Reversal of fibrinolysis by tranexamic acid is dependent upon fibrinogen concentration.

R. Hein, N. J. White.

**Background:** The antifibrinolytic drug tranexamic acid (TXA) can reduce hemorrhagic deaths when given after trauma, but for unknown reasons, only if given within 3 hours of injury. Fibrinogen quickly declines in plasma after trauma, which may limit the efficacy of TXA. To determine if TXA’s effect on fibrinolysis is dependent upon absolute fibrinogen concentration, we examined the effect of TXA on fibrinolysis induced by plasmin at various concentrations of fibrinogen.

**Methods:** Rotational thromboelastometry (ROTEM) was used to clot human fibrinogen in physiological buffer for one hour at 37deg C after activation by 1 IU/ml thrombin. Plasmin was added at 10 μg/ml to induce fibrinolysis. TXA was added at 14.7 μg/ml to inhibit fibrinolysis. Absolute fibrinogen concentration was titrated in 0.5mg/ml increments from 1-3 mg/ml. Control fibrinogen only, plasmin-only, and plasmin+TXA groups were compared at each fibrinogen concentration for clotting time, maximal clot firmness, and maximal lysis using two-way ANOVA with interaction.

**Results:** There were independent effects of fibrinogen concentration and TXA on clotting time, maximal clot firmness, and maximal lysis (ANOVA; fibrinogen conc. p <0.001, TXA p<0.001) At a fibrinogen concentration of 2mg/ml or less, TXA could not restore clotting time or maximal lysis to control values. Above 2mg/ml fibrinogen, TXA could fully recover clotting time (ANOVA interaction p<0.001) and maximal lysis (ANOVA interaction p=0.05).

**Conclusion:** The antifibrinolytic effect of TXA is dependent upon absolute fibrinogen concentration. This may explain why TXA is less efficacious when given later to bleeding trauma patients when fibrinogen concentration is most-likely to be decreased.

Nathan White M.D.
University of Washington Dept. of Emergency Medicine
Harborview Medical Center, Box 359702
Seattle WA 98104.
206-744-8465
whiten4@uw.edu