(e) ISSN Online: 2321-9599
(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

ASSESSMENT OF BLOOD PRODUCT ADMINISTRATION IN PATIENTS WITH OBSTETRIC HEMORRHAGE: A RETROSPECTIVE ANALYSIS

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ABSTRACT:

Background: According to World Health Organization (WHO), Haemorrhage constitutes 35% of deaths out of all global maternal mortality. Published data from the triennium 2008-2010 in South Africa indicate that if non-pregnancy-related sepsis is excluded, haemorrhage still ranks with hypertension as the most common cause of maternal deaths (24%). Labour and Welfare give little consideration to the pathophysiological mechanism or no standard for the appropriate dosage of blood product transfusion specific to obstetric hemorrhage. Therefore; we retrospectively reviewed blood product administration in patients with obstetric haemorrhage. **Materials & Methods:** Data was collected from January 1, 2012, and December 31, 2015 in which 252 obstetric patients underwent blood product transfusion in our tertiary perinatal institution. Their data were manually abstracted by our research staffs from our medical records, anonymized in an unlinkable fashion prior to our investigation, which exempted us from institutional review board approval. Blood products involved in this study are red cells concentrates (RCC), fresh-frozen plasma (FFP), and platelet concentrates (PC). Prothrombin activity was assayed by STA-R Evolution (Roche Diagnostics), a fully automated coagulation analyzer. Clotting times were converted to percent normal plasma prothrombin activity from a log-log standard curve prepared with dilutions of control pooled plasma. All the results were analyzed by SPSS software. Spearman's rank correlation coefficient and Kruskal - Wallis one-way analysis of variance was used to assess the level of significance. **Results:** 252 obstetric patients who underwent blood product transfusion, consisting of over 65% delivered by Cesarean section and over 30 % delivered vaginally were included in the present study. More than 30% of women were transported to our institution in their puerperium for our specialized management of obstetric hemorrhage. The median of FFP/RCC ratio was not significantly different between underlying obstetric disorders, but 2.0 or more except for uterine atony. **Conclusion:** In cases of massive obstetric hemorrhage where appropriate supplementation of coagulation factors is essential, the transfusion of RCC: FFP = 1 : 1.3–1.4 is desirable

Key Words: Hemorrhage, Obstetric, Transfusion

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This article may be cited as: Agarwal K, Das G. Assessment of blood product administration in patients with obstetric hemorrhage: A retrospective analysis. J Adv Med Dent Scie Res 2016;4(6):12-16.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2016.4.6.4

INTRODUCTION

If the World Health Organization (WHO) global maternal mortality by cause is examined for the period 1997-2007, Haemorrhage constitutes 35% of deaths. Published data from the triennium 2008-2010 in South Africa indicate that if non-pregnancy-related sepsis is excluded, haemorrhage still ranks with hypertension as the most common cause of maternal deaths (24%). So how can anaesthetists improve this situation and save lives? Sadly, the main reason for the appalling figures in respect of maternal deaths in sub-Saharan Africa is poor access to basic obstetric care, blood products and basic commodities, such as electricity, for the refrigeration of blood and drugs such as oxytocin[1]. In Japan, the Japanese Ministry of Health proposed "Principles for blood transfusion therapy" and "Principles of the use of blood products", Labour and Welfare give little consideration to the pathophysiological mechanism or no standard for the appropriate dosage of blood product transfusion specific to obstetric hemorrhage.[2]Therefore; we retrospectively reviewed blood product administration in patients with obstetric haemorrhage.

MATERIALS & METHODS

Between January 1, 2012, and December 31, 2015, 252 obstetric patients underwent blood product transfusion in our tertiary perinatal institution. Their data were manually abstracted by our research staffs from our medical records, anonymized in an unlinkable fashion prior to our investigation, which exempted us from institutional review board approval. Blood products involved in this study are red cells concentrates (RCC), fresh-frozen plasma (FFP), and platelet concentrates (PC). Two units of RCC (approximately 140 mL/unit), 3 units of FFP (approximately 80mL/unit), and 2 units of PC (approximately 20mL/unit) are derived from 400mL of whole blood, respectively, in this study.

MANAGEMENT PRINCIPLES FOR BLOOD PRODUCT TRANSFUSION (**Table 1**)

Since blood loss in vaginal delivery or Caesarean section is difficult to evaluate accurately and hemoglobin (Hb) concentration necessary to maintain appropriate hemodynamics and oxygen supply is ≥7 g/dL[3], Hb concentration <7 g/dL was determined to be an indication for blood product transfusion in principle. In addition to this principle, the patient's age, medical condition, state of hemorrhage, and blood test data were taken into consideration. Since the transfusion for patients with an Hb concentration ≥7 g/dL and stable vital signs may lead to excessive transfusion, RCC transfusion was performed with a goal Hb concentration of 7-8 g/Dl.[4] FFP was concomitantly transfused until the coagulation function normalizes.[5] We did not have any rule in advance to define the proportion of FFP to RCC in the present study. Cryoprecipitate, fibrinogen concentrate, or recombinant activated factor VII was not administered in general, since they are not approved or paid by public medical insurance in Japan. The following items were retrospectively evaluated: underlying disorders which required blood product transfusion, types of blood product and their transfused volume, and data of hemoglobin (Hb) concentration, percentprothrombin activity (%PT; normal range: 84–117% in our institution), activated partial thromboplastin time (aPTT; 25–36 sec), and fibrinogen concentration (150– 400 mg/dL) within 30 minutes before blood transfusion. Blood test data were excluded for further statistical analyses when they were obtained after blood product was transfused. Prothrombin activity was assayed by STA-R Evolution (Roche Diagnostics), a fully automated coagulation analyzer. Clotting times were converted to percent normal plasma prothrombin activity froma log-log standard curve prepared with dilutions of control pooled plasma.[6]All the results were analyzed by SPSS software. Spearman's rank correlation coefficient and Kruskal- Wallis one-way analysis of variance was used to assess the level of significance.

RESULTS

We have experienced 252 obstetric patients who underwent blood product transfusion, consisting of over 65% delivered by Cesarean section and over 30 % delivered vaginally as shown in **Table 2**. More than 30% of women were transported to our institution in their puerperium for our specialized management of obstetric hemorrhage. For 8 patients who had blood transfusion prior to or during transfer, we included the data on transfusion using their medical record of transfer source institution.**Table 3** shows the 220 cases with obstetric hemorrhage that required blood product transfusion. Most of the cases underwent blood transfusion in their peripartum, except for a few cases who had massive hemorrhage several days after their delivery. **Table 4** shows the number of cases and median volumesfor each blood product transfused for the 220 cases withobstetric hemorrhage shown in **Table 3**. No cryoprecipitate,fibrinogen concentrate, or recombinant factor VII wasadministered. Autologous whole blood was transfused for 24patients with placenta previa with or without placenta acreta,increta, or percreta. These patients who had autologousblood transfusion were excluded for the analysis.The median of FFP/RCC ratio for each patient was 2.0 in total, and 2.1 and 2.0 in subgroups with moderate (6–9 units) and massive (10 units or more) RCC transfusion, respectively (**Table 6**). The median of FFP/RCC ratio was not significantly different between underlying obstetric disorders, but 2.0 or more except for uterine atony.

Table 1: Principles of transfusion management

S No.	Goals
1	Rapid supplementation of coagulation factors until physiologic coagulation function is reached
2	Goal 1 is followed along with transfusion of 4–6 units of FFP at a time, and the coagulation function is evaluated after each transfusion
3	Vital signs stabilization
4	For achieving Hb level of 7-8 gm/dl, RCC transfusion should be done
5	Performing PC transfusion until unless platelet count above 50000/mm^3 is achieved
6	Generally, avoiding of administration of cryoprecipitate

Table 2: Demographic distribution of obstetric patients with blood transfusion

Parameters	Values
Mean Age (years)	33.5 years
Mean gestation age	36.1 weeks
Primipara, n	92
Multiple pregnancy, n	16
Caesarean delivery, n	167

Assisted vaginal delivery, n	28

Table 3: Obstetric hemorrhagic disorder with blood transfusion

Parameters	Values
Uterine atony	58
Genital tract trauma	52
Placental abruption	49
Placental previa without acreta	31
Placental previa with acreta	14
Uterine inversion	6
HELLP syndrome	14
Amniotic fluid embolism	2

Table 4: Blood products transfused for obstetric haemorrhage

Blood products	n	Median units (Range)
Red cell concentrate	190	7 (3-49)
Fresh frozen plasma	200	15 (3-110)
Platelet concentrate	65	21 (12-75)
Autologous whole blood	22	3 (1-7)

Table 5: Significant positive correlation between RCC and an FFP/RCC ratio in each obstetric hemorrhagic disorder

	N	Spearman's rank coefficient	p-value	FFP/RCC
Uterine atony/inversion	61	.7849	0.005	1.5 (1.2-2.5)
Genital tract trauma	52	.7845	0.006	2.3 (1.5-2.9)
Placental abruption	50	.7822	0.004	2.3 (1.5-3.0)
Placenta previa	21	.7772	0.003	2.0 (1.1-2.1)
HELLP syndrome	17	.5298	0.041	2.0 (1.9-2.8)
Total	202	.7771	0.002	2.0 (1.4-2.5)

Table 6: FFP transfusion volume and FFP/RCC ration in obstetric haemorrhage patients

RCC transfusion	n	FFP (units)	FFO/RCC
None	25	6 (4-8)	-
Minimal	48	7 (4-8)	1.5 (1.0-3.0)
Moderate	52	13 (10-20)	2.0 (1.3-2.7)
Massive	71	31 (21-42)	2.1 (1.5-2.5)

DISCUSSION

The Royal College of Obstetricians and Gynaecologists defined that primary postpartum hemorrhageas(PPH) that bleeding of .500 mL in the first 24 hours of child birth,[7] complicates 13% of deliveries.[8] Improved awareness, better obstetric care, and involvement of multidisciplinary teams has reduced the incidence of PPH overall, but temporal trends have shown an increase inmajor obstetric hemorrhage.[9, 10]Around 73 000 women die every year from hemorrhage due to childbirth in the United Kingdom, this remains in the top[3] direct causes of maternal death.[11] Management requires an appreciation of the underlying cause, allowing an individualized approach, with careful consideration to appropriate choice of medical, obstetric, and hematologic intervention. Hematologists need to focus their attention on patient blood management, acute coagulopathy, hemostatic monitoring with targeted use of blood components and hemostatic agents, the impact of massive hemorrhage packs, and efficiency of product delivery. Obstetricians need to be alert to the risk factors for PPH and early predictors of worsening hemorrhage, and consider the effects of different interventions. Attention to the placental site in women with previous caesarean delivery will help with identification and management of the morbidly adherent placenta. Research shows that most maternal hemorrhagic deaths occurred where there were shortfalls in the standard of care.[12] Hence, we retrospectively reviewed blood product administration in patients with obstetric haemorrhage.

Of the 220 patients with obstetric hemorrhage who underwent blood product transfusion, FFP was transfused for 92.3% (203/220) (Table 4), suggesting importance of coagulation factors in blood transfusion for obstetric hemorrhage. In the patients with obstetric hemorrhage who underwent only allogenic transfusion, there was a significant positive correlation between the volume of RCC transfused and that of FFP irrespective of underlying obstetric disorders (Table 5). A ratio of total transfused units of FFP to RCC and the median of FFP/RCC ratio in each patient was 2.1 and 2.0 (Table 5), respectively. Moreover, the median FFP/RCC ratio was 2.0 and 2.1 in subgroups with moderate and massive RCC transfusion, respectively (Table 6). Since two units of RCC and 3 units of FFP are derived from 400mL of whole blood, respectively, in this study, the RCC : FFP

ratio of 1 : 2.0–2.1 in units is equivalent to 1 : 1.3–1.4 when these volumes are converted to whole blood. This RCC : FFP ratio of 1 : 1.3–1.4 is almost consistent with the report of Borgman et al. who recommended the transfusion of RCC and plasma at a ratio of 1 : 1.4 for massive hemorrhage.[14]

Interestingly, there was a significant negative correlation also between the volume of RCC transfused and %PT as data of coagulation system tests, suggesting that coagulation dysfunction due to coagulation factor depletion may result in even more blood loss and increase in transfusion volume of not only FFP but also RCC. These results are consistent with studies showing an increase in blood loss due to secondary atonic bleeding unless coagulation factors are rapidly supplemented,[15] further dilution of coagulation factors and blood loss resulting from RCC and extracellular fluid supplementation alone without coagulation factors to pregnant and puerperal women with MOH[16], an increase in blood loss along with a decrease in coagulation factors, particularly with blood fibrinogen level less than 200 mg/dL[17], and the indispensability of coagulation factor supplementation when the blood fibrinogen level is ≤100 mg/dL.[18] Appropriate supplementation of coagulation factors normalizes the coagulation function in the early stage and reduces not only blood loss but also the volume of blood product transfusion.[19, 20] According to Figures 3 and 4, it is also noted that considerable number of patients with Hb, %PT, and fibrinogen values in the normal range were transfused with RCC and/or FFP. This may be because above-mentioned comprehensive evaluation of blood loss, cause of hemorrhage, vital signs, underlying disorders, and so forth has led to the clinical decision for blood product transfusion before the deterioration of their blood test values. On the other hand, Table 6 shows that 24 (12%) patients received FFP without RCC. In these patients consisting of 5 with placental abruptions, 7 with uterine atonies, 1 with genital tract trauma, and 11 with HELLP syndromes, RCC transfusion was not required since coagulation factors were promptly supplemented with FFP and their Hb levels could be maintained above 7 g/dL. Although some retrospective analyses reported that a percentage of patients were inappropriately transfused, [21, 22] we believe that prompt decision making is inevitable to avoid secondary atonic bleeding and DIC especially in life threatening obstetric hemorrhage.

CONCLUSION

For massive obstetric hemorrhage where appropriate supplementation of coagulation factors is essential, the transfusion of RCC : FFP = 1 : 1.3–1.4 in terms of whole blood is desirable according to our retrospective analysis as well as previous report.

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Source of support: Nil **Conflict of interest:** None declared