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Golden hour for fibrinogen concentrate infusion to improve post partum hemorrhage

Fibrinogen is the first agent to decrease in case of severe postpartum hemorrhage (PPH). It was also reported as an important predictor of PPH and of progression to severe PPH [1]. To date, maintaining fibrinogen levels above 2 g/L is a recommended therapeutic target in bleeding women [2]. However, the current level of scientific evidence of the timing of fibrinogen supplementation is still insufficient and controversial. The purpose of this letter to the editor is to describe our experience in the use of fibrinogen concentrate in PPH in this retrospective study.

After obtaining the approval from the medical committee of the Hedi Chaker University Hospital, we analyzed a database of patients who needed fibrinogen concentrate transfusion for the treatment of severe postpartum hemorrhage due to uterine atony after cesarean section delivery from January 2015 to December 2017. PPH was managed according to the clinical protocol of our institution in which fibrinogen concentrate was transfused at the dose of 2 g to treat coagulopathy (when plasmatic fibrinogen concentration < 2 g/L), or after massive transfusion, or earlier when practitioners in charge of the patient estimate that the bleeding may lead to coagulopathy (before the result of plasmatic concentration of fibrinogen).

Then, we assessed the blood loss estimated by Gross formula and the transfusion requirements.

Blood loss (Gross Formula) = total blood volume of a pregnant woman (80 ml/kg) × weight (kg) × [(Hb.i − Hb.d2)/((Hb.i + Hb.d2)/2] + 500 ml for every erythrocyte unit transfused.

Hb.i: Preoperative hemoglobin; Hb.d2: 2nd day post operative hemoglobin concentration.

The main outcome of this study was to determine if there is a correlation between the delay of fibrinogen transfusion (time from sulprostone infusion to fibrinogen transfusion) and the blood loss in severe PPH.

For statistics analysis, Quantitative variables are presented as mean ± SD. Pearson's correlation coefficient was adopted to test the correlation between the delay of administration of fibrinogen and the importance of uterine bleeding. We used student *T* test or Mann Whitney *U* test for comparison of continuous variables and Chi square test for the comparison of categorical variables. All statistical analyses were performed using SPSS 20.0. P value of < 0.05 was regarded as significant.

In this study, 33 patients were included. 12 patients who received fibrinogen concentrates within the first hour after delivery were called group E and the 21 who received it after (> 1 h) were called group L.

Demographic parameters (age, weight, patient's height, gestity and parity) and pre operative hemostatic status were comparable in both groups (Table 1). Blood loss was correlated to the delay of fibrinogen administration (Fig. 1). The Pearson correlation coefficient was 0.688. The mean blood loss was 2486 ml in group E versus 5310 ml in group L (p = 0.002) and the delay of fibrinogen transfusion was 27.5 min in group E versus 117 min in group L (p = 0.0001). Fibrinogen concentrates were given after massive transfusion in only 12 patients in group L. Prothrombin ratio and fibrinogen plasmatic concentration (before the fibrinogen transfusion) were respectively 78% and 2.54 g/L in group E versus 58% and 1.34 g/L in group L(p = 0.045, p = 0.002).

Red blood cell transfusion requirement was 4.58 units/patient in group E versus 8.14 in group L (p = 0.01). The need of fresh frozen plasma was 7 units/patient in group E versus 12.3 in group L (p = 0.045).

Surgical hemostasis like hypogastric arterial ligation was observed in 5 patients in group E versus 13 patients in group L (p = 0.529) and hysterectomy was needed in 3 patients in group E versus 13 patients in group L (p = 0.338). In our study 3 patients of group L died after multivisceral deficiency in the intensive care unit. However, only one patient died in group E by pulmonary embolism few hours after hysterectomy. In fact, we have no proof that this case of pulmonary em-

Table 1
Demographic parameters and pre operative hemostatic status (mean ± SD).

	Group E	Group L	p value
Age (years)	32.3 ± 4.3	32.9 ± 3.9	0.761
Weight (kg)	69.1 ± 8.5	69.1 ± 7.7	0.981
patient's height (cm)	149 ± 13	157 ± 12	0.623
Gestity	2.8 ± 1.1	2.6 ± 1.1	0757
Parity	2.5 ± 1.1	2.3 ± 1.1	0.631
Preoperative hemoglobin (g/dL)	10.5 ± 1.7	11.21 ± 1.9	0.261
Preoperative fibrinogen (g/L)	4.42 ± 0.7	4.21 ± 0.8	0.608
Preoperative prothrombin ratio (%)	92.9 ± 7	83 ± 15	0.299

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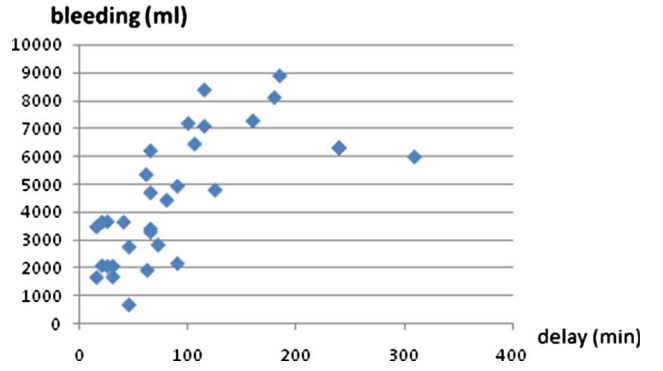

Fig. 1. the correlation between the blood loss and the delay of fibrinogen concentrates infusion.

bolism is related to fibrinogen transfusion.

Our study showed that early administration of fibrinogen (within the golden hour after delivery) may help to reduce blood loss and the need for transfusion after cesarean section delivery.

This may emphasize the utility of fibrinogen concentrate that can allow rapid therapy and rapid fibrinogen concentrations correction without blood type matching especially in emergent cesarean sections [2]. Even if it appears to be a promising therapeutic, there is still a need for randomized trials. However, there are limited data and no published randomized clinical trials in this field [3].

FIDEL study [3], a multi centric French study, whose results are not yet published, may give the answer for the best timing of fibrinogen concentrate infusion in severe PPH.

Even if our results (bleeding and transfusion) are in favor of early fibrinogen administration and aggressive therapeutic strategy, the safety of this strategy should be discussed [4]. Moreover, the risk of thromboembolic events associated with the use of fibrinogen concentrate has never been explored in this context (PPH).

Previous studies have suggested prophylactic fibrinogen transfusion to prevent PPH, while others denied its benefit [5]. However, according to our experience, the first hour following severe PPH (golden hour) seems to be the best timing for fibrinogen concentrate infusion to reduce the blood loss, transfusion requirements and surgical hemostasis.

Conflict of interest

None.

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