Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial


**SUMMARY:**

- Tranexamic acid (TXA) decreases bleeding by inhibiting the breakdown of fibrin blood clots; therefore, it theoretically could help in preventing or decreasing hemorrhage expansion in patients with intracerebral hemorrhage.

- The CRASH-3 trial was an international (29 country), multicenter (175 hospital), randomized, placebo-controlled trial examining the effects of TXA on death and disability in patients with traumatic brain injury.

- In this case, within 3 hours of injury, the study enrolled patients with traumatic brain injury who had either a bleed or Glasgow Coma Scale (GCS) score <13, and in whom the treating provider was unsure of whether TXA would have a benefit.

- When the trial started, the inclusion time was actually 8 hours but was decreased to 3 hours during the trial, on the basis of new data showing that TXA was unlikely to have benefits outside of 3 hours.

- The study enrolled 12,737 patients, 9,202 of whom were randomized within 3 hours; this number was slightly below the authors' goal of approximately 10,000 patients to have 90% power to detect a difference.

- The primary outcome, the risk of death related to head injury at 28 days, was observed in 18.5% of the TXA group versus 19.8% of the placebo group (RR 0.94).

- In a prespecified sensitivity analysis excluding patients with a GCS of 3 or bilateral unreactive pupils, the mortality was 12.5% in the TXA group versus 14.0% in the placebo group (RR 0.89).

- Importantly, the difference seen with TXA was in disease-specific mortality (head-injury-related death), but there was no difference in all-cause mortality.

- Early treatment was more effective than later treatment in patients with mild or moderate head injury (P = .005) but not in patients with severe head injury (P = .73).

- The authors then presented data to address the study's examination of subgroups that were not prespecified, according to the rationale that only the intermediate-illness group might benefit. The RR of death was 0.78 in patients with GCS >8 and 0.87 in patients with reactive pupils.

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**FULL ARTICLE:** https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32233-0/fulltext

**EDITOR’S COMMENTARY:** TXA appears safe in intracerebral hemorrhage, and in this RCT, the overall cohort showed a trend to benefit for head-injury-related death. Some subgroups may have a much larger benefit, but overall mortality was unchanged. Some people have already used the findings to suggest that a change in practice is mandated, while others claim statistical manipulation and overstating of benefits. The truth is probably somewhere in between.