Application of a plasmin generation assay to define pharmacodynamic effects of tranexamic acid in women undergoing cesarean delivery

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Tranexamic acid is a potent antifibrinolytic that reduces both tissue plasminogen activator (tPA)-mediated plasmin generation and breakdown of fibrin by plasmin. The efficacy of tranexamic acid in polytrauma patients is well known; reduced bleeding and mortality has been demonstrated when administered within the first three hours. Tranexamic acid is also indicated for perioperative bleeding, postpartum haemorrhage or in patients with haemophilia. However, potential adverse events such as increased incidence of thrombotic events or convulsions (associated with high doses) should be considered.

With the aim of finding the minimum effective dose, the authors succeeded in quantifying plasmin generation in plasma and compared this with the effects of tranexamic acid, measured by rotational thromboelastometry (ROTEM), from a group of pregnant women administered intravenous tranexamic acid (5, 10 or 15 mg/kg) during cesarean delivery. All doses of tranexamic acid significantly reduced plasmin generation in a similar magnitude. The maximum effect was achieved with a plasma concentration of 10 mcg/ml.

This is a new result and differs from previous literature, which questioned whether tranexamic acid reduced plasmin generation. These results suggest that tranexamic acid inhibits fibrinolysis at an early stage and therefore impacts multiple downstream effects of plasmin.
When assessing fibrinolysis, the development of an assay to measure plasmin generation allows differentiation between an alteration of fibrin stability, a deficit of plasmin production, or high or low plasmin activity. This can help identify the mechanisms underlying hyper- or hypo-fibrinolysis as observed in polytrauma patients and, therefore, optimise the therapeutic target.

The present study not only delves into the mechanism of action of tranexamic acid, but demonstrates an important advance in monitoring: the plasmin generation assay. Hopefully, one day this technology will be available as point-of-care and will help to provide a more complete view of the complex world of coagulation.