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Management of Postpartum Hemorrhage: Fibrinogen vs. Prothrombin Complex concentrate

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Postpartum hemorrhage (PPH) is the leading cause of maternal mortality. All women with a pregnancy beyond 20 weeks of gestational age are at risk of PPH and its sequelae. Although maternal mortality rates have greatly declined in the developed world, PPH remains a leading cause of maternal mortality. Incidence of PPH has recently increased in some countries which can be related to the increased use of oxytocin for labor augmentation and subsequent uterine atony (1). As members of the multidisciplinary team, critical care physicians should improve their expertise in fluid management, transfusion therapy, and intensive care management to prevent and treat the catastrophic events of PPH. There are many techniques for managing PPH (many guidelines and institution-specific protocols), some of which may reduce the incidence of maternal morbidity and mortality (2). Until now, no single trial has proven that a specific transfusion strategy or the use of any pro-hemostatic agent can improve maternal outcomes after PPH (3). Considering changes in maternal coagulation status during major PPH, fibrinogen can be an important therapeutic target. For treating hypofibrinogemia, we have three options: FFP (fresh frozen plasma), cryo and fibrinogen. The first two need larger volume for appropriate amount of fibrinogen replacement and also need blood type matching and thawing which may lead to significant time delay during management of major blood loss. Fibrinogen, as a glycoprotein, has some roles in hemostasis such as increasing platelet aggregation and activation and secondary hemostasis defined as starting fibrin polymerization after undergoing cleavage (4,5). Many studies have shown that low fibrinogen level (<2 g/L) is an independent predictor for PPH mortality (6-9). Results of two studies in which thromboelastography was used for management of PPH showed that functional fibrinogen deficiency could worsen the outcome of major PPH (9,10). If fibrinogen therapy is guided by results of ROTEM (Rotational thromboelastography), it will lead to reduced requirements for blood components and lower risk of circulatory overload (11). European society of anesthesiologists recommended an initial fibrinogen concentrate dose of 20-25 mL/kg in plasma fibrinogen concentration of less than 1.5-2 g/L or thromboelastography signs of functional fibrinogen deficit (12). Results of a recent multicenter trial recommended fibrinogen concentrate administration when fibrinogen levels are below 3.0 to 4.0 g/L in the presence of active bleeding (13); however, higher trigger levels (<4.0 g/L) were suggested in another study (14). It is reported that fibrinogen levels ≤2 g/L have a positive predictive value of 100% and levels >4 g/L have a negative predictive value of 79% for the development of severe PPH. A large recent multicenter trial failed to show the beneficial effect of preemptive administration of 2 g fibrinogen concentrate on PPH in normofibrinogenemia patients (15).

There are two types of prothrombin concentrate complex (PCC): a three-factor PCC and a four-factor PCC including factor VII. PCC is recommended for rapid reversal of warfarin therapy or vitamin K deficiency in patients exhibiting major bleeding manifestations and rapid reversal of warfarin therapy or vitamin K deficiency in patients requiring urgent (<6 hours) surgical procedures. As there are so many types of PCC with different dosage of composed factors, reaching an evidence-based approach is so difficult. There is insufficient published evidence available to allow a recommendation for the use or dosing of these products in PPH. Caution should be exercised if they are used in pregnancy, particularly in the peripartum/early postpartum period because of a heightened tendency to thrombosis (16).

Determining the true effect of fibrinogen concentrate or PCC is influenced by heterogeneity in hemorrhage etiology, the use of high volumes of colloidal solutions and the transfusion of other plasma derived concentrates, prothrombotics and antifibrinolytics within the similar time period (17). Based on predisposing factors and PPH etiology, more comparative effectiveness research is needed to assess the potential benefits of fibrinogen concentrates for PPH compared to more traditional approaches to fibrinogen replacement. Prompt and effective management, multidisciplinary involvement, more advanced coagulation monitoring and bedside assessment of the maternal coagulation profile can help physicians to provide more personalized goal-directed

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therapy for patients with PPH. The timely and rational use of coagulation factor concentrates may be more efficacious and safer than ratio-driven use of transfusion packages of allogeneic blood. Finally, fibrinogen appears to be a promising therapeutic option for PPH but there is no strong evidence for its routine use in the literature; on the other hand, lack of thromboembolic complications after fibrinogen is ideal. A large multicenter randomized double blinded trial is being performed with the aim of evaluating the effect of early administration of 3 g fibrinogen on PPH-induced coagulopathy in 412 patients (FIDEL trial) whose result can help for the better management of PPH in the future (18). The evidence for PCC in PPH is limited to case reports and the incidence of thromboembolic complications seems to be increased following its usage.

Therefore, despite the lack of conclusive evidence for optimal hemostatic resuscitation in PPH, viscoelastic hemostatic assays and appropriate fibrinogen usage may be potentially pivotal in the treatment of PPH.

Ethical Issues

Not applicable.

Conflict of Interests

The authors declare no conflict of interests.

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