

A00 Fibrinogen concentrate versus placebo for treatment of postpartum haemorrhage: a multicentre, prospective, double-blind randomised control study (OBS2)

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Introduction: A low fibrinogen is associated with progression of postpartum haemorrhage (PPH)¹ but it is unknown whether early replacement improves outcomes. In the absence of timely coagulation results, many centres use early fixed ratios of red blood cells (RBC) and fresh frozen plasma (FFP) to treat presumed haemostatic impairment. FFP is associated with adverse events and it is not known whether withholding FFP based on point of care testing is safe. We investigated Fitem-guided early fibrinogen replacement and FFP transfusion in moderate/severe PPH.

Methods: With consent, women with ongoing PPH (1000-1500 mL) were screened for enrolment into an MREC-approved multicentre double-blind randomised controlled trial. Fitem A5 was performed at enrolment and repeated after every 500 mL blood loss or for clinical concern; no FFP or fibrinogen was infused if Fitem A5 was >15 mm. If the Fitem A5 was ≤15 mm, women were randomised to fibrinogen concentrate or placebo. The primary outcome was the number of allogeneic blood products (RBC, FFP, cryoprecipitate, platelets) transfused.

Results: The study enrolled 653 women of whom 55 had a Fitem A5 <15 mm and were randomised: 28 to fibrinogen; 27 to placebo. The fibrinogen and placebo arms received a total of 58 and 75 allogeneic units, respectively; this was almost entirely due to a difference in FFP transfusion (18 vs 33 units). The adjusted incidence rate ratio (95% CI) for allogeneic products in the fibrinogen arm compared to placebo was 0.72 (0.30 to 1.70, $P=0.45$). Any transfusion was required in 53.6% of the fibrinogen and 55.6% of the placebo arm. In pre-specified subgroup analysis, the median [IQR] allogeneic units transfused in women with fibrinogen <2g/L in the fibrinogen (n=3) and placebo (n=4) arms was 1 [1-8] and 7[4-16], respectively. In women with a Fitem A5 <12 mm, allogeneic units transfused were 1 [0-4.5] for fibrinogen (n=13) and 3 [0-6] for placebo (n=15). Of the 653 women, 598 (92%) maintained a Fitem A5 >15 mm, indicating adequate haemostasis throughout. Of the 598 women, 23% received RBCs, 2% FFP and 82% had ≤1 invasive procedures to control bleeding.

Discussion: Haemostatic impairment is uncommon in moderate/severe PPH (<8%). Withholding FFP if Fitem A5 is >15 mm does not impair outcomes. Early fibrinogen replacement, triggered by a Fitem A5 ≤15 mm, was not associated with a statistically significant reduction in allogeneic transfusion although fewer units of FFP were transfused. Subgroup analyses support investigation of a lower intervention trigger for fibrinogen replacement.

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Reference

- Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. *Blood* 2014;124:1727-33