausal symptoms are common in these patients. Specialized care by skilled gynecologists should be offered to all post-BMT patients. Material and Methods: We assessed all post-BMT female patients followed at the GTD outpatient clinic (Molar pregnancy) and Post-BMT at Maternidade Escola Assis Chateaubriand - MEAC/ UFC from November 2015 to May 2016. Approximately 2,100 consultations were carried out in the clinic. Of these, less than 10% was of post-BMT patients. Results: The main indications for transplantation were bone marrow aplasia, Leukemia and Lymphoma. The main gynecological demands were safe contraception, fertility preservation and pre-menopausal symptoms. One of them, diagnosed with lymphoma, had part of her ovarian tissue cryopreserved and is currently awaiting cure criteria for reimplantation. Discussion: Proposed Clinical Protocol Post-BMT: 1. Monitoring: Asymptomatic Women: Refer to Gynecologist 1x/ year; Symptomatic Women: Refer to gynecologist with experience in post-BMT; Pediatric patients: Pediatric Gynecologist to be assessed by: Tanner Staging, inspection of the external genitalia and reevaluation every 3-6 months. 2. Therapeutic options: Intimate hygiene with water only. Lotions and perfumed soaps, as well as tight underwear should be avoided; Contraception: Oral (dienogest 2 mg): 01 tbl. 1x/ day OR transdermal (Norelgestromin 6 mg/ Ethinyl Estradiol 0.6 mg). Hormonal Therapy: If patient has a Uterus (E: Estradiol/ P: norethisterone): Transdermal: E (25 mcg)/ R (125 mcg) OR oral: E (1 mg)/P (0.5 mg): 01 tbl. 1x/ day; Hysterectomized (E: Estradiol): Transdermal: E (50 mcg/ day) OR oral: E (2mg): 01 tbl. 1x/ day; When there is vaginal atrophy, topical estrogen: Promestriene or Estriol. 3. Prevention of secondary gynecological tumors: Pap Cytology 1x/ year; Biopsy of genital lesions with suspected dysplasia or neoplasia; HPV vaccine for all young women (12-26 years). 4. Premature Ovarian Failure: Women with POF under 40 years should receive HRT regardless of symptoms up to the mean age for natural menopause (51 years); Early mammography after 25 years or eight years after TBI. For young women (<40 years) who wish to become pregnant or without defined offspring, they should be evaluated for the possibility of ovarian cryopreservation. Conclusion: The BMT services should provide adequate gynecological care, with options for safe contraception, hormone therapy and protocol in oncofertility (fertility preservation).

Keywords: Bone marrow transplant, gynecology, premature ovarian failure, oncofertility

P-151

Autologous Transplantation

Clinical evolution and current "status" of patients with severe Crohn's disease submitted to autologous hematopoietic stem cell transplantation. Crohn auto HSCT Project

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Crohn's disease (CD) is a severe disease that can be refractory and does not respond to conventional treatments. In this scenario of lack of therapeutic options, hematopoietic stem cell transplantation (HSCT) may be an alternative treatment. The objective of this study is to show the current status of a series of 20 patients submitted to autologous HSCT, with non-myeloablative regimen and no cell selection. The inclusion criteria for the procedure were: CD diagnosis, disease previously demonstrated by colonoscopy or capsule endoscopy, disease activity index (CDAI) >150, disease activity in Harvey & Bradshaw and Craig indexes, risk of new surgical resections, definitive implant or rectal amputation. The mobilization was: Cyclophosphamide (Cy) 60 mg/ kg day and G-CSF 10 mcg/ kg/ day from day 5 until the end of the collection of peripheral blood progenitors. Conditioning was: Cy 200 mg/ kg and Thymoglobulin 6.5 mg total dose, divided in 4 consecutive days. Clinical follow-up and evaluation of patients' CDAI occurred after 30 days, 3, 6, 12 months and annually after the procedure. The mean age of 11 male pts and nine female pts was 35 years and the stratification according to the Montreal classification was heterogeneous. The mean CDAI of the series prior to HSCT was 288.47 and after the 1st month: 104.1; at 3 months: 63.1; at 6 months; 83.5; at 12 months: 72.8. Colonoscopy was performed prior to HSCT, at 6 months, 12 months and annually after the procedure. Endoscopic improvement was observed in all patients in the study, with endoscopic remission in many cases, as well as significant clinical improvement and resolution of clinical symptoms and improved quality of life in most cases. The complications observed after the transplantation were restricted to a case with persistent hematuria after HSCT, which persisted for 1 month, and was resolved at the 2nd month after the procedure, in addition to a case submitted to hemorrhoidectomy nine months after the HSCT, unrelated to the disease. None of the described patients have required anti-inflammatory drugs, biological agents, immunosuppressants or corticosteroids to date, as there were no cases of disease recurrence up to now. This is the first series of cases of Crohn's disease treatment with HSCT being followed in Brazil.

Keywords: Intestinal Inflammatory Disease, Cell Therapy

P-152

Autologous Transplantation

Analysis of factors associated with the yield of hematopoietic progenitor cell apheresis in patients submitted to mobilization with biosimilar filgrastim for autologous transplantation

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Introduction: Hematopoietic stem cells (HSC) originating from peripheral blood are collected by leukoapheresis (AP) after their mobilization (Mob) with hematopoietic growth factors (usually filgrastim) alone or in combination with chemotherapy (CT) and/or with plerixafor. Objective: To evaluate factors that can affect the efficiency of HSC collection in patients submitted to the first Mob with biosimilar filgrastim (FI) for autologous transplantation (autoHSCT). Methods: A prospective cohort study was carried out in a university hospital from 01/01/2008 to 06/30/2015, which included patients candidates to the first autoHSCT using Mob only with FI and AP in a machine with discontinuous flow. The first AP was performed on day 5 after the start of FI. CD34 cell counts in peripheral blood pre-AP (CD34-SP) and post-AP unit were performed by flow cytometry (ISHAGE protocol). The target counting of HSC collection: ≥ $2x10^6$ CD34+ cells/ kg. When this cell target was not reached, a second Mob with FI was started on average 21 days after the first Mob. The analyzed variables were age, presence of obesity (BMI ≥30), primary disease, filgrastim dose/ kg, CD34-SP count on the first day of AP, number of chemotherapy lines, radiation therapy use and presence of thrombocytopenia (<100,000/ mm^3) prior to Mob. The statistical analysis used Fisher's exact test or x^2 in the univariate analysis and a logistic regression model in the multivariate analysis. Results: 99 patients were analyzed, 56 (57%) males, with a mean age of 48 years (SD = 15 years), of which 65 (66%) had multiple myeloma, 25 (25%) Hodgkin's disease and six (6%) non-Hodgkin's lymphoma. Twenty-one (21%) patients received ≥3 chemotherapy lines. Obesity was present in 28 (28%) cases. Thrombocytopenia and radiotherapy prior to the Mob occurred in six (6%) and 28 (28%) cases, respectively. FI mean dose in the first Mob was 11 μg/kg (standard deviation [SD] = 4 μg/kg). The mean of CD34-SP was 26 CD34/μL. The mean yield of the first Mob was 2.3x106 CD34 cells/kg (SD = 1.9 CD34/ kg). Thirty-three (33%) patients underwent the second Mob with a mean FI dose of 15 μg/kg (SD = 4 μg/kg). After the second Mob, 93 (94%) patients achieved the target HSC to undergo the autoHSCT. Univariate analysis showed that the following variables were significantly associated with good yield at the collection: primary disease (OR = 4.53; p = 0.001), CD34- SP ≥10 CD34/ μL (OR = 4.62; p = 0.003) and prior radiotherapy (OR = 0.36, p = 0.03). However, only the number of CD34-SP ≥10 CD34/ μL showed to be independently associated with this outcome in the multivariate analysis (OR = 4.7; CI: 1.7 to 13.0; p = 0.002). Conclusion: CD34 cell count in peripheral blood pre-leukoapheresis was the only independent factor associated with the yield of HSC collections, being a good parameter for the start of the first leukoapheresis and defining hematopoietic progenitor cell mobilization failure.

Keywords: Hematopoietic Stem Cell Mobilization, Filgrastim, Autologous Bone Marrow Transplantation

P-153

Autologous Transplantation

Logistics for the processing, cryopreservation and thawing of hematopoietic stem cells for autologous transplantation in children with central nervous system tumors

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Introduction: The performance of three sequential autologous transplants (transplants in tandem), has been studied as an alternative with less toxicity and possibly more effectiveness in the treatment of children with central nervous system (CNS) tumors. However, it is important to consider the space in freezers required to store several units of hematopoietic stem cells (HSC) and the logistics of defrosting for reinfusion. The processing of HSC allows reducing the volume of the product and increasing concentrations of total nucleated cells (TNC). As a result, the unit storage space is optimized. Because these are small children, removal of the cryopreservation agent dimethyl sulfoxide (DMSO) is indicated. In order to treat these patients, a strategy was created to ensure collections with adequate cellularity and also distribute them in at least three units, optimizing space in the freezers and the flow of infusions. Objective: To describe the logistics required for processing these units with pre-defined cellularity. Method: A retrospective evaluation of medical records of six patients with CNS tumors, each of them submitted to three infusions of HSC. Results: A median of two leukoaphereses per patient was collected in an automated blood cell separator COBE Spectra. A median of 20x10(8) TNC/ kg (8-62) and 12x10(6) CD34 cells/kg (6-239) was cryopreserved and distributed in at least three units (3-6), with a median total volume of 165 mL (90-214). The products were cryopreserved using albumin 4%, HAES 6% and DMSO 5%, without adjusting cell concentration and stored at -80°C in a freezer with negative tests for infectious diseases. For infusion, defrosting was carried out in a water bath at 37 °C and removal of DMSO according to the New York Blood Center protocol. The HSC were diluted at the ratio of 1:1 in Dextrano40+ 5% albumin immediately after defrosting and TNC counting was performed. Then, the unit was centrifuged at 2000 rpm and 4 °C for 20 minutes. The buffy coat was resuspended with the same solution, and sent to infusion. The sterility test was carried out after processing and after washing of the cells and there was no bacterial contamination. Age and weight medians were two years (1-5) and 12 kg (8-17), 50% of patients were males. All patients received three infusions, except one, who received two autologous infusions and a third, syngeneic infusion. The median cellularity infused was 4.7x10 (8) TNC/ kg (1.5 to 16), 2.5x10 (6) CD34/ kg (1-10) and 0.1 g/ DMSO/ kg prewash (0.1-0.4). All patients showed adequate neutrophil engraftment, with a median of 11 days (9-13) and all are alive. Only one patient has leftover units. Conclusion: The established logistics was essential for storing the number of bags and enough cells to guarantee infusions with satisfactory neutrophil engraftment and without compromising freezer space.

Keywords: Autologous BMT in Tandem, Cryopreservation of Hematopoietic stem cells, central nervous system, infusion of hematopoietic stem cells

P-154

Autologous Transplantation

Use of ondansetron, aprepitant and dexamethasone as antiemetic therapy in patients submitted to high-dose chemotherapy in Autologous Hematopoietic Stem Cell Transplantation.

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Introduction: Autologous hematopoietic stem cell transplantation is a therapy primarily used for the treatment of hematological malignancies and consists in the infusion of hematopoietic stem cells previously collected from the patient's own blood, so that faster marrow reconstitution occurs after aplasia induced by chemotherapy, because toxicity to bone marrow is a major limitation to therapy. Most patients receiving high dose chemotherapy have acute and severe complications, particularly nausea and vomiting. Objectives: The objective of this study was to analyze the therapeutic response of all patients who received prophylaxis for nausea and vomiting induced by chemotherapy using ondansetron, aprepitant and dexamethasone for the transplant conditioning in a public hospital in São Paulo, considering that the National Public Health System does not provide the three classes of recommended drugs. Materials and Methods: Data were obtained from electronic records, from which all adult patients were selected, from April 2013 to April 2015 submitted to high-dose chemotherapy at the autologous transplant conditioning phase and received the prophylactic regimen with ondansetron, aprepitant and dexamethasone. Results: The study sample consisted of 82 patients. As for the adverse events, 37.80% did not have any event related to nausea and vomiting, or even loss of appetite as a symptom. As for the nausea, patients who reported symptoms were 14.63% and for vomiting, 14.63% had at least 1 episode of vomiting during a 120-hour period. The overall complete response to vomiting was seen in 95.85% (CI: 95%) patients. An overall unsatisfactory response for vomiting was observed in 4.15% of the patients. The overall satisfactory response for nausea was observed in 95.60% (CI:95%) of patients. The overall unsatisfactory response for nausea was observed in 4.40% of patients. Discussion: The association of aprepitant to the antiemetic therapy showed to be effective in the acute and late phases. This study showed that in the late phase, our therapy was effective in 95.73% for nausea and 96.03% for vomiting. It can be observed that the mean daily cost of hospitalization of a patient with hematological malignancies is high and each extra day of hospitalization relevantly increases the cost of treatment. Conclusion: Adding aprepitant to the basic scheme offered by SUS (5-HT3 inhibitor and corticoids) increases the effectiveness of the antiemetic therapy without influencing the pharmacokinetics of the high-dose chemotherapy, resulting in greater adherence to treatment, shorter hospital length of stay and decreased treatment costs due to better control of adverse events.

Keywords: Pre-transplant conditioning, Vomiting, nausea, Antiemetic drugs

P-155

Autologous Transplantation

Mantle cell lymphoma – Experience from a single center transplant unit

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Introduction: Mantle cell lymphoma is a subtype of non-Hodgkin's lymphoma (NHL) derived from B-lymphocytes in the mantle zone, corresponding to 6% of all NHL. It usually has an aggressive clinical course and is characterized by a predominance of the male gender, a higher prevalence in the elderly and a propensity for extranodal involvement. The hematopoietic stem cells transplantation (HSCT) in mantle cell lymphoma is used as consolidation therapy after chemotherapy, leading to longer remissions and higher survival rates and, therefore, possible cures. Objectives: To describe the results of autologous hematopoietic stem cell transplantation in patients with mantle cell lymphoma in a Bone Marrow Transplant Unit from a single center. Material and Methods: An observational, retrospective, study was performed, with description of patients with mantle cell lymphoma submitted to autologous HSCT carried out from January 2013 to March 2016. Results: During the study period, , eight patients, all males, with a median age of 48 years and 88% from the Ceará state and 12% from Sergipe state were submitted to HSCT. At diagnosis, 62.5% had stage IV B. In relation to treatment, 25% were submitted to HyperCVAD protocol, 12.5% to CHOP + DHAP protocol, 12.5% to R–CHOP protocol, 12.5% to HyperCVAD + R - HyperCVAD protocol, 25% to Nordic Protocol and 12.5% to R - Maxi - CHOP protocol. Of the patients, 50% used G-CSF as CD34 cell mobilization protocol and all were submitted to conditioning with NEAM. At the post-HSCT evaluation, 87.5% of patients remained without signs of disease activity. Conclusion: The hematopoietic stem cell transplantation, used as consolidation therapy, showed to be a potentially curative regimen for patients with mantle cell lymphoma.

Keywords: Mantle Cell Lymphoma, Autologous of Hematopoietic Stem Cell Transplantation; Conditioning

P-156

Autologous Transplantation

C-reactive protein in patients submitted to autologous hematopoietic stem cell transplantation (HSCT) - evaluation of the dynamics and correlation with clinical outcomes

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Introduction: The use of inflammatory markers, such as C-reactive protein (CRP), has been employed aiming to improve the management of critically-ill patients. However, few data are currently available in patients submitted to HSCT. The aim of this study is to evaluate the association between the dynamics of quantitative CRP and its use as a predictor of the following outcomes: bacteremia, hospital length of stay, mucositis, granulocyte recovery and death. Method: A prospective cohort of patients submitted to autologous HSCT in two institutions (HCN and HUCFF) from 2012 to 2015, were assessed. To assess the dynamics, the CRP measurements were performed at the times: Pre-BMT, on the day of BMT infusion (D0), on the subsequent days D+3, D+6, D+9, and after D+11, at the start of febrile neutropenia, as well as at the time of granulocyte recovery (grafting CRP). The highest measurement of CRP was also evaluated (peak CRP). The negative reference and the unit suggested by the manufacturer (<0.3 mg/dL) were used. Data were expressed as medians with minimum and maximum values and graph analysis (BoxPlot). Statistical analysis was performed using Spearman's correlation test and Mann-Whitney test. Analysis of sensitivity and specificity was performed by the ROC curve. Results: 333 patients were analyzed; of these, 202 (61%) had been diagnosed with multiple myeloma and 126 (38%) with lymphoma. Death occurred in 8 (2.4%) patients. The pre-BMT CRP was > 0.3 mg/ dL in 66% of patients on admission. The median measurements were as follows: pre-BMT: 0.47 (<0.001 to 15.5), D0: 0.315 (<0.001 to 20.06), D+3: 0.68 (<0.001 to 86), D+6: 3.37 (<0.001 to 32.2); D+9: 7.86 (<0.001 to 32.31), post-D+11: 3.36 (<0.001 to 31.29), at grafting: 4.71 (<0.001 - 31.29), at peak: 11.8 (<0.001 to 32.79). There was no association between underlying disease, age and gender and Pre-BMT CRP measurement. There was an association between CRP measurements and the following outcomes: bacteremia (p <0.001), mucositis (p <0.001), time of neutropenia (p <0.001), hospital length of stay (p = 0.013), and death (p <0.001). The CRP measurement on D+6 was directly related to the degree of mucositis (p <0.001) with increasing medians between Grade 0 and Grade 4. The CRP on D+11 was strongly associated with mortality (p <.001). Conclusion: Quantitative CRP showed a significant association with important outcomes in patients submitted to autologous HSCT. The dynamics of CRP showed to be an important tool to assess risk for complications in this population. The search for cutoffs with good sensitivity and specificity is necessary.

Keywords: transplantation, complications, infection, marker

P-157

Autologous Transplantation

Retrospective evaluation of onco-hematological patients submitted to Autologous Hematopoietic Stem Cell Transplantation - analysis of early mortality and overall survival

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The autologous hematopoietic stem cell transplantation (HSCT) is regularly used to restore bone marrow function in patients with multiple myeloma or lymphoma after myeloablative chemotherapy. However, patients with comorbidities are more susceptible to toxicity and reduced quality of life after HSCT, and despite improvements in transplantation techniques and clinical support, the overall and early mortality rates remain high and are related to the procedure. Objectives: To evaluate the transplant-related mortality (TRM) in less than 100 days and overall survival in patients with multiple myeloma, Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) submitted to autologous HSCT from 1994 to 2015. Material and Methods: exploratory, observational and retrospective study that evaluated 532 patients, 298 with multiple myeloma, 142 with HL and 92 with NHL, submitted to autologous HSCT, by evaluating overall mortality post-HSCT, TRM, mortality causes and their association with the following prognostic variables: gender, age, pre-HSCT disease status and decade when the procedure was performed. Results: The overall mortality rate was 33.8% and the overall TRM was 6.6%. The main causes of overall mortality were disease progression (30.6%), infections (19.4%) and cardiac causes (0.6%). Median survival after HSCT was 97 months for the multiple myeloma group, 33 months in the NHL and was not reached in HD. The overall mortality rates were 32.2%, 31.7% and 42.4% and the TRM rates were 3.8%, 9.2% and 13% in the groups with multiple myeloma, HL and NHL, respectively. Predictors of higher TRM rates were not identified among the variables. Infections persisted as the main cause of TRM in all groups, configuring 91.7% of premature causes in the multiple myeloma group, 69.2% in the HL and 66.7% in the NHL group. There was no evidence of higher overall or early mortality in patients older than 60 years submitted to autologous HSCT. In multiple myeloma group, patients with lower tumor burden had lower overall mortality after HSCT (very good complete and partial response: 3.8% vs. stable disease or progression, 38.5%; $p = 0.002$) as well as in the HL group (response: 9.1% x progression: 63.6%; $p = 0.004$). It was also observed a reduction in mortality in HSCT performed between 2005-2015 in relation to the decade of 1994-2004 in the myeloma (58.3% vs. 41.7%; $p < 0.001$) and HL group (68.9% x 41%; $p = 0.006$). Significant predictors of mortality were not identified in the NHL group. Conclusion: Although the autologous HSCT offers increased potential for survival and shows improvements over the years, its results depend both on patient characteristics and the underlying disease, with disease progression being the main cause of post-HSCT overall mortality and infections as the major cause of TRM in the studied population.

Keywords: HSCT, prognostic factors, mortality, survival

P-158

Autologous Transplantation

Use of vinorelbine associated with filgrastim in stem cell mobilization for autologous transplantation

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INTRODUCTION: The hematopoietic stem cell transplantation (HSCT) is an important line of treatment in patients with multiple myeloma and those with recurrent high-grade lymphoma or lymphomas requiring HSCT at the first remission. To carry out this procedure, it is mandatory to perform the mobilization and collection of hematopoietic stem cells (HSC) before transplantation. Many of these patients, especially patients with lymphomas, are submitted during their treatment to multiple lines of chemotherapy or radiation therapy, which entails greater difficulty for the mobilization and collection of these cells. Currently, there are several regimens for performing HSC mobilization, always based on the use of filgrastim, which can be used alone or in combination with other drugs. Chemotherapy or plerixafor are the adjuvants that can be employed in combination with filgrastim. The use of vinorelbine associated with filgrastim is a new type of chemomobilization that does not require hospitalization for its administration and involves fewer adverse events and reduced costs when compared to traditional regimens. MATERIAL AND METHODS: We evaluated 20 patients diagnosed with multiple myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma and germ-cell tumors who used this association after failing the first mobilization regimen. RESULTS AND DISCUSSION: Nineteen patients achieved CD34 cell level in peripheral blood >10 cells/mm³ and were referred to collection by apheresis. Ten collected enough HSC on the 1st day of apheresis and five after two aphereses. Two had lower amounts collected, but underwent only one apheresis as they had cells stored from the first mobilization. Two did not reach the minimum CD34 cells in the collected units necessary for the HSCT. In the end, 17 patients collected enough CD 34 cells for HSCT with two mobilizations, the second using a combination of filgrastim and vinorelbine. CONCLUSION: This regimen seems to be effective, as well as safe and reduce costs in patients considered to be bad mobilizers.

Keywords: Vinorelbine; filgrastim; Mobilization; Bone marrow transplant

P-159

Autologous Transplantation

Autologous hematopoietic stem cell transplantation: experience of the bone marrow transplant unit at Walter Cantídio University Hospital with the first 100 transplanted patients

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Introduction: Currently, Brazil has one of the largest public organ and tissue transplantation programs in the world. Bone marrow transplantation (BMT) is used in the treatment of hematological, oncological, hereditary and immunological diseases. Objective: To characterize the epidemiological profile of patients submitted to autologous BMT in a reference center in the state of Ceará and outline the center operations. Method: This is an observational, prospective, descriptive and analytical study. The first 100 patients submitted to autologous bone marrow transplantation since the beginning of the unit operation in September 2008 until October 2013 were selected for the study. Results: Of the 100 patients submitted to autologous BMT, 64 were males and 36 were females. The mean age was 44 years (17-69 years). 57 patients underwent transplantation for the treatment of Multiple Myeloma, 26 to treat Hodgkin's lymphoma, 15 to treat Non-Hodgkin's lymphoma and 2 for the treatment of seminoma. The mean number of CD34 + cells collected was 4.88 x 106 cells/ kg (2.03 to 18.39 x 106 cells/ Kg). The mean neutrophil recovery (bone marrow grafting) was 10.7 days (7-21 days). The mean hospital length of stay was 21.85 days (11-50 days). The overall survival (OS) rate was 92.92%; there were 7 deaths and one patient was lost to follow-up, with the latter being excluded from the OS analysis. The mortality rate in the first 100 days was 6%. Conclusion: The analysis of the autologous BMT carried out in the state of Ceará showed excellent results when compared with data from the scientific literature.

Keywords: Bone Marrow Transplantation, Autologous, Multiple Myeloma, Lymphoma

P-160

Autologous Transplantation

Nutritional profile of patients submitted to hematopoietic stem cell transplantation in a university hospital in Fortaleza-CE

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) consists of several aggressive procedures that can lead to many complications for the individual and may affect the nutritional status which, in turn, can also influence the transplant outcome. Objective: To assess the nutritional status of patients submitted to hematopoietic stem cell transplantation. Method: This is a quantitative, retrospective study of the medical records of patients submitted to autologous HSCT during the hospitalization period at the Walter Cantídio University Hospital from 2009 to 2011. The data analyzed were gender, age, diagnosis, weight (before the conditioning, 5 and 13 days after the transplantation) and height, also calculating the body mass index (BMI) using the cutoff values determined by the World Health Organization (1995) for adults and Lipschitz (1994) for the elderly. Data were tabulated in a Microsoft Excel 2013 spreadsheet for analysis of results. Results: 23 patients older than 18 years participated in the study, in which males accounted for 70%, and the mean age of both genders was 39.9 ± 14.6 years. The elderly accounted for 9% of the studied population. The prevalence of the pathologies were: multiple myeloma (43.5%), Hodgkin's Lymphoma (39.1%) and non-Hodgkin's lymphoma (17.4%). The mean body mass index (BMI) before conditioning, five days and thirteen days after transplantation was 27.74 ± 4.6 kg/ m², 26.43 ± 4.0 kg/ m² and 27.17 ± 4.25 kg/ m², respectively. According to the nutritional status by the BMI, 4.3% of patients were undernourished, 26.1% had normal weight and 69.6% were overweight and all remained in the same classification before and after the transplantation. The mean weight loss was 3.1 ± 2.5 kg, and 73.9% of the patients showed weight loss during the HSCT process, whereas only 26.1% showed an increase in weight or showed no weight loss. Discussion: The study by Spexoto (2010) found that in pre-HSCT the mean BMI was 27 ± 5.0, whereas after HSCT it was 26 ± 5.0, similar to that found in the present study. The study by Sommacal et al (2010) found a mean of 6.27 kg of weight loss, being higher than that found in this study. It is necessary to say that patients who gained or did not lose weight can be justified by the presence of edema, which may not have been reported in the medical records. Conclusion: Therefore, it is known that maintaining a good nutritional status is especially important during the entire HSCT process.

Keywords: Weight Loss, Nutritional Status, Body Mass Index

P-161

Autologous Transplantation

Five-year experience in autologous hematopoietic stem cell transplantations in Hospital São Lucas in Ribeirão Preto – SP

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Introduction: Autologous hematopoietic stem cell transplantation (AHSCT) is a well-established therapeutic modality for the treatment of hematological malignancies, being the choice for patients with refractory lymphomas/ recurrence, acute and chronic leukemias and multiple myeloma. The procedure is not free of complications and requires care from a multidisciplinary specialized team and adequate hospital support facilities. Objectives: To report the experience of Hospital São Lucas AHSCT Unit in submitting patients with onco-hematological diseases to Autologous transplantation of hematopoietic stem cells. Material and Methods: A retrospective study of 63 patients submitted to AHSCT between November/ 2010 and May/ 2016 was performed. Results: 63 AHSCT were performed in the period. The median age of patients was 53 years (13-68 years), 65% were men. The AHSCT was performed in 32 patients with multiple myeloma, 11 relapsed/refractory Hodgkin's lymphoma and 17 with refractory non-Hodgkin's lymphoma, 2 with acute leukemia, 1 with systemic amyloidosis. Stem cell mobilization was performed with high-dose chemotherapy regimen and G-CSF for lymphomas (DHAP or ICE), and G-CSF for the other diseases. A patient with myeloma required cyclophosphamide use after collection failure with G-CSF alone. The conditioning chemotherapy regimen was BEAM (16) BUCyE (6) LACE (2), BUMEL (2), ThiotepaBC (1) in patients with leukemia and lymphomas, and MEL 200 mg/m^2 for multiple myeloma (32). All patients received cryopreserved peripheral hematopoietic stem cells. The median neutrophil recovery (neutrophil >500/mm^3) was 11 days for Lymphomas (9 to 18 days) and 10 days for myelomas (8 to 18 days). The median hospital stay was 24 days (19-31 days) for lymphomas and 18 days for myelomas (16-28 days). Four patients died in the peri-transplant period, 2 with myeloma (D +13 due to sepsis and D+50 due to cerebral bleeding caused by thrombocytopenia due to grafting failure) and 2 patients with lymphoma (D+16 due to neutropenic colitis and sepsis and the other on D+23 due to sepsis). The patients were admitted at an isolation unit following Decree 931 of May 2, 2006 of the Ministry of Health and received support from the medical, nursing, nutrition, social work, dentistry (selected), occupational therapy (selected) specialized teams. All patients had private health plans. Conclusion: The experience in performing AHSCT in a private institution has demonstrated consistent evolution in agreement with the literature. The patients were all treated by a trained multidisciplinary team that provided adequate and good-quality support equivalent to major transplant centers, providing an alternative for the treatment of patients.

Keywords: transplantation, autologous, myeloma, lymphoma

P-162

Autologous Transplantation

Autologous transplantation and increased overall survival of patients with multiple myeloma: an integrative review

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INTRODUCTION: Multiple myeloma (MM) is considered a malignant neoplasm. Among the clinical manifestations, bone disease and anemia are the most common. Regarding the epidemiology, it affects elderly patients, with a mean age of 65 years. MM is an incurable disease. Autologous transplantation has been chosen to provide an increase in the response rate to treatment and increase patient overall survival. During the pre-transplant period, nursing guidelines will contribute to a better understanding of the transplant process effectiveness. MM patients have many doubts about their survival after autologous transplantation and often ask the nurse who care for them about this. Due to this fact, as we are nurses working in a specialized outpatient clinic in onco-hematological diseases, the aim of this study was to identify in the national literature articles about autologous hematopoietic stem cell transplantation as treatment indication and increased overall survival and disease-free survival, favoring a better quality of life for patients diagnosed with multiple myeloma. METHODS: This is an integrative review of Brazilian scientific literature on the subject of autologous transplantation in patients with multiple myeloma, to increase their overall survival and disease-free survival, providing a better quality of life to these patients. For that purpose, we carried out a literature search, in which eleven (11) articles were reviewed, published in the last ten (10) years, described in the literature and available in full, which were not integrative reviews. In search for these articles, the following descriptors were applied: "Multiple Myeloma", "Autologous Hematopoietic Stem Cell Transplantation" and "Nursing", in order to find scientific articles that addressed the research object. RESULTS: As the autologous transplant developed by a multidisciplinary team that works directly with the Multiple Myeloma patient, it was observed that 81.8% of articles were mostly written by medical professionals, demonstrating the need for involvement of other professionals in the scientific reports. Regarding the study approach, 63.6% of the articles used a quantitative methodology, based on randomized clinical trials to obtain evidence of clinical practice in health. A large majority of articles, 54.5%, addressed autologous hematopoietic stem cell transplant associated with increased overall survival and disease-free survival in multiple myeloma. CONCLUSION: We identified an association between autologous transplant and increased overall survival and disease-free survival in multiple myeloma. This aspect brings a new perspective for patients, who sometimes have doubts about undergoing an autologous transplant. It also offers subsidies for professionals, especially those from the nursing area.

Keywords: Multiple Myeloma, Autologous Transplant, Nursing

P-163

Autologous Transplantation

Nursing care of the indwelling central venous catheter in a patient with Hodgkin's lymphoma submitted to autologous hematopoietic stem cell transplantation: a case report

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INTRODUCTION: Hodgkin's lymphoma (HL) is a prevalent disease in young adults and chemotherapy is the first choice of treatment; in refractory or relapsed HL, of autologous hematopoietic stem cell transplantation (HSCT) is the standard treatment. Chemotherapy treatment recommends the use of an indwelling central venous catheter (CVC); the adequate management by the nursing staff extends the life of the device and prevents complications. OBJECTIVE: To report a case of a patient with Hodgkin's lymphoma submitted to autologous HSCT and the nursing care of the indwelling central venous catheter. MATERIAL AND METHODS: Case report carried out from 2012 to 2015, in a patient with HL submitted to autologous HSCT with an indwelling CVC. RESULTS: RSMC, female gender, 26 years old, admitted to University Hospital in the city of Fortaleza to undergo autologous HSCT. The patient reported pain in January/ 2012, followed by cervical lymphadenopathy, night sweats, loss of 4 kg, daily fever and discharge of blood from the mouth. Immunohistochemistry of the cervical ganglion was compatible with Hodgkin's lymphoma, nodular sclerosis subtype grade II and immunophenotyping: CD15+ and CD30+, stage IVB (pulmonary nodules), mediastinal Bulky BM. In July/ 2012 the indwelling CVC was implanted for chemotherapy treatment; the patient was admitted at the outpatient chemotherapy unit for the maintenance phase, which began in August/ 2012. She underwent 20 sessions of radiation therapy, followed by chemotherapy (4 ABVD cycles); as the tumor mass persisted, she underwent 3 ICE cycles, resulting in residual mass. She was referred to autologous HSCT and remained with the indwelling CVC. The post-transplant PET/CT showed complete remission, followed by irregular maintenance of the indwelling CVC and eventual obstruction due to her not attending medical appointments until its removal in May/ 2015. DISCUSSION: The symptoms of HL in the chest are shortness of breath, chest pain, and B symptoms: fever, night sweats and weight loss. Patients with LH at a favorable early stage receive 3-4 ABVD courses; for Bulky Disease, radiation therapy is indicated. The ICE protocol is a rescue option for pre-autologous HSCT. Autologous HSCT occurs in patients up to 65 years without comorbidities, resistance to the first chemotherapy, recurrence after first-line treatment and/or chemosensitivity to the second-line therapy; it can lead to disease control and improved prognosis. The chemotherapy treatment has vesicant substances and therefore the indwelling CVC is recommended; nursing care prevents complications by using aseptic techniques when handling it: handwashing and antisepsis with chlorhexidine; washing with saline solution, heparinization every 30 days. When the catheter is adequately puncture, there is venous return in the catheter, as well as easy and painless infusion. CONCLUSION: Autologous HSCT is a treatment option for patients with refractory and relapsed HL. Chemotherapy is first choice treatment for LH, for which the use of indwelling CVC is recommended, of which handling is the responsibility of the nursing staff.

Keywords: Nursing, Hematological Disease, Hematopoietic Stem Cell Transplantation

P-164

Autologous Transplantation

Experience of a new center in Belo Horizonte with autologous hematopoietic stem cell transplantation (HSCT)

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Introduction: A private foundation specializing in cancer treatment inaugurated its autologous HSCT program on 09.02.2013. Objective: To report on the experience of this center, analyzing demographics, early mortality and survival according to payment source, diagnosis and pre-transplant clinical status. Material and Methods: Retrospective study of 109 patients (09/02/13 to 05/05/16). The variables analyzed were: gender, age, diagnosis, payment source, pre-transplant status, number of CD34 + cells, time to engraftment and hospital length of stay, presence of engraftment syndrome, death up to D+50, overall survival (OS) and progression-free survival (PFS). The cases were classified as: 1 - standard: MM patients transplanted in the first line after 4 to 6 cycles of induction, HL and diffuse large B-cell transplant in the 2nd line, T lymphoma and mantle in the first line. 2-nonstandard: MM in the first line after more than 6 cycles or more than one line of treatment, HL or NHL after the second line. 3-disease activity and 4-2nd transplantation for MM. OS and PFS assessment was carried out through telephone contact or chart review. Patients were censored at the last contact date. Data were analyzed using the SPSS program, version 23.0. Results: We transplanted 51 women and 58 men. The age ranged from 19.3 to 71.3 years (median 54.7). SUS was the payment source in 38 cases. Regarding the diagnosis: 67 cases of MM, 16 of HL, 21 of NHL, 2 cases of amyloidosis, 2 plasma cell leukemia cases and 1 case of promyelocytic leukemia. The number of collected CD34+ cells ranged from 1.8 to 43.7 (median 3.24) and time to engraftment ranged from 9 to 13 days. In 90.7% of cases engraftment occurred up to D+11 with no failure. The engraftment syndrome occurred in 16 cases. Hospital length of stay ranged from 14 to 37 days (median 20). Two patients died up to D+50 (1.8%). Recurrence or progression occurred in 28 of 104 analyzed patients (27%) and 13 deaths (12.6%) were observed, 11 due to progression of the underlying disease. The OS for all patients was 74.7% ± 9%. According to the payment source, the OS was 95.2% ± 5% for the SUS cases and 88.5% ± 4% for cases of supplemental health care agencies (p = 0.042). Analyzing the 62 MM cases, the OS for standard cases (n = 42) was 92.4% ± 5% and 100% (n = 10) for non-standard ones (p = NS). The PFS was 88% ± 6% and 67% ± 27%, respectively, for standard and nonstandard cases (p <0.001). Of the 16 cases of HL, OS was 100% for standard cases and 73% ± 16% for non-standard ones (p = NS). The PFS was 73% ± 16% ± 1.3% *versus* 18% for the standard and non-standard cases, respectively (p = 0.05). The several subtypes of NHL were analyzed together (21 patients). The OS for all NHL cases was 61.5% ± 13% and PFS was 50% ± 13%. Conclusions: The early mortality rate up to D+50 is in line with the expected. The interpretation of the results regarding the payment source requires a deeper analysis. According to the diagnosis, despite the small number of patients with MM and HL, the transplantation under the recommended conditions produced the best results.

Keywords: Autologous HSCT, multiple myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma

P-165

Autologous Transplantation

Pre-grafting early hospital discharge after autologous hematopoietic stem cell transplantation

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The outpatient model of autologous hematopoietic stem cell transplantation (AHSCT) with pre-grafting early discharge decreases costs and the incidence of infections, and improve patient quality of life. Objective: To demonstrate the feasibility of outpatient AHSCT and emphasize the main causes of hospital readmission and related toxicities. Methods: A retrospective study with data collection from medical records of patients submitted to AHSCT at the HCFMUSP with early discharge from January/2014 to May/2016. Patients eligible for early discharge should be residing in greater São Paulo, have a caregiver, easy access to the hospital, without severe comorbidities. A daily evaluation is performed at the day-hospital by a multidisciplinary team, with antimicrobial prophylaxis. If complications occur, patient evaluation is carried out in the day-hospital during the day shift or at the emergency department of HCFMUSP at night. Results: 41 patients with a median age of 48 years (23-67y) were assessed. 66% were males; 9 (22%) patients had Hodgkin's lymphoma, 7 (17%) had non-Hodgkin lymphoma and 25 (61%) had multiple myeloma (MM). 21 (52%) patients were in complete remission pre-BMT, 18 (44%) showed partial response, 1 (2%) had stable disease and 1 (2%) had active disease. As for the conditioning, 24 (59%) patients received high-dose melphalan, 10 (24%) BEAM, 6 (15%) BuMel and 1 (2%) LACE. The median neutrophil and platelet engraftment was 11 days and patient follow-up was 42 days. As for the treatment toxicity, 31 patients (76%) had febrile neutropenia (8 (20%) with microorganism isolated from cultures), 10 (24%) had oral mucositis grades 3-4, 8 (20%), had diarrhea grades 3-4 and 1 (2%) had vomiting grade 3. Of the total number of patients, 9 (22%) were readmitted, with a median time to readmission of 10 days. Among the causes of readmission, we emphasize sepsis and severe mucositis in 3 (7%) patients each. Severe GIT toxicity tended to an association with readmission in the univariate analysis. Severe sepsis was the cause of death in 3 cases (7%), which was comparable with the TRM of hospitalized patients evaluated in the same period. Among the patients who died, all were older than 50 years (58-67) and had a diagnosis of MM; only one was colonized by *Enterococcus faecium* (VRE). One patient had grafting failure; and two others had severe mucositis. Discussion: the study shows the applicability of AHSCT with early discharge in developing countries such as Brazil, with low infection rates that were microbiologically proven, with the daily use of prophylactic antimicrobials being feasible and, where necessary, treatment in the day-hospital. The readmission rate (22%) was comparable to others in the literature (18-26%), with sepsis and severe mucositis being the main causes of rehospitalization. Conclusion: The early discharge post-AHSCT is feasible in selected patients, with acceptable rehospitalization rates and overall survival comparable to that of inpatients, as well as tolerable toxicity.

Keywords: ambulatory autologous bone marrow transplant, early discharge, hospital readmission, toxicities

P-166

Autologous Transplantation

Unexpected reaction after standard conditioning regimen in a patient with plasma cell leukemia – a case report.

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Introduction: Plasma cell primary leukemia is a rare disease that accounts for less than 5% of plasma-cell neoplasms. It has a very poor prognosis when compared to multiple myeloma, with a median survival of 8-12 months. The results are disappointing with conventional therapy, but the autologous stem cell transplant can improve survival. Objectives: To report the case of a patient who received autologous transplantation for plasma-cell leukemia (PCL) at the bone marrow transplant unit, in Hospital São Lucas of Ribeirão Preto - SP and had an unexpected adverse reaction with the standard conditioning regimen. Material and Methods: A 60-year-old female patient, without comorbidities, was diagnosed with plasma-cell leukemia in November 2015 with bone pain, anemia and thrombocytopenia, 50% plasma cells in the bone marrow and 30% in peripheral blood and mild renal impairment. She was treated with 4 VCD cycles (intravenous bortezomib, 1.3 mg/m^2 on days 1,4,8 and 11; intravenous cyclophosphamide 300 mg/ m^2 on days 1, 8, and 15 and oral dexamethasone, 40 mg weekly) and showed a complete response after 4 cycles. She was submitted to the autologous transplantation followed by conditioning with melphalan 200 mg/m^2. On D+5, she developed a severe vasculitis-type skin reaction in the entire the body, acute renal failure and progressive mucositis up to grade IV. The bone marrow engraftment (neutrophils> 500/ mm^3) occurred on D+9. On D+12 she was referred to the Intensive Care Unit with signs of septicemia, requiring daily hemodialysis, very significant worsening of vasculitis with vesicle formation in the upper limbs and need for mechanical ventilatory support. She developed progressive decrease in neutrophils, requiring daily platelet transfusions, when on D+25, when she was in spontaneous ventilation, she had renal failure reversal and showed recurrence of leukemia with 40% of plasma cells in the bone marrow. Discussion: PCL is a rare and aggressive disease and frequent courses with early mortality due to disease progression. Autologous transplant is an important therapeutic option. Complications are known in most cases, but here we present a case with severe mucocutaneous and renal manifestations. The most likely explanation is that the reactions were secondary to the drugs. Conclusion: Even if the transplant leads to good response in some patients with PCL, this does not translate into prolonged survival and there is no way to predict some secondary adverse reactions to the treatment and their evolution.

Keywords: leukemia, transplantation, autologous, plasma, skin

P-167

Autologous Transplantation

Acute kidney injury after bone marrow transplantation

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INTRODUCTION: One of the possible complications post-bone marrow transplantation is acute kidney injury (AKI). Among the main risk factors for AKI are sepsis, associated with neutropenia and use of nephrotoxic drugs. OBJECTIVES: To investigate the occurrence of AKI in patients submitted to autologous bone marrow transplantation (BMT). MATERIALS AND METHODS: This was a retrospective study of 217 patients undergoing BMT in Tertiary Care Hospital in the city of Fortaleza, Ceará, from 2008 to 2016. The evaluation of the presence of AKI was established through the KDIGO criteria ("Kidney Disease Improving Global Outcomes") and statistical analysis was performed using SPSS v.20 program. RESULTS: Patients included in the study were aged between 16 and 71 years (mean 45.7 ± 14.8 years) and 134 were males (61.7%). In this group there were 36 cases (16.5%) of AKI. The mean age of patients with AKI was 45.3 ± 13.8 years, 24 (66%) males and 12 (34%) female patients, similar to the group of patients who did not develop AKI (p = 0.85). The mean creatinine at admission of patients with AKI was 1.6 ± 1.6 mg/ dL, whereas the mean creatinine at admission of patients without AKI was 0.7 ± 0.1 mg/ dL (p = 0.0001). In patients with AKI, we observed a mean maximum creatinine of 2.4 ± 1.6 mg/ dL, whereas in patients without AKI the mean maximum creatinine was 0.8 ± 0.2 mg/ dL (p = 0.0001). Renal function recovery was observed in 25 (67.5%) patients at the time of hospital discharge. DISCUSSION: BMT is an increasingly widespread therapeutic in the treatment of hematological malignancies. The literature shows that in the post-BMT period, AKI is a common complication and the incidence of AKI in patients submitted to autologous transplantation is much lower than in allogeneic transplantation. The incidence of post-BMT AKI reported in the literature (5-30%) is similar to that found in this study (16.5%). CONCLUSION: AKI is an increasingly common complication after BMT due to more frequent use of this procedure. Most patients recover renal function prior to hospital discharge. However, during AKI evolution, if there is no adequate intervention, the patient can die or develop chronic kidney disease.

Keywords: Acute kidney Injury, Bone Marrow Transplantation, Nephrology.

P-168

Autologous Transplantation

Hodgkin's lymphoma and Autologous transplantation - Experience of the first six years of the Hematology Service Transplant Unit of Hospital Universitário do Ceará

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Introduction: Patients diagnosed with refractory or relapsed Hodgkin's Lymphoma (HL) have rescue chemotherapy as the treatment of choice, aimed to define chemosensitivity, followed by the autologous Hematopoietic Stem Cell transplant (HSCT) as the consolidation therapy. There are no randomized studies comparing the efficacy of chemotherapy regimens before HSCT; the choice should be based on the service experience and patients' clinical characteristics. The best time to collect the stem cells and perform the autologous HSCT is after achieving remission, preferably reaching complete remission (CR). Objective: To describe the experience of the Bone Marrow Transplant Unit at the Hematology Service of UFC HUWC. Material and Methods: Observational study describing the findings of HL patients submitted to Autologous HSCT from January 2009 to May 2016. Results: 54 patients with LH were submitted to Autologous HSCT during this period, 32 men and 22 women, aged 16-51 years, median of 28 years. Twenty-eight patients were in complete remission and twenty-six in partial remission after rescue chemotherapy. The conditioning was carried out with BEAC regimen in 34 (63.1%) patients, NEAM in 13 (24.0%), BEAM in 5 (9.2%) and FEAM in 2 (3.7%). The most prevalent side effects observed during conditioning were nausea, vomiting, diarrhea and fever, with no difference between the different protocols. 24% of the patients had infection documented through culture. The mean time between the stem cell collection and the transplant was 83 days (26-274 days); mean neutrophilic grafting was 10 days (7-15 days) and mean hospital length of stay was 24 days (17-50 days). Six patients (11.1%) died, two due to infections related to the transplant (on D3 and D6, respectively); three patients died within the first twelve months post-BMT due to disease recurrence, and one patient died three years after the transplant also due to disease recurrence. The last patient assessment showed that 38 patients (70.3%) are in CR, 7 (12.9%) relapsed, all after D +100 and, of these patients, five are using Brentuximab as rescue therapy post-BMT; 3 (5.5%) patients are in partial response. Conclusion: The results show that autologous HSCT is an excellent rescue therapy regarding tolerance and overall survival.

Keywords: Transplantation, Autologous, Hodgkin's Lymphoma, Survival

P-169

Autologous Transplantation

Case report: Indications of Autologous Bone Marrow Transplantation in Hodgkin's lymphoma.

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Introduction: Hodgkin's lymphoma (HL) is the lymphoid neoplasia most often observed in young adults and adults older than 50 years, coursing with lymph node involvement mainly in the cervical, axillary and chest regions. At the histopathological analysis, it shows proliferation of neoplastic cells of variable morphology, the Reed-Sternberg cells (RSC), amidst the inflammatory infiltrate. Patient survival has been increasing, with cure rates of 80-85%, due to treatment advances. The Autologous Hematopoietic Stem Cell Transplantation (AHSCT) is indicated for patients with early disease relapse or treatment refractoriness and they are obtained from the patient's own cells. Objective: To ratify that the AHSCT is the best treatment for patients with recurrent/refractory HL after chemotherapy (CT). Material and Methods: This is a descriptive case report, based on clinical history and complementary exams. It was carried out in May 2016 in the city of João Pessoa-PB, together with the literature review. Discussion: P.I.A.J., 20 years, sought hematological medical assistance due to progressive increase in cervical lymph node on the left, as well as intense itching for the last 6 months. He was referred to excisional biopsy and histopathology was compatible with mixed cellularity HL, confirmed by immunohistochemistry. The first PET-CT showed lymph nodes above and below the diaphragm, clinically staged as IIIB. He started first-line chemotherapy for 8 cycles. After the 4th cycle, he achieved partial response, with still active residual disease. After the 8th cycle, localized disease progression was observed in the cervical region and, thus, radiation therapy (RT) 36 Gy was chosen. The PET-CT after RT showed diffuse disease progression, with the indication of 2nd line chemotherapy, with disease progression occurring during CT. A new 2nd line protocol exchange was performed and after the 2nd cycle, CTs showed stable disease. Due to relapsed/refractory HL, there was formal indication for AHSCT, which was uneventfully performed. Patient is in the post-transplant follow-up, with indication for Brentuximab monoclonal antibody (Anti-CD30) use to increase disease-free survival. Result: The case HL is of mixed-type cellularity, refractory to the first and second-line treatments. The patient is in post-transplant follow-up, still without evaluation with new imaging tests; however, because he had relapse/refractoriness to two or more chemotherapy regimens, he will undergo post-AHSCT maintenance with Brentuximab. Conclusion: The AHSCT is the best option for patients with relapsed/refractory HL, as it allows high-dose chemotherapy in an attempt to obtain a better therapeutic response, with subsequent hematopoiesis restoration.

Keywords: Lymphoma, use, refractoriness

P-170

Histocompatibilidade

Time elapsed between the initial unrelated donor search in Fanconi anemia patients and their transplantations in the period between 1993 and 2015

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Search for unrelated donors (URD) began at our institution in 1993, where the first unrelated bone marrow transplant (BMT) of Latin America was performed in 1995. Between 1993-1998, searches were carried out in international URD registries; after 1998, the Brazilian registry (REDOME) started donor drives all over the country and search for Brazilian donors became part of the process. This study aimed at evaluating the time elapsed between the start of URD search and BMT in Fanconi Anemia(FA) patients. From January/1993 to December/2015 a total of 266 patients were enrolled in the program. Of these, 115 (43.2%) underwent BMT with URD, and the time interval from the time donors were ready to donate and bone marrow infusion ranged from 13 to 431 days (M=124). From 1993 to 1998, the time of donor search for 6 patients who underwent BMT ranged from 203 to 704 days (M=312); from 1998 to 2007, when a significant increase in the number of new donors registered in REDOME occurred, time of donor search for 63 transplanted FA patients ranged from 57 to 2250 days (M=410). The median time decreased to 276 days (102-1629) for the 46 FA patients transplanted between 2008 and 2015. Of the 266 patients enrolled in the search process, 26 (9.8%) underwent haploidentical transplant, because a URD donor with an acceptable HLA compatibility could not be found (21-2782 days; M=886). In the same period, 47 patients (17.7%) died without transplant, and the duration of the search process ranged from 67 to 1597 days (M=317); 9/47 patients (19.1%) ended up finding an URD, but did not make it to the transplant due to disease progression. Among all patients enrolled in the program, 55 (20.7%) had the search canceled for various reasons, the most common being disease progression or patients' waiver, whereas 27 (10.1%) remain searching for a donor. Among the factors that can cause delay in the search time are the HLA gene polymorphisms, which makes the finding of a compatible donor difficult depending on the HLA genotype of the patient; sensitization of the patient against incompatible HLA antigens due to transfusion of blood components, which can induce allogeneic humoral response resulting in the production of anti- HLA antibodies; bureaucratic or financial problems; adjustment to changes in legislation; lack of beds to meet the demand of patients referred to BMT. In conclusion, this study was important to determine the waiting time for finding an URD. More recently, with the development of haploidentical BMT procedures, patients who do not find a compatible URD can be referred sooner to transplant. The use of alternative donors prevents the cost of long searches and allows the transplant to be performed in a timely manner, achieving better results. After patients find compatible URDs, the time until the transplant is still too long (median=124 days) demonstrating the need for more investments to provide more beds and meet the demand for hematopoietic stem cell transplants with unrelated donors.

Keywords: bone marrow, transplant, unrelated donor, time of transplant donor search

P-171

Histocompatibility

Next-generation sequencing for Class I and II HLA genes: Comparison of DNA samples obtained from oral mucosa and peripheral blood

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INTRODUCTION: The Next-Generation Sequencing (NGS) provides information of clonal sequences and has the potential to overcome many of the limitations of Sanger technique in HLA typing. The utilization of DNA from peripheral blood (PB) is commonly used in laboratory routine for HLA typing, but less invasive DNA sources are desirable. OBJECTIVES: To evaluate the HLA typing by NGS from DNA of PB samples, compared to those obtained from oral mucosa (OM) smear. METHODS: OM samples were collected from 8 patients treated at an oral diagnosis outpatient clinic of Hospital Universitário Antônio Pedro, using an endocervical brush and PB. All samples were submitted to genomic DNA extraction using the QIAamp DNA (Qiagen) kit. For the NGS technique, we used the NGSgo AMPX-384 (GenDx) kit. The amplified loci were HLA-A, -B, -C, -DRB1, -DQB1, -DPA1, -DPB1. Equimolar amounts of amplicons were gathered together in one tube per sample. The amplicon pools were enzymatically fragmented and then adapters were added at their ends. Then the cleaning step was performed, followed by selection by size of fragments through the use of magnetic microspheres. Libraries were forwarded for clonal amplification, followed by paired-ended sequencing in the HiSeq 2500® (Illumina) device. Data were analyzed in NGSengine® version 2.0.0.5095 (GenDx) software, the reads were aligned to the sequence-references of the IPD-IMGT/HLA Database, version 3.23.0. RESULTS: The interpretation was performed with the following parameters of program configuration: phasing algorithm: cluster, up to 1,000,000 reads, up to 8 digits typing, Minimum depth of 20 and allelic rate of 20%. The detection rate (%) and the mean reads depth determined by the program for OM and PB samples were: HLA-A: OM-87.5% (141) and PB-75% (143) HLA-B: OM-50% (128) and PB-87.5% (123), HLA-C: OM-100% (317) and PB-100% (296), HLA-DRB1: OM-62 5% (269) and PB-100% (333), HLA-DQB1: OM-50% (95) and PB-62.5% (592), HLA-DPA1: OM-12.5% (325) and PB-37.5% (107), HLA-DPB1: OM-87.5% (280) and PB-62.5% (378). All samples showed results ranging from 6 to 8 digits of resolution; there was disagreement of results in only one OM sample for DQB1. DISCUSSION AND CONCLUSION: The study by Erlich et al (2012) stipulated that a minimum of 50 reads per amplicon is required. All reads found in our study for the seven loci were over 50. The sample of the DQB1 locus of OM, where more than one possible genotype was observed, probably occurred due to the fact that they have different mean reads depth (64 MO x 762 PB). Adjustments in the hands on steps are possible to increase the detection rate. It is possible to use DNA from OM under appropriate conditions for HLA typing by NGS, and we confirm the use of this technique in the sequencing of unambiguous HLA alleles.

Keywords: next generation sequencing, HLA, high resolution, oral mucosa, genomic DNA

P-172

Histocompatibility

Influence of IL12 polymorphism on Chronic Periodontitis

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Introduction: Chronic periodontitis (CP) is a chronic inflammatory disease with a multifactorial infectious nature, which results in tissue damage, destruction of the periodontal ligament and bone support, causing tooth loss. Some cytokines are important in the pathological process of periodontitis. The interkeukin-12 (IL-12) is an immunoregulatory cytokine with an antagonistic effect to the Th1/Th2 balance and it provides a functional link between innate and acquired immune responses. This cytokine is a heterodimer of p35 and p40 subunits, which form the bioactive p70 protein. Higher levels of IL-12 production have been associated to CP. Objective: The aim of this study was to investigate the influence of IL12B polymorphism (rs3212227) on chronic periodontitis. Materials and Methods: Until now, a total of 97 individuals were selected from dental clinics of the Maringa State University (UEM) and Inga University. Participants from the chronic periodontitis group (N=46) consisted of individuals who had at least 5 sites in different teeth with probing depth (PD) ≥5 mm, clinical attachment level (CAL) ≥3 mm and more than 25% of bleeding on probing (BOP) and control group (N=51) consisted of individuals who did not have sites with reduced CAL, displayed a PD < 4 mm, and exhibited less than 25% of BOP. The inclusion criteria were age >30 years and the non-inclusion criteria were Asians descendants, subjects with diabetes mellitus and acute infections. All individuals signed a consent form. The IL12B was evaluated by PCR-SSP (polymerase chain reaction-sequence specific primers) using specific genotyping kits (Invitrogen®). Linear and logistic regression was used to analyze the association using SNPStats software. Genotypic differences adjusted for the effect of ethnicity, gender and smoking status were applied. Results: The distribution of alleles and genotype frequencies of IL12B were consistent with the Hardy-Weinberg equilibrium (P>0.05). In smokers and ex-smoker patients with CP, the IL12 AA genotype was more frequent (65% vs 35%; p=0.016; OR=2.37; CI 95%=1.06 – 5.45). Discussion: The progression of CP was related to a host inflammatory response that mediates tissue damage and several previous studies have associated immune genetic factors to the disease. Smoking habit is a predisposition factor of oral diseases. CP patients IL12B AA increased twice the risk of the disease. Although controversial, this genotype was correlated with a high expression of the cytokine. The higher expression of IL-12 could lead to an activation of Th1 response. Some studies had demonstrated low levels of IL-12 in the crevicular fluid in CP, although serum levels were higher than in controls. Conclusion: In smokers and ex-smoker patients, the IL12BAA was correlated to susceptibility to CP. However, more samples will be analyzed for further studies to elucidate the role of IL12 in CP.

Keywords: case-control, polymorphism, cytokine, periodontitis

P-173

Histocompatibility

The influence of Toll-Like Receptor 4 Asp299Gly and Thr399Ile and Interleukin 17A G197A and IL17F T7488C polymorphisms on chronic periodontitis.

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Introduction: Periodontitis is a chronic inflammatory disease that affects the tooth-supporting tissue and destroys alveolar bone. It is a multifactorial disease and as such, the significant elements not only include the presence of pathogenic bacteria and the immune mechanism, but also the genetic predisposition. Aim: Evaluate the possible association between Toll like receptor-4 gene Asp299Gly (rs4986790), Thr399Ile (rs4986791), IL17A G197A (rs2275913) and IL17F T7488C (His161Arg, rs763780) polymorphisms and chronic periodontitis. Materials and Methods: A case-control study was conducted in patients with chronic periodontitis (CP) and healthy controls. Genotypes were determined by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) method. Statistical analyses were performed using the Openepi and SNPStas software to calculate Chi square with Yates correction or Fisher's Exact tests, odds ratios (OR) and 95% confidence intervals (CIs), as well as Hardy-Weinberg equilibrium. Results: In smokers and ex-smoker patients with CP TLR4 Asp299Gly AA genotype was more frequent (OR=4.42, CI=1.76-11.13 and OR=3.74, IC=1.55–9.02; respectively) and also TLR4 Thr399Ile CC genotype (OR=4.49, CI=1.80-11.23 and OR=3.67, IC=1.53- 8.81; respectively). In both groups IL17A GG genotype (OR=16.43, IC=3.06-88.08 and OR=2.88, IC=1.04- 7.95) and IL17F TT genotype (OR=4.16; IC=1.76-9.80 and OR=3.73; IC=1.56-8.95) were also more frequent. IL17A GA genotype was more frequent in ex-smoker patients (OR=23.68; IC=2.67-209.97). Analyses of haplotypes (TLR4 Asp299Gly, TLR4 Thr399Ile, IL17A and IL17F) showed that smokers carrying ACGT or ACAT were susceptible to CP (OR=13.90, IC=2.64-73.22 and OR=4.96; IC=1.67- 14.73, respectively). Only TLR4 Asp299Gly and TLR4 Thr399Ile are in linkage disequilibrium (Δ'=0.8833). Discussion: In gram-negative infections, lipopolysaccharide (LPS) initiates signal transduction through the TLR4 receptor, and this pathway is enhanced by CD14 and MD-2, and is activated through NF-κβ and AP-1. Activation of TLR4 initiates intracellular signaling pathway to promote production of cyclooxygenase 2 (COX2), which induces prostaglandin E2 (PGE2). In another pathway, IL-17 induces PGE2 and simultaneously up-regulation of COX2. IL-17 can stimulate fibroblasts, epithelial and endothelial cells to produce IL-6, CXCL8/IL-8 too. IL-17 and TLR4 also induces the expression of receptor activator of nuclear factor kappa B ligand (RANKL) in osteoblasts and stimulates the differentiation and activation of osteoclasts, which can influence bone resorption mediated by these cells in CP. Conclusion: We can infer that TLR4 and IL17 polymorphisms together with smoking habits are associated to susceptibility to chronic periodontitis.

Keywords: Periodontitis, Chronic disease, Immunogenetics, PCR-RFLP.

P-174

Histocompatibility

False heterozygous at large-scale HLA typing: the impact of carry over on profile creation

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INTRODUCTION: The PCR-SSO methodology has a complex algorithm to define which combinations of the positive and negative beads found match with the known HLA haplotype profiles. The mixture of genetic material at critical steps of the methodology is an inherent risk to the technique, since typing by PCR-SSO is still mostly manual and, therefore, as any procedure involving human action, is liable to failure. Pipetting errors can cause the DNA carrying between samples, leading to an incorrect result in HLA genotyping. The strict and complicated feature of the analysis algorithm provides that the majority of cases where there is a mixture of genetic material between different individuals, the algorithm result is invalid, allowing a test repeat and further elucidation of the "quasi-error" typing. However, in some cases, this protective feature of the algorithm may not be sufficient, because it would be possible, theoretically, to have a valid result even after the DNA mixture of two individuals, creating a false *in vitro* heterozygous. This fact, in turn, would have a great chance of not being identified, particularly on a large-scale routine typing situation, such as the REDOME registry. This study aims to assess the possibility of creating a heterozygous profile by mixing two homozygous samples through genotyping using the PCR-SSO methodology, in which it is indistinguishable for the analysis algorithm of the HLA fusion interpretation software. MATERIALS AND METHODS: Typing of samples previously identified as homozygous in an allelic group for the HLA-A, B and DRB1 loci were performed. Samples with the haplotypic profile were selected: A*24:KCKB, A*24:KCKC and A*68:AEFNF A*68:AEFNF; B*07:AJFGS B*07:AJFGS and B*18:AGHXT and B18*AGGEJ; DRB1*15: AJEHB DRB1*15:AJEHA and DRB1*03:AGJKD, DRB1*03:AGJJZ. The extracted DNA samples were quantified and their concentration was adjusted to allow an equal mixture of the two samples. Then amplifications were performed with samples mixed at equal amounts, totaling the final volume of 200µL, necessary for using the PCR-SSO technique. RESULTS: The results show that it is possible to generate a plausible heterozygous genotyping profile in the analysis by HLA Fusion Software. It was also possible to identify that the found profile is completely indistinguishable from the natural profile of a heterozygous for the analyzed gene. CONCLUSION: The results are important to subsidize studies that seek strategies to minimize errors in the analytical process on a large scale, especially when performed with manual pipetting process, in addition to create a theoretical referential for research on the occurrence of the phenomenon of *in vivo* false heterozygosity, for instance, after transfusions.

Keywords: SSO, heterozygote, HLA

P-175

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Report of Interdisciplinary Experience among the Physical Therapy and Integrative Medicine teams in a Patient Submitted to Bone Marrow Transplantation and Long-Term Hospitalization in a Private Hospital

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INTRODUCTION: The hospitalization process brings some restrictions, such as adaptation to a new environment, sudden change in routine, physical and social life restraint. Prolonged hospitalization, as in the case of bone marrow transplantation (BMT), with isolation in the room, can bring not only physical consequences with the reduced activity, but also psychological and emotional ones, due to social life restrictions. OBJECTIVE: This report aims to present the interdisciplinary experience between the Physical Therapy and Integrative Medicine (IM) teams, aiming at the maintenance of physical activity, education in self-care, as well as physical and mental well-being of the patient during hospitalization. The IM is an approach aimed to a broader sense of healing, at treating the person as a whole: body, mind and spirit. CLINICAL CASE: Male patient, 34 years old, with Crohn's disease since he was 16, progressing with several complications, with protein-calorie malnutrition and receiving parenteral nutrition. He was submitted to related allogeneic BMT and remained in contact isolation virtually for the entire period of seven months of hospitalization due to multidrug-resistant microorganism. The patient had already started exercises for muscle mass gain during the previous hospital stay and physical therapy aimed to maintain the acquired muscle tropism, since the patient had no other demands. The sessions were carried out daily, except he had malaise and platelets were below 10,000. Resistance exercises were performed with dumbbells and ankle weights for upper and lower limbs for the major muscle groups, strengthening abdominals, stretching and breathing exercises. For the cardiovascular function, patient trained 15 to 30 minutes on the cycle ergometer. The body therapist from IM group worked two to three times a week, focusing on education for self-care and stress management, applying and teaching yoga techniques (light stretching, gentle movements, directed relaxation and attention to the present moment) with the aim to provide a wellness perception. The physical therapy sessions preceded the Integrative Medicine ones, because the muscle training required a lot from the patient and he liked to finish the training with the relaxation techniques. At hospital discharge, the patient had preserved muscle strength, a slight reduction of the initial muscle tropism, in addition to having learned techniques for stress management in self-care. During follow-up, the professionals from the two teams exchanged experiences during the visits respecting patient autonomy in performing the tasks. CONCLUSION: The complementary role of physical therapy followed by integrative medicine can provide multidimensional support to a patient undergoing a complex treatment, being essential for maintaining muscle strength, functional independence, autonomy and well-being.

Keywords: interdisciplinarity, self-care, wellness, exercise

P-176

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Admission of pre-transplant bone marrow patient: emotional aspects perceived by nurses

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BACKGROUND: Bone Marrow Transplantation (BMT) is a treatment performed in onco-hematological, hematological, immunological and hereditary diseases, when patients do not respond favorably to chemotherapy. There are two types of bone marrow transplantation: autologous and allogeneic. The procedure consists in the intravenous infusion of hematopoietic stem cells in order to restore bone marrow function. The conditioning in pre-transplant consists of high-dose chemotherapy, of which goal is the destruction of the diseased bone marrow to make room for the new one. Given the above, the time of patient admission is full of questions about life continuity, family life disruption and loss of privacy, which triggers anxiety, depression and expectations. OBJECTIVES: To report the emotional aspects perceived by nurses at the admission of the pre-transplant patient. MATERIALS AND METHODS: This is a qualitative study that used nurses' reports during clinical sessions. These were based on the experience as a nurse in a public hospital in Fortaleza, a reference in bone marrow transplantation, highlighting the nurse's role in patient admission. RESULTS: The emotional aspects evidenced as relevant at the time of patient admission involve questions about the hospital length of stay, family visits, alopecia triggered by the treatment, pain, lack of knowledge about stem cell transplantation, post-transplant limitations and the experience of faith. DISCUSSION: The admission for BMT involves the need to stay in isolation and following a strict protocol routine, in addition to predicting the reactions and side effects caused by the treatment. The study by ANDRADE, 2012, cites the isolation as an aggravating experience of the transplant process, given the fact that the subjects understand that this is necessary because the risk of infection to which they are exposed. Because it is a complex, long and aggressive process, the BMT involves emotional issues, as it is accompanied by stressful events, such as chemotherapy toxicity, the risk of complications and the implications for the patient's autonomy. When the patient is admitted, the nurse, through interviews, physical examination and guidance, complements the preparation process. This constructs the nurse/patient relation, which aims to minimize the impact of hospitalization, prepare the patient and family to face this new stage of treatment (LACERDA, LIMA, BARBOSA, 2007). CONCLUSION: It can be concluded that patients, when admitted, bring a series of questions that can generate a degree of anxiety that contribute unfavorably to their recovery. The participation of nurses, clarifying and demystifying perceptions of the BMT, contributes to an optimistic expectation for the resumption of daily activities.

Keywords: Bone marrow transplantation. Emotions. Patient admission.

P-177

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

The decision-making process in risk classification for patients undergoing cancer treatment in a pediatric emergency care unit with the application of the "WHITE" category

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INTRODUCTION: Ordinance n. 2048 of the Ministry of Health proposes to implement in the emergency care units the reception and the "risk classification screening." According to this Ordinance, this process "must be performed by a graduated health professional, with specific training, aiming to assess the degree of urgency of the patients' complaints, placing them in order of priority for the treatment" (BRAZIL, 2002). The risk classification uses colors for the priority order, where (RED) - Priority zero, refer straight to the resuscitation room, treatment within 15 min; (YELLOW) - Forward to immediate medical attention, waiting time up to 30 min; (GREEN) - forward to medical consultation, with waiting time of up to 1 hour for treatment; (BLUE), refer for care, priority in order of arrival. Childhood cancer is considered a rare disease. However, in recent years, cancer constituted the leading cause of death by disease in children under 15 years old. The practice of care in pediatric oncology is challenging, since it requires, in addition to specific materials and therapeutic resources, an attentive health staff regarding the childhood universe. Professionals with responsibility, commitment, preparation and sensitivity to child care are needed. OBJECTIVES: To expedite the emergency care of cancer patients in a pediatric emergency by applying the ''WHITE`` category. MATERIAL AND METHODS: This is a descriptive exploratory research with qualitative approach of an experience report type. RESULTS: In our daily practice in pediatric emergency, during the risk assessment, it is a routine to come across situations involving children with cancer, which in turn does not always have, at the arrival, a clinical priority that needs to be classified as urgent; however, as that is a child undergoing cancer treatment, we feel the need to prioritize this patient by using the ''WHITE`` category, which allows both the speed when caring for this patient, and the decision-making process regarding the admission and early medications that can be essential for the lives of children undergoing cancer treatment. CONCLUSION: We adopted the ''WHITE`` category following the model of Minas Gerais state, which was the pioneer Brazilian state in adopting the Manchester protocol, and therefore the first to include the ''WHITE`` category classification, described from different criteria, not only clinical but also administrative ones, which include episodes for which emergency care is needed. Depending on the context, the nurse needs to develop approach methods that perceive their care needs, individualizing care according to the uniqueness of each case, thus making the emergency care as agile as possible.

Keywords: Risk Classification, Pediatric Emergency, cancer treatment

P-178

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing care in the treatment of mucositis in patients submitted to bone marrow transplantation

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Introduction: Bone marrow transplantation (BMT) is a therapeutic procedure characterized by the infusion of progenitor cells capable of restoring bone marrow function in a patient. One of the side effects of BMT is oral mucosa inflammation, manifested by changes in color, atrophy, ulceration, edema and change in local perfusion. The first signs of mucosal involvement appear during the chemotherapy and/or radiotherapy conditioning, intensifying in the first two weeks after transplantation. Due to the impact of oral mucositis on the quality of life of BMT patients, we aimed to report the experience of a resident nurse in the care of bone marrow transplant patients. Material and Methods: This is a descriptive study of experience report type of a resident nurse at a public hospital in Ceará, in May 2016 in the Intensive Care Unit (ICU). Results and Discussion: Through the practice of nursing care in hospitals, during the multiprofessional residence, residents work in several sectors, experiencing different realities that contribute to their improvement and continuous professional training. During the period in which the resident nurse worked at the ICU, a bone marrow transplanted patient with oral mucositis received the nursing care. The performed care was: detailed inspection of the oral cavity, pain assessment by applying validated scales and administration of prescription painkillers, considering that mucositis causes pain and discomfort. Additionally, the nurse performed: oral hygiene with 0.12% aqueous chlorhexidine to reduce the entry of opportunistic microorganisms and intensive care of the patient due to severe clinical state. Conclusion: The need for evaluation and control of the pain in patients with severe mucositis is of utmost importance to improve quality of life of patients with these lesions. Another important factor of the experience report is the development of capacities, competencies and skills needed to care for patients with oral mucositis resulting from the BMT, with the patient benefitting the most from this training.

Keywords: oral mucositis, care, nursing, critical care

P-179

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Companion profile of patients submitted to bone marrow transplantation in a pediatric institution in the State of Parana.

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Summary: In 2011 the Bone Marrow Transplantation Unit of this institution started its operations by performing related, autologous and allogeneic transplantations. Since its implementation, this unit works with a multidisciplinary team consisting of doctors, nurses, nursing technicians, social worker, nutritionist, dentist and psychologist. Until April 2016, 68 BMT were performed, 52 allogeneic and 16 autologous, in children and adolescents of different age groups, from younger than 1 year up to 16 years old. The bone marrow transplantation is considered a highly complex procedure, involves significant changes in the patient's lifestyle and imposes physical changes resulting from the treatment side effects. These changes have an impact not only on the patient's life, but on the life and routine of the entire family. This research carried out a data collection through hospital records and traced a profile of the companions of patients undergoing bone marrow transplantation from May 2011 to May 2016; among the collected data are gender, age, age group, relationship with the patient, length of hospital stay and origin. Based on this survey we concluded that in most cases the companions came from other states, were women and were the patient's mother, considering that during the pre, peri and post-transplant periods, the patient experiences conflicts, which cause reactions and feelings of fear, anxiety, insecurity among others, and the whole disease process and treatment requires different and constant adaptations that lead the subject to a state of mental fragility. The companion, facing the intense emotional and physical demands from the child or adolescent, has a dual challenge: to support the patient and also deal with the conflicts generated by the situation. Based on the companions' profile, a literature review was carried out in order to identify and list the possible difficulties, expected reactions and probable psychological impact generated by the experience of accompanying a child or adolescent in the pre, peri and post-transplantation periods. As a result, we concluded that the emotional link and support must be started in the pre-transplantation period.

Keywords: Psychology, Social Services, companions, psychological impacts, HSCT.

P-180

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The relevance of attention to the psychosocial aspects of patients and companions in the scenario of pediatric BMT care.

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The Hematopoietic Stem Cell Transplantation (HSCT) has been one of the most promising procedures of the last decades; however, the treatment submits the patient to chemotherapy and, if necessary, to total radiation, leading to a severe state of immunosuppression, exposing the patient to several side effects and the significant risk of death. Internment is a solitary confinement for a significant time. These facts related to this procedure can have psychosocial effects on patients and their companions. Also, their psychosocial aspects can interfere with treatment. This quantitative and qualitative descriptive study analyses and integrates data from the Psychology Service and the Social Service of the BMT unit in a pediatric hospital, in Paraná, using data reports, social assessments, participatory observations and care of the mentioned services. The objective was to draw the profile of the patients and companions. This hospital performed 69 bone marrow transplants until May 2016, and the vast majority of patients came from other places, requiring them to stay in a support house during the peri and post-transplant period. The patient's post-transplantation permanence comprehends a period of one hundred days, or according to his/her evolution. In view of the important work of the multidisciplinary team, the professionals seek to have a comprehensive assessment of the subject-patient that extends to the companion, who is his/her reference of care, responsibility, affection and relationship with the health team, who considers the characteristics of the patient's development phase and analyzes the data from the survey, integrating them to the psychosocial aspects and effects. As a result, the research shows the importance of evaluation and identification of psychosocial aspects aiming at effective conducts and interventions in each case. It highlights the importance of the pre-assessment, the peri and post-transplantation follow-up, the integrated work of the multidisciplinary team, the difference in the contact with the patient, guidelines, risk assessment and psychosocial support. It identifies the impact of the patients' cultural aspects in adapting to the city, culture, the hospital, the hospitalization, necessitating care, support and management adequacy. Finally, this study showed improvements that can be made, such as proposing intervention actions and indicates the need to disclose more results for the multidisciplinary team. We believed in the possibility of sharing the experience of implementation of these services and working with them in a BMT unit, and we expect to warn all members and specialties involved in HSCT.

Keywords: HSCT, Pediatrician, Social Services, Psychology.

P-181

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Analysis of the profile of patients undergoing the bone marrow transplantation process and that required physical therapy intervention due to respiratory complications in a private hospital

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INTRODUCTION: Bone marrow transplantation (BMT) is the replacement of diseased cells from the bone marrow by healthy cells and it can be autologous, allogeneic or syngeneic type. There are several post-BMT complications and respiratory ones occur in 40-70% of patients, and of these, 30% die. OBJECTIVE: To identify the characteristics, such as age, gender and diagnosis, which may affect the use of positive pressure due to respiratory complications in BMT patients. MATERIALS AND METHODS: This is a quantitative/descriptive research, where digitized medical records of 74 patients were analyzed, all of them older than 18 years and who were submitted to bone marrow transplantation from April 2015 to April 2016. Of the total patients, 42 underwent autologous transplantation and 32 allogeneic. RESULTS: Among the 74 assessed patients, 51% (n = 38) were males and 49% (n = 36) females. The age of the study population ranged from a minimum of 20 and maximum of 76 years, with a mean of 53.7 years (SD 14.8). Of all patients, 82% (n = 61) had physical therapy intervention, and 6% (n = 5) required motor and/or analgesic therapy, 41% (n = 30) underwent respiratory and motor physical therapy without the use of positive pressure and 35% (n = 26) underwent motor and respiratory therapy with positive pressure due to some respiratory discomfort. The most common diagnoses in this population were myeloma, with 30% (n = 22), followed by non-Hodgkin's lymphoma in 15% (n = 11), myelodysplastic syndrome in 11% (n = 8) and acute myelogenous syndrome in 10% (n = 7). The data related to the type of the conditioning used were incomplete in the database. DISCUSSION: Considering the purpose of this study, the analyzed characteristics do not justify the use of positive pressure during BMT. However, if we observe the group of patients who required positive pressure (35% = 26 patients), we see 16 patients who underwent allogeneic transplantation and 10 patients who underwent autologous transplantation. According to Castro, Jr. (2001), the complexity and complications are higher in allogeneic transplantations, compared to autologous ones. The type of conditioning such as, for instance, the use of the chemotherapeutic drug busulfan, used in pathologies with indication for allogeneic BMT, can also be a source of respiratory complications. Thus, it is possible to justify the higher number of patients who underwent allogeneic BMT and were submitted to positive pressure than patients submitted to autologous transplant. CONCLUSION: When analyzing the profile of patients submitted to bone marrow transplantation, we found that age, gender and diagnosis characteristics are not, alone, a predisposing factor to respiratory complications that require the use of positive pressure. Other factors, such as the type of transplantation and chemotherapy drug used in the conditioning, can influence the development of respiratory complications, as identified in the analysis of this study together with the literature data.

Keywords: non-invasive ventilation, physical therapy, pulmonary complications

P-182

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Quality of life and functional capacity in post-bone marrow transplantation: a pilot study

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Introduction: Bone marrow transplantation (BMT) is one of the types of treatment proposed for hematological diseases. Patients undergoing this treatment suffer significant impacts due to cardiorespiratory complications and prolonged physical inactivity, which substantially interferes in their quality of life and functional capacity. Objectives: To analyze the functional capacity and quality of life of patients undergoing BMT, pre and post-BMT, in order to increase and deepen the knowledge of their physical therapy care needs. Materials and Methods: This is a quantitative prospective quasi-experimental study, of which sample consisted of 21 patients of both genders, aged between thirteen (13) and sixty (60) years, able to perform the proposed tests and submitted to autologous BMT, related allogeneic and/or unrelated allogeneic BMT, from April/2015 to October/2015. We excluded patients who had disabling cardiopulmonary diseases and/or severe or decompensated chronic obstructive pulmonary disease (COPD), severe or decompensated asthma, congestive heart failure; advanced chronic renal failure; muscular dystrophy, severe or decompensated liver disease; malignancies associated with the hematological cancer; Insulin-dependent diabetes; psychosis and dementia; ambulation incapacity =; Body mass index (BMI) <18 kg/m^2; osteoarticular and/or neuromuscular disorders that limit the performance of functional capacity tests. All patients underwent the following assessments: anthropometric, respiratory muscle strength (RMS), peak expiratory flow (PEF), inspiratory capacity (IC), Glittre test (GT) and application of abbreviated Whoquol-Bref questionnaire in the pre and post-BMT. Results: The sample consisted of three women and four men with a mean age of 34.9 ± 16,6 years. Patients had regular level of schooling, five did not complete high school and two completed high school. A significant difference in the mean PEF (L/m) (p-value 0.036) was verified, indicating significantly higher PEF after BMT, and for the remaining functional capacity measures and lung function, as well as among the areas of quality of life, there was no significant difference on the first day and after BMT. The results did not show a significant decrease in the quality of life and functional capacity of patients, between pre and post BMT. Also, we did not find significant correlations between quality of life and GT, RMS, body mass index and IC. Conclusion: The results did not show that the BMT has positive or negative effects on quality of life and functional capacity of patients during hospital stay. It is suggested to continue this study in order to achieve a representative sample and consequently, to point out the interventions that are adequate to the patients' needs.

Keywords: Quality of life, Exercise Capacity, Bone Marrow Transplantation, Physical therapy

P-183

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Peri-bone marrow transplantation weight loss at a university hospital

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Introduction: There is a lack of data on the nutritional status of patients with hematological diseases in the peri-bone marrow transplantation (BMT) period of hospitalization. Due to nutritional changes, a nutritional depletion is expected and, consequently, changes in anthropometric parameters. Objectives: To evaluate weight loss in patients undergoing BMT. Material and Methods: This was a retrospective longitudinal study. We used secondary data from medical records related to adult patients admitted for BMT between April 2015 and May 2016 at a Federal University Hospital. The weight loss between day T0 (day of admission) and T1 (day of discharge) was assessed, considering those equal to or greater than 5% (PP≥5%) during hospitalization. As independent factors we considered the changes in the gastrointestinal tract, as well as factors associated with food intake (days without reaching nutritional requirements, nutritional support indication, use of nutritional support, time of recovery of oral feeding, need for diet consistency change). To evaluate the weight loss between T0 and T1 we used the paired *t* test. The association between weight loss and the possible factors was evaluated using the chi-square test. Results: The sample consisted of 24 individuals, 66.67% males, mean age of 46.21 years (± 13). Most of them had myeloma (58.3%), followed by non-Hodgkin's lymphoma (20.8%); Hodgkin's lymphoma and bone marrow aplasia (8.3% each); and plasma-cell leukemia (4.2%). Only one individual was submitted to allogeneic BMT, whereas the remaining were treated with autologous BMT (95.83%). Nutritional diagnosis on admission was mild malnutrition (12.5%); well-nourished (29.17%); overweight (29.17%) and obese (29.17%). Changes in the gastrointestinal tract were hyporexia (95.83%), nausea (91.67%), diarrhea (87.5%) and vomiting (70.83%). The use of parenteral nutrition was observed in 3 patients (12.5%) and 2 were diagnosed with neutropenic enterocolitis. Unintentional weight loss was observed in 100% of patients (mean 4.09 kg; $p = 0.00$) and 41% ($n = 10$) had significant weight loss (PP ≥5%). There was no significant weight loss with the assessed independent factors. Discussion: Similar results were observed in previous studies with well-nourished patients on admission, but with nutritional depletion during hospitalization. There are reports of increased weight loss in allogeneic transplantation, which could not be confirmed in this sample. Although the gastrointestinal symptoms are pointed out as the cause of weight loss, usually this hypothesis is not statistically evaluated. Conclusion: Weight loss was observed during hospitalization, which was not associated with the gastrointestinal disorders evaluated in this study. Studies with longer follow-up, larger sample, food intake assessments, as well as energy expenditure assessments are suggested.

Keywords: bone marrow transplant, nutritional status, weight loss, gastrointestinal disorders, anthropometry

P-184

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nursing actions to promote patient safety in a Protected Environment Unit

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Introduction: In health care, safety is a basic principle and a requirement for the quality of care. Patient safety is defined as the reduction of unnecessary damage risk associated with health care, up to an acceptable minimum because, given the complexity of procedures and treatments, the potential for damage is real. Safe care results both from the right actions of healthcare professionals, as well as from appropriate procedures and systems in institutions and services, and also from the regulatory government policies, requiring a coordinated and sustained effort. Objectives: To describe nursing actions that are taken to promote patient safety in a Protected Environment Unit (PEU), which receives onco-hematological patients and patients submitted to Hematopoietic Stem Cell Transplantation in a university hospital in southern Brazil. Materials and Methods: This is a descriptive study, based on the experience report of PEU nurses of the institution. Results and Discussion: Currently, in order to promote patient safety in the PEU, the following nursing actions are carried out: correct patient´s identification, using name and medical record on the bracelet used by the patient; effective communication (double-checking of data obtained through verbal communication, such as alarming test results and medication use in emergency situations); high surveillance drug safety (adequate storage and controlled dispensing); hand washing and catheter care; reducing the risk of injuries caused by patient falls (using the Morse scale and identification bracelet for risk of falls); Thrombocytopenia Protocol implementation, which guides nursing actions to the thrombocytopenic patient; double-check the installation of some high-surveillance drugs, such as heparin solution, total parenteral nutrition and chemotherapeutic drugs, and blood components installation. These actions are highlighted by the World Health Organization (WHO) as promoting patient safety. In Brazil, the Ministry of Health established the National Program for Patient Safety, through Decree No. 529 of 1 April 2013, reinforcing a concern, already manifested worldwide, on this topic. However, it is necessary that the health teams are continuously trained, so that they can properly implement these actions. Conclusion: We observed that, in daily practice, these actions have become necessary for the safe care of the hospitalized patient in the PEU. We also conclude that it is necessary to build a patient safety culture, in which professionals and other services can share practices, values, attitudes and behaviors of harm reduction and promotion of care.

Keywords: Patient Safety, Security Management, Nursing Care.

P-185

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Physical therapy assistance in allogeneic HSCT: a case report.

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The hematopoietic stem cell transplantation (HSCT) comprises the intravenous infusion of hematopoietic tissue cells obtained from peripheral blood, bone marrow or cord blood, from a donor, into a recipient. Due to immune depression, resulting from chemotherapy and radiation, the HSCT patients are predisposed to infections and other complications. The physical therapist is an indispensable part of the multidisciplinary team, as the patient who performs HSCT is subject to long periods of protective isolation and exposure to toxic agents. The physical therapy intervention aims to minimize the reduction in functional capacity and prevent possible complications in cardiopulmonary function, contributing to a greater chance of successful transplantation. The aim of this study was to report the physical therapy assistance to a patient with acute lymphoblastic leukemia submitted to allogeneic HSCT. The patient, G.B.S, male, 20 years, submitted to unrelated allogeneic HSCT, was accompanied by physical therapy service from April 11 to June 10, 2016. The physical therapy was initiated on HSCT D-3. The patient had normal cardiopulmonary lung function, absence of pain complaints or muscle strength deficit in the upper or lower limbs. As conduct, metabolic and active free lower and upper limb exercises were performed, as well as static gait and ambulation, in order to minimize the effects of lower muscle activity period. Additionally, respiratory exercises were performed, emphasizing expansive ventilatory patterns. Neutrophil engraftment was confirmed on DAY+17, when the patient had hematuria and his hospital stay was extended until normalization of the clinical picture. The physical therapy conduct was maintained, with some adjustments on intensity according to the clinical condition of the patient, up to D+33, when the patient had pain at the movement and deep breathing, decreased lung sounds in the left hemithorax and radiological evidence of the left basilar atelectasis. The EPAP (expiratory positive airway pressure), expansive maneuvers and incentive spirometry were added to the physical therapy. After 7 days, the pulmonary atelectasis was reversed. As the patient remains hospitalized, aiming at normalization of hematuria, the physical therapy has continued up to now (HSCT D+57), aimed at maintaining the strength and muscle tropism and respiratory exercises aimed at maintaining lung function. Considering this case study, we can observe the importance of physical therapy for patients undergoing HSCT, by promoting functional independence, preventing muscle shortening, decreased tropism and muscle tone, stimulating activities of daily living, preventing and treating respiratory complications and, thereby, improving the quality of life of the patient.

Keywords: allogeneic bone marrow transplantation, physical therapy

P-186

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Assistance of the Integrative Medicine Group at the Hematopoietic Stem Cell Transplantation Inpatient Unit in a Private Hospital. Experience report.

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The hematopoietic stem cell transplantation (HSCT) is a treatment modality applied to onco-hematological diseases, congenital syndromes and autoimmune diseases. Increasingly advanced, this treatment has been the chance of survival for many patients. It represents a period of high complexity, long hospitalization regimen and critical periods of bone marrow aplasia. Integrative Medicine (IM) is the medical practice that reaffirms the importance of the relationship between the patient and the health professional; It is focused on the person as a whole; evidence-based; and uses all appropriate therapeutic approaches, all health professionals and all disciplines, in order to achieve the best of health and healing. Using integrative therapies that include mind and body practices such as yoga and stress management practices, with exercises focusing on breathing and mindfulness, moments of relaxation and well-being, encouraging the relaxation response, are offered to the patients, enabling the modulation between the sympathetic and the parasympathetic nervous systems. Objective: To report the experience of the introduction of IM practices in hospitalized patients submitted to HSCT. Method: This is an experience report of a HSCT inpatient unit. Results: The main goal of IM is to work together with conventional Medicine, encouraging the patient to actively participate in the process of health promotion and maintenance, emphasizing the body's innate ability with the help of integrative therapies. The IM service is offered to patients at the Oncology, Hematology and Bone Marrow Transplantation Center in a large private hospital in the state of São Paulo. The IM allows patients, even hospitalized ones, moments of wellness, comfort and self-care. Between 2014 and 2016, 142 HSCT were performed, where the autologous (43%) and unrelated allogeneic (25%) ones were the most prevalent. About 84% received care from the IM group, and approximately 1400 sessions were performed. Discussion: The interactions between the nervous, endocrine and immune systems include the impact of stress under the action of the immune system and health changes induced by it; the understanding of this interaction allows better use of practices of which aim is to stimulate the immune system. Current studies have emphasized the importance of behavior interventions, such as music, yoga and meditation, to reduce stress impact. We emphasize the importance of allowing patients to experience in-hospital pleasant moments, bringing the perception of their physical and psychological state, proposing tools to deal with possible psycho-emotional disorders. Conclusion: IM provides the relationship between health, mind and body, adding to the other areas of conventional Medicine, promoting interdisciplinary interaction. The inclusion of the IM approach was enriching for patients, family and the multidisciplinary team.

Keywords: Integrative Medicine, transplant, hematology

P-187

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Multidisciplinary team actions in the care of patients submitted to bone marrow transplantation

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Introduction: Bone Marrow Transplantation (BMT) is a therapeutic procedure that consists in the infusion of progenitor cells capable of reconstituting bone marrow function in a patient. The treatment based on BMT is very complex and requires a specialized multidisciplinary care, since the patient needs specific care to overcome the organic and social implications resulting from the treatment. Thus, our objective was to report the experience of resident professionals that comprise the multidisciplinary team caring for the patients submitted to BMT. Material and Methods: This is a descriptive study of the experience report type of the multidisciplinary care offered to patients submitted to BMT in a public hospital of Ceará, in April 2016 and at BMT unit. Results and Discussion: Through multiprofessional residency, the professional works in several sectors, seeking, during the experienced situations, resources for his/her improvement and, consequently, aiming to offer a better quality of life to the patient. During the period in which the resident professionals were in the BMT ward, the performance of each one was assessed individually and in the interdisciplinary manner. The nutritionist had the role to offer adequate nutritional support to the patient's needs; the pharmacist sought to address in a systematic way the problems related to medications and their doses; the social worker sought to know the problems experienced during the family and the patient's daily life that could somehow interfere with the treatment; the psychologist helped patient/ family to organize and plan the new routine during the different stages of treatment; the nurse provided more expressive care and educational activities, while in the assistance position, and the collaboration, coordination and supervision ones in the visit and management positions. Conclusion: Each health care professional has his/her specificity regarding the services provided to bone marrow transplant patients; however, the interventions of each service aim at improving the quality of life of patients and the provision of assistance covering the several individual dimensions, taking into account all the patient's needs. The role of the nursing staff, dietitians, pharmacists, social workers, doctors and psychologists, in an interdisciplinary and multidisciplinary manner, is of utmost importance to achieve good therapeutic results through specialized human resources, capable to provide adequate patient care, taking into account the high complexity of the treatment and all the patient's needs, therefore meeting the different dimensions of care.

Keywords: Bone marrow transplantation. multidisciplinary care. comprehensive health care.

P-188

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
The nurse's role in the collection of Hematopoietic Stem Cells (HSC) through aspiration puncture of bone marrow (BM): An experience report

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The collection of bone marrow (BM) through aspiration is performed in allogeneic donors when the patient usually has a benign pathology, given that bone marrow has a smaller population of mature lymphocytes, which leads to a lower risk of graft-versus-host-disease to the recipient. This study aims to report the initial experience of the authors with HSC collection from the donor by aspiration of BM, to perform the related allogeneic hematopoietic stem cell transplantation (HSCT). This is a descriptive study of the experience report type carried out at the Bone Marrow Transplantation Unit of Hospital Universitário de Fortaleza/CE, from December 2015 to May 2016. We obtained five donors who underwent HSC donation procedures by aspiration from the iliac crest, two of which were males and three females, aged 23-47 years (mean 33). The procedures were performed in the operating room under general anesthesia, with a mean duration of one hour. We used appropriate needles to remove the necessary amount of bone marrow for transplantation, with a maximum limit of 15 mL/kg of the donor's weight. To the collection bag with a closed valve system used for the procedure, 40 mL of heparin solution (83 IU/ml) was added and to every 300 mL of collected volume, it was added 0.5 mL of heparin. Upon reaching 600 mL, heparin was added to each 200 mL. The calculation of total nucleated cells (TNC) is made by counting the white blood cells obtained from the blood count sample, collected when 50% of the total planned volume it reached. After the collection, the filter set (850, 500 and 200 microns) is connected to remove bony spicules and fat. The final product is packed in up to 3 bags 600 mL each. There were no non-conformities in the cell collection in any performed procedure. Donor-related complications did not occur, with the only complaint being of pain at the puncture site, which was resolved with mild analgesics. All donors were discharged 24 hours after collection. The autologous erythrocyte concentrate transfusion was also performed in 100% of donors. To perform such a complex procedure, it is necessary a team with specialized knowledge and skills. The nursing staff is essential in this scenario, because they plan, perform and oversee the entire process.

Keywords: Nursing, Hematopoietic Stem Cell Transplantation

P-189

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Support offered by the support houses to patients undergoing hematopoietic stem cell transplantation

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Patients submitted to hematopoietic stem cell transplantation (HSCT) require care to prevent infections and other complications due to myelosuppression. Moreover, it is important that patients reside next to the health center in which they are being treated. The aim of this study was to describe three support houses located in the city of Porto Alegre-RS, which receive, among others, patients in pre and post-HSCT periods. This is an observational, descriptive and qualitative study (CAAE 51749615200005327). Three support houses in Porto Alegre-RS were visited in December 2015. These houses receive patients from cities in the state of RS and other states after patients are referred from hospitals. Considering the nearest referral hospital for transplantation, the first house is located 5.7 km away and receives up to 11 patients, of all ages, and their companions. The support house receives financial support from a church and donations, has an employee in charge of the local management and does not have volunteers or workshops. Regarding patient transportation, the house does not offer means of transportation, having as options the public or private transportation of which expenses are paid with the patients' own financial resources. The second house, located 5 km away from the same hospital, receives up to 10 patients of all ages, and their companions. It receives financial support from companies, food bank donations and has approximately 70 volunteers from several fields, as well as pedagogical coordinators, social workers and other hired employees. It has arts and craft workshops, computer classes, among other services. As for patients' transportation, it does not have vehicles, but has established a partnership with a private transportation service in order to reduce costs for patients. The third house is located close to the referral hospital, and receives up to 27 children and adolescents and their tutors. This house is maintained with resources from the hospital itself and support from an institute for children with cancer diagnosis and their families, offering workshops, psychological support, among others, in its headquarters in the vicinity of the house, in addition to providing volunteer caregivers. Among the site's own services, is the social service, in addition to other employees of the hospital itself. Despite their limitations, the support houses have suitable conditions to receive the immunocompromised patient; however, differences regarding certain characteristics are evident. The support of other entities, volunteers or donations do not occur in all of them, reducing the supply of other services and activities for these patients. Patients that stay in these houses are usually from remote locations and need help to stay close to the health center where they are being treated. Therefore, although there are improvements to be achieved, the support houses offer important support to patients undergoing HSCT, facilitating access to health services and treatment follow-up.

Keywords: transplantation, Hematopoietic stem cell transplantation

P-190

MULTIDISCIPLINARY (NURSING, PSYCHOLOGY, PHYSICAL THERAPY, OCCUPATIONAL THERAPY, PHARMACY, ORAL MEDICINE, SOCIAL SERVICE)

Bioelectrical Impedance Analysis in patients undergoing Hematopoietic Stem Cell Transplantation

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BACKGROUND: Bioelectrical Impedance Analysis (BIA) estimates the phase angle, fat and lean body mass. The test itself is inexpensive, easy to use, readily reproducible and appropriate for ambulatory and bedridden patients. Low phase angle by BIA is associated with increased morbidity and nutritional risk. The nutritional status of patients undergoing Hematopoietic stem cell transplantation (HSCT) is a prognostic indicator of this procedure. The protein-energy malnutrition and obesity increase the risk of comorbidities, mortality and length of use of immunosuppressive drugs. HYPOTHESIS: Study and correlate lean body mass, fat mas and phase angle in patients undergoing HSCT. METHODS: A retrospective study was performed, from May 2015 to January 2016, in 38 patients undergoing HSCT. The study took place at the Hematology-Oncology and Bone Marrow Transplantation Center of the Albert Einstein Hospital in São Paulo, Brazil. All patients were submitted to bioimpedance analysis prior to HSCT and the data were analyzed using the SPSS program. RESULTS: The study assessed 21 elderly patients (>55y) and 17 adult patients (<55y). In this pool, 52.6% were females and 47.4 males, with a mean age of 55.2±14.3 years, lean body mass of 71.1±7.9%, fat mass of 28.9±7.9% and phase angle of 5.6±1.02°. The bioimpedance test did not show sarcopenia in patients. Moreover, a negative correlation between age and phase angle (rp=0.5) was observed. In addition, the study showed a significant association between phase angle and older age ($p<0.05$). Finally, no significant difference was observed between lean mass, fat mass, and survival. CONCLUSION: This study shows that elderly patients have a significant association with low phase angle when compared with adult patients undergoing HSCT. As literature evidence suggests, low phase angle is associated with increased morbidity and nutritional risk. Therefore, preventive nutritional care should be applied to elderly patients that will be submitted to HSCT.

Keywords: Bioelectrical Impedance Analysis, Hematopoietic stem cell transplantation

P-191

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Evaluation of short-term central venous catheter in patients with autoimmune diseases submitted to autologous hematopoietic stem cell transplantation

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Patients with autoimmune diseases submitted to autologous hematopoietic stem cell transplantation (AHSCT) need a reliable and safe venous access. Maintaining this access allows the therapy to be administered and helps the successful treatment. Objective: we proposed in this study to evaluate the central venous catheter (CVC) in patients with autoimmune diseases submitted to AHSCT, identifying factors related to infection development and effectiveness of nursing actions. Method: Prospective study in a transplantation unit, from November 2015 to May 2016. The evaluation and filling out of the tool were carried out by the nurse on morning duty. Results and Discussion: During the AHSCT conditioning phase, eight patients were assessed, one with Multiple Sclerosis diagnosis and the other patients with Systemic Sclerosis. Six patients (75%) were females. The mean age was 37 years. All patients used a single double-lumen two-way CVC. The insertion site was the right internal jugular vein. In two cases the passage of the catheter was guided by ultrasound. The most commonly used conditioning regimen was cyclophosphamide and antithymocyte immunoglobulin (immunoablative therapy). The mean time of patients' neutropenia was 8 days. The polyurethane film cover was the most often used coverage. The advantage of this dressing consists in the possibility of continuous viewing of the insertion site and the skin around the wound and the time of permanence of the dressing, which prevents frequent changes and minimizes the risk of cutaneous trauma upon its removal. However, the presence of blood, especially in periods of thrombocytopenia, prevented its use, and this fact was the main reason for their exchange. Two patients experienced skin irritation, and skin erythema and swelling were the most prevalent incidents. Only one patient had a catheter infection, with the isolation of *Staphylococcus epidermidis* from the site. This patient had a skin reaction to all used dressing coverages and developed edema and skin loss. In immunosuppressed patients, the loss of the skin barrier facilitates the development of infections. All patients used antibiotic therapy, with febrile neutropenia being the main indication for its start. Blood cultures were collected every 24 hours in the presence of fever. The catheter permanence time was 18 days on average and its withdrawal predominantly occurred at the hospital discharge (75%); the other indications were suggestive signs of infection (12.5%) and confirmation of infections (12.5%). Conclusion: The constant and systematic monitoring of CVC has shown to be effective in the early identification and adoption of interventions in the presence of infection, and has brought subsidies for the creation and development of actions as educational measures for the staff, patients and caregivers, aiming at preventing infections and contributing to treatment success.

Keywords: Central venous catheterization, hematopoietic stem cell transplantation, immune system diseases

P-192

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Health demands of patients submitted to Allogeneic Hematopoietic Stem Cell Transplantation

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Introduction: Health demands are the result of a complex interaction between social, economic and cultural factors related to health services and professionals, often surpassing the search for medical attention, limited to health problems. In this context, the health demands could be encompassed in four major sets of needs: good living conditions, access to and use of health technologies, creation of effective relations between patient and staff/professionals and autonomy construction (Cecilio, Merhy 2002, 2003, 2014). Objective: To know the health needs of patients treated at the Hematopoietic Stem Cell Transplantation Assistance Program of a university hospital. Methodology: Qualitative research (CAAE 40328114500005327). The oral history technique was used for data collection. For data collection, we used interviews, through semi-structured script, from March to July 2015, and the subjects were 05 adult patients that met the inclusion criteria in that period. The data were analyzed using the Analysis of Content, based on Bardin (2009). Results and Discussion: The most recurring needs are related to housing-territory, work, issues related to changes in family income, family reorganization, loss of autonomy and affective relationships. The difficulties arise, as the lives of the subjects are interrupted by other processes and by the desire to restore their lives to "normal", beyond what is prescribed and recommended by the staff. The study showed that, although the concept of "health needs" is not explicit among the subjects, they understand the association between the social status and the health-disease process. The interviews allowed us to apprehend all the constitutive elements of the categories, *a priori* defined according to the Taxonomy of Health Needs. We identified that the social context where the subjects are included may have a strong influence on their health, and that the autonomy in decision-making is a necessity. The autonomy/self-care needs seem to be closely linked to the association with the health care team, since by reinforcing this relationship of trust, it is possible to strengthen the potential for facing the health-disease process. Final Considerations: The health needs are expressed in the health-disease process and demonstrate that the health conditions of the Brazilian people are disadvantaged and generate a great demand for health care. Regarding the HSCT, the people's care is often directed to health services in other locations, outside their territory, far from their family and community support groups, which further exposes the need for a close relationship between the comprehensive health care, access to social policies and quality of health actions and services.

Keywords: Needs and demands of health services, Hematopoietic stem cell transplantation, Comprehensive Health Care

P-193

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Nutritional profile of hematological patients pre-bone marrow transplantation

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Introduction: The nutritional status is considered a prognostic factor in patients undergoing bone marrow transplantation (BMT); however, there is scarcity of data on the nutritional status prior to BMT. For a better nutritional-therapeutic intervention and nutritional therapy indication, it is necessary to know the nutritional profile of these individuals. Objectives: To assess the nutritional status of patients admitted for BMT. Methods: This is a retrospective cross-sectional study. We used secondary data from medical records of adult patients prior to BMT between the months of April 2015 and May 2016 in a referral University Hospital for treatment of hematological diseases, located in northeastern Brazil. Nutritional screening was performed using the NRS-2002 form, considering patients with scores higher than and/or equal to 3 as being at nutritional risk. The anthropometry was evaluated by body mass index (BMI) and weight loss percentage (% WLP) in the last 6 months. We considered significant losses those above 10% of normal weight, with albumin being the biochemical indicator. Results: The sample consisted of 24 individuals, 66.67% males, with a mean age of 46.21 years (± 13). The hematological diagnoses were myeloma (58.3%, n = 14), non-Hodgkin's lymphoma (20.8%); Hodgkin's lymphoma (8.3%), bone marrow aplasia (8.3%) and plasma cell leukemia (8.3%). One individual was hospitalized to undergo allogeneic BMT, and the other patients were referred for autologous BMT (95.83 %). Only two patients (8.3%) were at nutritional risk according to NRS-2002. The mean weight was 78.5 kg (± 14,67 kg). Regarding BMI, the patients were classified as having mild malnutrition (12.5%, n = 3); normal weight (29.17%, n = 7), overweight/obesity (58.34%, n = 14), with 7 overweight and 7 obese individuals. Three individuals (12.5%) had shown significant weight loss in the six months prior to admission. Nine patients had hypoalbuminemia (albumin <3.5 mg/dL); however only one (4.2%) had severe hypoalbuminemia (albumin <2.5 mg/dL). Discussion: Regarding the anthropometric nutritional status, similar results (56% of overweight and obesity) were found in a study carried out in 2015 in southeastern Brazil. Although BMT represents a treatment with risk of malnutrition, overweight and obesity are not protective factors for survival after transplantation. The high weight is considered a risk for the development of Graft-versus-Host Disease (GVHD), and for causes of death unrelated to disease recurrence in post-transplant individuals. Conclusion: The description of the nutritional profile of patients eligible for BMT allows us to create strategies to control overweight/obesity in this population, helping to reduce post-transplant clinical complications.

Keywords: bone marrow transplantation, nutritional profile, overweight, obesity, anthropometry

P-194

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)
Main nursing care provided to patients submitted to bone marrow transplantation

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Introduction: Bone Marrow Transplantation (BMT) is a treatment procedure consisting of the intravenous infusion of bone marrow blood, obtained from a suitable donor, in a patient (recipient). Its purpose is the reconstruction of a hematopoietic organ injured by an autoimmune or toxic mechanism, or due to neoplastic or reaction cell proliferation. Due to the very severity of the disease and possible risks after BMT, patients should receive special care from the entire multidisciplinary team. Nursing care is essential for transplantation success and patient recovery, as nurses exercise the care 24 hours a day, assessing, caring and contributing to the overall condition of transplanted patients. Objectives: This study aims to outline the main nursing care procedures in patients post-bone marrow transplantation. Methods: This study consists of a literature review, which aims to know which are the main nursing care procedures offered to patients undergoing BMT. As data source we searched for articles available in the Capes journal portal, published in Portuguese, English and Spanish in the last five years. Twelve articles were selected and of these, only seven met the inclusion criteria: publications in Portuguese, English or Spanish, and date of publication between 2011 and 2016. Results and discussion: After reading the selected articles, seven were selected on the main nursing care procedures. The one with the highest prevalent referred to the care of the central venous access, related both to the daily practice of sterile dressing and the catheter patency. The use of a central venous catheter in patients undergoing BMT is of great importance because it allows the administration of drugs and fluids, repeated sample collection, etc. Another prevalent nursing care procedure is the evaluation of the oral cavity, identifying signs of complications and infections, as well as health education, guiding the patient on the maintenance of a satisfactory oral hygiene. Pain assessment and diet acceptance are also important. The first will promote patient comfort, and the second will allow the identification of problems that might interfere with the nutritional aspect of the patient, such as diarrhea or vomiting. Patients who undergo BMT must be careful to avoid infections, and because the nursing team is the one that is most frequently in contact with these patients, it has to be attentive to handwashing and to the adequate preparation of the procedures to be performed. Another important point refers to assessing the mental health of patients, observing signs of anxiety or depression that could impair adherence to treatment. Conclusion: By providing comprehensive care to the patient's health, nursing care is critical to patient post-BMT recovery. The care procedures performed by the nursing team meet both the physical as well as the emotional dimension requirements; these care procedures prevent complications and may disclose other problems that require intervention.

Keywords: bone marrow transplantation nursing, care

P-195

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Nursing care in patient preparation for hematopoietic stem cell collection: an experience report

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Introduction: Hematological disorders include a variety of significant abnormalities, accompanied by few or no symptoms, for which the main treatment is the Hematopoietic Stem Cell Transplantation (HSCT). The hematopoietic stem cell collection (HSCC) consists in the procedure employed, after therapy, to increase the number of these cells in peripheral blood, through the use of medication or collection of such cells directly from bone marrow. Objective: To report the nursing care experience in patient preparation for Hematopoietic Stem Cell Collection. Material and Methods: This is a descriptive study of the experience report type carried out in the Medical Clinic Unit of a public hospital in Fortaleza/CE from February to May 2016. Results: Nursing interventions concerning the patient preparation for hematopoietic stem cell collection include care upon admission, reduction of anxiety, nutrition control, performance and/or assistance in procedures, administration of prescription drugs, ensuring the continuity and/or appropriateness of continued use drugs, skin integrity maintenance, evaluation of the risk of falling in the hospital environment, health education, referrals and tests and supply control. Discussion: Nursing care should emphasize the correct identification of the patient; safety in handling central venous catheter, with an emphasis on hygiene in order to prevent infection; transportation safety and appropriate monitoring in taking the patient to the surgical center or apheresis sector; adequate use of medications and collection of laboratory tests and recommendations on drugs adverse events and procedures. Conclusion: The maintenance of quality when providing services in a systematic, clear and objective way depends on an individualized nursing care. To minimize adverse events during the performance of specific nursing procedures requires improvement of work processes and their assessment affords considerations on the professional's performance among those working in the onco-hematology inpatient unit, contributing to the treatment success of individuals who will undergo hematopoietic stem cell collection.

Keywords: Bone Marrow Cells, Hematopoietic Stem Cell Mobilization, Nursing Care

P-196

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Bone marrow donation: a survey of the nursing staff knowledge

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Introduction: Bone marrow transplantation is a treatment used in onco-hematological disorders for the purpose of restoring hematopoiesis. When the cells come from the individual's own blood, it is called Autologous, and when cells come from a different individual, Allogeneic. The donor can be related, when the recipient and the donor are consanguineous, and unrelated, when donor and recipient are not relatives. In the latter case, the Bone Marrow Donation is an essential procedure and the donor needs to be registered in the Brazilian Registry of Bone Marrow Voluntary Donors (REDOME). Objective: To identify the knowledge of nursing professionals on bone marrow donation. Methodology: A qualitative descriptive study was performed in June 2016. The sample consisted of 19 professionals that worked in an inpatient unit for onco-hematological patients from a public hospital in Fortaleza (CE). A semi-structured questionnaire on the theme, divided into two parts, was used: the first with fifteen (15) phrases to be marked as true or false, and the second with open questions. Results: The results showed that nursing professionals have little knowledge about bone marrow donation, as ten (10) of the participants reported that they do not feel capable of offering guidance to potential donors. Among the professionals, 14 (fourteen) declared themselves as non-bone marrow donors, with the most frequent reasons being the presence of health problems, lack of information, fear of the procedure and of pain. Discussion: Nursing professionals should receive appropriate guidelines inherent to the bone marrow donation process, in order to contribute to the health education of patients and families. Disseminating the correct knowledge ensures the proper use of health services and contributes to patient safety. Conclusion: Continuing education on the subject is essential for these professionals because, in addition to the need to provide reflections on their practice, they can be important partners in attracting future donors.

Keywords: Bone Marrow Donation, Hematopoietic Stem Cell Transplantation, Nursing

P-197

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Outcome analysis of patients submitted to hematopoietic stem cell transplantation in a private institution in São Paulo.

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Introduction: The hematopoietic stem cell transplantation (HSCT) is a therapeutic modality used as a possible cure for some onco-hematological diseases that used to be potentially fatal. It is a promising treatment, with increasing prospects of the best outcomes. With the increasing number of transplantation centers, and because it is a high-complex treatment, professionals are increasingly qualified and encouraged to make critical analysis of their results in order to plan their actions, seeking the best practices and clinical outcomes. Based on the analysis of these data, we obtain the knowledge of the patients' history in their several diagnoses and their therapeutic responses to the transplant. Objective: To observe the clinical outcome of patients who underwent HSCT, within one year after bone marrow infusion. Material and Methods: This is a descriptive and retrospective study performed in a large private hospital in the city of São Paulo, with analysis of the HSCT sector data from January 2013 to December 2014, from the computerized system of HSCT patients and from the information collected from the medical team. The analysis of the clinical evolution of patients was carried out during a one-year period after the marrow infusion (D0). After this period, the results of the clinical evolution were divided into five groups: disease-free, death during HSCT hospitalization, death within one year, disease relapse and no information on the evolution. Results: During the two-year period 48 HSCT were performed, being 30 (62.5%) autologous, 10 (20.8%) allogeneic and 8 (16.7%) haploidentical. Regarding the underlying disease that led to the treatment, 11 (22.9%) patients had non-Hodgkin's lymphoma, 9 (18.7%) had Hodgkin's lymphoma, 9 (18.7%) had Acute Myeloid Leukemia, 8 (16, 7%) had multiple myeloma, 5 (10.4%) Myelodysplastic Syndromes, 3 (6.3%) Lymphocytic Leukemia, 2 (4.2%) Primary Amyloidosis and 1 (2.1%) Myelofibrosis. After the classification, 26 (54.1%) patients were disease-free, 9 (18.7%) died during the HSCT hospitalization, 7 (14.6%) died within a year after the infusion, 3 (6.3%) relapsed and for 3 patients (6.3%) it was not possible to obtain information. Conclusion: After the data analysis, we observed that 54.1% of transplanted patients in our service were disease-free after one year of the hematopoietic stem cell infusion, whereas 6.3% had relapsed, concluding that HSCT is a therapeutic proposal that shows satisfactory response in patient overall survival. This survey provided knowledge of the clinical course of our patients, and prompted us to perform further studies in order to deepen the knowledge of the variables that influence the outcomes.

Keywords: transplantation, bone marrow, evolution, clinical

P-198

Multidisciplinary (Nursing, Psychology, Physical Therapy, Occupational Therapy, Pharmacy, Oral Medicine, Social Services)

Evaluation of oral mucositis treatment with a product based on avocado extract (Persea americana Mill) – A case study

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Introduction: Mucositis is the inflammation of the oral mucosa due to the side effects caused by chemotherapy in cancer patients, characterized by erythema, edema and painful ulcerations, which can affect the entire oral mucosa, causing pain, discomfort, affecting speech, in addition to changing the nutritional status due to difficulty in swallowing and affecting patient quality of life. Objective: This study aims to evaluate the clinical results regarding the efficacy and side effects of the medical product based on Persea americana Mill (avocado) extract on grade IV oral mucositis, in a patient with acute lymphoblastic leukemia (ALL) undergoing chemotherapy treatment. Material and Methods: To meet the proposed objective, the descriptive study of a clinical case was performed on a patient with grade IV oral mucositis, as experienced by the authors in a oncological hospital in the city of João Pessoa-PB. In order to document and monitor the treatment, a photographic record was carried out, after authorized by the patient through the signing of the free and informed consent by the mother and authorization from the Research Ethics Committee of the institution. Case report: Patient C.B.S.N, younger than 6 years old, female, white, submitted to chemotherapy for treatment of ALL with the ALL-BFM 02 (acute lymphoblastic leukemia – Berlin-Frankfurt-Munich) European protocol, at the remission induction phase, developed aplasia, with severe grade IV mucositis on the 8th day of treatment, as evidenced by ulcerated lesions on the semi-mucosa of the lip and in the tongue region, referring pain, dysphagia and loss of appetite. A topical therapy was started with the medical product based on avocado extract applied as sterile cold cream every 8 hours. Results and Discussion: 48 hours after the start of the topical therapy with the tested medical product, she showed improvement of the local clinical symptoms, with pain relief, healing of lesions and beginning of oral feeding. After 72 hours, the oral mucosa was regenerated, indicating that the stomatological management therapy had a positive effect, promoting better quality of life to the patient with nutritional status improvement and continued treatment. Conclusion: Oral mucositis is a common complication in cancer patients and its early treatment helps to minimize the side effects of chemotherapy. When associated with neutropenia and poor diet, it increases the risk of sepsis, modifying the patient's final prognosis by interrupting the dissemination of the disease. Due to this fact, the treatment is essential for the success of cancer therapy. With the lack of an ideal model, we chose the topical therapy with the medical product based on avocado extract, which showed excellent results in just 72 hours of product use on the oral mucosa of the child, with re-epithelialization of ulcerated areas and healing of lesions as evidenced by the good acceptance of the diet and improved nutritional status.

Keywords: nursing, oral mucositis, chemotherapy, topical therapy

P-199

Allogeneic Transplantation

Quantitative Growth in International Applications for REDOME Donors

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INTRODUCTION: The number of requests from patients of International Registries for REDOME registered donors has grown over the years. OBJECTIVES: To analyze the demand of requests made by the International Registries to REDOME from October 2010 to May 2016. MATERIALS AND METHODS: A data survey was carried out in the REDOME management system, between October 2010 and May 2016, considering the following variables: type of request, number of applications in the years and growth percentage. RESULTS AND CONCLUSION: The analysis showed that requests for confirmatory test (CT) and second-phase HLA class I and II in 2010 represented only 2% of all requests performed by REDOME, with 397 requests being made for international patients, and that in 2015 there was an increase of 518%, with a total of 8938 requests, which meant 36% of all requests to REDOME. Manual preliminary research, in which the search for potential donors is performed for patients in International Registries through REDOME management system, comprised a total of 11664 applications; however, in May 2016 we came to a total of 6300 applications over the year. When checking the amount of research on a quarterly basis, we can say that in the first quarter of 2015, 2347 preliminary searches were performed, and in the same period in 2016, a total of 3478 searches were performed, representing an increase of 48%. Currently, preliminary searches can also be automatically carried out via EMDIS (European Marrow Information System) and now they account for 81% of primary search performed by REDOME. We conclude that, over the years, REDOME has become more present internationally, being recognized as the third largest bone marrow donor registry in the world, with a significant growth percentage in the international area, offering quality and promptness in their services and products.

Keywords: strategy, internationalization, quality, resources, automation

P-200

Allogeneic Transplantation

One-week follow-up of a Volunteer Donor of HSCT - For National and International Recipient

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INTRODUCTION: The number of requests for unrelated HSCT has increased worldwide. The follow-up of donors for one week after donation is an activity that has been developed by REDOME (Brazilian Registry of Bone Marrow Unrelated Voluntary Donors). OBJECTIVE: To evaluate the one-week follow-up of national donors for national and international recipients, identifying and comparing specific characteristics among them. MATERIALS AND METHODS: 168 donors were assessed from October 2015 to April 2016, considering the following variables: age, gender, cell sources and more frequent symptoms. RESULTS: when analyzing the donors by gender, for national recipients: Male gender, 49 individuals donated bone marrow and 33 peripheral blood; Female gender, 30 individuals donated bone marrow and 16 peripheral blood. Regarding donors by gender, for international recipients: Male gender, 06 individuals donated bone marrow and 11 donated peripheral blood. Female gender, 04 individuals donated bone marrow and 19 peripheral blood. Regarding the donors' age, for national recipients: both for bone marrow and for peripheral blood, there is a greater concentration in the age group 18 to 39 years. Regarding donors by age, for international recipients: both for bone marrow and for peripheral blood, there is a greater concentration in the age group 30 to 49 years. The main symptoms reported by donors for the bone marrow biopsy collection are: pain at the puncture site 86%, fatigue and weakness 18%, and headache 15%. When the cell source is peripheral blood, they reported fatigue and weakness 28%, bruising 22% and pain in the arm 13%. CONCLUSION: The use of peripheral blood for international patients with Brazilian donors has become more evident than for domestic patients; the age range of the donors selected for international patients is older than that of donors for national patients. The symptoms and their frequency are similar to those reported in previous studies

Keywords: REDOME, donors, follow-up

P-201

Allogeneic Transplantation

Transportation of REDOME Donors for HSC Collection

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INTRODUCTION: There is an increasing number of HSCT with REDOME donors (National Registry of Unrelated Voluntary Donors of Bone Marrow), an institution regulated by the Ministry of Health. The Logistics for a shorter displacement of the donor to a collection center regulated by the Ministry of Health is one of the main REDOME tasks. OBJECTIVE: This study aims to demonstrate the donor's average displacement for the marrow collection procedure, and in which areas there is a need to implement collection centers, in order to reduce costs and time in transit. MATERIAL AND METHODS: The data of collections of the last 6 months of 2015 were assessed, crossing the data of the regions of donor´s origin and the states where the centers for HSC collections were located. RESULTS AND CONCLUSION: The analysis of results showed that the two donors from Northern Brazil, from the states of Amapá and Rondônia, had to travel an average of 3,293 km, since there is no collection center in the that region. In the Midwest, we had 16 donors and the average distance traveled was 589 km, as we have two collection centers in this region, and thus, the logistics is better. In the Northeast, where we have three collection centers, the average traveled distance was 700 km, and we had 6 donors. In the South region, we have a better scenario, with 5 collection centers and 17 donors who underwent collections, with the average traveled distance being 365 km. Finally, the Southeast Region, which has 12 collection centers and 46 donors undergoing collection in the period, with an average displacement of 352 Km. We can observe that this average displacement is long, because there is no collection center in the state of the Espírito Santo, and in the state of Minas Gerais there is no collection center to perform collections from peripheral blood. On the other hand, all 5 donors from Rio de Janeiro donated within their state and of the 22 donors from São Paulo, only 1 had to travel to another state. We conclude that in the South and Southeast regions we have an adequate number of collection centers, but the opening of additional centers in the Northeast and Midwest regions is necessary, being essential the opening at least one center in the North, to meet the demand of donors of that region.

Keywords: donors, REDOME, HSCT collection, logistics and displacement

P-202

Cell therapy

Adipose tissue-derived mesenchymal stromal stem cells and poly(L- lactic acid) scaffolds biocompatibility might lead to artificial trachea development through additive manufacturing and electrospinning.

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Introduction: Extensive tracheal resection uses temporary orthoses leading to infections requiring further surgeries. Regenerative Medicine might be an alternative. Mesenchymal Stromal Stem Cells (MSCs) have shown immunomodulatory ability, differentiation into mesodermal lineage capacity and are easily obtained from adipose tissue (AT). Biopolymers, such as Poly (L-lactic acid) (PLLA), guides the regenerative process without removal requirement due to their biodegradation and biocompatibility properties. This study aims to analyze AT-MSCs biocompatibility when cultured in PLLA scaffolds aimed at artificial trachea production. Material e Methods: PLLA was manufactured from L-lactide by ring opening polymerization, solubilized in chloroform/acetone and submitted to additive manufacturing and electrospinning procedure. Fibers were characterized by Scanning Electron Microscopy (SEM), Differential Scanning Calorimetry (DSC) and sterilized by ethanol 70% and U.V. AT was obtained by liposuction, digested by collagenase and harvested in DMEM low glucose and FBS medium. Adherent cells (fourth passage) were characterized as MSCs by flow cytometry, morphological changes (confocal microscopy) and mesodermal lineage differentiation capacity. Gene instability analysis was performed by telomerase enzyme activity and karyotype assays. AT-MSCs were seeded (3.0 x10E4) on PLLA scaffolds. Adhesion was analyzed by SEM, proliferation by MTT and cytotoxicity by Live/Dead. Prosthesis were transplanted into a swine model submitted to extensive tracheal resections. Results: PLLA fibers showed an average of 10μm diameter. DSC showed no residual solvent. Adherent cells were characterized as MSCs. Telomerase enzyme activity and karyotype analyses showed gene stability. AT-MSCs adhered and proliferated all over the scaffold maintaining viability. Conclusion: PLLA was biocompatible with AT-MSCs, being a promising alternative for tissue engineering.

Keywords: Tissue engineering, stem cells, mesenchymal stromal stem cells, biomaterial, regenerative Medicine

P-203

Cell therapy

Protocol optimization for chromosome analysis by gtg banding of mesenchymal stem cells

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Introduction: The use of stem cells (SC) in tissue regeneration suggests a promising future due to their self-renewal capacity and differentiation in many tissues. The use of these cells is of great interest worldwide, providing a steady increase in research in this area. However, lineages derived from SC, both embryonic and adult, may have genetic instabilities, causing chromosomal abnormalities that prevent the clinical use of these cells, in addition to reducing its reproducibility and reliability in experimental studies. Therefore, cytogenetic analyses are necessary to evaluate the stability of these cells. The conventional cytogenetics, chromosome analysis by G banding with Trypsin and Giemsa (GTG), is considered the gold standard for genetic evaluation of a cell lineage. However, several authors have reported difficulties in obtaining good-quality metaphases to enable this analysis, which is one of the reasons to choose molecular techniques. Objective: To optimize the chromosomal analysis protocol by GTG banding of mesenchymal stem cells, in order to obtain the highest number of good-quality metaphases of in each exam. Materials and Methods: For this study we used 7 samples of human mesenchymal SC, 4 of them from umbilical cord, 2 from bone marrow and 1 from nasal septum. In the second cell expansion (P2), the samples were seeded at concentrations of 0.1x106, 0.5x106 1.5x106 in three 150 cm^2 flasks. After 48 hours, the collection, preparation of slides and GTG banding of each material was performed. The analysis was performed under a microscope, by counting the number of metaphases per slide for each concentration, performed in triplicate and by two analysts. Results: The samples derived from umbilical cord had many metaphases, but with excessive chromosomal scattering, making it difficult to count. For samples derived from bone marrow and nasal septum, satisfactory results were obtained, indicating an increase in the number of metaphases in proportion to the concentration of seeded cells for cultivation, with a mean of 33, 198 and 340 metaphases per slide at the concentrations of 0.1x106, 0.5x106 and 1.5x106, respectively. Discussion: The results were compared with pre-established parameters, such as age and level of duplication of the cell population, and also compared with other data in the literature. Conclusion: The two largest concentrations, 0.5x106 and 1.5x106, were chosen to optimize the protocol, as they resulted in the largest number of metaphases obtained and a greater chance of finding good-quality metaphases for a safe analysis.

Keywords: mesenchymal stem cells, karyotype, tumorigenic potential, Cytogenetics, Metaphase.

P-204

Cell therapy

Mesenchymal stem cell culture of human dental pulp in scaffold manufactured with natural polymers

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Tissue engineering involves the use of biomaterials that act as templates, called scaffolds, in which stem cells can be cultured for the purpose of creating *in vitro* tissue. This study aimed to observe the growth of human dental pulp-derived mesenchymal stem cells (DPSCs) inside scaffolds manufactured with natural polymers. The pulp tissue was washed with PBS solution and submerged in a plate containing basal culture medium. The tissue was dissociated and kept in an incubator at 37 °C and humidified with 5% of CO_2. Upon reaching 80% of confluence, the primary cultures were trypsinized and cut. The presence of adherent cells, confluence and characteristic morphology were observed daily. For the analysis of the capacity to differentiate into mesenchymal lineages, cells were plated in 24-well plates at a density of 5x103 cells/cm^2. After reaching the appropriate confluence, the chondrogenic, adipogenic and osteogenic differentiation treatments were started. Cells were characterized by flow cytometry technique using the monoclonal antibodies CD14/FITC, CD45/FITC, CD105/FITC. Cell adhesion on the scaffolds were evaluated by Scanning Electron Microscopy (SEM). 105 cells were seeded onto the scaffold and incubated in an atmosphere of 5% CO_2 at 37 °C. After incubation, the cells were fixed, dehydrated, metallized and observed in a scanning electron microscope to evaluate cell adhesion within the scaffold. The cell morphology and adhesion on the scaffolds were also evaluated by their histological processing. Scaffolds impregnated with cells were fixed, dehydrated, embedded in paraffin, stained with hematoxylin/eosin, and viewed under an optical microscope. The DPSCs showed typical fibroblastoid morphology from the 10th day of *in vitro* culture, differentiation in mesenchymal lineages (osteocytes, chondrocytes and adipocytes), positive expression for CD105 and negative for CD14 and CD45. The SEM disclosed a porous matrix surface with the presence of cells fixed in its interior. Histological evaluation of the scaffold showed that DPSCs had a typical morphology, binding capacity and appropriate distribution within the matrix pores. Most cells had spherical morphology and were adhered to the membrane. Others showed fusiform and fibroblastoid morphology, also typical characteristics for DPSCs. The cell morphology and adhesion, demonstrated by histology and SEM, showed that they were viable within the matrix. The scaffold manufactured with natural polymers has applicability in *in vitro* cell culture, working as a support matrix for the growth of these cells, emerging as an important biomaterial to be used in surgical applications as support and mean of cell transportation in tissue regeneration processes.

Keywords: Tissue Engineering, Scaffolds, Mesenchymal stem cells, Natural Polymers

P-205

Cell therapy

Chronic myeloid leukemia cell (K562) and its derivative K562-Lucena, resistant to Vincristine, have cell proliferation inhibited by in vitro mesenchymal stem cell conditioned medium

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Introduction: Mesenchymal stem cells (MSCs) have broad applications in regenerative therapy, especially in bone marrow transplants after chemotherapy of cancer patients. These cells support the hematopoietic stem cells, which will recover the damaged hematopoietic system during chemotherapy. It is known that MSCs produce multiple substances, but little is still known about how these substances interact with other cell types, especially in tumors. There are conflicting reports in the literature indicating that MSCs can enhance *in vitro* and *in vivo* proliferation of tumor cell lines, and in other cases, inhibit it. But the vast majority of these studies are related to solid tumors, with a few studies on hematological tumors. Given the therapeutic usefulness of MSCs and their possible interaction in bone marrow transplants, it would be of great importance to study how these cells can interact with tumor cells that are chemotherapy-sensitive and resistant. Objectives: To determine the changes in cell viability and in cell proliferation *in vitro* of chemotherapy-sensitive (K562) and resistant tumor cells (K562-Lucena), compared to the substances released into the conditioned medium (CM) of MSC, derived from adipose tissue and amniotic fluid. Methods: The conditioned mediums were produced by incubating MSCs derived from adipose tissue (n = 3) and amniotic fluid (n = 3) with DMEM medium containing 10% FBS. These cells were obtained from the Laboratory of Genetics and Molecular Hematology of FMUSP. Cells were cultivated for 24 hours and then the CM was separated, centrifuged, filtered (0.22 um) and stored at -20 °C. The experiments were performed using chronic myogenic leukemia cells K562 (ATCC CCL-243) and its derivative K562-Lucena, resistant to vincristine. Changes in cell viability were determined by the MTT method. The degree of apoptosis in tumor cells treated with different CM was determined by using the annexin V/PI assay through High Content Screening microscopy and analysis by MetaXpress. The results were expressed as mean and standard deviation, and comparisons were performed using one-way ANOVA, considering $p < 0.05$ as significant. Results: In cell proliferation analysis, we observed reduced proliferation of K562 and K562-Lucena lineages when treated with CM, regardless of their origin. The cell viability analyses showed no significant increase in apoptosis; however, we observed a tendency to increase when compared to the control, indicating that the CM may be acting as a cytostatic agent on the tumor cells. Conclusion: The MSCs conditioned medium negatively modulates cell proliferation of leukemic lines.

Keywords: mesenchymal stem cells, conditioned medium, hematological lineage

P-206

Cell therapy

Analysis of serological examinations and nucleic acid test in the serum of mothers who stored their children's umbilical cord blood in private umbilical cord blood banks from 2013 to 2015.

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Introduction: Infections transmitted by bone marrow or umbilical cord blood transplantation are one of the biggest threats to the safety of these procedures. The introduction of the nucleic acid testing (NAT) in the analysis of the blood of mothers who decide to store umbilical cord blood cells of their children is not mandatory for Private Umbilical Cord Blood Banks (ANVISA - RDC 56/2010). For banks that have international accreditation, on the other hand, NAT tests for HCV and HIV are mandatory. The NAT technique is highly sensitive and specific for viral nucleic acids. It is based on the amplification of specific sequences of viral RNA or DNA and detect them before the serological screening methods and, therefore, reduces the duration of the immunological window, thus offering a much higher sensitivity for the detection of viral infections. Objective: This study aimed to analyze the serological examinations and nucleic acid test (NAT) in the serum of mothers who stored the umbilical cord blood of their children in a private bank from 2013 to 2015. Material and Methods: Retrospective descriptive observational study of the results of serological screening of 8057 maternal blood samples, collected at the birth of their children, from January/2013 to December/2015. The research was approved by the Research Ethics Committee - IPPMG - UFRJ (No. 608316). The samples were tested for blood-borne diseases in accordance with the resolutions of the National Health Surveillance Agency, which regulates the umbilical cord blood banks. Results: The analysis of 8057 clients' results revealed the presence of HIV infection in only one of the clients. All clients who were positive on serology for HCV also showed positive NAT, indicating the presence of hepatitis C virus particles. In the 86 positive tests for anti-HBc, only 6 had a positive NAT. Discussion: Although the results represent a portion of the privileged socioeconomic population, and despite the low number of active infections detected, these results demonstrate the importance of performing the HBV/DNA test during the prenatal tests of women who had only anti-HBc reagent (total antibodies). Conclusion: In addition to the possible detection of active virus, the nucleic acid test has the benefit of solving the false positive results of serological methods, which are very important for the notification and counseling of mothers with positive serology and care of the newborn. Because it is an autologous storage bank, the positivity in maternal serum is not an exclusion criterion for storage. The decision to keep the material stored, according to the current legislation, is made by the Bank together with the customer.

Keywords: NAT, ANVISA, HCV, HIV, HBV

P-207

Cell therapy

Comparative evaluation of genetic integrity and long-term expansion of human adipose-derived stromal cells from face and abdomen

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Background: Adipose tissue is a promising source of stem cells for use in regenerative therapies. Moreover, the genetic integrity of cells is essential for the success of therapy. Aims: In this context, we have comparatively evaluated the genetic integrity of adipose-derived stromal cell (ASC) isolated from facial or abdominal human adipose tissue. Methods: ASCs were obtained from skin samples discarded after rhytidectomies (face) and abdominoplasties (abdomen) at the University Hospital of Santa Catarina Federal University (Florianópolis, Brazil). Cell morphology was evaluated by phase contrast microscopy and cell senescence by cumulative population doubling. Nuclear abnormalities were assessed by cytokinesis-block micronucleus (CBMN) assay. The DNA damage response marker γH2AX was evaluated by immunofluorescence. Results: Both ASCF and ASCA displayed fusiform morphology. Less than 0.4% of cells showed nuclear damage such as nuclear buds and nucleoplasmic bridges despite of their facial or abdominal origin. Moreover, facial and abdominal ASCs have comparable levels of γH2AX. Conclusion: Therefore, we conclude that both facial and abdominal ASCs are good and equivalent sources of cells for cell therapy, able to maintain the genetic integrity after long-term expansion in culture. Ethics committee CEP-UFSC: 131.512

Keywords: adipose, face, abdomen, ASC, genetic integrity.

P-208

Cell therapy

Impact of the Research Program for SUS (PPSUS) in reducing regional disparities in cell therapy research funding

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INTRODUCTION: In Brazil there are large regional disparities in science, technology and innovation and the North, Northeast and Midwest regions have a smaller established scientific capacity and, consequently, lower financial contribution to research. In order to reduce such disparities, the Department of Science and Technology of the Science Technology and Strategic Inputs Secretariat of the Ministry of Health was created in 2004, the PPSUS, which has a shared management, with decentralization of sources and of decision-making power between federal and state government agencies. OBJECTIVE: To describe the panorama of research funding in cell therapy (CT) by Decit/SCTIE/MS in centralized funding modalities (Fomento Nacional - which announces edicts of broad national competition) and decentralized (PPSUS - which announces state edicts) between 2004 and 2015, and to evaluate the impact of the decentralized development strategy on the promotion of reducing regional disparities in CT. METHODS: The data (number of researchers and the number and value of the funded research) were extracted from the Pesquisa Saúde do Decit/SCTIE/MS (http://www.pesquisasaude.saude.gov.br) database and stratified into 2 geographical axes (South/Southeast SS and North/Northeast/Midwest NNM). To perform the association analysis between funding modality and number of funded projects (chi-square test - X^2), the data were expressed as a percentage. RESULTS: PPSUS funded 35 studies in CT, totaling R$ 4.5 million, comprising 31 researchers. It can be observed that the minority of financial resources (R$ 1 million, 22%), projects (9 projects, 26%) and researchers included (8 researchers, 26%) are located in the NNM axis. Similar pattern is observed for the of National Funding modality, which funded 167 studies in CT, totaling R$ 97.2 million including 168 researchers. Of these, the minority of financial resources (R$ 5.7 million, 6%), projects (14 projects, 8%) and researchers included (14 researchers, 8%) are located in the NNM axis. Despite the similar pattern, it was observed the existence of association between the type of funding and the geographical axis, indicating that the PPSUS supports more CT research, in terms of percentage, in the NNC axis than the National Funding modality (X^2 = 10.97). DISCUSSION AND CONCLUSION: The decentralization of research funding in CT by PPSUS has contributed to the reduction of regional disparities, as this funding modality funded, in terms of percentage, more studies in areas with lower established scientific capacity (NNM axis) than the Nacional Funding modality. However, the funding actions at the federal and state levels in the NNM axis cannot effectively impact on the reduction of these inequalities. Thus, decentralized funding strategies, such as PPSUS, are necessary to strengthen scientific capacity in CT in NNM regions.

Keywords: funding; Decit/SCTIE/MS; cell therapy

P-209

Cell therapy

Evaluation of murine macrophage behavior in cellulosic membranes associated with mesenchymal stem cells.

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INTRODUCTION: Tissue repair constitutes a series of orchestrated and complex events comprising regeneration and healing. Tissue engineering has focused on treatment options aiming to replace or regenerate, structurally and functionally, the injured tissues through the use of biomaterials, and in this scenario, polymers associated with mesenchymal stem cells has gained attention due to their efficiency in the regeneration of periosteum ligaments and because it is an auxiliary procedure in bone defect reconstruction. The resolution of the inflammatory response and progression of wound healing coincide with the differentiation of monocytes into macrophages, which are responsible for damage and premature degradation of the implant through their phagocytic capacity and enzyme secretion. In this context, this study aims to evaluate *in vitro* the mammalian macrophage behavior in cellulosic membranes associated with bone-marrow mesenchymal stem cells. MATERIAL AND METHODS: In order to evaluate the desired parameters, firstly the cellulosic membranes were grown in a 24-well plate with 1x105 bone marrow mesenchymal stem cells from rabbits for 24 hours, and after this period, murine peritoneal macrophages were added, and the plate was incubated again for 48 hours at 37 °C and 5% CO2. For the evaluation of phagocytic capacity after 48 h of incubation, 100 μL of stained zymosan solution was added and incubated for 30 min under the same conditions. Then, 1000 μL of Baker's fixative was added and, after 30 min., the supernatant was removed, 1000 μL of extraction solution was added and the reading was performed at 550 nm. To observe the induction of nitric oxide synthesis, after 24 hours of incubation, 25 μL of supernatants was transferred from the cell culture into a 96-well plate, and the nitrite assay was performed using the Griess reagent at 550 nm. RESULTS AND DISCUSSION: Our study showed that the cellulosic membrane associated with stem cells induced a subtle increase in phagocytic activity, but the result was not statistically significant, whereas regarding the production of nitric oxide, there was a nonsignificant increase in nitrite levels in the supernatant of the macrophage culture, which is a stable metabolite of nitric oxide radicals, known to be produced by activated macrophages. Studies show that low levels of nitrite oxide have an anti-inflammatory effect, and based on this fact, it is suggested that the presence of the membrane triggers a mild inflammatory response, considered beneficial. CONCLUSION: The cellulosic membrane associated with mesenchymal stem cells from bone marrow did not enhance macrophage activation capacity *in vitro*.

Keywords: Oxidative Stress, phagocytosis, stem cells, immunomodulation

P-210

Cell therapy

Analysis of the therapeutic potential of the human recombinant RSPO1 protein in small intestine regeneration in an animal model.

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R-Spondins (RSPO) are proteins that induce the WNT pathway, playing a pivotal and diversified role in cell proliferation, differentiation, migration and death during embryogenesis and in the adult individual. The critical role of RSPO1 for maintenance of small intestine crypt stem cells niche and its mitogenic activity in intestinal stem cells offer several therapeutic opportunities. We aimed to generate an overproduction of cell clones of the recombinant human RSPO1 (rhRSPO1) in CHO-dhfr-/- and HEK293 cells to obtain a purified and biologically active protein to be used in intestinal regeneration, individually or in combination with other recombinant peptide growth factors (VEGFs and/or PDGF-BB), to be tested in culture of murine intestinal organoid units using a Tissue Engineered Small Intestine (TESI) model in NOD/SCID receptor mice. The coding sequence of hRSPO1 was synthesized and subcloned into the pNU1 mammalian expression vector. CHO-dhfr-/- and HEK293 cells were stably transfected with this construct and underwent a gene amplification process by MTX and clone selection, respectively. Dot blot and ELISA assays were used to evaluate the hrRSPO1 expression levels. rhRSPO1 was produced in both expression systems at detectable levels and showed *in vitro* biological activity. A new protein purification protocol was established and RSPO1 was tested in the TESI model. Expression of a biologically active rhRSPO1 in mammalian expression systems allows the use of this protein in Tissue Engineering.

Keywords: Tissue Repair, Short Bowel Syndrome, Mammalian cell expression, Peptide Growth Factors, Intestinal Organoid Units

P-211

Cell therapy

Expansion and biointegration of bone marrow progenitor mesenchymal cells to bacterial cellulose membrane

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With the growing role of biotechnology, there are alternative biomaterials that become promising in regenerative Medicine. Studies of interactions between cells and substrates for tissue engineering are crucial for the success in biological implants. In this study, we evaluated the expansion and biointegration of mesenchymal stem cells from rabbit bone marrow associated with bacterial cellulose membrane (BCM). The bone marrow aspirates were diluted in PBS. The resulting content was filtered and deposited in a tube containing Falcom Ficoll® and centrifuged at 2000rpm for 25 min at 20 °C. The halo rich in mononuclear cells was aspirated and diluted in PBS with 1% antibiotic for washing and re-centrifuged. Bone marrow samples were resuspended in D-MEM Low Glucose supplemented growth medium. Samples were seeded in cell-culture plate wells at a concentration of 106 cells/well, kept in an incubator at 37 °C in 5% CO2 and 95% humidity. Primary cultures were replicated to reach 80% confluency and plated with twice the original area. For the osteogenic cell differentiation assay, 6x104 cells were seeded on a 24-well plate and stained with Alizarin Red. In chondrogenic differentiation, 3x105 cells were seeded on a 96-well plate and the analysis was performed using histological sections and Alcian Blue. To study the expansion and biointegration of mesenchymal stem cells to the bacterial cellulose membrane, we used the concentration of 2x104 cells on a 12-well plate, culturing them at three different times (1, 7 and 14 days). For analysis with Scanning Electron Microscopy (SEM), the samples were fixed with 3% glutaraldehyde. After that, they were washed once with PBS and subsequently submitted to dehydration through slow water exchange using a series of ethanol dilutions (30%, 55%, 70%, 88%, 96% and absolute) for 20 minutes at each concentration, and left to dry at room temperature. Subsequently, the samples were metallized and assessed by SEM. At the end of the experiment, it was observed that the bone marrow stem cells, in the first 24 hours, were anchored in BCM, and the analysis on day 7 of culture showed cytoplasmic spreading, and after 14 days the cells were completely incorporated to the biomaterial. Tissue engineering is being redrawn through promising studies that show great potential to create environments capable of forming functional tissues; cell expansion and integration into biomaterials depend very much on the quality and suitability of the biomaterial surface. In this context, the BCM showed to be a biomaterial that allowed cell growth and biointegration of progenitor cells from bone marrow, which can become a promising biomaterial in tissue engineering and regenerative medicine.

Keywords: Tissue engineering, cellulose, cell adhesion.

P-212

Cell therapy

Decellularization of murine pancreas and evaluation of the degradation of the extracellular matrix scaffold over time

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Introduction: The extracellular matrix (ECM) consists of a complex tissue stabilization network. Recent studies show that the ECM also plays a key role in the migration and phenotypic expression of resident cells, and influences the proliferation and differentiation through signal transduction. Such information has opened possibilities for several studies on the production of decellularized biological scaffolds. Our group has been studying the use of decellularized pancreatic scaffolds, in order to use them in rebuilding a bioartifical pancreas, as an alternative treatment for patients with Type I Diabetes Mellitus. Objectives: Therefore, the aim of this study is to assess by how long it is possible to keep these decellularized pancreatic matrices in the laboratory, in good conditions of preservation until the completion of the pancreatic reconstruction process. Methods: After extracting the murine pancreas (n = 12), the organs were decellularized by detergent perfusion through a protocol developed in the laboratory. After the decellularization step, pancreatic matrices are characterized and, then, preserved in three different manners, using: a) saline-phosphate buffer - without calcium and without magnesium (PBSA) at 4°C; b) PBSA supplemented with antibiotics and antimycotics at 4°C; and c) RPMI 1640 medium solution containing 10% dimethyl sulfoxide (DMSO) and 10% fetal bovine serum (FBS) at -80°C. Samples are removed for analysis after 1, 2, 4, 8, 12 and 16 weeks. Analyses of these samples include: a) evaluation by optical microscopy, using hematoxylin-eosin, Alcian blue and Picrosirius red; b) evaluation by transmission electron microscopy. Results: The murine pancreas were effectively extracted and decellularized, and assessed through histology and DNA quantification using the protocol developed in our laboratory. These matrices were incubated at different preservation conditions and, up to now, the samples corresponding to 1, 2 and 4 weeks were collected for analysis. The analysis showed that during the first four weeks, the pancreatic decellularized matrices showed no significant difference between the different conditions of preservation. Discussion: During the one-month period we found no differences in the methods used for the preservation of decellularized murine pancreatic matrices. In the literature, there are no studies evaluating the integrity of decellularized pancreatic extracellular matrix in a time-dependent manner. An assessment of the preservation of the pancreatic scaffold as a function of time is of utmost importance, since the knowledge of the best preservation condition and the time of the maintenance limit of this material in the laboratory will allow the increasing improvement of the recellularization technologies of such scaffolds for generate a partially or fully functional organ.

Keywords: Decellularization, Bioengineering, pancreas, extracellular matrix, type 1 diabetes

P-213

Cell therapy

Comparative preclinical study of platelet-rich plasma (PRP) use and a biomaterial, associated with human skin-derived mesenchymal stem cells (SMSCs) in burn healing process

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In order to provide viability for the tissue regeneration in burns, studies have been developed with the use of biomaterials, particularly with the dermal regeneration matrix (DRM), associated to other components of tissue engineering. Within this perspective, the Platelet-Rich Plasma (PRP) and skin-derived mesenchymal stem cells (SMSCs) emerge as a viable alternative to treating these injuries, and the combination of these items could provide an increase in the reduction of hospital length of stay in burned individuals, as well as better scar tissue. The aim of this study is to evaluate the association of tissue engineering products (SMSC + PRP + DRM) in burn wound healing, regarding time, in a preclinical study. Methodology: Inbred mice strain C57BL/6 were used and the population consisted of 36 animals, which were submitted by surgical intervention, to an injury corresponding to a full burn and received treatments with SMSC, PRP and DRM, divided into three groups of four different interventions in each group. We performed a daily macroscopic evaluation of the injury in the established groups, where the animals were sedated in an isoflurane chamber and the lesion circumference was measured with the use of calipers to determine two values expressed by crosses of the lesion diameter. According to the groups (1, 2 and 3,) on days 03, 07 and 18 after the lesion, the animals were euthanized and skin biopsies were obtained for future histological, immunohistochemistry and molecular evaluations. Data were tabulated in Microsoft Excel and analyzed through statistical software using ANOVA and regression model. Results: In the morphometric analysis of the lesion there was a decrease in the diameter of the lesions, according to time, in all studied groups, and the group treated with DRM + SMSC showe better results regarding the reduction of these diameters. Statistical significance was observed between the groups in the reduction of the lesion diameters using $p < 0.05$. Discussion: The scientific literature corroborates the results obtained using SMSC in reducing the diameter of the lesions, and when using PRP in combination with SMSC, there is still no standardization and consensus regarding the amount and how to prepare it for use. Conclusion: In the study, the group treated with DRM + SMSC had a better performance in reducing the diameter of the lesions.

Keywords: Mesenchymal Stem Cell, Healing, Cell Therapy

P-214

Cell therapy

Evaluation of in vitro cytotoxicity of the bacterial cellulose membrane to use with mesenchymal stem cells

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INTRODUCTION: Bioengineering is a science that includes concepts and techniques that go beyond the limits of cell biology, reaching the foundations of engineering and materials science. This area investigates the use of biocompatible materials that act as matrices for cell growth, called scaffolds. Equivalently, the bacterial cellulose (BC) is seen as a promising biopolymer, and stands out as one of the most prosperous biomaterials for the health area. However, it is necessary to investigate the biocompatibility of this product with the host´s cells, aiming to establish possible adverse effects inherent to the use of membrane in therapies. In this context, the study aims to investigate the potential toxic effects of a bacterial cellulose membrane on mesenchymal stem cells and mononuclear cells of mammals. MATERIAL AND METHODS: For the assessment of the cytotoxicity, we used the methylthiazolyldiphenyl-tetrazolium bromide (MTT) method (Sigma-Aldrich, St. Louis, USA). For the cytotoxicity parameter in mesenchymal stem cells, we used bone marrow mesenchymal stem cells from mammals. The cells were cultured at 104 cells in the cellulosic membrane on a 24-well plate with 1000 µL of supplemented Low Glucose DMEM and the cells were incubated for 7 days at 37 °C and 5% CO2. As for the assessment of cytotoxicity on nuclear mammalian cells, on a 24-well plate, we added about 2 x 105 macrophages per well with the bacterial cellulose membrane and incubated for 48 hours at 37 °C and 5% CO2 in RPMI-1640 medium. After the aforementioned incubation periods, MTT was added and incubated for 4 hours. Finally, the reading was performed at 550 nm in a Biotek microplate reader (model ELx800) for both tests. RESULTS AND DISCUSSION: During the experiment we did not detect morphological changes in the cell shapes under an optical microscope, when compared to cells found in control. MTT is a gold-yellow tetrazolium salt and soluble in water which, when incubated with cells in full metabolic activity, is reduced to solubilized crystals of DMSO. Thus, cell viability is directly proportional to the color intensity. Our results showed that there were no significant differences in cell viability, thus the cellulosic membrane did not exert toxic effects on bone marrow mesenchymal stem cells and similarly did not show toxic effects on the immune system cells. CONCLUSION: The cellulosic membrane showed no toxic effect on mammalian cells, and can be safely used in therapeutic applications.

Keywords: Polymers, Biocompatibility, Therapies, Stem Cells

P-215

Cell therapy

Umbilical Cord and Placental Blood Bank - UCPBB. Data on the collections performed in private and public hospital networks. Centro de Hematologia e Hemoterapia do Ceará - HEMOCE

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INTRODUCTION: We started our activities in April 2012. The UCPBB is a public bank that aims to collect voluntarily donated umbilical cord and placental blood (UCPB). The UCPB is a source of hematopoietic stem cells (HSC), as well as the bone marrow. The HSC play an important role in bone marrow reconstitution after myeloablative chemotherapy. Thus, the UCPB has become an alternative source of HSC to bone marrow in unrelated allogeneic transplantation. OBJECTIVE: To analyze the number of units collected in public and private maternity wards, as well as the profile of the mothers who donated UCPB. MATERIALS AND METHODS Analysis of the data obtained from UCPB donors and from the collected and processed units in the UCPBB -Fortaleza/HEMOCE. RESULT: We analyzed the profiles of 403 mothers who donated UCPB, in seven different hospitals, two Public Hospitals and five from the private network. In the analyzed period, 183 UCPB units were collected in the private network and 220 in public hospitals. Of the 403 units that comprise this study and which were separately analyzed, we obtained the following results: Private Network, 82.5% of cryopreserved bags and 17.5% discarded; in the Public Network, 61.8% of cryopreserved and 38.2% discarded for several reasons. The age range of mothers who donated in the private network was 54.6% between 26 and 33 years old, 26.3% between 18 and 25 years and 19.1% between 34 and 41 years. In the public network, 51% were between 18 and 25 years, 37% between 26 and 33 years, 11% between 34 and 41 years and 1% were 42 years old or more. Regarding the number of pregnancies, in 51.4% and 59.1% of the analyzed mothers that was not their first pregnancy in the Private Network and Public Network, respectively. Regarding miscarriages abortion, 19.5% of the mothers had miscarriages in the public hospital network and 12.6% in private hospitals. Regarding the type of delivery at the time of collection, cesarean sections prevailed in private hospitals and normal delivery in the public network. CONCLUSION: According to the results, we can analyze the collected units yield. We found a better use of the bags collected in the private network, where the number of discarded bags was lower compared to the public network. According to the donors' profile, the age group that prevailed in the private network was 26 to 33 years and the in public network, from 18 to 25 years. When analyzing the number of mothers at the first pregnancy, the higher number was observed in the private network, and regarding mothers who reported miscarriages, there was a higher number of mothers/donors from the public hospital network.

Keywords: mothers who donated UCPB

AUTHORS INDEX

B

C

D

E

F

K

L

M

N

O

P

R

S

T

U

V

W

Y

Z