Transfusion and Apheresis Science 53 (2015) 373–377

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

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

An analysis of transfusion support in haematopoietic stem cell transplantation – report from a centre in India

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ARTICLE INFO

Article history:
Received 14 April 2015
Received in revised form 2 May 2015
Accepted 10 July 2015

Keywords:
Haematopoietic stem cell transplantation
Matched related donor
Matched unrelated donor
ABO compatibility
Transfusion support
GvHD

ABSTRACT

Background: Transfusion support in haematopoietic stem cell transplantation (HSCT) can be very demanding and challenging. The conditioning regimen, stem cell dose, donor type, presence of GvHD, infection all influence transfusion therapy in haematopoietic stem cell transplantation (HSCT). We retrospectively analysed the first 100 days transfusion requirements among HSCT recipients with haematological as well as non-haematological malignancies in our centre.

Materials and Methods: Transfusion data were retrieved for 100 patients who had undergone HSCT over a period of two years. The HSCT recipients were divided into three groups: autologous, allogenic and haplo-identical. Allogenic group was subdivided into matched related donor (MRD) and matched unrelated donor (MUD). The allo and haplo groups were then classified on the basis of the ABO compatibility as major, minor, bi-directional and compatible. We analysed the mean requirement of blood components (RBC, RDP, SDP and FFP) within the first 100 days of HSCT in each category.

Results and Discussion: Haematologic malignancies constituted 97% of the indications for HSCT. Allo-HSCT constituted 50% of the HSCT, of which 92% were MRD. Auto and haplo-HSCT constituted 40% and 10% respectively. Mean requirement for all products – RBC, SDP, RDP and FFP – was highest in the haplo category, followed by the allo category and then the auto HSCT category. The mean product requirement in the MUD category was significantly higher than in the MRD category ($p < 0.05$). The mean product requirement in the major and bidirectional ABO incompatible group was significantly higher as compared to the minor and ABO compatible group ($p < 0.05$).

Hence our data may help transfusion medicine specialists to understand the transfusion requirement in stem cell transplant settings from developing countries like India. The average number of blood donors required for each group of stem cell transplant patients can also be roughly predicted from this study.

1. Introduction

Haematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for many patients with haematological as well as non-haematological malignancies. Transfusion support in haematopoietic stem cell transplantation (HSCT) can be very demanding and challenging. The conditioning regimen, stem cell dose, donor type, presence of GvHD, infection all influence transfusion therapy. Patients are usually dependent on blood products until engraftment of stem cells. Previously high-dose conditioning regimens have been used for disease eradiation and immunosuppression in HSCT [1]. But due to high toxicity of myeloablative regimen, the uses of nonmyeloablative and reduced intensity regimens (RIC) have been started for the conditioning. Conventional myeloablative conditioning consisted of cyclophosphamide and total body irradiation, cyclophosphamide/total body irradiation and etoposide, or

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http://dx.doi.org/10.1016/j.transci.2015.07.006
1473-0502/

busulfan/cyclophosphamide. Whereas RIC consisted of fludarabine/total body irradiation, fludarabine/busulfan/antithymocyte globulin or cyclophosphamide with or without anti-thymocyte globulin. Cyclosporine combined with short-term methotrexate/mycophenolate mofetil (MMF) or cyclosporine alone was administered for GvHD prophylaxis as post-grafting immunosuppressor [2]. An early study involving small numbers of patients showed reduced transfusion requirements among nonmyeloablative compared to myeloablative recipients of human leucocyte antigen (HLA)-identical sibling HSCT [3]. Transfusion therapies are also influenced by the type of stem cell donor. Studies have shown that fewer transfusions were required for recipients of HLA-related compared to HLA-unrelated stem cell donors [4,5]. Major ABO incompatibility between donors and recipients has been associated with delayed red blood cell recovery, transient pure red cell aplasia and, thereby, prolonged need for red blood cell (RBC) transfusions in HSCT setting [6]. Only limited information is available about the transfusion requirements in the HSCT setting from India due to the high cost of treatment and lack of referral institutes for stem cell transplantation across the country.

This is a retrospective analysis of the transfusion requirements for the first 100 days following transplantation. HSCT recipients were patients with haematological as well as non-haematological malignancies at our centre. We have compared the mean requirement of blood components (RBC, RDP, SDP and FFP) among patients of auto-HSCT, allo-HSCT and haplo-HSCT and among the allo-HSCT, between matched related donor (MRD) and matched unrelated donor (MUD). We have also analysed the effect of ABO incompatibility between donor and recipient on transfusion requirements.

2. Materials and methods

2.1. Patients

The study analysed mean requirement of blood components (RBC, RDP, SDP and FFP) during the first 100 days of HSCT among recipients suffering from haematological as well as non-haematological malignancies. Transfusion data were retrieved for 100 patients who had undergone HSCT over a period of two years from 2012 to 2014. Most of the patients were Indian in origin. The standard institutional treatment protocol was followed for each case and most of the patients had received reduced intensity conditioning (Table 1). The HSCT was performed using peripheral blood stem cells (PBSC), harvested on the Cobe spectra cell separator following mobilization by G-CSF or G-CSF + plerixafor. The dose of transfused stem cells ranged from 2×10^6/kg to 5×10^6/kg CD34+ cells. Donors were matched for A, -B, and -C antigens of HLA class-I and DRB1 antigens of HLA class-II either by intermediate resolution DNA typing or by high-resolution technique. DNA typing was performed by SSOP (sequence specific oligonucleotide probes) method (Luminex-xMAP technology) in the HLA laboratory. But in a few occasions it was done by the SBT (sequence based typing) method (HistoGenetics laboratory) as a part of unrelated HLA-matched stem cell donor search programme from an international bone marrow registry system.

2.2. Donors

The stem cells were collected either from the patient or from the HLA-matched donor. Depending on the source of stem cell donor, we have classified the HSCT recipients into three categories - autologous, allogenic and haplo-identical HSCT. Allogenic category was further subdivided into two groups - matched related donor (MRD) and matched unrelated donor (MUD). All of the donors in MRD category were HLA-matched sibling donors and in case of MUD stem cells were obtained from the bone-marrow registry under national marrow donor program (NMDP) or from DATRI, an Indian bone marrow registry organization. For patients who did not have any matched related or unrelated donors, haplo-identical HSCTs were performed.

2.3. ABO-incompatible transplants

The allo and haplo groups were classified on the basis of the ABO compatibility as major, minor, bi-directional and compatible. ABO-incompatible transplantations were performed according to the standard institutional practice guidelines [7]. Minor ABO-mismatches were characterized by the presence of anti-recipient isohaemagglutinins in donors, e.g., O-type donors and A-, B- or AB-type recipients; major ABO-mismatches were characterized by the presence of anti-donor isohaemagglutinins in recipients, e.g., A-, B- or AB-type donors and O-type recipients; bi-directionally ABO-mismatches were characterized by the combination of major and minor ABO-mismatches, e.g., A-type donors and B-type recipients, or B-type donors and A-type recipients.

2.4. Engraftment

Patients are usually dependent on blood products until engraftment of stem cells. The engraftment criteria consists of an absolute neutrophil count (ANC) of 0.5×10^9/l or more for 3 consecutive days along with platelet count of 20×10^9/l or more without any transfusion support for consecutive 7 days. The time of engraftment of myeloid and platelets is listed in Table 2. Red cells engraftment was delayed in major ABO-mismatched or bi-directional HSCT compared to the minor ABO-mismatched or ABO compatible HSCT. In our study, median RBC engraftment time in major/bi-directionally

Table 1
Conditioning regimens for HSCT.

Diagnosis	Conditioning regimen
Multiple myeloma	Auto-HSCT in CR or VGPR; conditioning by Melphelan: 200 mg/m^2
Myelo-dysplastic syndrome	Auto/allo-HSCT ± Decitabine
Non-Hodgkin's and Hodgkin's lymphoma	BEAM protocol (Carmustine + Etoposide + Cytarabine + Melphelan) followed by auto/allo-HSCT
Acute leukaemia	Fludarabine + Busulphan/cyclophosphamide protocol followed by allo- or haplo-HSCT in CR