



Journal of Nursing

Revista de Enfermagem

UFPE On Line

ISSN: 1981-8963

ORIGINAL ARTICLE

ADVERSE REACTIONS RELATED TO HEMATOPOIETIC STEM CELL INFUSION REAÇÕES ADVERSAS RELACIONADAS À INFUSÃO DE CÉLULAS TRONCO HEMATOPOÉTICAS REACCIONES ADVERSAS RELACIONADOS LA INFUSIÓN DE CÉLULAS MADRES HEMATOPOYÉTICAS

Natália Costa Bezerra Freire¹, Andrea Bezerra Rodrigues², Paulo César de Almeida³, Liduina de Souza Costa⁴,
Fernando Barroso Duarte⁵

ABSTRACT

Objective: to identify adverse reactions related to hematopoietic stem cell infusion. **Method:** a descriptive exploratory, level II, retrospective study with a quantitative approach, carried out in the BMT unit of the Walter Cantídio University Hospital (HUWC) from August 2008 to July 2012. The research project has been approved by the Research Ethics Committee under Protocol 049.07.12. **Results** the average age was 42 years and the majority (73.3%) were men. 83.3% of the patient had some sign or symptom during infusion of CTH. On the correlations between adverse reactions and gender ($p=0.705$), age ($p=0.830$), storage time ($p=0.299$), conditioning regimen ($p=0.616$) there was no statistically significant correlation. The most common reactions were respiratory (26.4%) and cardiovascular problems (29.5). **Conclusion:** most patients presented at least one adverse effect, with an equal percentage of occurrence of adverse reaction in the DMSO group at 5% and 10%. **Descriptors:** Hematopoietic Stem cell transplantation; Dimethyl Sulfoxide; Toxicity

RESUMO

Objetivo: identificar as reações adversas relacionadas à infusão de células tronco hematopoéticas. **Método:** descritivo exploratório, nível II, retrospectivo e com abordagem quantitativa, realizado na Unidade de TMO do Hospital Universitário Walter Cantídio (HUWC) entre agosto de 2008 a julho de 2012. O projeto de pesquisa foi aprovado pelo Comitê de Ética em Pesquisa, protocolo 049.07.12. **Resultados:** a idade média foi de 42 anos sendo a maioria (73,3%) homens. 83,3% dos pacientes apresentaram algum sinal ou sintoma durante a infusão de CTH. Nas correlações entre reações adversas e gênero ($p=0,705$), idade ($p=0,830$), tempo de estocagem ($p=0,299$), regime de condicionamento ($p=0,616$) não houve correlação estatisticamente significativa. As reações mais comuns foram as respiratórias (26,4%) e cardiovasculares (29,5). **Conclusão:** a maioria dos pacientes apresentou pelo menos um efeito adverso, com igual percentual de ocorrência de reação adversa no grupo de DMSO a 5% e a 10%. **Descritores:** Transplante de Células Tronco Hematopoéticas; Dimetil Sulfóxido; Toxicidade.

RESUMEN

Objetivo: identificar reacciones adversas relacionadas con la infusión de células madre hematopoyéticas. **Método:** descriptivo exploratorio, nivel II, enfoque retrospectivo y cuantitativo, realizado en la Unidad TMO Hospital Universitario Walter Cantídio (HUWC) entre agosto de 2008 y julio de 2012. El proyecto de investigación fue aprobado por el Comité de Ética de la Investigación, protocolo 049.07.12. **Resultados:** la edad promedio fue de 42 años y la mayoría (73,3%) hombres. 83,3% de los pacientes mostró signos o síntomas durante la infusión de HMC. Las correlaciones entre las reacciones adversas y de género ($p = 0,705$), la edad ($p = 0,830$), el tiempo de almacenamiento ($p = 0,299$), régimen de acondicionamiento ($p = 0,616$) no hubo correlación estadísticamente significativa. Las reacciones más frecuentes fueron las respiratorias (26,4%) y cardiovascular (29,5). **Conclusão:** la mayoría los pacientes tenían al menos un efecto adverso, con igual porcentaje de aparición de reacciones adversas en 5% grupo DMSO y 10%. **Descriptores:** El trasplante de Células Madre Hematopoyéticas; Sulfóxido de Dimetilo; Toxicidad.

¹Resident Nurse specialist in Onco-Hematology, Federal University of Ceara-UFC. Fortaleza (CE), Brazil. Email: natalia.costa.b@hotmail.com; ²Nurse, Nursing Specialist, PhD in nursing, Federal University of Ceara-UFC. Fortaleza (CE), Brazil. Email: andreabrodrigues@gmail.com; ³Statistician, Master Professor in Biostatistics, PhD in Public Health, State University of Ceará / UECE. Fortaleza (CE), Brazil. Email: pc49almeida@gmail.com; ⁴Nurse, Specialist in Oncology, Nursing Coordinator, Bone Marrow Transplant Unit of HUWC. Fortaleza (CE), Brazil. Email: costalidu@yahoo.com.br; ⁵Hematologist Doctor, Head of Bone Marrow Transplant Unit at HUWC. Fortaleza (CE), Brazil. Email: nutriquimio@uol.com.br

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is the intravenous infusion of hematopoietic stem cells (HSC), which can come from bone marrow, peripheral blood or umbilical cord, in order to restore hematopoiesis in patients with an injured spinal cord function. Regarding its modality, HSCT can be classified as autologous, allogeneic or syngeneic. Autologous transplantation uses the patient's own cells previously collected, stored and, after the infusion of the chemotherapy regimen, infused. In allogeneic transplantation, the patient receives HSC from a donor family (related or unrelated), or a donor who comes from a bone marrow bank (unrelated or unrelated) so that there is a compatibility in the human leukocyte antigen (HLA). The syngeneic transplant occurs when the patient and the donor are twin brothers identical twins.^{1,2}

The HSC is defined as a cell with great capacity for self-renewal and proliferative potential, which enables their differentiation into progenitor cells of all the bloodlines and the hematopoietic reconstitution of the population. The HSC phenotype includes the expression of a transmembrane glycoprophosphoprotein called CD34+. In basal conditions, only a small number of CD34+ cells are released in the peripheral blood. In autologous HSCT, the patient performs first recruitment of HSC CD34+ bone marrow environment for the peripheral blood, this process called mobilization. The mobilization occurs through the use of granulocyte growth colony stimulating factor (G-CSF), associated or not with chemotherapy, with the aim of increasing the number of progenitor cells in the peripheral blood.³

The next step consists in collecting these cells, which is accomplished through the Apheresis process, usually performed on consecutive days, after the mobilization. So that spinal cord grafting occurs successfully there is a minimum consensus count of 2.0×10^6 CD34+ cells per kilogram of weight.⁴

The HSC are then forwarded to the field of cryobiology to be preserved. To carry out this procedure cryoprotective agents are used that capable of inhibiting the formation of intra and extracellular crystals and therefore cell death. The standard cryoprotectant is dimethylsulfoxide (DMSO) in order to reduce the formation of intracellular ice and osmotic stress during the freezing of living cells. The DMSO is used in concentrations between 5%

and 10% and can be combined with saline, albumin and other cryoprotectant solutions.⁵

Once prepared, the HSC is stocked in the freezer at negative 80°C. The patient then is subjected to the conditioning regimen, which includes high doses of chemotherapy, with the goal of inducing the medullar aplasia for the infusion of HSC.^{6,7}

The HSC are thawed on the edge of the bed, in water bath to a temperature between 37-40 degrees C and immediately infused through via a unique central venous catheter. During the infusion of HSC adverse reactions may occur, generally mild and short-lived.⁶

The occurrence of adverse reactions during the infusion has been traditionally associated with the amount of DMSO infused, as cryoprotectant induces histamine release and bradykinin. The most common reactions are: nausea, vomiting, and abdominal pain, occurring in 50% of patients, as well as hypotension, bradycardia, and headache. More rarely occur severe reactions, involving the cardiovascular system and the respiratory system, such as hypertension, tachycardia, arrhythmias, respiratory failure, diffuse alveolar hemorrhage and neurological complications.^{5,8,9}

Thus, it is imperative that the rigorous and continuous monitoring of the patient, as well as early identification of adverse reactions by the healthcare team. In this highly specialized and complex treatment scenario, it is necessary that the HSCT nursing staff is scientific and technically skilled to meet the possible complications that can occur at every stage of the transplant in order to intervene early, minimizing the adverse effects and restore the patient's medical conditions.¹⁰

OBJECTIVES

- To identify adverse reactions related to hematopoietic stem cell infusion.
- Correlate these adverse reactions during the hematopoietic stem cell infusion with the time interval between the collection of the HSC and its infusion, counting the CD34+ cells present in the infused bags, infusion time of HSC, the volume of HSC case, the amount and concentration of DMSO present in the HSC bags, the age and sex of the patient and the type of conditioning regimen carried out.

METHOD

Exploratory, retrospective descriptive study and quantitative approach, performed in the Bone Marrow Transplant Unit of the Walter Cantídio University Hospital, Fortaleza, CE.

The unit has two beds and has performed autologous HSCT since August 2008.

The service that performs the preparation of the HSC infusion is the Cryobiology Service Center of Hematology of Ceará (Hemoce). Initially, the addition of the cryopreservation Protocol 58ml albumin 20% and the 26,4ml of DMSO at 99% was adopted as at a 500 ml of stock solution of non-activated cryopreservation, consisting of electrolytes and glucose. After mixing, the solution becomes activated, being increased in proportion of 1: 1, the HSC, resulting in a final concentration of DMSO 5%.

From October 19, 2011, by the difficulty of acquiring the cryopreservation solution, Hemoce began to adopt a new protocol for the cryopreservation of HSC. In this new process, we use 40% autologous plasma, 40% to 6% hydroxyethyl starch and 20% to 99% DMSO as cryoprotectant solution added at a ratio of 1: 1, to the HSC bag, resulting in a final concentration of DMSO 10%.

The different processes of cryopreservation and the different concentrations of DMSO resulted in two groups of patients undergoing the HSCT were analyzed separately.

The study population was composed of 30 records of patients who were undergoing HSCT at the above-mentioned unit that had their CTH preserved in the service of the Hemoce, in the period of August 2008 and July 2012. The medical records of patients undergoing infusion of HSC bags with different percentages of DMSO concentration were excluded from medical records of patients who had their hematopoietic stem cells cryopreserved in another center of cryopreservation and records no records of adverse reactions.

This project was approved by the Ethics Committee of the Walter Cantídio University Hospital Research (HUWC) under protocol number 049.07.12.

In each patient's medical information was analyzed, both in relation to clinical evolution and evolution of nursing, and annotations of reactions during the cell infusion.

This study considered that the occurrence of the adverse effect expression of at least one sign or symptom in any of the infused HSC bags.

The statistical analysis was used average, standard deviation and the Mann Whitney likelihood ratio. For the inferential analysis $p < 0.05$ was set as statistically significant. The data were processed in the EPI-INFO software.

RESULTS

The average age was 42 years, ranging from 17 to 65 years, with the majority (73.3%) of male gender. The most frequent diagnoses were: multiple myeloma (MM) (50%) and Hodgkin's Lymphoma (HL) (26.7%), non-Hodgkin's Lymphoma (NHL) (20%) and seminoma (3.3). As for the conditioning regimen, 40% carried out the Melphalan Protocol 200 mg/m², 26.7% BEAC Protocol, 10% the BEAM, R-BEAM 10%, 6.7% Melphalan 140 mg/m², Melphalan 3.3% 100 mg/m² and 3.3% used Carboplatin and Etoposide.

83.3% presented adverse reactions during the infusion of HSC. As for the storage time of HSC, 33.3% of them were stored between a month and a half to three months, 30% between 15 days to a month and a half, 26.7% between four to twelve months and 10% between three to four months. Regarding the percentage of DMSO used in the cryopreservation process, 63.3% had 5% of the cryoprotectant in HSC and 36.7% showed 10% concentration.

The group that had the least amount of DMSO (DMSO 5%) to have received an average of 0.06 g/kg of DMSO. They were infused on average 4.63 bags of HSC which had an average of 1.85×10^6 CD34+ cells. The group with concentration of DMSO 10%, the average concentration of the cryoprotectant per kilogram of patient weight is 0.15 g / kg. Having been infused an average of 3.81 HSC bags, which contained an average of 2.2×10^6 CD34+ cells.

When we analyzed the occurrence of reactions per patient in the group that had received HSC bag with DMSO 5% at a percentage of 89.5%. In the Group of patients that received HSC with DMSO 10%, the percentage found was 72.7%.

Considering that each patient received on average 4.3 bags, it has been estimated adverse reactions not only for patients, but also per bag of infused HSC.

If we consider the manifestation of reactions not more per patient ($n=30$), but each bag infused ($n = 131$), the percentage found adverse effects for the whole of HSC bags infused is 56.5%

When examining the prevalence as the DMSO concentration is that, of the total number of bags with the DMSO 5% infused, 57.5% led to some adverse reaction and the Group of DMSO 10% the value found was 54.5%, statistically equal values ($p= 0.75$) (table 1).

Table 1. The occurrence of adverse reactions by HSC bag infused according to the percentage of DMSO.

Reactions	DMSO 5%		DMSO 10%		Total	
	N	%	N	%	N	%
Yes	50	57.5	24	54.5	74	56.5
No	37	42.5	20	45.5	57	43.5
Total of bags infused	87	100	44	100	131	100

On the correlations between adverse reactions and the variables, gender, age, time of storage, conditioning regime there was no statistically significant correlation, namely: gender ($p=0.705$), age ($p=0.830$), storage time ($p=0.299$), conditioning regimen ($p=616$).

As each infused bag can cause more of an adverse reaction, for better analysis, we decided to combine the reactions for organic systems and as the percentage of DMSO present in the bag.

In both groups (DMSO 5% and 10%) non-occurrence of the reaction is presented as the majority (42.5% and 45.5%, respectively) (Tables 2 and 3). The Group of DMSO 5%

regarding the affected system, respiratory was shown as most prevalent (26.4%) (Table 2). In the group that received bags with DMSO 10%, the manifestations on the cardiovascular system were more prevalent (29.5 percent) (Table 3).

In the gastrointestinal system symptoms were abdominal pain, nausea and vomiting. In the respiratory tract were coughing and throat irritation. In the cardiovascular system patients had bradycardia, tachycardia, hypotension, hypertension and chest pain. Regarding the neurological symptoms there were eye irritation, chills, rash on the face, cold, shivering and drowsiness.

Table 2. Distribution of the number of adverse reactions by HSC bags with DMSO 5% concentration.

Number of reactions	DMSO 5%	
	n	%
Respiratory System	23	26.4
Cardiovascular System	19	21.8
Gastrointestinal System	16	18.4
Neurological System	08	9.2

Note: There is the possibility of more than one reaction per bag.

Table 3. Distribution of the number of adverse reactions by HSC bags with DMSO 5% concentration.

Number of reactions	DMSO 10%	
	n	%
Cardiovascular System	13	29.5
Gastrointestinal System	12	27.3
Respiratory System	09	20.5
Neurological System	04	9

Note: There is the possibility of more than one reaction per bag.

In the group that received HSC bags of DMSO 5% concentration when conducting correlation tests between the reactions systems and not any reaction with the amount of DMSO in grams per kilogram of body weight and the volume infused by time in minutes, is not statistically significant.

However, when evaluating the correlation of bags infused with DMSO 5% with no adverse reactions and the CD34+ cell count, there was a statistical significance ($p=0.036$).

When you have the volume infused per pound of weight of the patient, showing statistical significance with the occurrence of reactions in the gastrointestinal system ($p=0.002$) and non-occurrence of reactions ($p=0.002$) (table 4).

Table 4. Correlation between adverse reactions in patients receiving DMSO 5%, counting CD34+, the volume per kilogram of weight and volume per time.

Number of reactions	DMSO(g/kg)	Cont. CD34+	Vol/kg	Vol/time
No reactions (n=37)	0.099	0.036	0.002	0.747
Respiratory system (n=23)	0.659	0.206	0.074	0.094
Cardiovascular System (n=19)	0.139	0.064	0.154	0.073
Gastrointestinal system (n=16)	0.018	0.112	0.002	0.312
Neurological system (n=8)	0.224	0.806	0.918	0.231

Regarding the group with concentration of DMSO 10%, the only system that was statistically significant was the respiratory system with variable amount of DMSO per kilogram body weight (p=0.029) and the volume of stock per kilogram of weight patient (ml / kg) (p=0.029) (Table 5).

Table 5. Correlation between adverse reactions in patients receiving DMSO 10%, counting CD34+, the volume per kilogram of weight and volume per time.

Reactions	DMSO(g/kg)	Cont. CD34+	Vol/kg	Vol/time
No reactions (n=20)	0.507	0.077	0.507	0.741
Cardiovascular System (n=13)	0.546	0.205	0.546	0.145
Gastrointestinal system (n=12)	0.293	0.757	0.293	0.124
Respiratory system (n=9)	0.029	0.946	0.029	0.598
Neurological system (n=4)	0.389	0.056	0.389	0.252

*g= gram ∞ kg=kilogram £ vol= volume

DISCUSSION

DMSO has been used extensively as a cryoprotectant for freezing the HSC by reducing intracellular ice formation and osmotic stress during freezing.¹¹

The infusion of thawed HSC has been related to reversible generally mild side effects that include gastrointestinal effects such as nausea, vomiting and abdominal pain,¹² respiratory cough and dyspnea as, cardiovascular as hypotension, hypertension and bradycardia and neurological and dermatological effects such as flushing of the skin, rash.¹¹ These effects, in general, are resolved in a few minutes or hours, having rarely fatal repercussions.¹² An incidence of adverse reactions is describe between the 13.5% being only 0.4% 67.3 the percentage described for serious damage.¹⁴ The percentage of adverse events per patient from the infusion of HSC this study was quite superior to that described in other reviews (83.3%).

The amount and the percentage of DMSO showed themselves as factors that strongly influence the occurrence of reactions¹¹there is a description of lower concentration of cryoprotectant DMSO, the 5%, would lead to a lower incidence of adverse effects¹⁵and a reduction of the DMSO would entail in a smaller overall toxicity.¹⁶ In this study a higher occurrence was obtained of 89.5% reaction in the group that received bags with DMSO 5% and 72.7% in the group that received the DMSO 10%, diverging from the data described in the literature. Since there is a larger number of patients in the Group of DMSO 5% (n=19) than in DMSO 10% group (n=11).

Furthermore, the average infused into the bags of the DMSO 5% group is higher than DMSO 10% group (4.63 and 3.81 respectively).

However, analyzing the data, with the number of HSC sample units infused, has been in the Group of DMSO 5%, 57.5% of the total number of bags led to some clinical manifestation, when compared to 54.7% DMSO 10% group, statistically they are equal values (p=0.75). There is no difference between the manifestation of reactions between the DMSO 5% group and the DMSO 10% group.

In the study the stock volume ratio per kilogram of patient weight was shown to be strongly related to the occurrence of reactions in the gastrointestinal system and with no occurrence of adverse effects on the DMSO 5% concentration group. Nausea and vomiting are related to vagal response due to the infusion of large volumes of cold liquid.¹³

In the study the lower rate of CD34+ cells showed statistical significance with the non-occurrence of reactions in the DMSO 5% group. A greater number of granulocytes is associated with the manifestation of more adverse effects.^{3,21}

As factors predisposing to adverse reactions some studies describe the genre as one of them, showing that women have more reactions than men,^{17,8} and that the elderly have fewer adverse manifestations.¹⁷As for the infusion time it describes that the slower the infusion, the smaller the percentage of cardiovascular reactions.¹³ These Factors that this study analyzed, but showed no statistically significant correlation. Other studies also showed no correlation between age and the manifestation of adverse effects⁸ as well as the gender.¹¹

Infusion volume is another factor related to adverse effects in some studies,^{11,18,19} should be between 2 to 24 ml per kilogram of weight of the receiver.²⁰ In this research by analyzing the volume infused per kilogram of weight of the receiver has an average of 6.15ml / kg, which was within the margin referred to in the literature.

Other factors involved in the occurrence of reactions, which were not analyzed in this study and are described in the literature are the amount of red blood cells in the product of apheresis,¹¹ free hemoglobin,²¹ and bacterial contamination.¹⁴

Some studies have different prevalence rates when analyzing the main adverse effects. Some have reported gastrointestinal manifestations as the most frequent,^{8,11} others report cardiovascular diseases²² and there are also reports of allergic reactions like rash, facial flushing and bronchospasm.¹⁷

Relate the occurrence of adverse events to release of histamine, products of cell lysis¹⁵ and complement activation.²³

Several strategies to minimize such complications have also been studied, among them the reduction of DMSO for the cryopreservation, washing the cells prior to infusion in order to also reduce the cryoprotectant fractionated infusions.¹³

The registration of clinical manifestations presented by the patient during infusion of HSC becomes paramount to the analysis and understanding the main injuries. Thus the nursing staff can be trained and be prepared to provide a specialized and qualified nursing care to the patient subject to autologous HSCT.

CONCLUSION

In the Group of studied most of the patients (83.3%) presented at least one adverse effect. Organic systems most affected by adverse reactions were the respiratory and cardiovascular. When correlated to occurrence of reactions and the storage time of the purse, the conditioning regime, the age and gender of the patient there was no statistical significance.

However, the quantity in grams of DMSO per kilogram of the patient's weight of the as well as the percentage of DMSO concentration in the HSC revealed statistical significance with gastrointestinal and respiratory reactions with no demonstration of adverse effects.

There was a higher percentage of occurrence of at least one adverse reaction in the DMSO 5% group with respect to the DMSO 10% group when evaluating the patient.

However when analyzing bags infused HSC has a percentage of 57.5% in the DMSO 5% group showing symptoms and 54.5% in the DMSO 10% group percentage prevalence with no statistical difference.

REFERENCES

1. Castro Jr CG, Gregianin LJ, Brunetto JL. Transplante de medula óssea e transplante de sangue de cordão umbilical em pediatria. *Jornal de Pediatria* [Internet]. 2001 [cited 2013 May 31]; 77 (5):345-60. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0021-75572001000500004
2. Okane ESH, Machado LN. Introdução/Histórico. In: MACHADO LN et al. *Transplante de Medula Óssea - Abordagem Multidisciplinar*. São Paulo: Lemar; 2009. p.23-29.
3. Souza CA, Marques Júnior JFC, Bouzas LFS. Fontes, Mobilização e Coleta de Células-Tronco Hematopoéticas. In: Voltarelli JC. *Transplante de células tronco hematopoética*. São Paulo: Editora Atheneu; 2009. p.565-88.
4. Cantor AB, Lazarus HM, Laport GG. Cellular basis of hematopoiesis and stem cell transplantation. In: Gregory SA, McCrae KR. *American Society of Hematology Self - Assessment Program (ASH-SAP)*, 4 ed.; 2010. p.331-71.
5. Berz D, McCormack EM, Winer ES, Colvin GA, Quesenberry PJ. Cryopreservation of Hematopoietic Stem Cells. *Am J Hematol* [Internet]. 2007 [cited 2013 May 31];82(6):463-72. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2075525/>
6. 6 Santis GC, Prata KL. Criopreservação de células-progenitoras hematopoéticas. *Medicina (Ribeirão Preto)*. 2009; 42(1): 36-47.
7. Machado LN. Papel do Enfermeiro nas Diferentes Fases do TMO. In: Machado LN et al. *Transplante de Medula Óssea - Abordagem Multidisciplinar*. São Paulo: Lemar, 2009. p.59-67.
8. Bojanic I, Cepulic BG, Mazic S, Batinic D, Nemet D, Labar B.. Toxicity related to autologous peripheral blood haematopoietic progenitor cell infusion is associated with number of granulocytes in graft, gender and diagnosis of multiple myeloma. *Vox Sanguinis* [Internet]. 2008 [cited 2013 May 31]; 95:70-75. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18422859>
9. Schroeder T, Fenk R, Saure C, Czibere A, Bruns I, Zohren F et al. The Mexican Way: a feasible approach to avoid DMSO toxicity. *Bone Marrow Transplantation* [Internet]. 2011

[cited 2013 May 31];46:469-71. Available from:

<http://www.nature.com/bmt/journal/v46/n3/full/bmt2010140a.html>.

10. Ortega ETT, Stelmachuk AM, Cristoff C. Assistência de Enfermagem no Transplante de Células-Tronco Hematopoéticas. In: Voltarelli JC. Transplante de células tronco hematopoética. São Paulo: Editora Atheneu; 2009. p.1031-98.

11. Martín-Henao GA, Resano PM, Villegas JM, Manero PP, Sánchez JM, Bosch MP et al. Adverse reactions during transfusion of thawed haematopoietic progenitor cells from apheresis are closely related to the number of granulocyte cells in the leukapheresis product. *Vox Sanguinis* [Internet]. 2010 [cited 2013 May 31];99:267-73. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20840341>.

12. Hayakawa J, Joyal EG, Gildner JF, Washington KN, Phang OA, Uchida N et al. 5% Dimethyl sulfoxide (DMSO) and pentastarch improves cryopreservation of cord blood cells over 10% DMSO. *Transfusion* [Internet]. 2010 [cited 2013 May 31];50(10):2058-66. Available from:

<http://www.ncbi.nlm.nih.gov/pubmed/20492608>.

13. Calmels B, Lemarié C, Esterni B, Malugani C, Charbonnier A, Coso D et al. Occurrence and severity of adverse events after autologous hematopoietic progenitor cell infusion are related to the amount of granulocytes in the apheresis product. *Transfusion* [Internet]. 2007 [cited 2013 May 31];47(7):1268-75. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17581163>

14. Khera N, Jinneman J, Storer BE, Heimfeld S, O'Meara MM, Chauncey TR et al. Limiting the Daily Total Nucleated Cell Dose of Cryopreserved Peripheral Blood Stem Cell Products for Autologous Transplantation Improves Infusion-Related Safety with No Adverse Impact on Hematopoietic Engraftment. *Biol Blood Marrow Transplantation* [Internet]. 2012 [cited 2013 May 31]; 18:220-28. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21703976>.

15. Akkøk CA, Liseth K, Nesthus I, Løkeland T, Tefre K, Bruserud O et al. Autologous peripheral blood progenitor cells cryopreserved with 5 and 10 percent dimethyl sulfoxide alone give comparable hematopoietic reconstitution after transplantation. *Transfusion* [Internet]. 2008 [cited 2013 May 31];48(5):877-83. Available

from:

<http://www.ncbi.nlm.nih.gov/pubmed/18298599>.

16. Chen-Plotkin AS, Vossel KA, Samuels MA, Chen MH. Encephalopathy, stroke, and myocardial infarction with DMSO use in stem cell transplantation. *Neurology* [Internet]. 2007 [cited 2013 May 31];68:859-61. Available from:

<http://www.ncbi.nlm.nih.gov/pubmed/17353475>.

17. Cordoba R et al. The occurrence of adverse events during the infusion of autologous peripheral blood stem cells is related to the number of granulocytes in the leukapheresis product. *Bone Marrow Transplantation* [Internet]. 2007 [cited 2013 May 31]; 40:1063-67. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17906706>.

18. Donmez A, Tombuloglu M, Gungor A, Soyer N, Saydam G, Cagiran S. Clinical side effects during peripheral blood progenitor cell infusion. *Transfusion and apheresis science* [Internet]. 2007 [cited 2013 May 31];36:95-101. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17236813>.

19. Bachier C, Potter J, Potter G, Sugay R, Shaughnessy P, Chan K et al. High White Blood Cell Concentration in the Peripheral Blood Stem Cell Product Can Induce Seizures during Infusion of Autologous Peripheral Blood Stem Cells [Internet]. 2010 [cited 2013 May 31]; 2012: 1-6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22178402>.

20. Saver-Heilborn A, Kadidlo D, McCullough J. Patient care during infusion of hematopoietic progenitor cells. *Transfusion* [Internet]. 2004 [cited 2013 May 31]; 44(6):907-16. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1537-2995.2004.03230.x/abstract>.

21. Foïs E, Desmartin M, Benhamida S, Xavier F, Vanneaux V, Rea D et al. Recovery, viability and clinical toxicity of thawed and washed haematopoietic progenitor cells: analysis of 952 autologous peripheral blood stem cell transplantations. *Bone Marrow Transplantation* [Internet]. 2007 [cited 2013 May 31];40: 831-35. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17724443>.

22. Konuma T, Ooi J, Takahashi S, Tomonari A, Tsukada N, Kobayashi T et al. Cardiovascular toxicity of cryopreserved cord blood cell infusion. *Bone Marrow Transplantation* [Internet]. 2008 [cited 2013

Freire NCB, Rodrigues AB, Almeida PC de et al.

Adverse reactions related to hematopoietic...

May 31]; 41:861-65. Available from:
<http://www.ncbi.nlm.nih.gov/pubmed/18209718>.

23. Benekli M, Anderson B, Wentling D, Bernstein S, Czuczman M, McCarthy P. Severe respiratory depression after dimethylsulphoxide-containing autologous stem cell infusion in a patient with AL amyloidosis. Bone Marrow Transplantation [Internet]. 2000 [cited 2013 May 31];25:1299-301. Available from:
<http://www.ncbi.nlm.nih.gov/pubmed/10871736>

Submission: 2013/08/30

Accepted: 2014/12/20

Publishing: 2015/01/15

Corresponding Address

Natália Costa Bezerra Freire
Especialista em onco-hemtologia
Centro de Ciências da Saúde
Universidade Federal do Ceará
Rua Mozart Pinto, 533
Bairro Monte Castelo
CEP 60325-670 – Fortaleza (CE), Brazil