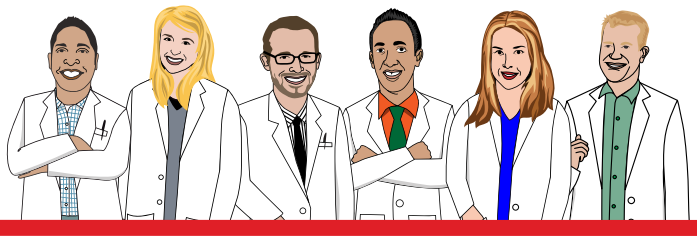
Emergency Medical Abstracts



Abstract Editor: Sanjay Arora MD

Effect of out-of-hospital tranexamic acid vs placebo on 6-month functional neurologic outcomes in patients with moderate or severe traumatic brain injury

Rowell SE, Meier EN, McKnight B, et al. JAMA. 2020;324(10):961-974.

SUMMARY:

- Tranexamic acid (TXA) decreases bleeding by inhibiting the breakdown of fibrin blood clots; therefore, it could theoretically help prevent or decrease hemorrhage expansion in patients with intracerebral hemorrhage.
- With TXA, earlier administration is generally believed to be better. In this trial, the authors examine the value of TXA administered within 2 hours of injury on 6-month neurologic outcomes in patients with moderate or severe traumatic brain injury (TBI).
- This was a 3-arm trial with patients randomized to receive an out-of-hospital TXA 1-g IV bolus and an in-hospital TXA 1-g 8-hour infusion (bolus + maintenance); an out-of-hospital tranexamic acid 2-g IV bolus and in-hospital placebo 8-hour infusion (bolus only); or an out-of-hospital placebo bolus and an in-hospital placebo 8-hour infusion (placebo).
- The target population for the trial was patients 15 years or older with moderate or severe blunt or penetrating TBI, a Glasgow Coma Scale (GCS) score of 3-12, at least 1 reactive pupil, and a systolic blood pressure of at least 90 mm Hg before randomization.
- The primary outcome was the functional neurologic outcome at 6 months after injury, on the basis of the Glasgow Outcome Scale-Extended (GOSE), dichotomized into favorable (GOSE score >4, indicating moderate disability or good recovery) or poor (GOSE score ≤4, indicating severe disability, vegetative state, or death) outcomes.
- The study examined many secondary outcomes, including 28-day mortality, progression of intracranial hemorrhage and ICU course.
- The authors planned to examine the 2 TXA groups separately but, because of power concerns, ultimately combined the groups and compared them with the placebo group.
- Over 2 years, 966 patients were randomized and analyzed. The characteristics were similar across groups: most patients were male and approximately 40 years old, almost 100% had blunt injury, the median Injury Severity Score was 17, and the mean GCS score was 8.
- A 6-month follow-up was completed on 84.8% of the sample.
- Good neurologic outcomes were seen in 65% of patients in the TXA groups vs 62% in the placebo group; no statistically significant differences were observed in the 28-day mortality (14% TXA vs 17% placebo, 6-month Disability Rating Scale score (6.8 vs 7.6), or progression of intracranial hemorrhage (16% vs 20%).
- In terms of safety, thrombotic events were more frequently observed in the bolus-only (9%) and placebo (10%) groups than in the bolus + maintenance group (4%).
- The use of a large single bolus is a unique aspect of this trial. Although there was no clear indication that this treatment improved outcomes, a signal of increased harm in the form of seizures (5% vs 2%) was found.
- This article has multiple limitations, including that 20% of the enrolled patients had a GCS score ≥13 in the ED and therefore would not have been considered TXA candidates by most providers, and that this trial enrolled patients with TBI in the prehospital setting before a CT and consequently administered TXA to many patients who had no potential for benefit with either no/minimal brain injury or nonsurvivable injury (43%).

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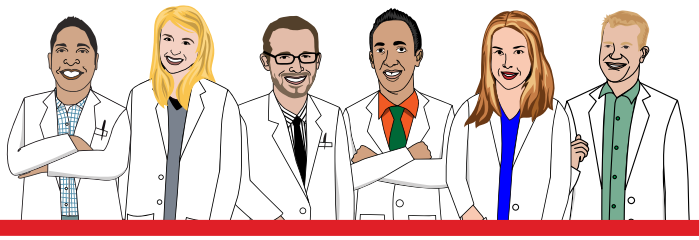

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EDITOR'S COMMENTARY: In this RCT, the authors try to maximize the benefit of early TXA administration in patients with TBI by randomizing patients in the prehospital setting and administering TXA around the 40-minute mark after injury. Similarly to the CRASH-3 study, this study did not find a statistically significant benefit for all comers, but some methodological issues make me wonder if the small effect they saw would be more robust in a larger trial. I think TXA is safe and may have benefits in some patients with intracranial hemorrhage. We just need to figure out which exactly which subgroups will actually see this benefit.

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