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Partial matching of blood group antigens to reduce alloimmunization in Western India

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ABSTRACT

Red blood cell alloimmunization occurs due to the genetic disparity of red cell antigens between donor and recipient. In the present study, we report a spectrum of red cell alloantibodies characterized in patients with different clinical conditions in a reference center in India. Majority of the antibodies identified were against the blood group antigens c, D, E, M, N, S, s and Jka. Hence, apart from ABO and RhD, we recommend partial antigen matching between donor and patients for other Rh (C, c, E, e) and MNS blood group antigens to potentially reduce the risk of alloimmunization by 75%. Matching of Kell antigen is not recommended in Western India.

1. Introduction

Genetic disparity of RBC antigens between donor and recipient leads to sensitization against foreign antigens which may result in the development of alloantibodies. The most common routes of alloimmunization are via blood transfusions, transplantation or feto-maternal hemorrhage. Red cell alloimmunization complicates cross matching procedures and thereby delays issuing of compatible blood units. This problem may further be aggravated by the presence of multiple alloantibodies and the chances of finding compatible blood units are further reduced. About 25% of alloimmunized patients requiring blood transfusions receive unsatisfactory transfusion support and also in some cases, it may even be impossible to find suitable units [1]. Blood transfusion also predisposes the formation of autoantibodies in a patient [2], which may result in the development of automimmune hemolytic anemia (AIHA), and can cause increased hemolysis of transfused RBCs. Multiparous women with complicated obstetric history are at the risk of alloimmunization against other Rh antigens C, c, E and e [3,4]. Also, maternal antibodies against other minor blood group antigens have been implicated in hemolytic disease of the fetus and newborns (HDFN) [5–7].

The incidence of alloantibodies produced against different blood group antigens ranges from 0.3 to 38% among different study groups [8]. However, higher alloimmunization rates have also been reported among some patient groups [9]. Among the frequently encountered antibodies, Rh and Kell blood group specific antibodies have been the most common [10–13]. In order to reduce risk of alloimmunization, various study groups have suggested partial matching of blood group antigens between donors and patients [14–18].

Various studies in India have reported the incidence of alloimmunization between 1.25 and 18.8% among multitransfused patients, antenatal women and in patients with chronic renal failure. The commonly encountered antibodies among these patients were anti-E, anti-c and anti-K [19–29]. Our center, being a reference laboratory, receives samples from various blood banks and hospitals for characterization of alloantibodies in patients with different clinical backgrounds. Here, we report the spectrum of antibodies encountered among these patients and based on these findings recommend three levels of partial antigen matching to reduce risk of alloimmunization.

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2. Material and methods

One hundred and twenty five blood samples which were referred to the Department of Transfusion Medicine, National Institute of Immunohaematology (Indian Council of Medical Research), Mumbai, over a period of 3 years (2011–2014) for resolving problems related to blood grouping and cross matching from Western India were taken in the present study. Among these, thirty-six were cases of autoimmune hemolytic anemia (AIHA). The remaining samples included seven cases having autoimmune disorders, 18 cases of thalassemia, four cases of sickle-cell anemia, 25 cases of pregnancy related alloimmunization, six blood donors and 29 cases of anemia, jaundice, hereditary spherocytosis and etc. For all the patients, a proforma containing details of name, age, sex, previous history of transfusion, illness and obstetric details was filled at the time of sample collection.

Initially, direct antiglobulin test (DAT) on patient's red cells and indirect antiglobulin test (IAT) on patient's serum was carried out on each of the samples using O pooled cells and patient's own red cells (for autocontrol). Patients' sera were then tested using in-house antibody screening cells by saline, enzyme (papain-cysteine) and IAT technique at 37 °C and by saline and enzyme at 22 °C and 4 °C. All the tests were done by tube technique using standard protocol. Samples showing a positive screen were then tested for identifying the specificity of the antibody using in-house and commercial reagent red cell panels. For AIHA cases, as the DAT was positive, eluates were prepared by ether elution technique. The serum and eluate both were subjected to antibody identification test using reagent red cell panels.

In case of multiple antibodies, after the identification of one antibody, the known antibody was adsorbed with antigen positive red cells and then the serum was retested using reagent red cell panel for identifying the specificity of other antibodies. Red cell phenotyping of patient's RBCs for clinically significant blood group antigens was performed using commercially available antisera (Immucor, Inc., USA) as per manufacturer's instructions by tube technique to confirm the nature of the antibody(allo or auto).

3. Results

In the present study, 105 alloantibodies occurring as single or along with another antibody were detected in 89 patients with different clinical conditions. Specificity of the antibodies could be identified in 74 cases. Among these, antibodies against a single specific blood group antigen was found in 82.4% of the cases, while in the remaining cases, antibodies of multiple specificities were observed. In 15 cases the specificity of the alloantibody could not be determined. Pan-reacting autoantibodies were detected in 35 cases of AIHA. As all these samples were referred to our laboratory from various blood banks for characterization of antibodies, the rate of alloimmunization was not determined.

The specificities of single and multiple antibodies identified in multi-transfused patients, multiparous women and donors are shown in Table 1. Among single specific antibodies identified, 51% were against Rh blood group antigens. In 13 cases with multiple antibodies, 77% showed the presence of at least one Rh antibody. Anti-c and anti-M reacting

Table 1
Specificity of the antibodies identified in 74 cases.

Clinical background		Single specific antibody		Multiple antibodies	Total cases
		Antibodies against Rh blood group system	Antibody against antigens of other minor blood group systems		
Multi-transfused (44)	AIHA or other autoimmune disorder	anti-c(3), anti-e(1)	Anti-Fy^b(1), anti-S(1), anti-Fy^a(1)	Nil	7
	Hemoglobinopathy (Thalassemia and Sickle cell anemia)	Anti-c(3), anti-E(2), anti-e(1)	Anti-Jk^a(1), anti-K(1), anti-M(3), anti-s(1), anti-P_1(1), anti-Lu^a(1), anti-Le^a(1)	anti-S + E + Jk^a(1), anti-c + Jk^b + S(1), anti-Jk^a + Fy^b(1), anti-C + D(1), anti-c + Jk^b(1), anti-c + S + Fy^a(1), anti-c + other(1)	22
	Other*	Anti-E(3)	Anti-Fy^a(1), anti-Jk^a(2), anti-M(4), anti-N(2)	anti-Le^b + N(1), anti-N + I(1)	14
Pregnancy related alloimmunization		Anti-D(9), anti-c(5), anti-E(2), anti-e(1)	Anti-N(2), anti-S(1), anti-Fy^a(1)	anti-C + D(2), anti-c + E(1), anti-D + other(1)	25
Donors		Anti-c(1)	anti-Jk^a(1), Anti-P_1(2), anti-M(1), anti-N(1)	Nil	6
Total					74

* Includes cases of jaundice, anemia, hereditary spherocytosis, Leukemia, alcoholic liver disease, renal disorder.