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Original Research Article

Frequency of red blood cell alloimmunization in sickle cell patients and healthy donors: the influence of racial and antigenic pattern differences

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ABSTRACT

Background: Red blood cell (RBC) transfusions are frequently used in patients with sickle cell disease (SCD) to treat and prevent of their disease complications. However repeated blood transfusions are often complicated by RBC alloimmunization. Race and antigenic pattern differences are the common risk factor to develop alloimmunization. This study was performed to determine the frequency of RBC alloimmunzation in sickle cell patients and healthy blood donors.
Methods: This is a cross sectional study that has been done on 140 patients with SCD and 140 healthy blood donors from April 2015 to April 2016. The RBC phenotype of all patients and donors investigated by Tub method and all panel test phases were done at immunohematology laboratory of Iranian Blood Transfusion Organization of Ahwaz.
Results: Of all SCD patients 61 (43.6%) were male and 79 (56.4%) were female. 68 (48.5%) were HbSS and 72 (51.4%) were S/B thalassemia. The mean age of patients was 19.69 (range: 2-60) years. Of all patients, 114 (81.25%) had received transfusion. The RBC alloimmunization rate among SCD patients was 7.1% and 50% of the RBC alloimmunization had anti-Kell and 30% had anti-Rh. The comparison of the RBC phenotypes between the group of patients with SCD and the group of blood donors (non-Arab) revealed a statistically significant difference in the frequency of S (54% vs. 67%, p=0.024), M (82.7% vs. 90.7%, p=0.049), and FYb (73.4% vs. 55.7%, p=0.002).
Conclusions: Althoguh alloimmunization rate in SCD patients in this study was lower than reported by other studies but cross matchining at least for the Rh and Kell systems from the time of initial transfusion may decrease the incidence of alloimmunization.

Keywords: Alloimmunization, Sickle cell disease, Transfusion

INTRODUCTION

Sickle cell disease (SCD) is a hereditary disease caused by substitution of the amino acid valine instead of glutamic amino acid in the sixth position of the beta chain and sickle hemoglobin production is caused. Sickle hemoglobin in the time of lack of oxygen, has less soluble than normal hemoglobin A and by forming a rod-like bodies within the red blood cells provide their destruction. Sickle gene of red blood cells, a common mutation in the areas of malaria which protect them against cerebral malaria Falysparm diseases.[1-3]

History of the sickle gene along with the recognition and the incidence of malaria. Nuclear and mitochondrial DNA analysis shows populations living in Africa have this mutation 50000 years ago. SCD include all cases of Hbs homozygous and all cases of compound

heterozygote mutation that one gene get mutation sickle and another gene get other mutations include Hbs, thalassemia, HbD, Hbo Arab. In SCD hemoglobin homozygous not produce and RBC include 90-100% of S hemoglobin. In compand homozygous, Hbs was more than HbA and in sickle form, RBC 20-40% of Hbs.[1-3]

Iran sickle cell with higher f hemoglobin more similar to Suadia and Indian-Asian type.[4]

The severity of signs in the SCD is more different and some of them without sign and recognized only in screening programs and some others suffered to pain. Complications of SCD including sickle cell dactylitis, sepsis, acute chest syndrome, pulmonary hypertension, kidney disease. Some patients to prevent attacks, strokes, cardiovascular failure, hematuria long-term, repeated Pysm fairies require repeated and chronic blood injections.[1-3]

Some of patients need for repeated blood injection has Immune response against the antigen in RBC which this phenomenon called Alloimmunization.[1-6]

The rate of alloimmunization in some areas reported 7-20% and in North American 8-50%.[1,5,7]

Age, sex, number of transfusions, unknown racial and genetic factors differences between recipients and blood donors are involved in the creation of alloimmunization.[1-3,5]

Given that SCD after thalassemia is the second common hemoglobinopathy and also racial and phenotype differences among SCD patients and blood donors as one of the effective and important causes in the development of alloimmunization, the aim of this study was to determine the frequency of alloimmunization in patients with SCD and blood donors.

METHODS

This cross-sectional study has been done on 140 patients with SCD and 140 randomly selected blood donors from April 2015 to April 2016. At admission time, a questionnaire included questions about time of last blood donor; IVIG and antibiotic receiving were asked patients. Patients with transfusion less than one month and getting IVIG not included in the study. Blood samples from SCD patients and donors were phenotyped, using standard techniques recommended for the following red-cell antigens: A, B, C, D, E, C, E, K, k, M, N, s, S, FYa, FYa, JKb and JKa. Consent form completed for all patients and patients didn't pay any money for their experiments. Collected data analyzed by statistical methods in SPSS.16.

RESULTS

In this study 140 patients with SCD were studied. 61 (43.5%) of them were male and 72 (51.5%) were thalassemia sickle cell which of them, 45 (32%) cases were positive beta sickle and 27 (19.2%) zero thalassemia sickle. The mean age of patients was 16.7 (range 2-60). The mean of hemoglobin was 8.2 (range 6-13). 31 (22%) of patients have splenomegaly and 23 (16.4%) have splenectomy. Most of patients with history of exchange transfusion have severe pain attack (72.2%) (Table 1).

Table 1: Characteristics of the study participants with SCD.

Variables	n	%
Sex		
Male	61	43.5
Female	79	56.5
Type of sickle cell		
Homozygous	68	48.5
Thalassemia	72	51.5
History of blood transfusion (yes)	114	81.3
Start age of bloodletting in transfused patients		
<3	47	41.2
>3	67	58.8
History of exchange transfusion (yes)	18	12.8

Table 2: Comparison between frequency of RBC in SCD patients and healthy Arabian donors.

RBC antigen	Arabian donors (%)	SCD (%)	P value
e	92/9	97/9	70.0
c	80	80/7	0/9
E	32/9	40	0/3
C	74/3	79/3	0/41
D	91/4	95	0/31
S	50	67/1	0/016
N	61/4	65	0/6
M	78/6	90/7	0/015
K	0	6/4	0/79
s	77/1	88/5	0/035
F.y.b	75/4	55/7	0/006
F.y.a	63/8	55/7	0/26
J.k.b	69/6	68/6	0/88
J.k.a	72/5	72/9	0/95

The RBC alloimmunization rate among SCD patients was 7.1% which 70% of them were female and rest of them were males. Of alloimmunization cases 90% have bloodletting age more than three years and the incidence of alloimmunization increased significantly by increasing the first age of blood transfusion. In this study there wasn't significant relation between alloimmunization and rate of injection volume. The frequency of allo-antibody orderly were 50% anti-Kell, 30% anti-E and 10% anti-D and 10% unknown, respectively. The frequency of minor blood groups in two groups were in phenotype S (50% in

healthy Arabian donors vs. 67.1% in sickle cell patients, p=0.016), phenotype M (78.6% in healthy Arabian donors vs. 90.7%, p=0.01), phenotype s (77.1% in healthy Arabian donnor and 88.5% sickle cell patients, p=0.035) and FYb (75.4% in healthy Arabian donors vs. 55.7% in sickle cell patients) and the difference between two groups were significant (Table 2).

Table 3. Comparison between frequency of RBC in SCD patients and healthy non-Arabian donors.

RBC antigen	Non-arabian donors (%)	SCD (%)	P value
e	97/1	97/9	0/74
c	68/6	80/7	0/05
E	42/9	40	0/69
C	80	79/3	0/9
D	97/1	95	0/47
S	57/1	67/1	0/15
N	55/7	65	0/19
M	87/1	90/7	0/42
K	21/1	6/4	0/05
s	84/3	88/5	0/4
F.y.b	71/4	55/7	0/028
F.y.a	68/6	55/7	0/07
J.k.b	55/7	68/6	0/06
J.k.a	80	72/9	0/25

The significant difference only was seen in phenotype FYb between blood groups in two groups (55.7% in sickle cell patients vs. 71.4% in non-Arabian healthy donors, p=0.028) (Table 3).

Table 4: Comparison between frequency of RBC in SCD patients and healthy Arabian/ non-Arabian donors.

RBC antigen	Donors (%)	SCD (%)	P value
e	95	97/9	0/19
c	74/8	80/7	0/23
E	38/1	40	0/74
C	77	79/3	0/64
D	94/2	95	0/78
S	54	67/1	0/024
N	58/3	65	0/24
M	82/7	90/7	0/049
K	20	6/4	0/06
s	80/6	88/5	0/07
F.y.b	73/4	55/7	0/002
F.y.a	66/2	55/7	0/07
J.k.b	62/6	68/6	0/29
J.k.a	76/3	72/9	0/51

There was significant difference in four blood types between SCD patients and Healthy Arabian and Non-Arabian donors that included S(54% in healthy donors vs. 67% in sickle cell patients, p=0.024), M (82.7% in healthy donors vs. 90.7% in sickle cell patients, p=0.049) and FYb (73.4% in healthy donors vs. 55.7% sickle cell patients, p=0.002) (Table 4).

DISCUSSION

The frequency of RBC alloimmunization rate in this study was 7.1% and in other studies this rate in SCD patients reported in range 4-40%. Several studies have indicated that the prevalence of RBC alloimmunization in SCD patients is in ranged from 9.9-30% which higher than our study results.[11-16]

In a study on major thalassemia patients, this rate reported 18.75% which was higher than our study report.[15]

In Gilberto Moreira et al study, the rate of RBC allo-immunization rate was 12.9% and 80% of alloantibodies against Kell and Rh phenotypes. Elliott and et al showed that 67% of Alloantibodies against Kell, E, C and JKb.[10,12]

Given the inherently high immunogenicity of blood groups Kell and Rh, the prevalence of alloantibody in our study and other studies were similar. In this study there wasn't significant difference between alloimmunization and the amount of transfused blood based cc/kg/year. In sickle cell patients at Brazil, there wasn't any significant difference between alloimmunization frequency and the volume of transfused blood.[12]

The transfused blood age was effective in allo-immunization incidence rate so that the frequency of allo-immunization in infants with first transfused blood less than three years significantly lower than other infants (20.9% vs. 47.5%, p=0.03). [14]

In this study, the frequency of RBC alloimmunization has relation with age of blood transfusion. Even though, of 10 patients with RBC alloimmunization, 7 patients were female but the difference wasn't significant and this result in line with other studies.[13]

There was significant in compare phenotype of RBC in SCD patients with non-Arabian healthy donoors in monor blood groups type FYb (71.4% in non-Arabian healthy donors vs. 55.7% in SCD patients, p=0.028) but there wasn't any significant between other phenotypes. FYb and FYa are the common Alleles in Asian and Europian races and anti FYa and anti FYb found in transfusion reactions. Anti FYa cause mild hemolytic anemia but FYb didn't.[1]

There was significant difference between healthy donors and SCD patients at three phenotypes FYb, M and S. Although in our study there wasn't found any effective allo-antibody on FYb, M and S but a significant difference in the frequency of minor blood groups will predispose alloimmunization in repeated transfusions and sometimes inevitable in SCD patients. Alloantibodies M,

N and S usually not associated with clinical signs and in cases without history of transfusion can be positive. [1]

In a study in Brazil only the group type C has significant difference between healthy donors and SCD patioents.[12] This study showed that racial differences in SCD patients is one of the causes of the SCD in patients.[1,12-13]

In compare minor blood groups between SCD patients (commonly are from Arabian races) and healthy non-Arabian donors, the difference was only seen in FYb phenotype but in whiten healthy and sickle cell Arabian races the difference between three blood groups was significant that could be related due to racial diversity among Iranians Arabs (from Sudan, Iraq, Yaman, Behraine). In other words, inter-ethnic blood transfusions in this study can be associated with the higher risk of alloimmunization in patients.

CONCLUSION

Patients with SCD, for many reasons such as severe pain, acute chest syndrome and stroke are needed regular blood transfusions and alloimmunization is one of the dangerous side effects of transfusion. Although in this study, the phenotype of blood groups of non-Arabian healthy volunteers and SCD patients except FYb weren't difference but in compare the phenotype of patients with blood donors at least in three phenotypes S, M and FYb was significant difference. So it is recommended that a database containing comprehensive information about phenotype of blood groups of healthy volunteers of both race and SCD patients is essential but its formation seperatly between SCD patients and Arabian donors not necessary.

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