The role of tranexamic acid in trauma — a life-saving drug with proven benefit

Ian Roberts and Francois-Xavier Ageron

Uncontrolled bleeding is a leading cause of death after traumatic injury. Evidence from large-scale randomized trials shows that urgent treatment with tranexamic acid (TXA) reduces bleeding deaths and all-cause mortality, without increasing the risk of thrombotic adverse events[1,2]. TXA also reduces head injury deaths in patients with traumatic brain injury[3]. In their article (Moore, E. E. et al. Trauma-induced coagulopathy. *Nat. Rev. Dis. Primers* **7**, 30 (2021)), Moore and colleagues[4] argue that TXA should only be used if patients have viscoelastic haemostatic assay (VHA) evidence of hyperfibrinolysis. In the pre-hospital setting, where VHA results are unavailable, the authors suggest that TXA use should be limited to severely injured patients, based on the belief that shock is the main driver of fibrinolytic dysregulation.

Their claims are unsupported by evidence from randomized trials. These analyses show that the effect of TXA on death due to bleeding is similar regardless of mechanism of injury, systolic blood pressure and baseline risk of death due to bleeding[5,6]. Recent pathophysiological studies show that early empirical TXA prevents admission fibrinolysis and reduces mortality but does not increase late mortality regardless of the fibrinolysis pattern in the 24 h after injury[7].

Despite the data from large, international trials being available, the authors paid more attention to the smaller trials conducted in the USA (The STAAMP trial and The Prehospital TXA for TBI trial)[8,9]. Although there was no statistically significant difference in mortality between the TXA and placebo groups in these small trials, their results are entirely in accord with those from the large international trials and only strengthen the conclusion that TXA is safe and effective in a wide range of patients with trauma (FIG. 1).

In their discussion on the complex pathophysiology of trauma-induced coagulopathy and use of VHAs, the authors also overlook the fact that TXA safely reduces bleeding in elective surgery. A meta-analysis of randomized trials of TXA in surgery show that TXA reduces blood loss by nearly one-third irrespective of the type of surgery[10]. Moreover, data from more than 100,000 patients found no evidence of thrombotic adverse effects[11]. None of these surgical patients has trauma-induced coagulopathy and, because their blood pressure is closely monitored by the attending anaesthetist, none will have haemorrhagic shock. These results suggest that TXA reduces surgical and traumatic bleeding whether or not patients have shock or 'hyperfibrinolysis'. Limiting the use of TXA to only the most severely injured will deny many patients a life-saving treatment with an excellent safety profile.

There is a reply to this letter by Moore, E. E., Moore, H. B. & Sauaia, A. *Nat. Rev. Dis. Primers* https://doi.org/10.1038/s41572-022-00368-4 (2022).

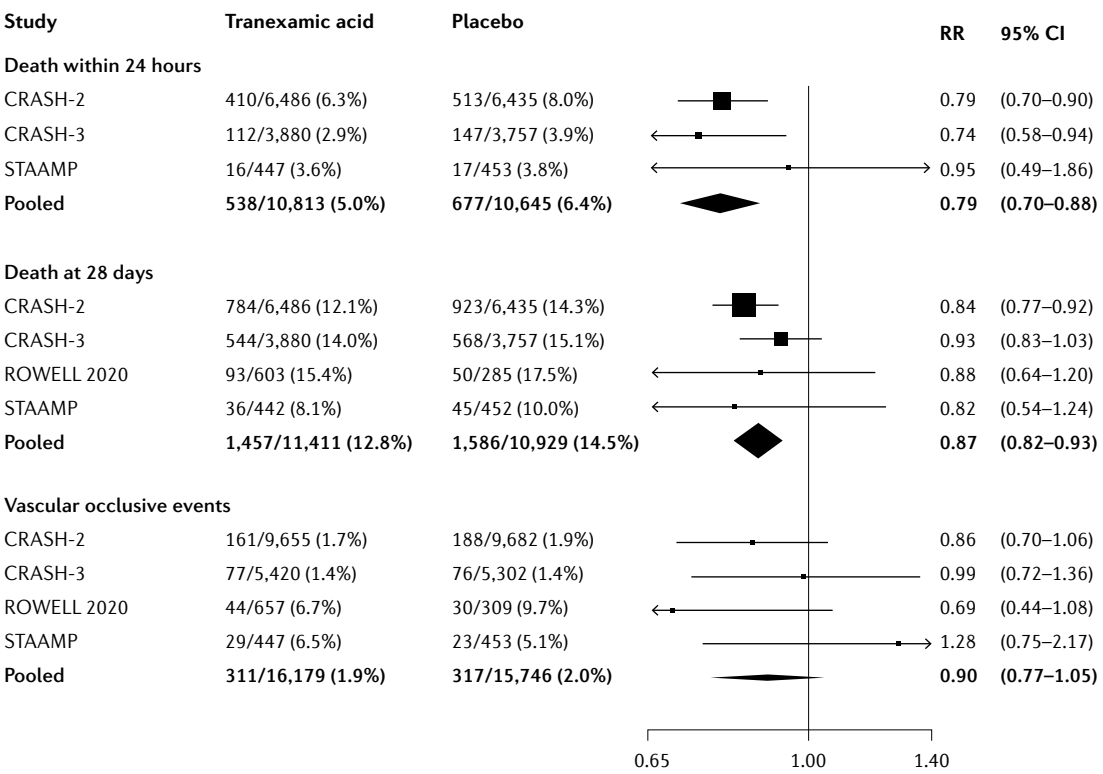

Fig. 1 | **The effect of TXA on all-cause mortality at 24 hours and 28 days.** Forest plot based on data from published randomized trials with >500 participants (CRASH-2 trial[1], CRASH-3 trial[3], STAAMP trial[8] and Prehospital TXA for TBI trial[9]). A relative risk (RR) <1 indicates fewer deaths or vascular occlusive events with tranexamic acid (TXA) treatment. Reprinted with permission from REF.[12], Thieme.

Ian Roberts[1] ✉ *and Francois-Xavier Ageron*[2]
[1]*Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK.*
[2]*Department of Emergency Medicine, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland.*
✉*e-mail: Ian.Roberts@LSHTM.ac.uk*

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Competing interests
The authors declare no competing interests.

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