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Pathology

INCIDENCES OF ALLOIMUNIZATION IN MULTITRANSFUSED CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT Alloimmunization is one of the major complications in patients who are repeatedly transfused. This can occur during transfusion of antigen positive blood into antigen-negative individuals, or during pregnancy when the mother lacks a blood group antigen that is present on the fetal RBCs. A total of 40 multitransfused patients who received at least 5 units of PRBCs were included in our study. Antibody screening and detection was done using Column Agglutination Technology (CAT). There was no association of gender (male/female) with the rate of alloimmunization as seen in the study. The use of phenotypically or genotypically matched red cells for major antigens from the beginning of a chronic transfusion regimen can prevent alloimmunization to a significant degree.

KEYWORDS : Alloimmunization; Antigen; RBCs;

Introduction

Alloimmunization consists of the induction of immunity in response to foreign antigen(s), resulting from exposure to cells or tissues from a genetically different member of the same species. It is one of the major complications in patients who are repeatedly transfused.

Blood group antigens can be immunogenic in individuals who lack the corresponding antigen on their red blood cells (RBCs). This can occur during transfusion of antigen positive blood into antigen-negative individuals, or during pregnancy when the mother lacks a blood group antigen that is present on the fetal RBCs. This can result in immunization and the production of alloantibody.[1]

Each component in a unit of blood is capable of producing antibodies. Antigens such as HLA Class I & II, granulocyte specific antigens, platelet specific antigens and RBC specific antigens can stimulate the immune system and produce alloantibodies.[2,3]

Red cell transfusions are a valuable health care resource especially for thalassemics, patients of myeloproliferative disorders, hematological disorders, end-stage renal failure, leukemia, and organ transplant.[4]

The antigens most frequently involved in alloimmunization belong to the Rh, Kell, Kidd, Duffy, Lewis and MNS blood group systems. In a study by Dhawan, *et al.*[2,9], an Indian study, it is reported that out of total 23 alloantibodies detected in 319 transfused thalassemic patients, 87.17% belong to Rh and Kell blood group system.

Strategies for prevention or treatment of alloimmunization vary from provision of RBCs matched for all the major antigens associated with clinically significant antibodies to blood matched only for antibodies that have already been made. In the first approach an extended RBC phenotype (ABO, Rh, Kell, Kidd, Duffy, Lewis, and MNS) of the patient is done before starting transfusion therapy. Antigen-matching for C, E and K antigens is performed for patients without prior alloantibody formation.[6]

The transfusion of matched blood is essential for chronically multitransfused patients in order to avoid alloimmunization in a great percentage of transfused patients. Over 90% of the immunized patients develop antibodies which generally are considered clinically significant (e.g. anti-D, E, K, Fy^a, Fy^b, Jk^a, Fy^b). The low rate (3.7 %) of alloimmunized patients who have received blood matched for the Rhesus and Kell systems from their initial transfusion is an eloquent and supportive measure for this patients.[8]

The present study is based on the selected population of patients with, chronic renal disease who undergo regular blood transfusions, and are followed up systemically in our blood center for alloimmunization to red cell antigens.

Materials and Methods

A prospective cross sectional study was conducted in the Department of Transfusion Medicine of our institute between the periods of January 2017-July17. A total of 40 multitransfused patients who received at least 5 units of PRBCs were included in our study. The clinical history, previous transfusion history and detail of transfusion reactions, if present, were carefully noted in a proforma. Patients requiring multiple transfusions in dependent chronic kidney disease were included in the study. All samples that had a positive reaction with a commercially available cells with(ID DIA CELL I II III) 3 cell panel were further tested using an (ID DIA CELL I-XI) 11 cell panel. All samples with a history of multiple transfusions, which also showed an incompatible cross match on testing, were subjected to 11 cell panel testing even if the 3 cell panel was negative. All samples that showed pan agglutination with a 3 cell panel and also had a positive DCT, were not subjected to further testing with an 11 cell panel. Five ml blood in plain vial was obtained aseptically after informed consent was obtained from the patient. Serum separated in the blood bank laboratory was kept in deep freezer at -40°C till screened for alloantibody. ABO grouping and Rh typing was also done in the laboratory. Antibody screening and detection was done using Column Agglutination Technology (CAT).

Observation & Discussion

Alloimmunization of red blood cells (RBCs) is a common and potentially serious consequence of blood transfusions. The risk of alloimmunization is especially high in patients who receive multiple transfusions, such as patients with thalassemia, aplastic anaemia, and haematological malignancies. The frequency of alloimmunization varies in different patient populations. The risk of developing RBC alloantibodies depends on the age, sex, and genetic makeup of the patient, as well as the I number and frequency of transfusions that he or she has received.[9,11]

This study was carried out in the Department of Transfusion Medicine of our institute from January 2017 to July 2017. A total of 40 multiply transfused patients receiving at least 5 units of non-leukodepleted packed red blood cells were selected for the study. In the present study the alloimmunization rate was found to be 5%. A low rate of alloimmunization may be expected when there is homogeneity of RBC

antigens between the blood donors and recipients.[1] This homogeneity between the patient and blood donor population may be the reason of low rate of alloimmunization in our study. Use of leucodepleted blood could have contributed to further decrease in alloimmunization as found by Singer, *et al.*

There was no association of gender (male/female) with the rate of alloimmunization as seen in the studies of Ameen, *et <al.* El Danasoury, *et al.*and Hendrickson, *et al*. who also had depicted that gender was not a significant factor in the development of alloimmunization (12,13). In the present study, the detected alloantibodies belonged to the Rh and Kell blood group system. Among them, Anti-E and Anti-K were detected (Figure-1).

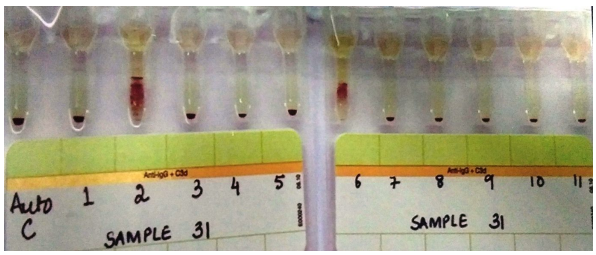
The overall specificity of RBC alloantibodies in transfused patients in an Indian study was as follows; with anti-E being the most common (36.3%), followed by anti-D (16%), anti-c (6.4%), anti-c + E (6.4%), anti-C + D (5.1%), and anti-K (4.5%) (13, 14). The alloimmunization rate of CKD patients was 5% in our study. It corroborates to findings of other literatures that ranges from 6-14%. Many patients with CKD undergoing dialysis require intermittent or regular blood transfusions to treat symptoms associated with anaemia. Uremic patients are a multitransfused group in which the altered humoral and cell-mediated immune response to several antigen systems has been documented.[17] Even though renal failure patients have a suppressed immune response; formation of red cell alloantibodies is not significantly suppressed. The reported prevalence of RBC 6-14 % in CKD patients.[15,16]

In our study, all the disease groups studied, and the alloimmunization rates was in accordance to the studies[15,18] conducted for each of them (p value: < 0.0001). The factors affecting alloimmunization are complex and involve at least three main contributing elements: (1) the RBC antigenic difference between the blood donor and the recipient; (2) the recipient's immune status; (3) the immunomodulatory effect of the allogenic blood transfusions on the recipient's immune system.[8] As most of the alloantibodies are against limited red cell antigens, the benefits of extended red cell phenotyping to minimize alloimmunization has been debated in the literature. Spanos, *et al.* have observed that when patients were transfused with blood matched for three parameters, ABO, Rh, and Kell, the rate of alloimmunization was low (3.7%), while if it was matched for ABO and Rh only, the immunization rate was high (15.7%). Matching for antigens other than ABO or Rh would be cost effective only if a multitransfused patient has a history of one or more alloantibodies.

Conclusions

The use of phenotypically or genotypically matched red cells for major antigens (D, C, c, E, e, and Kell) from the beginning of a chronic transfusion regimen can prevent alloimmunization to a significant degree. Those who have already developed alloantibodies, corresponding antigen negative blood units are to be issued to them. Apart from antigen matched units, another strategy to reduce alloimmunization is leukodepletion of blood and blood components.

Figure-1



Sample 31 contains (3+) in cell 2 and contains (-ve) in cell 1, 3, 4, 5
Sample 32 contains (3+) in cell 6 and contains (-ve) in cell 7, 8, 9, 10, 11
Alloantibodies belonged to the Rh and Kell blood group system and identifies as Anti-E and Anti-K

REFERENCES:

1. Pandey H, Das SS, Chaudhary R. Red cell alloimmunization in transfused patients: A silent epidemic revisited. Asian J Transfus Sci 2014; 8(2):75-7.
2. Lo SC, Chang JS, Lin SW, Lin DT. Platelet alloimmunization after long-term red cell transfusion in transfusion-dependent thalassemia patients. Transfusion 2005; 45(5):761-5.
3. Walters AH, Minchinton RM. Clinical problems due to alloimmunization to platelet and granulocyte antigens. The Journal of the Royal College of Pathologists of Australia 1981; 13(2):391-92.
4. Sood R, Makroo RN, Riana V, Rosamma NL. Detection of alloimmunization to ensure safer transfusion practice. Asian J Transfus Sci 2013; 7(2):135-139.
5. Dhawan HK, Kumawat V, Marwaha N, Sharma RR, Sachdev S, Bansal D, et al. Alloimmunization and autoimmunization in transfusion dependent thalassemia major patients. Study on 319 patients. Asian J Transfus Sci. 2014; 8(2): 84-8.
6. Singer ST, Wu V, Mignacca R, Kuypers FA, Morel P, Vichinsky EP. Alloimmunization and erythrocyte autoimmunization in transfusion-dependent thalassemia patients of predominantly Asian descent. Blood. 2000; 96:3369-73.
7. Makroo RN, Bhatia A, Gupta R, Phillip J. Prevalence of Rh, Duffy, Kell, Kidd & MNSs blood group antigens in the Indian blood donor population. Indian J Med Res. 2013 Mar; 137(3):521-26.
8. Spanos T, Karageorga M, Ladis V, Peristeri J, Hatziliami A, Kattamis C. Red Cell Alloantibodies in Patients with Thalassemia. Vox Sang. 1990; 58(l):50-5.
9. Schonewille H., Van De Watering, L. M.G., Loomans, D. S.E. and Brand, A. Red blood cell alloantibodies after transfusion: factors influencing incidence and specificity. Transfusion 2006; 46; 250-256.
10. Olujohungbe A, Hambleton I, Stephens L, et al. Red cell antibodies in patients with homozygous sickle cell disease: a comparison of patients in Jamaica and the United Kingdom. Br J Haematol. 2001; 113(3):661-5.
11. Philip J, Biswas AK, Hiregoudar S, Kushwaha N. Red blood cell alloimmunization in multitransfused patients in a tertiary care center in Western India. Lab Med 2014 Fall; 45(4):324-30.
12. E1 Danasoury AS, Eissa DG, Abdo RM, Elalfy MS. Red blood cell alloimmunization in transfusion- dependent Egyptian patients with thalassemia in a limited donor exposure. program. Transfusion. 2012; 52(1):43-7
13. Hedrickson JE, Desmarets M, Deshpande SS, et al. Recipient inflammation affects the frequency and magnitude of immunization to transfused red blood cells. Transfusion. 2006; 46 (9) : 1526-36.
14. Zaman S, Chaurasia R, Chatterjee K, and Thapliyal RK, "Prevalence and Specificity of RBC Alloantibodies in Indian Patients Attending a Tertiary Care Hospital," Advances in Hematology, 2014.
15. Blumberg N, Peck K, Ross K, Avila E. Immune response to chronic red blood cell transfusion. Vox Sang. 1983; 44(4):212-7.
16. Doman RE, Ramirez G. Red cell alloimmunization in chronic renal failure patients undergoing hemodialysis. Nephron. 1988; 48(4): 284-5.
17. Kangiwa U, Ibegbulam O, Ocheni S, et al. Pattern and prevalence of alloimmunization in multiply transfused patients with sickle cell disease in Nigeria. Biomarker Research (2015); 3:26.
18. Coles SM, Klein HG, Hollond PV. Alloimmunization in two multitransfused patient populations. Transfusion. 1981; 21(4):462-6.