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Original article

Unrelated hematopoietic stem cell transplantation in the pediatric population: single institution experience

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ABSTRACT

Objective: Hematopoietic stem cell transplantation has been successfully used to treat the pediatric population with malignant and non-malignant hematological diseases. This paper reports the results up to 180 days after the procedure of all unrelated hematopoietic stem cell transplantations in pediatric patients that were performed in one institution.

Methods: A retrospective review was performed of all under 18-year-old patients who received unrelated transplantations between 1995 and 2009. Data were analyzed using the log-rank test, Cox stepwise model, Kaplan–Meier method, Fine and Gray model and Fisher's exact test.

Results: This study included 118 patients (46.8%) who received bone marrow and 134 (53.2%) who received umbilical cord blood transplants. Engraftment occurred in 89.47% of the patients that received bone marrow and 65.83% of those that received umbilical cord blood (p-value < 0.001). Both neutrophil and platelet engraftments were faster in the bone marrow group. Acute graft-versus-host disease occurred in 48.6% of the patients without statistically significant differences between the two groups (p-value = 0.653). Chronic graft-versus-host disease occurred in 9.2% of the patients with a higher incidence in the bone marrow group (p-value = 0.007). Relapse occurred in 24% of the 96 patients with malignant disease with 2-year cumulative incidences of 45% in the bone marrow group and 25% in the umbilical cord blood group (p-value = 0.117). Five-year overall survival was 47%, with an average survival time of 1207 days, and no significant differences between the groups (p-value = 0.4666).

Conclusion: Despite delayed engraftment in the umbilical cord blood group, graft-versus-host disease, relapse and survival were similar in both groups.

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Introduction

Allogeneic hematopoietic stem cell transplantation (HSCT) is an accepted treatment for a number of inherited and acquired hematopoietic diseases in children, especially diseases for which an alternative treatment is not available or no longer effective.[1,2]

Human leukocyte antigen (HLA)-matched sibling donors are available only for around 25% of such children. However, there has been substantial progress over the last four decades in the use of alternative donors, including unrelated volunteer donors.[3–5]

The known advantages of unrelated umbilical cord blood (UCB) over unrelated bone marrow (BM) are well documented and include: significantly faster availability of banked cryopreserved UCB units, no risk to the donor, reduced transmission of viral illnesses such as cytomegalovirus (CMV) and Epstein Barr virus (EBV), tolerance of HLA disparity between the donor and recipient, and reduced risk and severity of acute graft-versus-host disease (GVHD). However, the main problem of using UCB for transplantation is the low number of hematopoietic progenitor cells, which results in increased risk of graft failure, delayed hematopoietic engraftment and delayed immune reconstitution.[6,7]

HLA matching, the use of high-dose chemotherapy and/or radiotherapy and the need of immunosuppressive drugs represent the causes of onset of many complications following HSCT.[8,9]

GVHD is a common complication, mainly in unrelated HSCT or in the presence of any HLA allele mismatch.[10] At an incidence of 40%, acute GVHD occurs in the early period after transplant with the skin being the most commonly affected tissue. Risk factors for the development of GVHD include the recipient's age, CMV serostatus, HSC donor source and HLA disparity.[11,12] Chronic GVHD is observed in 30–90% of recipients of HSCT.[3]

In patients with malignant diseases, GVHD is associated with the graft-versus-leukemia effect (GVL), thus resulting in a decreased incidence of relapse.[13,14]

In recent decades, the overall survival (OS) in children who received HSCT is much higher, about 60% one to two years after transplant, depending on the disease, clinical conditions prior to transplant and complications after the transplant.[2,6] Therefore, this study aimed to analyze the results of unrelated HSCT in pediatric patients up to 180 days after the procedure and to compare the stem cell sources used.

Methods

Patients

This is a retrospective study. Between January 1995 and December 2009, 261 under 18-year-old patients received unrelated HSCT at the Hospital de Clínicas, Universidade Federal do Paraná (UFPR), Brazil. Of the 261 patients, nine were excluded from the analysis for the following reasons: seven patients had insufficient data for analysis and two patients were recipients of peripheral blood transplants. One hundred and eighteen patients received BM and 134 UCB grafts. The characteristics of the 252 cases that were assessed are listed in Table 1.

Table 1 – Features of patients and treatment.

Variable	
Age – mean (range) years	8 (0.2–18.0)
Diagnoses – n (%)	
Malignant disease	96 (38.1)
Marrow failure	95 (37.7)
Immune deficiency	42 (16.7)
Metabolic disorders	19 (7.5)
Source of stem cell – n (%)	
Bone marrow	118 (46.8)
Umbilical cord blood	134 (53.2)
Degree of HLA match – n (%)	
Without incompatibility (BM)	71 (60.2)
One/more incompatibility (BM)	47 (39.8)
Without or one incompatibility (UCB)	76 (56.7)
Two/more incompatibility (UCB)	58 (43.3)
Conditioning regimen – n (%)	
CFA + FLU	106 (42.4)
CFA + TBI	47 (18.8)
CFA + BU	58 (23.2)
CFA + BU + MEL	8 (3.2)
Others	31 (12.4)
ATG	174 (69.0)
GVHD prophylaxis – n (%)	
CsA + MTX	144 (57.1)
CsA + steroids	91 (36.1)
Others	17 (6.7)

CFA: cyclophosphamide; FLU: fludarabine; TBI: total body irradiation; BU: busulfan; MEL: melphalan; ATG: anti-thymocyte globulin; CsA: cyclosporine; MTX: methotrexate.

HLA typing and unrelated donor selection

The units were selected on the basis of best HLA matching and a critical minimum cell dose at the discretion of the treating physicians and source from National and International Public Banks. Class I typing was performed by serological or molecular techniques and Class II typing by molecular techniques; it was only in 2008 that the analysis of the locus C was frequently performed.

Conditioning regimen and prophylaxis against graft-versus-host disease

The conditioning regimen and prophylaxis for acute GVHD varied according to the underlying disease, stem cell source and HLA incompatibilities (Table 1).

Transplantation

The units of BM grafts used for transplantation contained an average of 4.39×10^8 total nucleated cells (TNC) (range: 0.3–10.8 cells) per kilogram of recipient's body weight after thawing. The units of UCB grafts used for transplantation contained an average of 5.2×10^7 TNC (range: 1.4–36.5 cells) and