STATE OF MAINE

DEPARTMENT OF PUBLIC SAFETY

MAINE EMERGENCY MEDICAL SERVICES

152 STATE HOUSE STATION

AUGUSTA, MAINE 04333

PAUL R. LEPAGE

GOVERNOR

JOHN E. MORRIS

COMMISSIONER

SHAUN A. ST. GERMAIN

DIRECTOR

MEDICAL DIRECTION AND PRACTICES BOARD

WHITE PAPER

Tranexamic Acid (TXA)

BACKGROUND

Hemorrhage is the leading cause of preventable death in trauma. In recent years, the MDPB has written several protocols to help stop bleeding early including the use of tourniquets and hemostatic agents. Tranexamic acid (TXA) is an intravenous drug shown to reduce mortality in patients suffering from hemorrhagic shock[1,2]. Specifically, it has been shown to have the greatest benefit when given within 1 hour of traumatic injury[1]. The addition of TXA to the Maine EMS protocols allows paramedics who identify hemorrhagic shock to administer TXA in addition to controlling hemorrhage and managing hypotension.

How is TXA given?

TXA is initially given as a bolus of 1 gram over 10 minutes. This will require mixing 1 gram of TXA from a vial into a 250cc bag of IV fluid and given as a bolus over 10 minutes. It does not require being placed on an IV pump, although this is acceptable. Do not push the 1 gram bolus as an IV push – it may cause hypotension. A second gram given as an infusion may be initiated by the hospital after this initial bolus.

What is TXA?

TXA is a drug that has been used since the 1960s to treat surgical bleeding. During the war in Afghanistan it was tested to treat hemorrhage from severe trauma and has since been evaluated in two very large prehospital trials (CRASH-2 and MATTERs). It is now recommended by the Tactical Combat Casualty Care as a Class I recommendation for the treatment of victims of combat related trauma[5].

PHONE: (207) 626-3860 TTY: (207) 287-3659 FAX: (207) 287-6251

With offices located at the Central Maine Commerce Center, 45 Commerce Drive, Suite 1, Augusta, ME 04330

How does TXA work?

The short version:

TXA helps the body maintain any clots that have formed, combating the coagulopathy of trauma.

TXA does not create new clots.

The long version:

TXA works by preventing clot breakdown, a process called fibrinolysis. Fibrin is one of the final products in the common pathway of the coagulation cascade, and functions to cross-link and strengthen clots. The lysis of fibrin (fibrinolysis) is cutting those cross-links. Plasmin is an enzyme that breaks down fibrin to weaken and dissolve clots. [*In the event of a stroke, we give tPA (tissue plasminogen activator) to create more plasmin, and break down more clots.*] In the setting of hemorrhagic shock, as patients enter the lethal triad of hypothermia, acidosis, and coagulopathy they can develop hyper-fibrinolysis – breaking down all clots including those that are working to stop life threatening hemorrhage. To help protect any clots that have formed, TXA prevents plasmin from performing fibrinolysis.

Since TXA works at the end of the coagulation cascade when clots have already formed, it does not cause patients to be hypercoagulable. So, it does not cause extra clots to form. No increase in clot formation (PE or DVT) has been documented[1,2].

Who benefits from TXA?

The two largest prehospital studies to date have evaluated the use of TXA in patients exhibiting signs of hemorrhagic shock. The CRASH-2 trial[1,3], was a randomized placebo-control trial of 20,000 patients at 240 civilian hospitals. It demonstrated a decrease in mortality to patients who received TXA <3 hours from the time of injury and an especially dramatic improvement in mortality when given within 1 hour of the time of injury.

The MATTERs trial[2], was a retrospective review of ~900 patients requiring blood transfusions at a military hospital in Afghanistan. These patients were overall more injured (based on Injury Severity Scale) and required more blood transfusions than the patients in the CRASH-2 trial. This trial confirmed the mortality benefit of TXA and showed a decrease in the number of blood product transfusions patients required.

Based on these studies, the MDPB has used the following inclusion criteria to identify patients who may benefit from TXA:

- Patient ≥16 years old who has suffered a blunt or penetrating injury within the last 3 hours

- Have evidence of hemorrhagic shock (tachycardia, hypotension, or other signs of hemodynamic instability)

Who should not receive TXA?

Patients < 16 years old: The data in pediatric trauma is extremely limited (a single non-randomized study[D]). More data is needed before the MDPB can recommend the use of TXA in pediatric trauma.

Patients with isolated head injuries: TXA has not been adequately studied in patients with isolated traumatic brain injuries (TBI), only in patients with multi-system trauma. A multisite randomized clinical trial to evaluate its use in isolated head injury is currently underway (CRASH-3) and may provide information about use in this patient population in the future.

Patients > 3 hours from traumatic injury: TXA has been shown to have a time-dependent effect[1,3]. The earlier it is given, the better outcomes in mortality and reduction in blood transfusions. In the CRASH-2 study, patients who received TXA >3 hours from the time of injury had an increased risk of death[1,3].

Women who are known or suspected to be pregnant with fetus of viable gestational age (>24 weeks or fundus above the umbilicus). TXA has not been adequately studied in pregnant trauma patients and a theoretical concern of TXA crossing the placental barrier exists.

Other important information:

Blood products should not be transfused through the same IV/IO as TXA. When TXA is administered, the vascular access used should be clearly noted and communicated to the receiving staff.

Some patients on anticoagulant medications (like warfarin) may receive a reversal agent to restore their normal coagulation cascade. These include activated clotting factors or prothrombin complex concentrate (PCCs). These reversal agents may be contraindicated if TXA is given. For this reason, the MDPB recommends contacting OLMC prior to administering TXA if your patient is known to be on an anticoagulant medication.

In the bleeding patient, appropriate hemorrhage control and resuscitation remain the priority. Prehospital TXA use should never supersede bleeding control techniques i.e. tourniquets, IV fluids, rapid transport to a trauma center.

Works Cited:

1. CRASH-2 Collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2); a randomised, placebo controlled trial. *Lancet*. 2010;376:23-32.

2. Morrison JJ, et al. Military application of tranexamic acid in trauma emergency resuscitation (MATTERs) study. *Arch Surg*. 2012;147(2):113-119.

3. CRASH-2 Collaborators. The importance of early treatment with tranexamic Acid in bleeding trauma patients: An exploratory analysis of the CRASH-2 randomised control trial. *Lancet*. 377; 2011:1096-101.

4. Eckert MJ. et al. Tranexamic acid administration to pediatric trauma patients in a combat setting: the pediatric trauma and tranexamic acid study (PED-TRAX). *J Trauma Acute Care Surg*. 2014;77(6):852-858.

5. Dickey NW and Jenkins D. Addition of Tranexamic Acid to the Tactical Combat Casualty Care Guidelines 2011-06. Defense Health Board Memorandum: September 23, 2011.