Guidance Document Regarding the Pre-Hospital Use of Tranexamic Acid for Injured Patients

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Tranexamic acid (TXA) is a synthetic lysine analog that competitively inhibits the activation of plasminogen to plasmin. It was approved by the US Food and Drug Administration in 1986 for short-term use as an injection to reduce or prevent bleeding during tooth extraction in hemophilia patients. The oral form is approved to treat menorrhagia. All other uses are off-label.

TXA has the potential benefit of decreasing fibrinolysis in the injured bleeding patient. The 2010 results of the Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage (CRASH-2) trial showed a decrease in all-cause mortality of 1.5% and a decrease in risk of death secondary to hemorrhage of 0.8% in patients receiving TXA. While CRASH-2 was the largest randomized study to date, many are critical of the findings, such as the lack of modern resuscitative practices in many of the participating centers. Retrospective studies, such as the Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) study, also showed a mortality benefit in patients receiving TXA, but suggested an increase in thromboembolic events.

A subgroup analysis of the CRASH-2 study examined the timing of administration. In bleeding patients, a significant reduction in mortality resulted from TXA administration within 1 hour of injury. This benefit continued up to 3 hours post-injury, but after 3 hours, TXA administration was found to be harmful. Some in the prehospital community have embraced this finding, suggesting that an early administration approach is most beneficial to the patient and thus the drug is ideal for the prehospital environment. Our organizations recognize that TXA is being administered already in many prehospital air and ground systems. We recognize that insufficient evidence exists to support or refute the prehospital administration of TXA and are awaiting the results of several prehospital studies currently in progress before making a recommendation regarding prehospital use of this agent. Therefore, we have created this document to aid agencies and systems in best practices for TXA administration based on currently available best evidence.

System integration is paramount

Definitive hemorrhage control and rapid transport to a trauma center is the key to survival in the bleeding patient. TXA administration should never delay transport. Furthermore, TXA administration involves a bolus dose followed by an infusion over 8 hours. The receiving center should endorse the prehospital use to not only ensure the infusion is initiated but also to avoid a repeat bolus. EMS agencies are encouraged to engage with their leading regional trauma centers to agree on protocols for prehospital TXA use. It is also encouraged that a clear hand-off of care report be given by EMS providers specifically noting that the TXA bolus has been given during transport so that the infusion is begun at the receiving center.

Administration to bleeding patients

Limited evidence suggests that more venous thromboembolic events (VTE) occur when TXA is given to patients not requiring massive transfusion. This discrimination can be difficult in the field where rapid decisions must be made with minimal diagnostics or time for evaluation. Objective measurements

should be used to guide prehospital TXA administration protocols. The focus for management of compressible, external bleeding should be on pressure dressings, hemostatic agents, wound packing, or tourniquets. Evidence of injury consistent with non-compressible hemorrhage (e.g. penetrating thoracoabdominal trauma, unstable pelvis fractures) along with heart rate > 120 bpm and SBP < 90 mmHg are suggested criteria. Agencies may consider vital sign adjustments for the geriatric population.

Transport to a trauma center

Compressible bleeding should be managed with pressure dressings, hemostatic agents, wound packing, or tourniquets. Prehospital TXA should be administered only to patients with non-compressible bleeding. Thus, definitive surgical control at a trauma center is essential. Patients receiving prehospital TXA should be preferentially transported to a Level I or II trauma center if available. If geographic or other factors preclude direct trauma center transport, the first receiving hospital should be capable of continuing the TXA infusion and implementing hemorrhage control procedures.

Monitoring and Quality Improvement

Given the lack of data available, our organizations recommend prehospital TXA administration be monitored closely in a prehospital and/or trauma registry. Administration should be reviewed and protocols improved to avoid unnecessary or incomplete doses, inappropriate patient selection, or lack of infusion following the initial bolus. TXA dosing, timing, blood transfusion requirements, and any adverse events should be included in the registry. If TEG is being used to guide resuscitation, fibrinolysis as measured by %LY30 should be collected in the trauma registry for future research.

Caution in cases of known anticoagulation

The effect of administering TXA in conjunction with other medications to reverse anticoagulants, such as 4-factor Prothombin Concentrate Complex (PCC) is unknown and could potentially lead to more thrombotic complications. In the case of trauma patients known to be on chronic anticoagulants, medical control should be consulted prior to TXA administration if specific protocols for this situation have not been developed.

Communication is key

Repeat bolus doses of TXA should be avoided. Prehospital TXA administration should be clearly communicated with the next receiving provider. Simple adjuncts, such as stickers or wristbands applied to patients, may be used to aid in the information transfer.

Pediatrics

Children were excluded from the CRASH-2 Trial. The best studies of TXA efficacy in children to date are in craniofacial surgery, where there is Level I evidence that TXA decreases transfusion requirements. An acknowledged risk of TXA is seizures, which has been seen mainly in the pediatric cardiac surgery population. With the extremely limited information concerning TXA use in pediatric trauma, prehospital TXA use is not currently recommended outside of a research study.

Don’t Forget the Basics

In the bleeding patient, hemorrhage control and appropriate resuscitation are still priority. Prehospital TXA use should never supersede field bleeding control techniques, rapid transport to a trauma center, or the administration of blood or plasma.

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