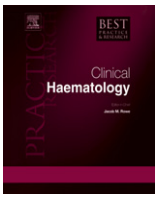
Best Practice & Research Clinical Haematology 23 (2010) 259–274

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beha



11

Haematopoietic transplants combining a single unrelated cord blood unit and mobilized haematopoietic stem cells from an adult HLA-mismatched third party donor. Comparable results to transplants from HLA-identical related donors in adults with acute leukaemia and myelodysplastic syndromes

Ana Sebrango, MD, Senior Haematology Medical Residents [a,b,1], Isabel Vicuña, MD, Senior Haematology Medical Residents [a,b,1], Almudena de Laiglesia, MD, Associate Haematologists [a,b,1], Isabel Millán, PhD, Senior Biostatistician [a,b,1], Guiomar Bautista, MD, Associate Haematologists [a,b,1], Trinidad Martín-Donaire, PhD, Research Assistant [a,b,1], Carmen Regidor, MD, PhD, Chief of the Haematopoiesis and Criobiology Unit [a,b,1], Rafael Cabrera, MD, PhD, Chief of the Haematology [a,b,1], Manuel N. Fernandez, MD, PhD, Professor, Emeritus Consultant Haematologiat [a,b,*]

[a] *Universidad Autónoma de Madrid, Hospital Universitario Puerta de Hierro, Siguero 59, 28035 Madrid, Spain*
[b] *Hospital Universitario Puerta de Hierro Majadhonda, c/ Joaquín Rodrigo, 2 Majadahonda, 28222 Madrid, Spain*

Keywords:
cord blood
transplantation
haematological malignancies
acute leukaemia
myelodysplastic syndromes

We describe results of the strategy, developed by our group, of co-infusion of mobilized haematopoietic stem cells as a support for single-unit unrelated cord blood transplant (dual CB/TPD-MHSC transplants) for treatment of haematological malignancies in adults, and a comparative analysis of results obtained using this strategy and transplants performed with mobilized haematopoietic stem cells from related HLA-identical donors (RTD) for

* Corresponding author at: Universidad Autónoma de Madrid, Hospital Universitario Puerta de Hierro, Siguero 59, 28035-Madrid, Spain. Tel.: +34 666507904, +34 913163955; Fax: +34 911917882.
E-mail addresses: anasebrango@hotmail.com (A. Sebrango), isabelicu@yahoo.es (I. Vicuña), adelaiglesial@yahoo.es (A. de Laiglesia), imillan.hpth@salud.madrid.org (I. Millán), gbautista.hpth@salud.madrid.org (G. Bautista), trini40l@hotmail.com (T. Martín-Donaire), mregidor.hpth@salud.madrid.org (C. Regidor), jcabrera.hpth@salud.madrid.org (R. Cabrera), manueln.fernandez@uam.es (M.N. Fernandez).
[1] Tel.: +34 911916000; Fax: +91 191 7862.

1521-6926/$ – see front matter
doi:10.1016/j.beha.2010.05.002

treatment of adults with acute leukaemia and myelodysplastic syndromes. Our data show that the dual CB/TPD-MHSC transplant strategy results in periods of post-transplant neutropenia, final rates of full donor chimerism and transplant-related mortality rates comparable to those of the RTD. Final survival outcomes are comparable in adults transplanted because of acute leukaemia, with different incidences of the complications that most influence these: a higher incidence of infections related to late recovery of protective immunity dependent on T cell functions, and a lower incidence of serious acute graft-versus-host disease and relapses. Recent advances in cord blood transplant techniques allow allogeneic haematopoietic stem cell transplantation (HSCT) to be a viable option for almost every patient who may benefit from this therapeutic approach. Development of innovative strategies to improve the post-transplant recovery of T cells function is currently the main challenge to further improving the possibilities of unrelated cord blood transplantation.

Introduction

In this paper we first summarize our results using the strategy of co-infusion of mobilized haematopoietic stem cells as a support for single-unit unrelated cord blood transplants (dual CB/TPD-MHSC transplants) for the treatment of haematological malignancies in adults. Next, we perform a comparative analysis of results obtained in our institution using this strategy and those of transplants performed with mobilized haematopoietic stem cells from related HLA-identical donors (RDT) for the treatment of adults with acute leukaemia (AL) and myelodysplastic syndromes (MDS).

Background

In the two decades elapsed since cord blood transplant (CBT) was introduced to clinic practice [1], this modality of haematopoietic stem cell transplant (HSCT) has evolved into an effective option for the treatment of number of haematological malignancies and non-malignant disorders requiring haematopoietic reconstitution, for patients lacking a readily available adequate related or unrelated volunteer donor [2–4]. Recognized advantages of CBT include easy procurement without risks for the donor, reduced risk of transmitting infections, rapid accessibility, and a relatively low incidence and severity of graft-versus-host disease (GVHD), despite tolerance of up to three out of six HLA mismatches. At least one cord blood (CB) unit with a minimum of four out of six A–B DR HLA matches (antigenic for loci A and B and allelic for locus DR) may be found nowadays for the great majority of patients in the worldwide network of CB banks. On the other hand, the main disadvantages of unrelated CBT transplantation are the limited number of haematopoietic stem cells (HSC) in the amount of cord blood (CB) that can be collected after birth, the possibility of transmitting undetected haematological pathologies and the unavailability of the donor for additional donations [5–10].

Slow and low rates of engraftment, infections during lengthy post-transplant neutropenia and toxicity of preparative regimens have been recognized as factors for early transplant-related mortality (TRM) of CBT in large registry-based observational studies [11–18]. Low cell content in the transplanted product and a higher degree of HLA incompatibility are, in turn, the main factors for graft failure and late engraftment [2,5]. In the past, all of these have a limited wider use of CBT, especially in adults. Another concern with CBT was the possibility of poor development of anti-tumour and adaptive immunity against pathogens. Obviously, a high rate of engraftment is a necessary pre-requisite for an adequate evaluation of CBT immune-related GVHD, graft-versus-tumour (GVT) effect and adaptive immunity. Strategies pursued to obtain high rates of engraftment include *ex-vivo* expansion of HSC of an aliquot of the transplanted CB, intraosseous infusion, infusion of two CB units, and the co-infusion of TPD-MHSC proposed by our group, all which can be combined with reduced intensity conditioning.