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Tranexamic Acid for Cesarean Delivery: Evidence of Fibrinolysis?

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CONFLICTS OF INTEREST:
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Dear Editors:

We have read the letter "Tranexamic Acid for Cesarean Delivery: Induction of a Regimen for Post-Partum Hemorrhage?" in response to our publication "Tranexamic Acid Administered During Cesarean Delivery in High-Risk Patients: Maternal Pharmacokinetics, Pharmacodynamics, and Coagulation Status." We agree that using systemic whole blood to detect postpartum hyperfibrinolysis with rotational thromboelastometry (ROTEM®) may have limitations. Consistent with this, we saw no evidence of hyperfibrinolysis in peripheral samples by comparing EXTEM vs. APTEM clotting time (CT) and maximum clot firmness (MCF). Lack of peripheral hyperfibrinolysis may indicate an absence of hyperfibrinolysis, or early localized hyperfibrinolysis sequestered within the uterus. Despite these limitations, ROTEM has previously identified profound hyperfibrinolysis and can demonstrate coagulopathy during severe postpartum hemorrhage (PPH).

The authors inquire whether our FIBTEM testing indicated platelet-driven clot retraction and not actual clot lysis. Our EXTEM and FIBTEM results showed no evidence of this, as EXTEM maximum lysis (ML) was zero in 18 (90%) of our patients, and no lysis > 15% was detected in any sample from 30 minutes to 5 hours. There was no control group as our primary endpoint was to evaluate the central tendency and variability of TXA plasma concentrations after 1g given intravenously. We agree that studies are warranted to identify which assays detect clinically significant peripheral or localized hyperfibrinolysis, such as D-dimers or plasmin-antiplasmin complexes, and which patients would benefit most from antifibrinolytic therapy. Our study does provide evidence against significant systemic hyperfibrinolysis on ROTEM at the reported TXA plasma concentrations during PPH.
We found a weak positive correlation between TXA concentration and both EXTEM MCF ($r = 0.32$, 95% CI 0.21, 0.46) and FIBTEM MCF ($r = 0.30$, 95% CI, 0.16, 0.44). While TXA has been associated with increased MCF, it is reassuring that the MCF in our cohort remained within the normal range for pregnancy. As the authors note, the dynamic process of PPH with fluid shifts during resuscitation may alter TXA concentrations. If the correlation of plasma TXA concentrations with MCF was caused erroneously through hemodilution or hemoconcentration, then that is reassuring in terms of the thrombosis risk of TXA. We agree that additional work is needed in this area, as our study was not powered to evaluate these secondary aims. We also agree that further studies are warranted to refine the optimal threshold for TXA plasma concentrations in the context of PPH to optimize effective and safe dosing regimens.

References:

