Prevalence of alloimmunisation in patients with beta thalassaemia major

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Dear Sir,

Alloimmunisation, a reaction of the immune system to foreign antigens, is one of the most important side effects of regular blood transfusions. The rate of red blood cell alloimmunisation following the transfusion of a single unit of blood is 1 to 1.6%, while the rate in patients receiving regular blood transfusions may be as high as 60%[1]. When regular blood transfusions start at an older age, the chance of alloimmunisation increases. Under certain conditions, such as infection, surgery or pregnancy, patients with intermediate thalassaemia may receive blood transfusions at an older age. In the presence of alloimmunisation, the life span of red blood cells is shortened and the patient's need for blood increases. Identification of the types of antigens present and transfusion of fully compatible blood may prevent alloimmunisation. Currently, if a patient has a haemolytic reaction, his or her blood serum will be evaluated in order to identify antibodies present and the transfusion of blood with the relative antigens should be restricted. In some instances there is such a broad diversity of antibodies present that finding appropriate blood for the patient is almost impossible, and though the person suffers from severe anaemia, he or she cannot receive blood.

In order to examine the presence of alloimmunisation, 218 patients with β-thalassaemia major referred to the Thalassaemia Research Centre, Sari, Iran, were assessed. The average age of the patients was 22.5±7 years and gender distribution was 45.9% males and 54.1% females. The patients started to receive blood transfusions at the age of 2.3±2 years. Among this group, 40 patients had a history of allergic reactions, consisting of fever, rash or both symptoms, during blood transfusion. The Biotestcell-P3 screening kit (Biotest, Deireich, Germany) was used to detect antibodies against C, C^w, Le^a, E, Lu^a, Le^b, K, Jk^b, N, P1, D, Jk^a, M, S, Xg^a, e, Fy^a, s, c, Fy^b, k, Kp^a, Js^b, Lu^b and Co^a antigens in patients' blood samples. All specimens were microscopically evaluated for agglutination with three red blood cell panels from the kit (*panel 1:* $R_1{}^wR_1$, D, C, e, C^w, k, Kp^b, Js^b, Fy^a, Lu^b, Jk^a, M, S, s, Le^a, Xg^a, Co^a; *panel 2:* R_2R_2, D, E, c, k, Kp^b, Js^b, Fy^b,Lu^a, Lu^b, Jk^a, M, S, s, Le^b, Xg^a, Co^a ; *panel 3:* rr, c, e, Cw, K, k, Kp^b, Js^b, Fy^a, Fy^b, Lu^b, Jk^b, N, s, P^1, Co^a). Data were processed using descriptive statistics and 95% confidence intervals calculated by SPSS V17.0 software (IBM Corporation, New York, USA).

Alloantibodies were detected in 88 cases (40.4%; 95% CI: 33.9-46.9), of whom 46 were female and 42 male. Alloantibodies against C, C^w and Le^a red blood cell surface antigens were the most frequently detected alloantibodies (Table I). In this study no significant correlation was found between emergence of alloantibody and age at first transfusion (before or after 3 years of age) (r: 0.07, P=0.32) or frequency and years of blood transfusion (r: 0.08, P=0.25).

This study showed that up to 47% of our patients had at least one type of alloantibody. These results are comparable with those of a study by Aygun *et al.*, in which alloantibodies were detected in 29% of children and 47% of adult sickle cell anaemia and thalassaemia patients[2]. In a different study, pregnant women and people with post-accident blood transfusions showed alloimmunisation rates of 1 to 3%, while this rate was about 70% in patients receiving regular blood transfusion[1].

Table I - Frequency of different alloantibodies in patients with beta thalassaemia major at the Thalassaemia Research Centre, Sari, Iran, in 2010.

Reaction with panels	Possible present alloantibodies	Frequency (%)
1	C, C^w, Le^a	40
2	E, Lu^a, Le^b	24
3	K, Jk^b, N, P_1	13
1+2	D, Jk^a, M, S, Xg^a	11
1+3	e, Fy^a, s	6
2+3	c, Fy^b	5
1+2+3	k, Kp^b, Js^b, Lu^b, Co^a	1

During the process of blood transfusion, compatibility of the major blood groups of the donor and recipient is always taken into consideration, thus the high prevalence of the phenomenon of alloimmunisation is attributed to the effects of minor blood groups that initiate immune system responses in recipients. This issue highlights the importance of choosing appropriate and sensitive compatibility tests, such as antibody screening, in the detection and identification of these antibodies.

In regions where appropriate and compatible blood cannot be provided for patients, the rate of alloimmunisation is completely dependent on the genetic diversity of the population. For instance, in a study of 161 thalassaemia patients in Pakistan, alloantibodies were detected in only 5% of the cases[3]. The low rate of alloimmunisation was explained by the fact that genetic variance in that community is very low. The authors concluded that given the low probability of alloimmunisation in that region, searching for the presence of different antigens in all patients is neither necessary nor cost-effective.

Evaluating 564 patients with malignancies or blood disorders, Schonewille *et al.* showed that 9% of all the patients studied were alloimmunised and that anti-E and anti-c were the most frequently detected alloantibodies[4]. In a study by Gupta *et al*. the rate of alloimmunisation was 20% and the most common antibodies were anti-E and anti-K[5]. In our study, antibodies against Le^a, C^w and C were the most frequently found antibodies.

There may be several reasons for the variance in prevalence of alloantibodies in different countries in a region: varied levels of immunogenicity of the common blood antigens in a population, homogeneity of the population and percentages of natives versus immigrants, and the source of transfused blood, i.e. whether it is from inside or outside the region.

Schonewille *et al.* evaluated patients who had regular blood transfusions and found that up to 60% of these patients may produce alloantibodies. In a 20-year follow up they discovered an increase in antibody diversity in each patient[4]. They believed that an appropriate cross-match test could prevent 83% of all cases of alloimmunisation. There are certain strategies that can be used to reduce the rate of alloimmunisation: antibody screening tests for patients who have recently received a transfusion and finding people who have raised alloantibody, and creating an antigenic profile of these recipients through molecular methods. In comparison with classical blood group typing through an agglutination method, molecular laboratory approaches are more reliable, as there is no donor's red blood cell present in the laboratory process and the chance of possible mistakes in identifying minor blood groups is reduced.

The Authors declare no conflicts of interest.

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