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Frequency of irregular Red Cell Alloantibodies in Patients with Thalassemia Major: a Bicenter Study

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Abstract

Objective: To provide frequency and distribution pattern of various types of irregular red cell alloantibodies in patients with thalassemia major.

Methods: This is a descriptive study conducted at two centers from January to December 2001. Purposive sampling was done and all patients diagnosed to have thalassemia major were included in the study. Antibody identification was carried out on serum employing commercial two-cell panel using standardized blood bank methods. If patients were found to have an irregular red cell alloantibody then the antibody identification was performed using 16 panel cells.

Results: A total of ninety-seven patients were included in the study. Fifty-three patients were males and 44 females. Mean age was 10.6 years. Irregular red cell alloantibodies were found in 9 (9.2%). Mean age of patients who developed red cell alloantibody was 11.9 years. Three (33.3%) patients developed anti-K while two (22.2%) had non-specific antibody. One patient each developed anti-D (11.1%) and anti-E (11.1%). Two had anti-D (11.1%) and anti-C while the other one (11.1%) developed anti-E and anti-K.

Conclusion: We concluded that there is relatively high rate of alloimmunization in our set of patients when compared to data from our region. We also suggest that red cell alloimmunization should not be overlooked in patients receiving regular blood transfusions (JPMA 55;563:2005).

Introduction

Appropriate and regular red cell transfusion remains the main treatment choice for a large number of patients with thalassemia major. These patients who are maintained on hypertransfusion regimen can develop various complications due to multiple transfusions, one of them being allosensitization to red cell antigens. As blood is routinely matched with respect to major blood group antigens i.e. ABO and Rh D antigen, there is a high probability that the donor will have minor blood group antigens not present in the recipients which will result in alloimmunization.

Alloimmunization significantly concerns the Rhesus, Kell, Duffy and Kidd system which are clinically significant.¹ They can cause, not invariably haemolytic transfusion reactions and limit the ability of safer transfusion while, others are clinically insignificant.¹

Factors for immunization are complex and involve at least three main contributing elements. This includes RBC antigenic difference between the blood donor and the recipient, the recipient's immune status and immunomodulatory effect of the allogenic blood transfusions on the recipient's immune system.²

In thalassemia major, red cell alloantibody production usually occurs after the age of 6 years after multiple transfusions. Perhaps this is due to immune tolerance developed by periodic blood transfusion started in early age.³ The relation between the number of units of blood transfused and antibody formation is unknown in thalassemia major but it is an important factor for increased alloimmunization. However, it has been said that the earliest sensitization if any, appears usually after ten transfusions.⁴

The aim of this descriptive study is to provide frequency and distribution patterns of various types of irregular red cell alloantibodies in patients with thalassemia major at two centers.

Patients and Methods

This is a case series conducted at two centers from January to December 2001 using the purposive sampling method.

All patients diagnosed to have thalassemia major on haemoglobin electrophoresis were included in this study. These patients were on hypertransfusion regimen, receiving packed cells cross - matched for ABO and Rh D antigen.

Patients with any other haemoglobinopathy or haematological disorder receiving multiple transfusions were excluded from the study.

Informed consent was taken from all patients prior to collection of blood sample. Antibody identification was carried out on serum employing two cell panel (Immucor, INC, Norcross, GA, U.S.A.) using standardized blood bank methods.⁵ If patients were found to have an irregular red cell alloantibody, then the antibody identification was performed using 16 panel cells (Immucor, INC, Norcross, GA, U.S.A.).⁵

The variables noted were age, gender along with frequency and distribution of irregular red cell alloantibodies. Also noted was the frequency of transfusion in patients who developed irregular red cell alloantibodies.

Results

A total of ninety-seven patients diagnosed to have thalassemia major were screened for the presence of red cell alloantibodies. Forty-seven patients from Aga Khan University Hospital and fifty patients enrolled at Hussainy Blood Bank and Transfusion Center for regular blood transfusion were included in this study.

Fifty three (54.6%) patients were males and 44 (45.3%) were females. Mean age was 10.6 years (age range 2-24 years). All the patients were receiving blood transfusion at an interval of 2-4 weeks.

Irregular red cell alloantibodies were found in 9 (9.2%) patients. Mean age of patients who developed red cell alloantibody was 11.9 years (range 2.5-24 years). Male to female ratio was 2:1. Frequency of transfusion was 2-3 weeks in six (66.6%) patients while in three (3.33%) patients it was 3-4 weeks.

Three (33.3%) patients developed anti-K while two (22.2%) patients developed non-specific antibody. One patient each developed anti-D (11.1%) and anti-E (11.1%). Two patients developed two irregular red cell alloantibodies. One patient (11.1%) developed anti-D and anti-C while the other one (11.1%) developed anti-E and anti-K.

Discussion

This study was conducted to demonstrate the frequency of irregular red cell alloantibodies in patients with thalassemia major. In our study, the rate of development of red cell alloimmunization is high (9.2 %) when compared to another study from our region, which showed frequency of irregular red cell alloantibodies to be 3.6%.² The red cell antibodies developed in this report were anti-Lewis a, anti-c, anti-N, anti-S, anti-C and anti-Fy, while our study revealed red cell alloantibodies mainly from Rhesus and Kell system.

Various centers all around the world have reported different frequencies of immunization. The majority of these reports have a high rate of alloimmunization but a few centers have reported low rates when compared to our data.^{2,4,6} Most of this published data have similar types of irregular red cell alloantibodies as ours.

A study in Italy among patients of thalassemia major by Sirchia et al³ revealed a rate of alloimmunization of 5.2% red cell alloantibodies were found in 74 out of 1432 patients. A total of 136 alloantibodies were found in 74 patients which were entirely confined to the common antigens of Rhesus, Kell, Kidd, Duffy and MNS system. Twenty one (28%) patients had two alloantibodies and seventeen (23%) had more than two alloantibodies.

Another study conducted in Hong Kong among patients of Asian descent by HOR - Kung Ho et al⁷ showed a total of nine alloantibodies in 68 (7.4%) patients. The red cell alloantibodies found were anti-E, anti-M, anti-HLA, anti-BG, anti-BW 22. In this study anti-K was not encountered. This is in contrast to our data where anti-K was seen in three patients.

However, many studies have also reported a high rate of red cell alloimmunization. A study by Singer et al², reported frequency of alloimmunization of 22% in patients with thalassemia major. He reported that 19 red cell alloantibodies were seen in 14 out of 64 patients. Three antibodies were detected in one patient while two antibodies in three patients. Anti-Kell was most often identified. This report also interestingly states that patients who receive blood matched for Rhesus and Kell system from their first transfusion, the rate of alloimmunization is found to be relatively low. Hence they inferred that transfusion of blood phenotypically matched for Rh and Kell systems compared to blood phenotypically matched for the standard ABO-RhD system could prove to be effective in preventing alloimmunization.

Vasilikil Michail et al⁶ found rate of alloimmunization to be 19.16%, that is, 23 children developed alloantibodies out of 120 patients with thalassemia major receiving regular blood transfusion. They reported alloimmunization in two groups of children. One was the better-matched

group which comprised of children who received blood compatible with ABO, Cc, Ee, D and K antigen while the usual-match group received blood compatible with ABO and RhD antigen. They also found that the overall frequency of alloimmunization between the usual-match and better-match group was not statistically significant. In this study, the antibodies belonged to Rhesus, Kell, Duffy, Kidd, Lewis and MNS system. In the usual match group the distribution frequency of alloantibodies was RhD: 35.8%, Kell: 25.6%, Duffy: 10.2%, Kidd: 12.8% and MNSs and Lewis: 7.6% each.

Spanos et al⁴ also found a high frequency of red cell alloimmunization in 220 (22.6%) out of 973 thalassemic patients receiving blood matched for ABO and RhD antigen. Alloantibodies belonged to the following systems: 34% to Rhesus, 29.8% to Kell, 7.9% to MNS, 8.1% to Kidd, 6.6% to Bg, 5.9% to Lewis, 4.1% to Duffy and 1.32% to P. Almost half (51.8%) had formed only one alloantibody and the rest (48.2%) produced more than one antibody.

Hence we concluded that there is relatively high rate of alloimmunization in our set of patients when compared to data from our region. However more data is required from various other large centers. We also concluded that

red cell alloimmunization should not be overlooked in patients with thalassemia major receiving regular blood transfusion. It should always be considered if the patient repeatedly suffers from haemolytic transfusion reaction or not being able to maintain haemoglobin at a desired level inspite of regular transfusions. Regular screening for red cell alloantibodies would add towards the better management of these patients.

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