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Transfusion in autoimmune hemolytic anemia: comparison of two different strategies

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Abstract

Objective: Autoimmune Hemolytic Anaemia (AIHA) is a condition in which red blood cells (RBC) are destroyed by autoantibodies. Clinicians tend to avoid the transfusion in AIHA patients who has difficulties during pre-transfusional testing. Depending on the institutional policy, the transfusion of the selected least incompatible RBC unit is a strategy. Since ORh(-) RBCs are the universal RBC donor type, the transfusion of the group ORh(-) RBC is selected in AIHA patients. In this study, we compared the effects of group ORh(-) RBC or least match incompatible same type of blood product transfusion in AIHA patients.

Material and Methods: The study included newly-diagnosed AIHA patients without active bleeding who required transfusion due to symptomatic anemia. ORh(-) RBC was transfused to the patients who had different blood groups and for the other patients, the least match incompatible same type blood product was transfused. Pre- and post-transfusion hematological and biochemical indicators were reported and compared.

Results: We determined that; there was no significant difference between groups regarding the increase in Hb levels and hemolysis parameters. In correlation analysis, the lower the pre-transfusion MCV value, the higher the LDH change. The lower the pre-transfusion MCV value, the decrease in hemolysis was higher.

Conclusion: Clinicians should not avoid transfusion for critically anemic AIHA patients for whom compatible RBC has not been found. Both group ORh(-) types of RBCs and same type least incompatible RBCs can be preferred for transfusion in critically patients when further compatibility testing procedures for alloantibodies detection cannot be performed.

Keywords: Autoimmunity, Hemolytic Anemia, Transfusion Reaction

Introduction

Autoimmune Hemolytic Anaemia (AIHA) is a condition in which red blood cells (RBC) are destroyed by autoantibodies and removed from the bloodstream by the immune system before their normal lifespan is over. If the rate of hemolysis is greater than hematopoiesis, severe symptoms of acute anemia develop and patients may become decompensated. In the literature, there is no absolute contraindication to RBC transfusion for AIHA patients, as it remains a safe procedure (1). According to the recent guidelines, if a patient has cardiopulmonary symptoms due to anemia, transfusion recommended regardless of hemoglobin level(2). However, generally, clinicians avoid transfusion due to the difficulties in pre-transfusion testing to provide the serologically compatible RBCs. Alloantibodies that were hidden by auto-antibodies, found in up to 40% of AIHA patients and may cause a new hemolytic status(3,4). Special tests are recommended to determine the presence of an alloantibody and proper cross-matching since triggering a new hemolytic status.

In clinical practice, procedures cannot be routinely performed in all transfusion centers due to the cost-effectiveness and time-consuming.

As difficulties experienced during pre-transfusion testing, transfusion of the selected least incompatible RBC unit is a strategy in some centers(5). Since O, Rh(D)-negative RBCs are the universal RBC donor type, mostly use of these RBCs before the completion of compatibility testing is advised, such as the setting of trauma or patients with the unanticipated hemorrhage who require an urgent transfusion (6). Depending on the institutional policy, the transfusion of group O, Rh(D)-negative RBC is selected in AIHA patients with difficulties during pre-transfusion testing. In this study, we aimed to determine the efficacy and safety of transfusion strategies by analyzing demographic and clinical characteristics of the patients in the era of different transfusion strategies

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Material and Methods

Baseline Characteristic

The study included newly-diagnosed warm-type AIHA patients without active bleeding who required transfusion due to symptomatic anemia with the hemoglobin (Hb) level of <7gr/dl. Other causes of acquired or hereditary hemolytic anemia, such as paroxysmal nocturnal hemoglobinuria and glucose-6-phosphate dehydrogenase deficiency were excluded. The patients had no previous history of transfusion or hematological disease but had comorbidities including diabetes mellitus, coronary heart disease or hypertension.

The selected patients had difficulties to find a compatible RBC unit during cross-match testing. Blood grouping was confirmed and further immunological testing included DAT, auto-antibody detection, auto-control, and indirect antiglobulin test (IAT) were applied to incompatible RBC units using gel technology (DiaMed, BİoRAd, Switzerland). Groups were randomized according to age comorbidities and blood grouping. O Rh (-) blood product was transfused to the patients who had different blood groups (group 1). For the other patients, the least match incompatible same type of blood product was transfused (group 2). Least incompatible type-specific RBC units were selected in the bank reserve. All procedures in the laboratory and selection of the RBC product were made by the technician on duty. Methylprednisolone 1mg/kg/day was initiated at the diagnosisof all patients for AIHA treatment.

Transfusions and Hemolysis Parameters

In this study, the age of the patients, chronic disease status, hemodynamic instability, and Hb status were considered when deciding to transfusion. Without comorbidity and/or younger patients who cannot tolerate a sudden decrease in Hb were transfused due to hemodynamic instability. None of the patients had any premedication such as steroids or antihistamines before transfusion. Transfusions were observed by medical professionals to identify any evidence of acute hemolysis. Each patient received 2 consecutive RBC units in a single procedure. Each transfusion was started from the same vascular access and finished as rapidly as tolerated, with the complete transfusion not exceeding 4 hours. Vital signs and complaints of patients attributed to possible acute transfusion reactions such as dyspnea, headache, hypotension, back pain, fever, tachycardia, and chills were recorded by the observer. Symptoms indicating hemolysis were observed, and in case of an attributable sign, the transfusion was stopped.

Pre- and post-transfusion (24 hours after transfusion) hematological and biochemical indicators of hemolysis, including Hb, hematocrit (HCT), percentage of reticulocyte (RETIC %), serum lactate dehydrogenase (LDH), serum total and unconjugated bilirubin levels were reported and compared. The increase in Hb levels (Hb Δ) calculated with the formula (post-transfusion Hb level - pretransfusion Hb level) was compared by pre- and post-transfusion hemogram parameters.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS version 20.0 software (Chicago, IL, USA). Categorical variables were stated as number (n) and percentage (%), parametric variables as mean ± standard deviation, and non-parametric variables as median and range values. In the comparison of parametric and non-parametric data between two dependent groups, the Paired Samples t-test or the Wilcoxon test was applied, respectively.

Variables and outcomes between two independent groups were compared using the Mann-Whitney U and Independent Sample-t-test for non-parametric and parametric variables, respectively.Chi-square tests were used to compare categorical variables. Pearson or Spearman correlation analyses were performed. All statistical tests were two-sided, and a value of $P<0.05$ was considered statistically significant.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. As a standard of care/action in our department, the patient records confirmed that all the study patients gave informed consent at the time of hospitalization and before the transfusion and other relevant diagnostic/therapeutic standards of care.

Results

Patients Characteristic

Totally 17 units of RBCs transfused to 35 newly-diagnosed AIHA patients (28 males, 7 females) with a mean age of 62.63± 1.98 years. 34 units of group O, Rh(D)-negative RBC were transfused to 17 AIHA patients and 36 units of type-specific RBC were transfused to 18 patients.

The mean age and sex frequency of groups were similar. All patients (100%) had IgG type autoantibodies whereas 10 patients (58.8%) in group 1 and 14 patients (77.7%) in group 2 had C3d + type autoantibodies. The demographic data of all the patients and the transfusion units are presented in Table 1. All the transfusions in two groups were completed without any complications or signs of hemolysis.

Hematological parameters

The increase in Hb levels (Hb Δ) was observed in both patient groups following the transfusions (1.50±0.54 for group 1 and 1.67±0.66 for group 2). However, no statistically significant difference was found between the two transfusion strategies ($p>0.05$).

There was no correlation between Hb Δ and a pre-transfusional parameter which may affect Hb increments. Parameters related to pre- and post-transfusion were detailed in Table 2.

Biochemical parameters

Hemolysis parameters that including LDH, total and unconjugated bilirubin were decreased in both groups after transfusion. Parameters indicating hemolysis were not found statically different in two methods (p:0.79, 0.17 and 0.22 resp.).

Detailed biochemical parameters are given in Table 2. In correlation analysis, there was significant correlation only with LDH Δ and pre-transfusion MCV (p:0.001, r:-0.53) and bilirubin (p:0.002, r:-0.51) levels (Table 3.)

Table1. The demographic and antibody data of the patients

Parameter	Total (n=35)	According to transfused blood product	
		Group1(n=17)	Group 2(n=18)
Age	62.63±1.98	62.82±2.94	62.44±2.76
Gender			
Male	28(80%)	13 (76.5%)	15(83.3%)
female	7 (20%)	4(23.5%)	3(16.7%)
Direct coombs (n. %)			
IgG(+)	35 (100%)	17 (100%)	18 (100%)
IgG(+). C3(+)	24 (68.5%)	10 (58.8%)	14 (77.7%)
Indirect Coombs(+) (n. %)	26 (74%2)	15 (88.2%)	11 (61.1%)

Table2. Pre- and post-transfusional hematological and biochemical assessment

Parameter	*Group 1 (N=17)*	*Group 2(N=18)*	*p*
Pre-Transfusion	5.78±0.18	5.58±0.27	*0.57*
Hb (g/dL) (Mean±SD) Hct (%)	16.94±0.63	18.11±1.07	*0.36*
(Mean±SD) MCV(fL)	111.76±1.79	110.94±2.13	*0.77*
(Mean±SD)	878.0 (577.55-1304.80)	802.0(644.58-1696.52)	*0.47*
Median LDH (range)	4.05±0.39	4.60±0.64	*0.48*
Total bilirubin (mg/dL) (Mean±SD)	3.38±0.36	3.85±0.55	*0.48*
Unconjugated bilirubin (mg/dL) (Mean±SD)			
Post-Transfusion	7.28±0.17	7.26±0.22	*0.94*
Hb (g/dL) (Mean±SD) Hct (%)	21.88±0.69	22.00±0.80	*0.91*
(Mean±SD) MCV(fL)	103.76±1.83	105.83±2.05	*0.46*
(Mean±SD)	688.0 (470.37-938.69)	677.0 (478.90-1296.76)	*0.49*
Median LDH (IU/L) (range)	2.90±0.30	3.60±0.51	*0.21*
Total bilirubin (mg/dL) (Mean±SD)	2.23±0.27	3.06±0.45	*0.13*
Unconjugated bilirubin (mg/dL) (Mean±SD)			
Δ value Hb (Mean±SD)	1.50±0.54	1.67±0.66	*0.40*
Median LDH (range)	-120.0 (-26.0 -1528.0)	-161.0 (-18.0 -1203.0)	*0.79*
Median Total bilirubin (range)	-0.70 (0 -3.40)	-0.65(0 -2.0)	*0.17*
Median Unconjugated bilirubin (range)	-0.90 (0 -3.0)	-0.60(0.10 -2.9)	*0.22*

Table3. Pre- and post-transfusional hematological and biochemical correlation

Parameter	Δ Hb	Δ Total Bilirubin P value (r*)	Δ Unconjugated bilirubin P value (r*)	Δ LDH P value (r*)
Age	0.22	0.38	0.7	0.11
Sex	0.28	0.37	0.12	0.35
Pre- transfusion				
Hb	<0.001	0.32	0.53	0.25
Hct	0.27	0.18	0.14	0.15
Mcv	0.004	0.42	0.69	0.001(-0.53)
LDH	0.16	0.64	0.98	0.59
Total bil	0.44	<0.001(-0.67)	<0.001(-0.72)	0.002(-0.51)
Unconjugated bil	0.44	<0.001(-0.65)	<0.001(-0.67)	0.002(-0.49)
Post-transfusion				
Hb	0.69	0.74	0.86	0.73
Hct	0.65	0.59	0.56	0.64
Mcv	0.1	0.92	0.77	0.14
LDH	0.32	0.98	0.67	0.88
Total bil	0.72	0.12	0.2	0.14
Unconjugated bil	0.61	0.15	0.33	0.15

Discussion

In this study, we compared the effects of O Rh (-) RBC or least match incompatible same type RBC transfusion in AIHA patients and we determined that; there was no significant difference between groups regarding the increase in Hb levels and hemolysis parameters. In correlation analysis, the lower the pre-transfusion MCV value, the higher the LDH change. The lower the pre-transfusion MCV value, the decrease in hemolysis was higher.

There is no absolute contraindication to RBC transfusion in AIHA patients, as it remains a safe procedure. But autoantibodies often cause laboratory problemsdetermining ABO and Rh groups problematic and preventing effective antibody screening due to cross-reacting antibody (7). Therefore, clinicians tend to avoid transfusion in AIHA patients who has difficulties during the pre-transfusional test. For these patients, serological investigations are recommended to determine the presence of alloantibodies and proper cross-matching since trigger a new hemolytic status. However, despite providing phenotypically matched RBC reduces the risk of hemolysis, it does not totally eliminate the transfusion-related hemolytic status. Furthermore, the feasibility of these tests seems to be disadvantageous as time-consuming for patients who require urgent transfusion.

Depending on the institutional policy, mostly transfusion of the least incompatible RBC unit selected by seeking out all RBC products in the bank reserve. Recently, some reports demonstrate the safety and feasibility of this strategy (8-10). Different than the other studies, we investigated the Hb increments and hemolysis risk of transfusion with Group O, Rh(D)-negative RBC which is the universal RBC donor type. In these patients matching blood with the patient's own type is recommended due to the risk of transfusion reaction due to underlying alloantibodies theoretically(11). However, to the best of our knowledge, there is no any report that is confirmed by studies.

In the current study, a significant elevation in Hb levels was recorded in both groups following transfusions. Furthermore, a statically significant difference was not noticed between the groups. Due to severe anemic symptoms of the patients, two units of RBC transfused for each patient. Since the age of donors RBCs was expected to be younger, two units of RBC were transfused to clarify Hb increments. Parks et al. compared the post-transfusion Hb and hemolysis parameters in AIHA patients positive for alloantibodies only or those without RBC-specific antibodies (9). They reported the findings did not support newly-developed hemolysis in all groups. In our study, a decrease in hemolysis parameters was observed in the following days of transfusion which was associated with the regression of hemolysis over time. We consider that initiated steroid therapy may be effective to control the hemolysis.

Recently Chen et al. reported a large retrospective study on hospitalized AIHA patients. They analyzed the rate of transfusion reactions with the use of least incompatible RBCs (10). They found that patients who had lower Hb levels at baseline were the most benefited group from the least incompatible RBC transfusion. The remission rate was found higher in AIHA patients with Hb<6g/dl at admission. In our study efficacy of transfusion may be associated with mean initial Hb level was <6 g/dL.

A concerning problem in the transfusion of group O RBC to non-O recipients is limited number of group O products. It is not recommended routinely in daily practice except emergency. Therefore, we suggest to use the group O RBC only in cases where a sufficient number of products cannot be scanned for compatibility testing due to the reserve in the bank.

The limitations of the current study were the retrospective design and the small number of the patient population. Since two units of RBC were transfused to the patients, we could not determine the increase corresponding to the 1 unit RBC transfusion.

Conclusion

Clinicians should not avoid transfusion of O Rh (-) types for critically anemic AIHA patients for whom compatible RBC has not been found. Both group O Rh (-) types of RBCs and same type least incompatible RBCs can be preferred for transfusion in critically patients when further compatibility testing procedures for alloantibodies detection cannot be performed. Further, larger prospective studies are warranted to determine the clinical effects of O Rh (-) types for critically anemic AIHA patients.

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References

1. Petz LD. A physician's guide to transfusion in autoimmune haemolytic anaemia. Br J Haematol. 2004;124:712-6.

2. Carson JL, Grossman BJ, Kleinman S, Tinmout AT, Marques MB, Fung MK, et al. Red blood cell transfusion: a clinical practice guideline from the AABB*. Ann Intern Med. 2012;157:49-58.

3. Sokol RJ, Hewitt S, Booker DJ, Morris BM. Patients with red cell autoantibodies: selection of blood for transfusion. Clin Lab Haematol. 1988;10:257-64.

4. Laine ML, Beattie KM. Frequency of alloantibodies accompanying autoantibodies. Transfusion. 1985;25:545-6

5. Ziman A, Cohn C, Carey PM, Dunbar NM, Fung MK, Greinacher A et al. Warm-reactive (immunoglobulin G) autoantibodies and laboratory testing best practices: review of the literature and survey of current practice. Transfusion. 2017;57:463-77.

6. Dutton RP, Shih D, Edelman BB, Hess J, Scalea TM. Safety of uncrossmatched type-O red cells for resuscitation from hemorrhagic shock. J Trauma. 2005;59:1445-9.

7. Maley M, Bruce DG, Babb RG, Wells AW, Williams M. The incidence of red cell alloantibodies underlying panreactive warm autoantibodies. Immunohematology. 2005;21:122-5.

8. Das SS, Zaman RU, Safi M. Incompatible blood transfusion: Challenging yet lifesaving in the management of acute severe autoimmune hemolytic anemia. Asian J Transfus Sci. 2014;8:105-8.

9. Park SH, Choe WH, Kwon SW. Red Blood Cell Transfusion in Patients With Autoantibodies: Is It Effective and Safe Without Increasing Hemolysis Risk?. Ann Lab Med. 2015;35:436-44.

10. Chen C, Wang L, Han B, Qin L, Ying B. Autoimmune hemolytic anemia in hospitalized patients: 450 patients and their red blood cell transfusions. Medicine (Baltimore). 2020;99:e18739.

11. Milkins C, Berryman J, Cantwell C, Haggas R, Jones J, Rowley M et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. British Committee for Standards in Haematology. Transfus Med. 2013;23:3-35.