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Tranexamic Acid for Cesarean Delivery: Induction of a regimen for post-partum hemorrhage?

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Dear Editor,

We have read with great interest the study by Seifert et al. who assessed the pharmacokinetics (PK) and pharmacodynamics (PD) of tranexamic acid (TXA) administered to women at risk for post-partum hemorrhage (PPH) undergoing cesarean delivery. A combined assessment of PK and PD is meaningful in elucidating a clinically effective level of TXA as multiple modifiers of bleeding and fibrinolysis interact during PPH. The authors empirically selected a target TXA plasma concentration (>10 mg/L). All patients had a TXA level >10 mg/L at 1 hour, which was maintained in more than half of patients at 3 hours. While this data seems to suggest that the studied TXA dosing should cover a post-partum surge of tPA, it is difficult to assess the overall hemostatic function at the patient level. TXA concentration per se does not prove antifibrinolytic efficacy or clinical hemostasis.

To assess the PD, the authors used a serially measured tissue factor-activated test (EXTEM) of rotational thromboelastometry (ROTEM®; Instrumentation Laboratory, Bedford, MA). There are several potential issues with using EXTEM in the assessment of localized or systemic fibrinolysis. First, EXTEM maximum clot firmness (MCF) or maximum lysis (ML) parameters are rather insensitive to in vivo plasmin generation reflected on D-dimer or plasmin-antiplasmin complex levels.2 A half-life of tPA is rather short (5 min)3, and EXTEM test performed in peripheral venous blood is unlikely to capture localized fibrinolysis in the post-partum uterus. The low incidence of hyperfibrinolysis may simply represent the insensitivity of EXTEM test. Second, even if higher ML values were present, it is important to consider the possibility of platelet-mediated clot retraction. Arnolds and Scavone previously observed increased clot lysis (>3%) at 30 min (Ly30) on kaolin-activated thromboelastography (TEG) in 12.7% (15 of 118) of 118 PPH cases.4 However, simultaneously performed functional fibrinogen test using abciximab
failed to demonstrate any clot lysis in 13 of the 15 cases (86.7%). Clot retraction is driven by platelets, and thus a platelet inhibitor allows differentiation from clot lysis. Seifert, et al. also performed an assay (FIBTEM) with a platelet inhibitor, cytochalasin D, but the results were not reported. Third, the authors comment “TXA concentration was associated with enhanced clot strength” was based on a weak positive correlation between TXA concentration and EXTEM-MCF ($r = 0.32$). For cases with significant bleeding, it is plausible that the accompanying hemodilution lowered both TXA and MCF and caused this correlation.


