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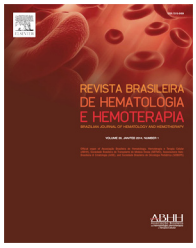

Original article

Determination of an unrelated donor pool size for human leukocyte antigen-matched platelets in Brazil

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ABSTRACT

Background: Successful transfusion of platelet refractory patients is a challenge. Many potential donors are needed to sustain human leukocyte antigen matched-platelet transfusion programs because of the different types of antigens and the constant needs of these patients. For a highly mixed population such as the Brazilian population, the pool size required to provide adequate platelet support is unknown.
Methods: A mathematical model was created to estimate the appropriate size of an unrelated donor pool to provide human leukocyte antigen-compatible platelet support for a Brazilian population. A group of 154 hematologic human leukocyte antigen-typed patients was used as the potential patient population and a database of 65,500 human leukocyte antigen-typed bone marrow registered donors was used as the donor population. Platelet compatibility was based on the grading system of Duquesnoy.
Results: Using the mathematical model, a pool containing 31,940, 1710 and 321 donors would be necessary to match more than 80% of the patients with at least five completely compatible (no cross-reactive group), partial compatible (one cross-reactive group) or less compatible (two cross-reactive group) donors, respectively.
Conclusion: The phenotypic diversity of the Brazilian population has probably made it more difficulty to find completely compatible donors. However, this heterogeneity seems to have facilitated finding donors when cross-reactive groups are accepted as proposed by the grading system of Duquesnoy. The results of this study may help to establish unrelated human leukocyte antigen-compatible platelet transfusions, a procedure not routinely performed in most Brazilian transfusion services.

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Introduction

Platelet alloimmunization is commonly seen in patients with hemato-oncological disorders requiring frequent red blood cell and platelet transfusions[1] and may be associated with refractoriness to platelet transfusions (RPT). There may also be an association between platelet transfusion failure and patient survival, which increases the clinical importance of RPT.[2]

RPT is defined as inappropriately low platelet count increments following exposure to antigens after two or more (usually consecutive) transfusions and must be determined by objective data which determine platelet transfusion outcomes.[3] This condition may be caused by immune and non-immune factors. More than 80% of RPT cases are related to non-immune causes. Thus, immune causes occur in less than 20% of the cases involving alloimmunization against human leukocyte antigens (HLA) and, to a lesser extent human platelet antigens (HPA), following exposure after transfusion, pregnancy, or transplantation. Among the immune causes, HLA antibodies are responsible for approximately 80–90% of RPT cases and HPA antibodies for approximately 10–20% of cases, associated or not with HLA antibodies.[4]

Providing an adequate post-transfusion platelet count increment to refractory patients is not an easy task; transfusion of HLA-matched platelets is one possibility.[5] However, it is very difficult to find multiple HLA-compatible related donors for one individual.

The HLA system is highly polymorphic[6] and the probability of finding identical matches may be around 10% of donations.[7,8] When a full match cannot be found, different strategies are used to select partially HLA-matched donors. HLA class I specificities can be grouped into cross-reactive groups (CREG), mismatches with antigenic similarity that result in less allorecognition or immune activation.[9] The grading system described by Duquesnoy et al. in the 1970s[10] (Table 1) is defined according to the presence of HLA CREGs and is still widely used by transfusion services. Although in some cases, the selection of mismatched donors based on HLA CREGs may fail to produce adequate increments,[11] this strategy can increase the number of potential donors in the same donor base.[8]

Pool size calculations can be an essential component for the rational planning of platelet support programs.[12] It is estimated that to provide at least five completely compatible donors for more than 80% of patients, 500, 1000, and 1500 donors would be needed for the Japanese, European Caucasoid and North American Caucasoid populations, respectively.[13] However, for a highly mixed population such as in Brazil, which is comprised of European, African and Amerindian roots,[14] the pool size required to provide these patients with adequate platelet support is unknown.

The unrelated donor pool size that might be necessary if a center wants to provide patients with unrelated HLA-compatible platelets was estimated using a random sample from the Brazilian population. A mathematical model was created for compatibility analysis and its application was illustrated in a population of 154 cancer patients. The findings of this study may help to establish the transfusion of unrelated HLA-compatible platelets, which currently is not a routine procedure in many Brazilian centers.

Methods

Study database, design and setting

A group of 154 HLA-typed patients who were submitted to bone marrow transplantation or who were candidates for this procedure at Hospital Israelita Albert Einstein (São Paulo, Brazil) between January 2006 and December 2009 were included in this retrospective study to illustrate a possible patient population.

A database of 65,500 HLA-typed bone marrow donors, registered in the LIG Laboratório de Imunogenética Ltda, São Paulo, Brazil was used in this study as the potential donor population. This database includes samples from the southeastern (mainly), southern and northeastern regions of Brazil and represents a section of the National Registry of Bone Marrow Donors. According to a Brazilian demographic census, these regions are related to 80% of the population[15] and may represent a good picture of the HLA phenotype diversity of the Brazilian population. This study was approved by an Ethics Committee and the Local Review Committee.

Measures and statistical analysis

Patients and donors

HLA typing was performed by the polymerase chain reaction sequence specific oligonucleotide probe (PCR-SSOP) method for loci A and B.

Table 1 – Description of the grading system of Duquesnoy.

Grade	Description	R/D	HLA typing			
		R	A1	A2	B7	B8
A	HLA identical – all 4 antigens	D	A1	A2	B7	B8
BU	Only 3 antigens detected – all identical	D	A1	–	B7	B8
B2U	Only 2 antigens detected – both identical	D	A1	–	B8	–
BX	4 antigens detected – 3 antigens identical and 1 cross-reactive	D	A1	A24	B7	B8
BUX	3 antigens detected – 2 identical and 1 cross-reactive	D	A1	A24	–	B8
B2X	4 antigens detected – 2 antigens identical and 2 cross-reactive	D	A1	A24	B7	B64
C	1 antigen mismatch, out-of-CREG	D	A1	A32	B7	B8
D	All other ≥2 antigen mismatches	D	A1	A32	B7	B64

R: recipient; D: donor; HLA: human leukocyte antigen; –: undetected antigens.