

Phenotype frequencies of blood group systems and alloantibodies to red blood cells in blood transfusion recipients in Kayseri (Turkey)

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Abstract

Aim: In this study, we aimed to assess the antigen and phenotype frequencies of various blood groups among recipients of erythrocyte suspensions in Kayseri.

Material and Methods: The study was conducted as retrospective, cross sectional and multicenter study. In all, 48750 blood recipients old typed in terms of the ABO, Rh, MNS, Duffy, Lewis, P, Kell, Lutheran, and Kidd systems were subjected to erythrocyte phenotyping using a gel centrifugation method within the age group of 18-60 years.

Results: Of the ABO blood group, A was most frequent (44%) followed by O, B, and AB (30.3%, 16.2%, and 6.5%, respectively). The frequencies of Rh antigens were 88% D-positive and 12% D-negative. Alloantibodies were detected by screening in 196 (0.4%) of 48,750 patients, and decreased in the order anti-E (62%), -C (43%), -D (42%), -C (11%), -c (11%), -e (8%), -M (7%), -Fy a (5%), -Jk a (5%), -Kp a (4%), -Le a (3%), -Jk b (2%), -S (2%), -Le b (1%), and -P (1%). The most frequently detected alloantibodies were anti-E (31.6%) and -K (21.9%).

Conclusion: Knowledge of the phenotypic frequencies of red blood cell antigens allows the creation of banks of appropriate antigen-negative blood, thus preventing transfusion reactions in patients requiring multiple transfusions or who express alloantibodies.

Keywords: Blood Group Systems; Alloantibody; Kayseri; Phenotype Frequency.

INTRODUCTION

In routine practice, safe and effective erythrocyte transfusion requires donor blood of the appropriate ABO and Rh blood group systems. A total of 308 red blood cell (RBC) antigens are recognized by the International Society of Blood Transfusion, 270 of which are assembled in 30 blood group systems. Of these, nine are considered to be major blood group systems (ABO, Rh, Kell, Kidd, Duffy, MNS, P, Lewis, and Lutheran) (1,2). Immunogenic reactions leads to alloimmunization, which is a serious problem especially in patients receiving multiple transfusions (3-6).

Alloantibody data banks can be obtained by determining the antibody profile of the community by screening for the RBC antigen phenotype (7). Therefore, the potential development of alloimmune transfusion reactions can be avoided. With the exception of the frequencies of ABO and Rh antigens (8-10), there are no previous reports regarding the frequencies of RBC antigens in Turkey.

Erythrocyte antibody screening to prevent alloimmunization reactions in erythrocyte suspension recipients has been routinely performed at Erciyes University in Kayseri, a city in central Anatolia, Turkey, since January 2008. This is the first report of the frequencies of RBC antigens and phenotypes of different blood groups in Kayseri, Turkey.

MATERIAL and METHODS

The study was conducted as retrospective, cross sectional and multicenter study. The data on which this study was fetched from the transfusion records of patients at the Erciyes University and Kayseri Training and Research Hospital Blood Bank. Informed consent was not obtained due to the retrospective nature of the study. Ethical approval was obtained from Erciyes University Ethical Committee (number: 298/2017). The records for 48750 blood recipients typed for the ABO system, Rh system, and other blood groups between January 2009 and July 2011 within the age group 18-60 years were retrieved. Patients

Received: 20.06.2017 Accepted: 17.07.2017

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were also screened for the presence of autoantibodies.

To screen and identify the ABO group types and Rh specificities of the blood samples is used the microtyping kit (DiaMed-ID Micro-typing System, DiaMed AG, Cressier sur Morat, Switzerland) by gel centrifugation. The screened blood group antigens in the recipients were as follows: Kidd (Jka and Jkb), Kell (K, kpa, and kp6), Duffy (Fya and Fyb), MNS (M, N, S, and s), Lewis (Lea and Leb), P (P), Lutheran (Lua and Lub), and Xg (Xga). ID card antigen profile-I (P1, Lea, Leb, Lua, and Lub), ID card antigen profile-II (K, k, kpa, Kpb, Jka, and Jkb), and ID K typing cards were used with a 5% RBC suspension for phenotyping. ID card antigen profile-III (M, N, S, s, Fya, and Fyb) was used with RBC suspensions prepared in 0.8% LISS. Antigen typing was performed in accordance with the manufacturer's instructions (DiaMed AG). The gel test results were graded between +4 and +1 according to the structure of the red line produced by agglutinated cells.

Statistical analysis

IBM SPSS for Windows ver. 21.0 (IBM Corp., Armonk, NY) used for statistical analysis. Values were presented as frequency (%).

RESULTS

A retrospective analysis of the transfusion history and medical records of 48750 patients who had received at least one transfusion indicated that 196 (0.4%) of the patients had developed antibodies. Of the patients whose antibody test results were positive, 28 (14%) were found to have autoantibodies.

The autoantibody-positive patients consisted of 114 (58%) females and 82 (42%) males. Of the female patients, 40 (35%) were postpartum. All patients were evaluated before transfusion. Of these patients, 96 (57%) were from various surgical clinics and 72 (43%) were followed up for different hematological disorders. Of these patients, 15 (7.6%) were found to have two antibodies and 181 (92%) were found to have a single antibody.

Indeed, of the 42997 screened patients, 86.4% (37837) had Rh (+) and 13.6% (5850) had Rh (-) test results. E antigen was found to have the highest frequency (31.6%), followed by D, C, c, and e (21.4%, 5.6%, 5.6%, and 4.1%, respectively), Table 1. Overall, 55 (0.94%) of the 5850 Rh (-) patients were found to have antigens, with frequencies of 76.3% (42) for D, 16% (9) for C, 7.3% (4) for Kpa, and 5.5% (3) for M. Double antigens were detected in nine patients, with D and C being the most commonly seen concurrent antigens (n = 8). The red cell antigen and phenotype frequencies of the other blood group systems (Kell, Kidd, Duffy, MNS, P, Lewis, and Lutheran) and Xga antigens are shown in Table 2.

In the Kell blood group system, 22% (43/196) of the recipients were typed as positive for K antigen. This rate was 0.08% (43/48750) in the screened population. A rare Kpa phenotype was found with a frequency of 2.04% (4/196) in the recipients. For the Kidd and Duffy blood group systems, the Jka rate was 2.5% (5/196), the Jkb rate

was 1.02% (2/196), and the Fy (a+) rate was 2.5% (5/196). Neither the Lutheran nor Xga phenotype was observed in the study population. M+ and S+ were the most common phenotypes observed for the MNS blood group system (3.6% and 1.02%, respectively). According to the Lewis blood group system, Lea and Leb antigens were observed at frequencies of 1.5% and 0.5%, respectively, whereas the frequency of P1 antigen was 0.5%.

Table 1. Gene frequency and distribution of Rh antigens D (+) and D (-) patient (n=4299/5850)

Gene	Antigens	AF in D (+) Patients Number (%) n = 4299(88 %)	AF in D (-) Number (%) n = 5850 (12 %)
D	D (+)	0	42 (76.3%)
E	E (+)	62	9
C	C (+)	2	9 (16%)
e	e (+)	8	0
c	c (+)	11	0

AF, Antigen frequency

Table 2. Incidence of red cell antigen and gene frequency in Turkey blood recipients (n= 186).

	Number	%	Antigens	Number	%
Kell			MNSs		
K	43	23.11	M	7	3.76
Kpa	4	2.15	N	0	0
Kidd			S	2	1.07
Jka	5	2.68	s	0	0
Jkb	2	1.07	Lewis		
Duffy			Lea	3	1.61
Fya	5	2.68	Leb	1	0.53
Fyb	0	0	Lutheran		
P			Lua	0	0
P1	1	0.53	Lub	0	0
Xga	0	0			

DISCUSSION

Alloimmunization against RBC antigens is stimulated by the transfusion of blood products. In addition to RBC alloimmunization, immunological complications due to repeated blood transfusions can cause difficulties in finding appropriate blood and lead to the development of autoantibodies, as well as acute and delayed hemolytic transfusion reactions (4-5).

RBC antigens vary by ethnicity. The city of Kayseri, which is located in central Anatolia, Turkey, is homogeneous in terms of ethnicity and reflects the whole of the country in terms of the ABO and Rh blood group systems (11).

This is the first report regarding the antigen frequencies of various blood group systems in central Anatolia, Turkey. The overall frequency of alloimmunization in multi-transfused pediatric patients in Turkey (thalassemia and

other inherited hemoglobinopathies) is 47% (12). This rate is on the low side of the wide range of frequencies reported in the literature, with the highest rate of 76% in the United Kingdom (13), 34% in the United States (14), and 21.1% in Greece (15).

According to our study, the rate of alloimmunization was 0.4% in the healthy population, which is similar to data reported from different parts of Turkey (8,10). The rate of alloimmunization decreases when the donor and recipient are from the same ethnic group (6,7).

Although Rh antigen shows variations in ethnic groups around the world, its frequency varies between 85% and 95%. In the present study, the D antigen frequency was 88%, which is the lowest rate reported to date in Turkey. In addition, we investigated the frequencies of other antigens in the Rh system (C, c, E, and e) in the population of Kayseri. We found a marked difference in the frequency of E antigen in this population compared to the general frequency in Turkey (16). The frequencies of the C, c, and e antigens were 5.6%, 5.6%, and 4.1%, respectively. D antigen (76.4%) and C antigen (16.4%) were seen more frequently in Rh (-) recipients than in Rh (+) recipients.

Based on the antibody test results, patients prepared for surgical intervention reflected the general population, and hematological patients reflected those undergoing multiple transfusions. The rates of antigen frequency were similar between these two groups. In the present study, anti-E, anti-K, and anti-D were the most frequently detected alloantibodies. Although the frequencies of anti-M and anti-K alloantibodies were similar to those in other studies, the rates of anti-C and anti-D alloantibodies were different from those reported in Saudi Arabia and North India (6, 7).

The rate of warm antibody formation was 9.7% following multiple RBC transfusions, which is similar to the rates reported in other countries (3,7). In addition, the rate of dual antigen positivity was 7.5% in this study. Limitation of this study is the nondetermine age groups.

Multiple antigen detection is a significant problem in blood banking. In patients undergoing chronic transfusion, if hemoglobin levels decrease suddenly and a requirement for transfusion frequency increases without any other cause, the probability of multiple antibodies ought to be thought. In addition, the application of transfusions at different centers increases the antibody rate as a result of different transfusion practices.

CONCLUSION

Logical alloantibody screening can stop from transfusion reactions in patients undergoing multiple transfusions if a data bank can be created. Antibody screening tests, particularly in recipients, would reduce both time and financial losses.

Conflict of interest

The authors have no conflicts of interest associated with this publication.

Acknowledgments

We are grateful to all of the workers who graciously gave up their time for data collection. The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: <http://www.textcheck.com/certificate/X5yPqJ>

REFERENCES

1. Daniels G, Castilho L, Flegel WA, Garratty G, Henry S, Jorgensen J, et al. International society of blood transfusion committee on terminology for red cell surface antigens: vancouver report. *Vox Sang* 2003;84(3):244-7.
2. Calhoun L, Petz LD. Erythrocyte antigens and antibodies. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, Seligsohn D (Eds). *Williams Hematology*. New York: Mc Graw-Hill; 2001.p.1843-58.
3. Castellino SM, Combs MR, Zimmerman SA, Issitt PD, Ware RE. Erythrocyte autoantibodies in paediatric patients with sickle cell disease receiving transfusion therapy: frequency, characteristics and significance. *Br J Haematol* 1999;104(1):189-94.
4. Wheeler CA, Calhoun L, Blackall DP. Warm reactive autoantibodies: clinical and serologic correlations. *Am J Clin Pathol* 2004;122(5):680-5.
5. Aygun B, Padmanabhan S, Paley C, Chandrasekaran V. Clinical significance of RBC alloantibody and autoantibodies in sickle cell patients who received transfusions. *Transfusion* 2002;42(1):37-43.
6. Gader AG, Al Ghumlas AK, Al-Momen AK. Transfusion medicine in a developing country-alloantibodies to red blood cells in multi-transfused patients in Saudi Arabia. *Transfus Apher Sci* 2008;39(3):199-204.
7. Thakral B, Saluja K, Sharma RR, Marwaha N. Phenotype frequencies of blood group systems (Rh, Kell, Kidd, Duffy, MNS, P, Lewis, and Lutheran) in north Indian blood donors. *Transfus Apher Sci* 2010;43(1):17-22.
8. Akbay T, Demiröz P, Güneş C. Türkiyede kan gruplarının coğrafi bölgelere göre dağılımı. *GATA Bult* 1989;31(3):391-402.
9. Dilek I, Demir C, Bay A, Akdeniz H, Oner AF. ABO and Rh blood groups frequency in men and women living in eastern Turkey. *UHOD* 2006;1(16):23-6.
10. Ergin A, Yardımcı S. Distribution of ABO and Rh blood groups in Turkey. *Ankara Üni Tıp Fak Mec* 1993;46(2):527-33.
11. Torun YA, Kaynar LG, Karakükcü C, Yay M, Kurnaz F, Mutlu H, et al. ABO and Rh blood group distribution in Kayseri province, Turkey. *Turk J Haematol* 2012;29(1):97-8.
12. Canatan D, Karadogan C, Oguz N. Red cell antibodies in patient with Beta-thalassemia major. *Blood Banking and Transfusion Medicine* 2003;1(1):121-3.
13. Olujuhongbe A, Hambleton I, Stephens L, Serjeant B, Serjeant G. 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.
14. Vichinsky EP, Earles A, Johnson RA, Hoag MS, Williams A, Lubin B. Alloimmunization in sickle cell anemia and transfusion of racially unmatched blood. *New Engl J Med* 1990;322(23):1617-21.
15. Spanos T, Karageorga M, Ladis V, Peristeri J, Hatziliami A, Kattamis C. Red cell alloantibody in patients with thalassemia. *Vox Sang* 1990;58(1):50-5.
16. Canatan D, Acar N, Kılıç B. Rh subgroups and kell antigens in patients with thalassemia and in donors in Turkey. *Turk J Med Sci* 1999;29(2):155-7.