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Prehospital tranexamic acid administration during aeromedical transport after injury

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ABSTRACT

Background: Tranexamic acid (TXA) has been shown to reduce mortality in the treatment of traumatic hemorrhage. This effect seems most profound when given early after injury. We hypothesized that extending a protocol for TXA administration into the prehospital aeromedical setting would improve outcomes while maintaining a similar safety profile to TXA dosed in the emergency department (ED).

Materials and methods: We identified all trauma patients who received TXA during prehospital aeromedical transport or in the ED at our urban level I trauma center over an 18-mo period. These patients had been selected prospectively for TXA administration using a protocol that selected adult trauma patients with high-risk mechanism and concern for severe hemorrhage to receive TXA. Patient demographics, vital signs, lab values including thromboelastography, blood administration, mortality, and complications were reviewed retrospectively and analyzed.

Results: One hundred sixteen patients were identified (62 prehospital *versus* 54 ED). Prehospital TXA patients were more likely to have sustained blunt injury (76% prehospital *versus* 46% ED, $P = 0.002$). There were no differences between groups in injury severity score or initial vital signs. There were no differences in complication rates or mortality. Patients receiving TXA had higher rates of venous thromboembolic events (8.1% in prehospital and 18.5% in ED) than the overall trauma population (2.1%, $P < 0.001$).

Conclusions: Prehospital administration of TXA during aeromedical transport did not improve survival compared with ED administration. Treatment with TXA was associated with increased risk of venous thromboembolic events. Prehospital TXA protocols should be refined to identify patients with severe hemorrhagic shock or traumatic brain injury.

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Background

Hemorrhagic shock is a leading cause of early, potentially preventable death after trauma.[1,2] Trauma-induced coagulopathy (TIC) affects up to one-quarter of trauma patients and plays a critical role in ongoing hemorrhage during resuscitation.[3] Despite the adoption of damage control strategies for blood product–based replacement of intravascular volume and clotting factors, mortality from exsanguination has remained relatively unchanged over the past 3 decades.[4] Hyperfibrinolysis, which is present in up to 7% of all trauma patients, is a critical component of TIC and correlates with mortality from hemorrhage, making it a potential therapeutic target.[5-7]

Tranexamic acid (TXA) is a lysine analog that limits fibrinolysis via plasminogen inhibition. Although several large trials have demonstrated significant survival benefit for patients who receive TXA early in traumatic hemorrhage,[8,9] concerns remain about the generalizability of the existing data, which were accrued mostly in austere environments.[1,10] Nonetheless, while questions persist about TXA's efficacy, dosing, and indications, the low cost and seemingly low risk of TXA have led to its widespread use even in mature health care systems.[11-13]

As the literature indicates that TXA is most efficacious when given early after injury, our trauma center initiated a clinical practice guideline for the prehospital administration of TXA by our helicopter emergency medical service. In this study, we investigated the outcome and complication rates in trauma patients who received TXA either in the emergency department (ED) of our urban level 1 trauma center or in this prehospital setting. We hypothesized that the earlier, prehospital dosing of TXA in an aeromedical setting would improve outcomes while maintaining a similar safety profile when compared with TXA dosed in the ED.

Methods

Study setting

This is a single-center, retrospective cohort study spanning an 18-mo period from April 2014 to October 2015, after the initiation of a prehospital aeromedical TXA administration protocol. The University of Cincinnati Medical Center is an American College of Surgeons–accredited level I trauma center that serves 1.8 million people and maintains a registry of all patients evaluated and admitted after traumatic injuries. The trauma services perform approximately 3800 trauma evaluations and 2900 admissions annually. This study was approved by the Institutional Review Board of the University of Cincinnati.

Identification of participants

Using an institutional pharmacy database and trauma registry, we identified and cross-referenced all patients who received TXA in the ED or during aeromedical transport (from the scene or during interfacility transfer) during the study period. All TXA doses given during aeromedical transport were provided by the inpatient pharmacy at University of Cincinnati Medical Center and therefore were captured for billing purposes in the pharmacy database.

Criteria for TXA administration

Criteria for TXA administration in both groups required the following: age greater than 16 y; evidence of high-risk mechanism by history or physical exam (e.g., ejection from automobile; fall greater than 20 feet; or penetrating injury to head, neck, torso); suspicion for severe hemorrhage (e.g., positive Focused Assessment with Sonography for Trauma, bleeding requiring a tourniquet, unstable pelvic fracture); and at least one clinical marker of hemodynamic instability (systolic blood pressure <90 mm Hg, heart rate >110 bpm, tachypnea >24 breaths per min, clinical findings of peripheral vasoconstriction) or one or more laboratory values that would trigger the initiation of a massive transfusion protocol (LY30 > 3%, point of care international normalized ratio >1.5, base deficit < −6 mmol/L, hemoglobin <11 g/dL, platelet count <200,000).[14] For prehospital aeromedical transport patients, TXA was considered for use only in patients receiving blood products. However, helicopter medical providers (emergency medicine resident physicians) could consult with medical control for those patients whom they felt demonstrated signs of impending hemodynamic instability or for whom they had clinical suspicion for traumatic brain injury (TBI), and thus might benefit from early administration of TXA without meeting the aforementioned criteria.

The protocol excluded all patients with evidence of active intravascular thrombotic disease or disseminated intravascular coagulation; recent or anticipated treatment with prothrombin complex concentrate, factor VIIa, or factor IX complex concentrates; suspected or confirmed pregnancy; previous hypersensitivity reaction to TXA; or acquired disturbance of color vision.

Intervention

TXA administration only was considered within 3 h of injury. In both the prehospital and ED settings, patients who met the aforementioned criteria for TXA administration received a bolus of 1 g (g) of TXA in 100 mL of either 0.9% normal saline or lactated Ringers over 10 min through a dedicated intravenous or intraosseous access point. For both groups, subsequent dosing of another 1 g of TXA over the next 8 h was left to clinician judgment and evaluation of fibrinolysis according to the percent clot lysis in 30 min (LY30) parameter on rapid thrombelastography (rTEG).

Data collection, definitions, and outcomes

Once patients who received TXA were identified, clinical data was extracted from the institutional trauma registry and supplemented with additional queries into the electronic medical record. Patient demographics including age, gender, mechanism of injury, injury severity score (ISS), and interfacility transfer status were collected. Prehospital and initial ED vital signs including systolic blood pressure, heart rate, Glasgow coma scale (GCS), and shock index (SI) were recorded.