The role of fibrinogen in massive postpartum haemorrhage, a case report

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1. Summary

In the following case report, a 32-year old G2P1 will be presented with a complicated obstetric history of severe postpartum haemorrhage (7 L). Pro-active management by fibrinogen supplementation during labour, in addition to standard active management, will be discussed as an effective means to reduce blood loss. In our case, intensive collaboration with the anaesthesiologist during pregnancy and labour significantly reduced obstetric haemorrhage during her second delivery and illustrates the importance of a multidisciplinary approach.

2. Case Presentation

2.1. Obstetric History

A 30 year old woman of Asian origin, primigravida, BMI 17 (1.63 m and 44 kg at the start of antenatal care) was referred to our hospital by her attending midwife because of long-term rupture of the membranes at term.

Labour was induced by intravenous oxytocin and she received epidural anaesthesia. Because of foetal distress, a ventouse delivery was performed and a healthy daughter was born. Placenta and membranes followed spontaneously within 5 min. The third stage was complicated by severe haemorrhage following delivery of the placenta. Oxytocin was administered intravenously and 800 μg of misoprostol was given rectally. The bleeding persisted and she was admitted into the operating room at 8 centimetre dilation. Second stage was uncomplicated and in 15 min she delivered a healthy girl. Immediately after delivery she received oxytocin and a urinary catheter was inserted. In the OR fibrinogen level was measured again and was decreased to 2.3 g/L. Her haemoglobin level was 6.3 mmol/L, platelets 71 10e 9/L and fibrinogen 2.9 g/L, again showed a decrease. She was taken to the intensive care unit, where a radiologist with spongostan, an absorbable haemostatic gelatine sponge. By then she had lost 7 L of blood, for which she received six packed cells, four fresh frozen plasma and two thrombocytic units. In the next days in the ICU, she was diagnosed with an occlusion and dissection of the left internal iliac artery. Stent-assisted mechanical thrombectomy was performed successfully. Six days after the delivery she went home in relatively good condition with a haemoglobin level of 5.7 mmol/L. She failed to attend our preconception care clinic prior to the next pregnancy, and was referred in the second trimester of her second pregnancy by another medical centre where she was under antenatal care.

3. Second Pregnancy

In her second pregnancy our patient was assessed at the anaesthetic outpatient clinic.

At a gestational age of 33 weeks and 2 days her haemoglobin level was 6.9 mmol/L, platelets 125 10e 9/L and fibrinogen 3.7 g/L. At 35 weeks and 5 days von Willebrand factor was 191 and factor VIII 144% (normal levels in pregnancy). At 37 weeks and 1 day her fibrinogen level showed a decreased level of 3.2 g/L. This was interpreted as abnormal, presuming that fibrinogen levels increase during pregnancy. The medical staff decided that she would deliver in the operating room and that fibrinogen levels would have been measured during delivery.

4. Second Delivery

At term, a planned induction was initiated by artificial rupture of membranes and oxytocin at a gestational age of 38 weeks and 1 day. Pre-labour her haemoglobin level was 7.0 mmol/L, platelets 93 10e 9/L and fibrinogen 2.9 g/L, again showed a decrease. She was taken to the operating room at 8 centimetre dilation. Second stage was uncomplicated and in 15 min she delivered a healthy girl. Immediately after delivery she received oxytocin and a urinary catheter was inserted. In the OR fibrinogen level was measured again and was decreased to 2.3 g/L. Her uterus was again hypotonic and she lost 600 mL of blood when the placenta was delivered. 800 μg of misoprostol was given rectally, oxytocin was replaced by sulproston, 2 mg of methylergometrine, 2 g of fibrinogen was administered and 1 g of tranexamic acid. Thereafter, the bleeding stopped and no further interventions were necessary. During delivery and postpartum her prothrombin levels were measured and stayed at 10 s. Total blood loss was 2.0 L. Postpartum her haemoglobin level was 6.3 mmol/L, platelets 71 10e 9/L and fibrinogen 3.0 g/L, calcium 1.17 mmol/L.
5. Outcome and Follow-up

One day after the second delivery she was discharged with her daughter in good condition. Six weeks later the mother and her daughter were doing well and she was satisfied about the management during this second delivery.

6. Investigations

The questions arise as to why this woman had such extended haemorrhage during delivery and how to prevent this from happening again in a second delivery.

Charbit et al. published evidence of low fibrinogen levels in women with severe postpartum haemorrhage (PPH). He suggested that simple fibrinogen measurement can predict the severity of PPH. Their results also indicated that women more prone for severe bleeding had a lower body weight than women with non-severe bleeding [1].

Fries et al. showed that in pigs, substitution of fibrinogen together with packed cells can enhance coagulation and final clot strength, thereby reducing blood loss and the severity of PPH and finally reducing morbidity [2].

As suggested by Ickx (2010): ‘Serious bleeding in women with uterine atony, abruption of the placenta, and placenta praevia is often associated with excessive fibrinolysis and fibrinogenolysis, often results in very low levels of plasma fibrinogen and high levels of fibrin D-dimer. Fibrinogen substitution may therefore play an important role as a therapy in this subgroup. However, the efficacy of the administration of fibrinogen concentrates has thus far not been studied in the obstetric setting’ [3].

7. Fibrinogen

Fibrinogen (factor I) is a soluble plasma glycoprotein, that is converted by thrombin into fibrin during blood clot formation. It is synthesized in the liver by the hepatocytes. The concentration of fibrinogen in healthy, non-pregnant adults is between 2.0 and 4.0 g/L. In massive blood loss, fibrinogen levels may drop below 2.0 g/L, rapidly making the blood clot formation more difficult and contributing to more severe bleeding.

Studies have shown that the aggressive and early replacement of fibrinogen can improve clot strength and survival. A pasteurized fibrinogen concentrate has recently been developed. Use of the fibrinogen concentrate in bleeding patients resulted in significant reductions in red blood cell, fresh frozen plasma and platelet requirements along with a significant reduction in blood loss [4].

8. Discussion

We presumed that fibrinogen levels played a role in our patient's excessive blood loss at first delivery. Because of her clinical history and the decreasing fibrinogen levels in this pregnancy, a detailed plan for delivery was made in collaboration with gynaecologists, interventional radiologists, anaesthesiologists and operating staff.

9. Key Message

Major postpartum haemorrhage can be reduced by active management during third stage. Collaboration with anaesthesiologists in an early stage, as in our case presented and administration of fibrinogen supplementation in case of low maternal serum levels, can be of significant importance for favourable obstetric outcome. Fibrinogen levels may play an important role in the majority of the postpartum haemorrhage. Perhaps we could prevent major haemorrhage during future deliveries by fibrinogen.

Further research should give more insight in this matter: Leiden University Medical Centre has recently set up a multi-centre prospective cohort study (TeMpOH 2) to identify coagulation parameters predictive of progressing from mild postpartum haemorrhage into major obstetric haemorrhage.

References

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