UAMS Journal Club Summary
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Critical Bottom Line
The two publications discussed below reached different conclusions, lacking consensus when it comes to the use of TXA in GI bleeds. There does not appear to be an improvement in mortality between the two groups. Trial 1 found no improvement and suggests increased risk of thromboembolic events and seizures. Trial 2 did find a significant decrease in risk of rebleeding and need for surgery. Based on the evidence, we do not recommend routine TXA in GI bleeding, however it may be considered for severe or refractory cases.

PICO
P - Patients with upper GI bleeds presenting to ED
I - TXA
C - Placebo
O - Change in mortality, rebleeding, and/or rate of adverse effects

Background
Upper GI bleeds are a relatively common presentation to the emergency department. Unfortunately they come with significant morbidity. The current mainstay of treatment involves protecting the airway, volume resuscitation, and depending on the etiology of the bleed rocephin, octreotide, and a PPI. Ultimately these patients will need EGD or open surgery for definitive management. However, TXA has often been discussed as a way to temporize the bleeding. It has shown inconsistent effects in other bleeding pathology, and these studies look to assess the utility of TXA in upper GI bleeds. In theory, it should slow bleeding resulting in improved morbidity and mortality.

Trial 1

HALT-IT Trial Collaborators. Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial. Lancet. 2020 Jun 20;395(10241):1927-1936.

PubMed link: https://pubmed.ncbi.nlm.nih.gov/32563378/

Validity Rating: Very well powered, arguably overpowered

The Basics:
This trial compared patients with upper GI bleeds presenting to 164 emergency departments across the 15 countries, with a focus on those that are critically ill. This was a double blind placebo trial which resulted in the practitioners administering placebo or TXA for 24 hour infusion.

Inclusion Criteria:
Patients were included if they were considered an adult in their respective country (>16 vs >18 years old). These adult patients were included if they presented with an upper GI bleed which was deemed significant based on hypotension, tachycardia, signs of shock, or those likely to need surgery. Additionally, the provider must have reported that they were “uncertain” whether to use TXA.

Exclusion Criteria:
There were no explicit exclusion criteria stated in this study. The only individuals that were excluded were those that withdrew consent or did not receive the treatment.

Primary Outcomes:
Death due to bleeding within 5 days of randomization.

Secondary Outcomes:
Death due to bleeding within 24 hours and 28 days.
All-cause and cause specific mortality at 28 days.
Rebleeding within 24 hours, 5 days , and 28 days.
Surgery or radiological intervention.
Blood product transfusion.
Arterial Thromboembolic Events.
Venous Thromboembolic Events.
Seizures.
Other complications.
Days spent in the ICU.
Functional status at admission and at 28 days.

Results:
This large RCT included 12,009 patients found that there was no difference in the primary outcome, death due to bleeding at 5 days (RR 0.99, 95% CI 0.82 - 1.18). The lack of difference maintained even with subgroup analysis. Additionally, there was no difference in the death due to bleeding at the other time points included in the secondary outcomes. The remainder of the secondary outcomes also did not show any significant difference with exception of venous thromboembolic events (RR 1.85 95% CI 1.15-2.98) and seizures (1.95 95% CI 1.09-3.50).

Limitation/Bias:
This was a large, well-designed, and well-executed study without many shortcomings. However, one concern is that the research team did change the primary outcome after sample size calculations were made. Initially the primary outcome examined all-cause mortality. With respect to the sample size, it may be argued that this trial was over powered, inflating the risk of VTE and seizures.

Trial 2

Burke E, Harkins P, Ahmed I. Is There a Role for Tranexamic Acid in Upper GI Bleeding? A Systematic Review and Meta-Analysis. *Surg Res Pract*. 2021;2021:8876991. Published 2021 Jan 29. doi:10.1155/2021/8876991

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/33564713

The Basics: This was a review article that evaluated previously written studies to determine the effect of TXA on GI bleeds. TXA is an antifibrinolytic that is used in trauma and obstetrical hemorrhage, but has undetermined affect on other types of hemorrhage. This study looked specifically at rate of mortality, rebleeding, and adverse events in patients with upper GI bleeding when compared with placebo, as well as the need for surgery and blood product transfusion.

Methods: Searches were performed on PubMed, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL). A random effects meta-analysis was then performed to determine the risk ratio.

Inclusion Criteria:

-Randomised controlled clinical trials
-Adult patients (definition depending on jurisdiction >16 or >18)
-Suspected or endoscopically verified upper GI bleeding
-Intervention: tranexamic acid, either intravenous or oral administration
-Comparator: placebo
-Outcome: must have primary outcomes reported and ideally secondary outcomes

Exclusion Criteria:
-pediatric participants

Results:

A total of 8 studies were included totaling 12994. Risk ratio of TXA on mortality across all studies was 0.95, though the confidence interval crossed 1 with a wide range and was not statistically significant. 6 of the studies showed an increased risk ratio of 0.64 for rebleeding rate which was significant. Increased risk of thromboembolic event in 3 of the studies was 0.93; however, this also was not statistically significant. Risk ratio was 0.59 for need for surgery in 7 studies and was statistically significant with a 95% CI ranging from 0.38 to 0.94. The authors concluded that the use of TXA in upper GI bleeding is beneficial for decreasing the risk of re-bleeding and decreasing the need for surgery. However, there was not a statistically significant effect on need for blood transfusions, risk of thromboembolic events, or effect on mortality.

Limitations/Bias: The major limitation was the differences in studies selected studies including sample size, dose of TXA used, and duration of treatment as well as having different primary and secondary outcomes reported.