—Report on Experiments and Clinical Cases—

Association between Fibrinogen Levels and Severity of Postpartum Hemorrhage in Singleton Vaginal Deliveries at a Japanese Perinatal Center

Yoshie Shibata, Daisuke Shigemi, Marie Ito, Kayoko Terada, Kazuho Nakanishi, Masahiko Kato, Miwa Igarashi and Shunji Suzuki

Department of Obstetrics and Gynecology, Japanese Red Cross Katsushika Maternity Hospital

Abstract

Objective and Methods: We examined the relationship between low fibrinogen levels (<200 mg/dL) and the severity of postpartum hemorrhage in singleton vaginal deliveries after 22 weeks' gestation complicated by postpartum hemorrhage requiring transfusion at our hospital.

Results: During a 10-year period, 61 women (0.38%) received transfusions owing to postpartum hemorrhage within the first 24 hours after delivery. Of these women, 13 (21%) had low fibrinogen levels (mean, 123±68 mg/dL) when postpartum hemorrhage was diagnosed, and the other 48 (79%) had normal fibrinogen levels (mean, 305±50 mg/dL). Neither total blood loss nor the incidence of additional therapies, such as hysterectomy, differed between the 2 groups of women. Women with low fibrinogen levels started to receive transfusions significantly earlier (98±58 minutes after delivery) than did women with normal fibrinogen levels (142±75 minutes after delivery, p=0.03) and received more units of fresh-frozen plasma (p=0.03).

Conclusion: The early transfusion of fresh-frozen plasma in women with postpartum hemorrhage and low fibrinogen levels might help prevent adverse outcomes.

(J Nippon Med Sch 2014; 81: 94–96)

Key words: postpartum hemorrhage, fibrinogen level, singleton vaginal delivery, fresh-frozen plasma

Introduction

A low fibrinogen level at the diagnosis of postpartum hemorrhage (PPH) has been reported to be a marker of exacerbation[1]. For example, Charbit et al.[2] and Cortet et al.[3] have observed that fibrinogen levels <200 mg/dL are independently associated with an increased risk of severe PPH. However, these studies contained data of twin deliveries or cesarean deliveries or both, which are associated with increased risks of PPH[4]. Therefore, in the present study we examined the relationship between low fibrinogen levels (<200 mg/dL) and the severity of PPH in singleton vaginal deliveries after 22 weeks' gestation complicated by PPH requiring transfusion at our hospital.

Correspondence to Shunji Suzuki, MD, Department of Obstetrics and Gynecology, Japanese Red Cross Katsushika Maternity Hospital, 5–11–12 Tateishi, Katsushika-ku, Tokyo 124–0012, Japan
E-mail: czg83542@mopera.ne.jp
Journal Website (http://www.nms.ac.jp/jnms/)

Methods

The protocol for this study was approved by the Ethics Committee of the Japanese Red Cross Katsushika Maternity Hospital. In addition, informed consent was obtained from each subject before delivery.

We retrospectively analyzed the medical charts of women with PPH requiring transfusion in singleton vaginal deliveries after 22 weeks' gestation at Japanese Red Cross Katsushika Maternity Hospital from April 2003 through March 2013. We examined the relationship between low fibrinogen levels (<200 mg/dL) and clinical characteristics and perinatal outcomes associated with the severity of PPH.

Data are presented as number (%) or mean±SD. For statistical analysis, the χ^2 test with Yates' correction for categorical variables was used. Student's *t*-test was used for continuous variables. Differences with $p<0.05$ were considered significant.

Results

During the 10-year period, 15,978 women had a singleton vaginal delivery, and 61 of these women (0.38%) received transfusions owing to PPH within the first 24 hours after delivery (**Table 1**). Of the 61 women, 13 (21%) had low fibrinogen levels (mean, 123±68 mg/dL) at PPH diagnosis, and the other 48 (79%) had normal fibrinogen levels (mean, 305±50 mg/dL).

The incidence of low Apgar scores (<7) associated with both placental abruption and amniotic fluid

Table 1 Clinical characteristics and perinatal outcomes of singleton vaginal deliveries complicated by postpartum hemorrhage (PPH) with and without low fibrinogen levels at PPH diagnosis

	Normal fibrinogen	Low fibrinogen	P-value
N	48	13	
Maternal age (years)	32.0 ± 4.1	33.3 ± 5.2	0.34
Nulliparity	26 (54%)	10 (77%)	0.56
Gestational age at delivery (weeks)	39.4 ± 1.4	39.5 ± 1.7	0.83
Oxytocin use	21 (43%)	4 (31%)	0.40
Instrumental delivery	9 (19%)	5 (38%)	0.13
Neonatal birth weight (g)	3,292 ± 515	3,085 ± 330	0.18
Apgar score <7 at 1 minute	1 (2%)	5 (38%)	<0.01
Before delivery			
Hemoglobin level (g/dL)	11.1 ± 0.7	11.3 ± 0.8	0.38
Platelet level (giga/L)	24.0 ± 5.7	22.8 ± 6.3	0.36
At transfusion start			
Time from delivery (minutes)	142 ± 75	98 ± 58	0.03
Hemoglobin level (g/dL)	7.1 ± 1.6	6.3 ± 1.3	0.10
Platelet level (giga/L)	19.7 ± 5.6	13.2 ± 3.2	<0.01
Fibrinogen level (mg/dL)	305 ± 50	123 ± 68	<0.01
Blood loss (mL)	1,880 ± 480	1,490 ± 510	0.01
PPH etiology			
Uterine atony	31 (65%)	7 (54%)	0.47
Genital tract trauma	13 (27%)	0 (0%)	0.03
Placental abruption	2 (4%)	4 (31%)	<0.01
Amniotic fluid embolization	0 (0%)	1 (8%)	0.05
Others	2 (4%)	1 (8%)	0.60
Total blood loss (mL)	2,630 ± 980	2,750 ± 890	0.69
RCC transfusion (units)	7.1 ± 1.2	6.6 ± 3.4	0.40
FFP transfusion (units)	2.6 ± 5.7	6.3 ± 4.6	0.03
Hysterectomy	2 (4%)	1 (8%)	0.60
Arterial embolization/ligation	0 (0%)	1 (8%)	0.05

Abbreviations: PPH, postpartum hemorrhage; RCC, red cells concentrates; FFP, fresh-frozen plasma.

embolism in the low-fibrinogen group was significantly higher than that in the normal-fibrinogen group ($p<0.01$). In addition, compared with the normal-fibrinogen group, the low-fibrinogen group had significantly lower platelet levels ($p<0.01$), started receiving transfusion significantly earlier ($p=0.03$), and received more units of fresh-frozen plasma (FFP; $p=0.03$). However, the groups did not differ in total blood loss or the incidence of additional therapies, such as hysterectomy.

Discussion

There has been increasing research interest in how the maternal coagulation profile changes during major PPH, and fibrinogen has been identified as an important factor that may influence the overall severity of blood loss[1–3]. In the postpartum period, maternal fibrinogen levels decrease by a mild-to-moderate degree after removal of the placenta, and a low fibrinogen level during the early phase of bleeding has been identified as an important predictor of severe PPH[1–3]. In addition, the degree of hypofibrinogenemia and the timing of fibrinogen replacement may influence the severity of PPH-related maternal morbidity and the rates of morbidity and mortality.

In the present study, PPH with low fibrinogen levels was associated with the incidence of placental abruption. Placental abruption has been reported to increase the risk of neonatal asphyxia due to acute fetoplacental circulatory disturbance[5]. In addition, it has been reported to be associated with an increased risk of maternal disseminated intravascular coagulation[5]. The present results are supported by several earlier studies[1–3,5].

On the other hand, total blood loss and the incidence of additional therapies in the present study seem to disagree with several previous important studies[1–3]. In the present study, total blood loss and the incidence of additional therapies did not differ significantly between women with low and normal fibrinogen levels at PPH diagnosis. A possible reason for this result is the small number of subjects, who included only women with singleton deliveries. Another possible reason for this result is our rapid management, including aggressive blood transfusion with packed red blood cells and FFP, if available, for patients who have PPH and low fibrinogen levels according to the current Japanese guidelines for the treatment of "obstetrical critical hemorrhage"[6,7]. For example, the volume of blood loss at PPH diagnosis in women with low fibrinogen levels was less than that in women with normal fibrinogen levels. Therefore, we believe that both early coagulation testing and early transfusion of FFP for patients with PPH and low fibrinogen levels, because of the early detection of bleeding without coagulation, have contributed to the prevention of adverse outcomes at our institution.

The present results remind us that patients with PPH require rapid obstetric and medical care.

Conflict of interests: The authors report no conflict of interests. The authors alone are responsible for the content and writing the paper.

References

1. Butwick AJ: Postpartum hemorrhage and low fibrinogen levels: the past, present and future. Int J Obstet Anesth 2013; 22: 87–91.
2. Charbit B, Mandelbrot L, Samain E, et al.; PPH Study Group: The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. J Thromb Haemost 2007; 5: 266–273.
3. Cortet M, Deneux-Tharaux C, Dupont C, et al.: Association between fibrinogen level and severity of postpartum haemorrhage: secondary analysis of a prospective trial. Br J Anaesth 2012; 108: 984–989.
4. McLintock C, James AH: Obstetric hemorrhage. J Thromb Haemost 2011; 9: 1441–1451.
5. Oyelese Y, Ananth CV: Placental abruption. Obstet Gynecol 2006; 108: 1005–1016.
6. Japan Society of Obstetrics and Gynecology, Japan Association of Obstetricians and Gynecologists, Japan Society of Perinatal and Neonatal Medicine, Japanese Society of Anesthesiologists, Japan Society of Transfusion Medicine and Cell Therapy: The Japanese guidelines for the treatment of "obstetrical critical hemorrhage". 2010; http://www.jspnm.com/topics/data/topics100414.pdf
7. Minakami H, Hiramatsu Y, Koresawa M, et al.: Japan Society of Obstetrics and Gynecology; Japan Association of Obstetricians and Gynecologists. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2011 edition. J Obstet Gynaecol Res 2011; 37: 1174–1197.

(Received, October 31, 2013)
(Accepted, November 25, 2013)