Effects of cooperative blood transfusion and homologous blood transfusion on the production of red blood cell irregular antibodies in obstetric patients

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Abstract. Effects of cooperative blood transfusion and homologous blood transfusion on the production of red blood cell irregular antibodies in obstetric patients were investigated. A total of 300 obstetric patients who underwent blood transfusion in the Maternity and Child Health Care of Zaozhuang from February 2016 to February 2018 were enrolled. There were 150 obstetric patients receiving the same type of transfusion who were included in the control group. Due to special circumstances the remaining 150 obstetric patients with ABO and Hr with cooperative blood transfusion were included in the research group. The positive detection rate of blood cell irregular antibody, the effectiveness of blood transfusion and the incidence of adverse transfusion reaction were observed in the two groups after the comparison of blood transfusion of both groups. The total positive detection rate of erythrocyte irregular antibody in the research and control groups was not statistically significant (P>0.05). There were no significant differences in the red blood cell counts, hemoglobin concentration, hematocrit and platelet count between the research and control groups after infusion (P>0.05). Comparing all the groups, the red blood cell counts, hemoglobin concentration, hematocrit and platelet count after infusion in both the research and control groups were significantly higher than before the infusion, and differences were statistically significant (P<0.001). There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). The effect of blood transfusion and homologous blood transfusion on the positive detection rate of red blood cell irregular antibody in obstetric patients, the efficiency of blood transfusion and the incidence of adverse transfusion reactions are similar, and all have high clinical application value.

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Introduction

Obstetric patients have adverse reactions to blood transfusion and difficulty in matching blood, mainly due to the production of red blood cell irregular antibodies in the body due to immune stimulation during pregnancy or massive blood transfusion (1,2). Red blood cell irregular antibodies can cause neonatal hemolysis in newborns, therefore the incomplete antibody test is performed on the patients who need blood transfusion before transfusion to understand the production of blood group antibodies in patients, and the patient's adverse reaction of transfusion is avoided as much as possible (3,4). Related studies have confirmed that negative screening of irregular antibodies does not mean that there are no irregular antibodies at all, and cross-matching before blood transfusion is also very important (5,6). To ensure the safety of blood transfusion, WHO-related documents require pregnancy screening or short-term need to receive multiple blood transfusions must be screened for irregular red blood cell antibodies (7). Incomplete antibody screening for obstetric patients is helpful for the diagnosis of hemolytic disease in newborns (8).

Blood transfusion is based on the principle of homologous blood transfusion. ABO, RhD homologous blood transfusion is an important method for the treatment of obstetric patients with severe blood loss (9). For obstetric patients, the time of transfusion treatment is crucial. Once the optimal blood transfusion time is delayed, it can cause death of the patients. However, in some critically ill patients, there is a lack of homologous blood in the blood bank or a difficult blood type. Then cooperative blood transfusion becomes an important approach (10,11). Cooperative type blood transfusion is used to determine the compatibility of blood transfusion on the basis of blood type identification. Then, the blood recipient and the blood donor can use the cross-matching blood test to confirm that both do not have blood group incompatibility agglutination, and avoid agglutination reaction for the blood recipient due to the antibody antigens, which could cause a transfusion accident (4,10,12).

The aim of the present study was to investigate the effect of cooperative blood transfusion and homologous blood transfusion on the production of red blood cell irregular antibodies in obstetric patients.

Patients and methods

General information. A total of 300 cases of obstetric patients who underwent blood transfusion therapy in the Maternity and Child Health Care of Zaozhuang (Zaozhuang, China) from February 2016 to February 2018 were enrolled. A total of 150 obstetric patients receiving homologous blood transfusion were included in the control group, and 150 cases of obstetric patients who underwent ABO and Rh with cooperative blood transfusion were included in the research group. The age range of the research group was 22-40 years, and the average age was 25.79±7.38 years; the age range of the control group was 22-38 years, and the average age was 26.04±5.24 years. Inclusion criteria were that all subjects who were diagnosed as critically ill and required transfusion therapy were clinically diagnosed, and all were treated according to WHO special circumstances emergency rescue blood transfusion program. Any subjects with coagulophagy, liver dysfunction, renal dysfunction or other hematological diseases were excluded.

Patients and their families were required to sign informed consent in advance. The study was approved by the Ethics Committee of Maternity and Child Health Care of Zaozhuang.

Main methods

Reagents and instruments. SA-2000 automatic blood type blood matching analyzer (Shanghai Hanfei Medical Instrument Co., Ltd., Shanghai, China), FYQ type immune microcolumn incubator (Beijing Zhuochuan Electronic Technology Co., Ltd., Beijing, China), anti-human globulin gel card (Changchun Bo Xun Biotechnology Co., Ltd., Changchun, China), BC-5000 automatic five-class blood cell analyzer (Shanghai Yuyan Scientific Instrument Co., Ltd., Shanghai, China), poly-condensed amine method kit (Beijing Ovia Biotechnology Co., Ltd., Beijing, China), micro-column gel reagent Box (Beijing Ovia Biotechnology Co., Ltd.) were used in the study.

Method. Firstly, the SA-2000 automatic blood type blood matching analyzer was used to identify the ABO positive, negative and RhD blood type in the two groups. The research group received ABO and Rh main antigen cooperative blood transfusion due to special circumstances, and the control group received homologous blood transfusion therapy. Before the infusion and 24 h after the blood transfusion, 5 ml of fasting venous blood was taken in the early morning, centrifuged at 3,000 x g for 10 min at 4˚C, and the serum was separated and incubated in an FYQ immunomicrocolumn incubator for 15 min. Irregular antibodies were screened by the microcolumn gel and polybrene methods.

Specific procedures. i) Microcolumn gel method. The instructions of the micro-column gel method kit was strictly followed. First 50 μl of cells to be screened and 50 μl of self-cells were added to the microcolumn anti-human globulin gel card, and then 50 μl separated plasma was added. The plasma was incubated at 37˚C for 15 min and finally centrifuged at 1,500 x g for 10 min at 20˚C and the results were recorded.

ii) Polybrene method. The instructions of the polybrene method kit were adhered to: first, 1 drop of blood donor red blood cells at a concentration of 2% and 2 drops of blood serum from the recipients to the main side were added, then 1 drop was added to the secondary side at a concentration of 2% from the blood donor and 2 drops of blood serum from the blood recipient. Then 0.6 ml of no. I solution and 2 drops of no. II solution were added to the prepared primary and secondary tubes respectively, and centrifuged at 1,500 x g for 1 min. After centrifugation, the supernatant was aspirated and 2 drops of no. III solution were added and slowly mixed. Positivity was shown by a blood group incompatibility agglutination within 1 min, and negativity if it expanded within 1 min.

Judging criteria. The judgment of erythrocyte irregular antibody positive in this study refers to the judgment standard of erythrocyte irregular antibody positivity by WHO (13).

Observation index. The positive rate of erythrocyte irregular antibody was observed in the research and the control groups. After 24 h of transfusion treatment, the red blood cell count, hemoglobin concentration, hematocrit and platelet count were compared to analyze the transfusion efficiency of the two groups. The incidence of adverse transfusion reactions between the research and the control groups were observed.

Statistical analysis. Statistical analysis was carried out using the SPSS 17.0 (Beijing Bo Yi Zhixun Information Technology Co., Ltd., Beijing, China) software system. The enumeration data were expressed by [n (%)], and the χ^2 test was used to compare the enumeration data groups. The measurement data are the mean ± standard deviation. The Students' t-test was used to compare the data of the measurement. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Comparison of positive detection rates of red blood cell irregular antibodies in the two groups. There was no positive red blood cell irregular antibody detection in the research and the control groups before transfusion. After 30 days of transfusion, the total positive detection rate of red blood cell irregular antibody in the two groups was 2.67 and 4.00%, respectively. The groups were not statistically significant ($P>0.05$; Table I).

Comparison of blood transfusion efficiency of research and control groups

Comparison of red blood cell counts before and after red blood cell transfusion in the two groups. The red blood cell counts of the research and the control groups before the infusion were 2.02±0.16 and 2.03±0.18 10^{12}/l, respectively. There was no significant difference between the two groups ($P>0.05$). The red blood cell counts of the study and the control groups were 4.00±0.29 and 3.98±0.30 10^{12}/l, respectively. There was no significant difference between the two groups ($P>0.05$). Within the group, the red blood cell counts of the research and the control groups were significantly higher than before the infusion, and the difference was statistically significant ($P<0.001$; Table II and Fig. 1).

Comparison of hemoglobin concentration before and after red blood cell transfusion in the two groups. The hemoglobin

Table I. Comparison of positive detection rates of red blood cell irregular antibodies in two groups [n (%)].

Group	Research group (n=150)	The control group (n=150)	χ^2	P-value
Rh blood group system antibody				
Before infusion	0 (0.00)	0 (0.00)	-	-
After infusion	1 (0.67)	3 (2.00)	1.014	0.314
ABO blood group system antibody				
Before infusion	0 (0.00)	0 (0.00)	-	-
After infusion	1 (0.67)	2 (1.33)	0.337	0.562
Total positive detection rate				
Before infusion	0 (0.00)	0 (0.00)	-	-
After infusion	4 (2.67)	6 (4.00)	0.414	0.520

Table II. Comparison of red blood cell counts ($x10^{12}$/l) before and after red blood cell infusion.

Group	Research group (n=150)	Control group (n=150)	t	P-value
Before infusion	2.02±0.16	2.03±0.18	0.509	0.611
After infusion	4.00±0.29	3.98±0.30	0.587	0.558
t	73.220	68.260		
P-value	<0.001	<0.001		

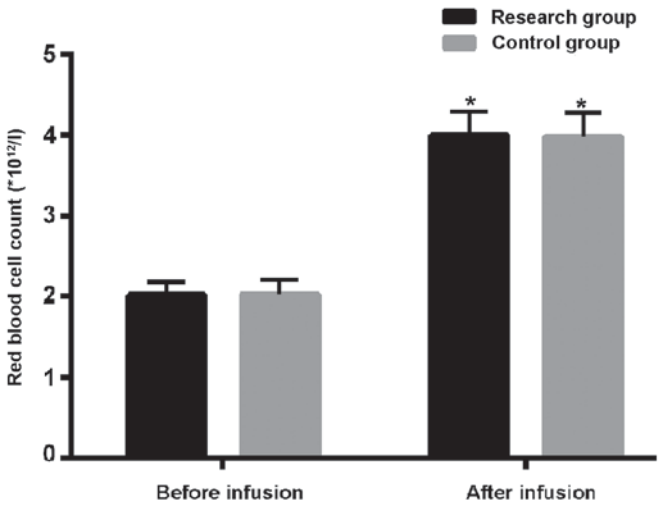

Figure 1. Comparison of red blood cell counts before and after infusion of red blood cells. There was no statistically significant difference between the two groups (P>0.05). There was no statistically significant difference in the red blood cell count between the two groups after infusion (P>0.05). The red blood cell counts of the control group were significantly higher than before the infusion, and the difference was statistically significant (P<0.001). *P<0.001, indicates that the difference between the group and the pre-infusion is statistically significant.

concentration of the research and the control groups before the infusion were 91.77±7.96 and 90.46±8.93 g/l, respectively. There was no significant difference between the two groups (P>0.05). The hemoglobin concentration of the study and the control groups were 128.18±10.08 and 127.32±11.56 g/l, respectively. There was no significant difference between the two groups (P>0.05). Within the group, the hemoglobin concentration of the research and the control groups were significantly higher than that before the infusion, and the difference was statistically significant (P<0.001; Table III and Fig. 2).

Comparison of hematocrit before and after red blood cell transfusion. The hematocrit of the research and the control groups before the infusion were 0.18±0.01 and 0.17±0.09, respectively. There was no significant difference between the two groups (P>0.05). The hematocrit of the study and the control groups were 0.24±0.02 and 0.23±0.09, respectively. There was no significant difference between the two groups (P>0.05). Within the group, the hematocrit of the research and the control groups was significantly higher than that before the infusion, and the difference was statistically significant (P<0.001; Table IV and Fig. 3).

Comparison of platelet counts before and after red blood cell transfusion in the two groups. The platelet counts of the research and the control groups before the infusion were 12.36±1.03 and 12.45±1.01 10^9/l, respectively. There was no significant difference between the two groups (P>0.05). The platelet counts of the study and the control groups were 28.12±1.34 and 28.09±1.37 10^9/l, respectively. There was no significant difference between the two groups (P>0.05). Within the group, the red blood cell counts of the research and the control groups were significantly higher than that before the infusion, and the difference was statistically significant (P<0.001; Table V and Fig. 4).

Comparison of adverse reactions between the research and the control groups. The total incidence of hemolysis, non-hemolytic fever, allergic reaction, post-transfusion purpura, graft-versus-host disease, transfusion color disease were compared between the two groups. The results showed that the differences between the two groups were not statistically significant (P>0.05; Table VI).

Table III. Comparison of hemoglobin concentration (g/l) before and after red blood cell infusion.

Group	Research group (n=150)	Control group (n=150)	t	P-value
Before infusion	91.77±7.96	90.46±8.93	1.341	0.181
After infusion	128.18±10.08	127.32±11.56	0.687	0.493
t	34.720	30.900		
P-value	<0.001	<0.001		

Table IV. Comparison of hematocrit before and after red blood cell infusion.

Group	Research group (n=150)	Control group (n=150)	t	P-value
Before infusion	0.18±0.01	0.17±0.09	1.353	0.177
After infusion	0.24±0.02	0.23±0.09	1.328	0.185
t	32.860	5.774		
P-value	<0.001	<0.001		

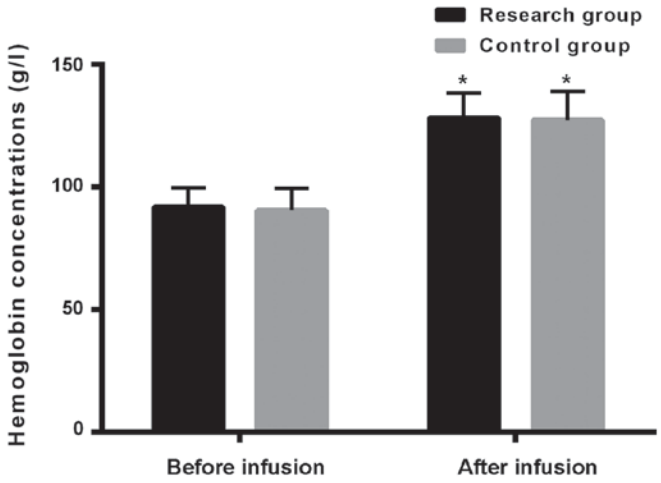

Figure 2. Comparison of hemoglobin concentrations before and after infusion of red blood cells. There was no statistically significant difference between the two groups (P>0.05). There was no statistically significant difference in the hemoglobin concentration between the two groups after infusion (P>0.05). The hemoglobin concentration of the control group was significantly higher than the hemoglobin before the infusion, and the difference was statistically significant (P<0.001). *P<0.001, indicates that the difference between the group and the pre-infusion is statistically significant.

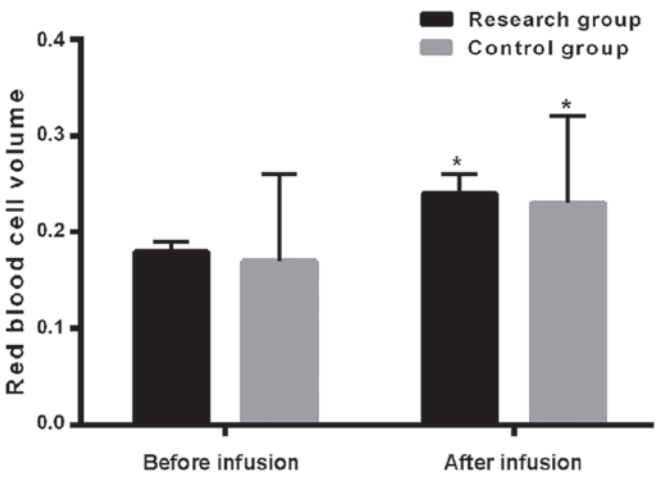

Figure 3. Comparison of hematocrit before and after infusion of red blood cells. There was no statistically significant difference between the two groups (P>0.05). There was no statistically significant difference in the hematocrit after infusion between the two groups (P>0.05). Comparing the groups, the hematocrit of the research group and the control group were significantly higher than that before infusion, and the difference was statistically significant (P<0.001). *P<0.001, indicates that the difference between the group and the pre-infusion is statistically significant.

Discussion

Obstetric hemorrhage is the main cause of maternal death, ranking the third cause of maternal death; most of the causes of death involve insufficient blood transfusion treatment, and rapid disease progression, leading to hemorrhagic shock (14,15). Blood transfusion therapy is one of the important means of treating obstetric patients, but in the process of massive blood transfusion, the body produces red blood cell irregular antibodies due to immune stimulation (3). Irregular antibodies produced during maternal transfusion can cause hemolytic disease and harm to newborns (16,17). It is the same type of blood transfusion as the first principle of blood transfusion, which is a common clinical blood transfusion method. However, when an emergency of blood transfusion occurs, such as the blood bank cannot provide the same type of blood, cross-matching blood and antibody screening positivity are imperative. Due to the above reasons, obstetric emergency patients are in danger if they do not undergo immediate blood transfusion. Moreover, insisting on the same type of blood transfusion will lead to the patient missing the best time for therapy. Therefore, under special circumstances, the use of cooperative blood transfusion, or insisting on the same type of blood transfusion has become a difficulty of clinical blood transfusion (18,19). This study investigated the effects of cooperative blood transfusion and homologous blood transfusion on the production of red blood cell irregular antibodies in obstetric patients.

Table V. Comparison of platelet counts (x10^9/l) before and after red blood cell infusion.

Group	Research group (n=150)	Control group (n=150)	t	P-value
Before infusion	12.36±1.03	12.45±1.01	0.764	0.445
After infusion	28.12±1.34	28.09±1.37	0.192	0.848
t	114.200	112.500		
P-value	<0.001	<0.001		

Table VI. Comparison of adverse reactions between the research and control groups [n (%)].

Group	Research group (n=150)	Control group (n=150)	χ^2	P-value
Hemolysis reaction	1 (0.67)	2 (1.33)	0.337	0.562
Non-hemolytic fever	1 (0.67)	1 (0.67)	-	-
Allergic reaction	1 (0.67)	1 (0.67)	-	-
Purpura after transfusion	1 (0.67)	2 (1.33)	0.337	0.562
Graft-versus-host disease	1 (0.67)	1 (0.67)	-	-
Transfusion color disease	1 (0.67)	1 (0.67)	-	-
Total incidence number	6 (4)	8 (5.33)	0.300	0.584

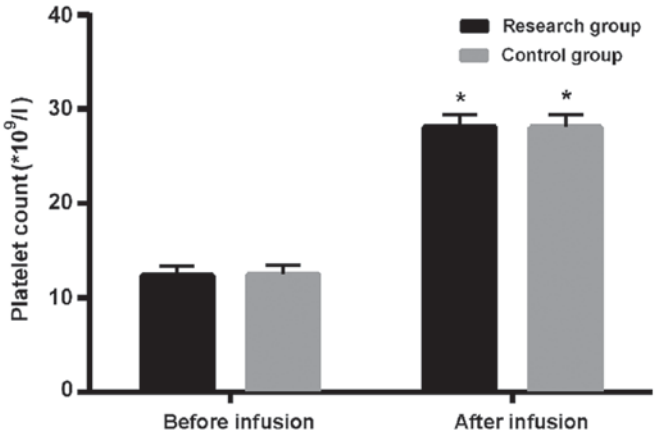

Figure 4. Comparison of platelet counts before and after red blood cell infusion in two groups. There was no statistically significant difference between the two groups (P>0.05). There was no statistically significant difference in platelet count between the two groups after infusion (P>0.05). The platelet counts of the control group were significantly higher before the infusion, and the difference was statistically significant (P<0.001). *P<0.001, indicates that the difference between the group and the pre-infusion is statistically significant.

In this study, we included 150 obstetric patients receiving homologous blood transfusion in the control group, and 150 obstetric patients who underwent ABO and Rh with cooperative transfusion in special cases were included in the research group. The two groups were compared before and after red blood transfusion. The positive rate of regular antibody detection showed that there was no positive red blood cell irregular antibody detection in the research group or the control group before transfusion. After 30 days of blood transfusion, the total positive rate of erythrocyte irregular antibody in the research and the control groups were 2.67 and 4.00%, respectively, and there was no significant difference between the two groups (P>0.05), which suggests that the type of red blood cell irregular antibody produced by the obstetric patients is similar to the cooperative blood transfusion or homologous blood transfusion. Guzman *et al* (19) also compared the occurrence of irregular antibodies in the red blood cells of patients with cooperative blood transfusion and patients with the homologous blood transfusion. The results showed that after transfusion, the patients with cooperative blood transfusion and patients with homologous transfusion had similar irregular antibodies in the red blood cells, and the difference was not statistically significant (P>0.05). This is an excellent demonstration of the results of this article. We then compared the transfusion efficiency and the incidence of adverse transfusion reactions after treatment for 24 h, the results of which showed that there was no significant difference in the red blood cell count between the research and the control groups after infusion (P>0.05). Comparing the groups, the red blood cell counts of the research and the control groups were significantly higher before the infusion, and the differences were statistically significant (P<0.001). There was no significant difference in hemoglobin concentration between the research and the control groups after infusion (P>0.05). Comparing the groups, the hemoglobin concentration in the research and the control groups was significantly higher before the infusion. The differences were statistically significant (P<0.001). There was no significant difference in the hematocrit between the research and the control groups after infusion (P>0.05). Comparing the groups, the hematocrit of the research and the control groups was significantly higher before the infusion, so the hematocrit was statistically significant (P<0.001). There was no significant difference in platelet count between the research and the control groups after infusion (P>0.05). Comparing the groups, the platelet counts of the research and the control groups were significantly higher before the infusion, the difference was statistically significant (P<0.001). There was no significant difference in

the total incidence of hemolysis, non-hemolytic fever, allergic reaction, post-transfusion purpura, graft-versus-host disease, transfusion color disease and adverse reactions between the two groups (P>0.05).

Following comparisons, findings of numerous related reports demonstrated the effective index values of cooperative transfusion and homologous transfusion with the adverse reactions after transfusion. There was no statistically significant difference (P>0.05) (20,21). Therefore, we speculated that both cooperative blood transfusion and homologous blood transfusion have high effectiveness.

This study has a limited number of subjects and this may have some impact on the experimental results.

In summary, the effect of cooperative blood transfusion and homologous blood transfusion on the positive detection rate of red blood cell irregular antibodies in obstetric patients, the efficiency of blood transfusion and the incidence of adverse transfusion reactions are similar, both have high clinical application value. The optimal blood transfusion protocol should be selected clinically based on the patient's blood transfusion needs.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JL and SW conceived and designed the study. DS and JL collected the data of the patients. JL and GC analyzed and interpreted the data of cooperative blood transfusion and homologous blood transfusion on the production of red blood cell irregular antibodies in obstetric patients. SW and DS performed the Microcolumn gel and Polybrene method. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Maternity and Child Health Care of Zaozhuang (Zaozhuang, China). Each patient who participated in this research, signed an informed consent and had complete clinical data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Sarnaik S, Schornack J and Lusher JM: The incidence of development of irregular red cell antibodies in patients with sickle cell anemia. Transfusion 26: 249-252, 1986.
2. Boonstra JG, Overbeeke MA, de Rijke YB and Duvekot JJ: A pregnant woman with irregular erythrocyte antibodies for whom no compatible packed red blood cells were available. Ned Tijdschr Geneeskd 149: 2633-2636, 2005 (In Dutch).
3. Li H, Xu HM, Zhang Y and Cui JX: Analysis of patients' irregular antibody screening and identification results before blood transfusion. Zhongguo Shi Yan Xue Ye Xue Za Zhi 23: 861-865, 2015 (In Chinese).
4. Garg N, Sharma T and Singh B: Prevalence of irregular red blood cell antibodies among healthy blood donors in Delhi population. Transfus Apheresis Sci 50: 415-417, 2014.
5. Gaur DS, Negi G, Chauhan N, Kusum A, Khan S and Pathak VP: Utilization of blood and components in a tertiary care hospital. Indian J Hematol Blood Transfus 25: 91-95, 2009.
6. Bhattacharya P, Samanta E, Afroza N, Naik A and Biswas R: An approach to incompatible cross-matched red cells: Our experience in a major regional blood transfusion center at Kolkata, Eastern India. Asian J Transfus Sci 12: 51-56, 2018.
7. Aneke JC and Okocha CE: Blood transfusion safety; current status and challenges in Nigeria. Asian J Transfus Sci 11: 1-5, 2017.
8. Perelman R: Hemolytic disease of newborn. Med Infant (Paris) 66: 3-71, 1959 (In French).
9. Enosolease ME and Bazuaye GN: Distribution of ABO and Rh-D blood groups in the Benin area of Niger-Delta: Implication for regional blood transfusion. Asian J Transfus Sci 2: 3-5, 2008.
10. Liu W, Le AP, Liu JH and Lan JC: Experimental study on neonatal ABO or RhD compatible blood transfusion. Zhongguo Shi Yan Xue Ye Xue Za Zhi 25: 916-920, 2017 (In Chinese).
11. Coghlan G, McCreary J, Underwood V and Zelinski T: A 'new' low-incidence red cell antigen, LOCR, associated with altered expression of Rh antigens. Transfusion 34: 492-495, 1994.
12. Chan AH, Chan JC, Wong LY and Cheng G: From maximum surgical blood ordering schedule to unlimited computer crossmatching: Evolution of blood transfusion for surgical patients at a tertiary hospital in Hong Kong. Transfus Med 6: 121-124, 1996.
13. Zhao XR, Gao C, Zhang Y and Yu YH: The malignant transformation of retrorectal cystic hamartomas with blood irregular antibodies positive: A case report. Medicine (Baltimore) 94: e2253, 2015.
14. Friedman AJ: Obstetric hemorrhage. J Cardiothorac Vasc Anesth 27 (Suppl 4): S44-S48, 2013.
15. Rudra A, Chatterjee S, Sengupta S, Wankhede R, Nandi B, Maitra G and Mitra J: Management of obstetric hemorrhage. Middle East J Anaesthesiol 20: 499-507, 2010.
16. Wu KH, Chu SL, Chang JG, Shih MC and Peng CT: Haemolytic disease of the newborn due to maternal irregular antibodies in the Chinese population in Taiwan. Transfus Med 13: 311-314, 2003.
17. Deng ZH, Seltsam A, Ye YW, Yu Q, Li Q, Su YQ, Liang YL and Zang H: Haemolytic disease of fetus and newborn caused by ABO antibodies in a cisAB offspring. Transfus Apheresis Sci 39: 123-128, 2008.
18. Muta T, Ozaki M, Tokuyama T, Izumi K, Matsushita M, Nishiyama N, Nakanishi H, Ueda Y, Fujisaki T and Yokota E: Anti-haptoglobin antibody detection after febrile non-hemolytic transfusion reactions in a non-haptoglobin-deficient patient. Transfus Apheresis Sci 41: 171-173, 2009.
19. Guzman LR, Streeter E and Malandra A: Comparison of a commercial blood cross-matching kit to the standard laboratory method for establishing blood transfusion compatibility in dogs. J Vet Emerg Crit Care (San Antonio) 26: 262-268, 2016.
20. Dubey L, Chatterjee S and Ghosh A: Hepatic and hematological adverse effects of long-term low-dose methotrexate therapy in rheumatoid arthritis: An observational study. Indian J Pharmacol 48: 591-594, 2016.
21. Sahu S, Hemlata and Verma A: Adverse events related to blood transfusion. Indian J Anaesth 58: 543-551, 2014.