

Is low dose Tranexamic acid less effective than a standard dose at reducing blood loss and inhibiting hyperfibrinolysis in hemorrhagic caesarean section? Multicenter double-blind placebo-controlled dose-ranging (TRACES) trial.

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Abstract

Objective: To study the effect of a low (0.5g) or a standard (1g) tranexamic acid (TA) dose compared to placebo on clinical and biological endpoints in women experiencing postpartum hemorrhage (PPH) **Design:** TRACES trial is a double-blind, randomized, placebo-controlled, dose-ranging study **Setting:** 8 women hospitals in France. **Population:** Women experiencing PPH > 800 mL during caesarean section. **Method:** After informed consent, patients were randomized to receive either TA 0.5g (n=57), TA 1g (n=58), or a placebo (n=60). Data were collected at 8 time-points. **Main outcome measures:** Efficacy: additional blood loss after study drug, maternal morbidity, safety, biology: D-dimers, plasmin-antiplasmin complexes (PAP), simultaneous-generation-thrombin-plasmin-potential. **Results:** Compared to 1g dose, 0.5g TA was less effective to reduce additional blood loss (300 mL [95% confidence interval (95%CI) 68 to 630] vs 134 mL [95%CI 50 to 419] (p=0.042)). Compared to placebo, 1g TA, but not 0.5g, inhibited hyperfibrinolysis as shown by plasmin generation potential, % increase in D-dimers from injection to 120 minutes (93% [95%CI 68 to 118] vs 58% [95%CI 32 to 84] (p=0.06) vs 38% [95%CI 13 to 63] (p=0.003) and % increase in PAP from injection to 30 minutes (56% [95%CI 25 to 87] vs 13% [95%CI 18 to 43] (p=0,051) vs -2% [95%CI -32 to 28] (p=0.009)). **Conclusions:** In this study, fibrinolysis inhibition was more sustained after the administration of 1g TA compared to 0.5g TA or a placebo. Further pharmacokinetic-pharmacodynamic modelling will be needed to determine the optimal TA dose to be administered in PPH. NCT 02797119

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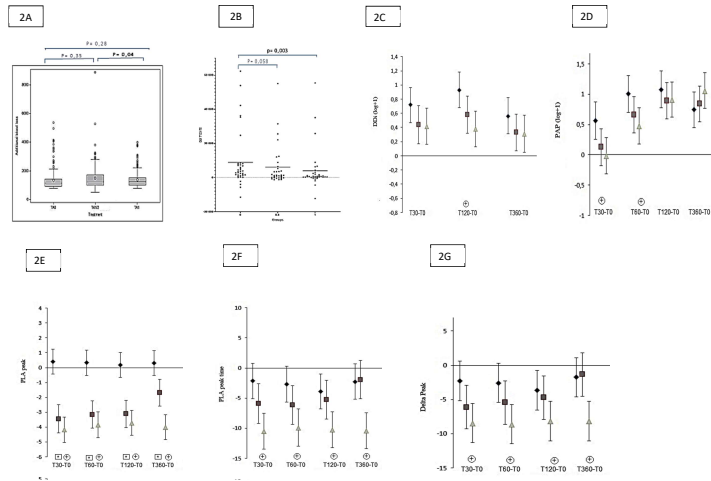
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TAB_1_baseline_VF_30102021.docx available at <https://authorea.com/users/355339/articles/543982-is-low-dose-tranexamic-acid-less-effective-than-a-standard-dose-at-reducing-blood-loss-and-inhibiting-hyperfibrinolysis-in-hemorrhagic-caesarean-section-multicenter-double-blind-placebo-controlled-dose-ranging-traces-trial>

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Figure 2: Dose-ranging impact of TA ½ g and TA 1 g compared to placebo on additional blood loss (2A) and fibrinolysis inhibition: D-dimers (2B and 2C), plasmin-antiplasmin (2D) and plasmin generation potential (2E,2F,2G) profile between injection and 6 hours later.



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Table 2_TA_concentrations.docx available at <https://authorea.com/users/355339/articles/543982-is-low-dose-tranexamic-acid-less-effective-than-a-standard-dose-at-reducing-blood-loss-and-inhibiting-hyperfibrinolysis-in-hemorrhagic-caesarean-section-multicenter-double-blind-placebo-controlled-dose-ranging-traces-trial>