Procedure: The following patients may benefit from early (within 3 hours of injury) administration of TXA:

- LY30 ≥ 3% and ongoing transfusion requirement
- LY30 ≥ 3% and severe traumatic brain injury with evidence or risk of bleeding
- LY30 ≥ 3% and severe solid organ injury with significant potential for bleeding

***USE OF TXA 3 HOURS OR MORE AFTER INJURY INCREASES MORTALITY AND IS NOT INDICATED

Dosing:

a. Infuse 1 gram of tranexamic acid in 100 ml of 0.9% NS over 10 minutes intravenously (more rapid injection has been reported to cause hypotension).

b. Infuse a second 1-gram dose intravenously in 100 ml of 0.9% NS over 8 hours.

Background:

Management Principles for Damage Control Resuscitation

The major principle of damage control resuscitation is to prevent development of or exacerbation of trauma induced coagulopathy by dilution of factors needed to provide hemostasis. In order to support this goal, the MHH Blood Bank must provide components at an appropriate ratio throughout the entire resuscitation process. The transfusion goal of the patient who has suffered significant bleeding is to deliver a ratio of PRBCs to plasma to platelets of 1:1:1. This approach has resulted in decreased use of blood components and improved survival in severely injured trauma patients.1-4

With the advent of routine admission TEG evaluation of Code 3 trauma patients, we have found that while fibrinolysis occurs rarely in seriously injured patients (n = 1225), when present it is associated with increased mortality.

LY30 ≥ 5% results in mortality of 58% (n = 42)
LY30 ≥ 4% results in mortality of 35% (n = 70)
LY30 ≥ 3% results in mortality of 20% (vs. 10% in those <3%; p<0.001) (n = 137)

Pharmacologic efforts to correct this pathologic fibrinolysis may improve survival.

Tranexamic acid (TXA), an anti-fibrinolytic agent, has been used to decrease bleeding and the need for blood transfusions in coronary artery bypass grafting (CABG), orthotopic liver transplantation, hip and knee arthroplasty, and other surgical settings. The safety and efficacy of using TXA to treat trauma patients was recently evaluated in a large randomized, placebo-controlled clinical trial.5 In this
trial, 20,211 adult trauma patients in 274 hospitals in 40 countries with, or at risk of, significant bleeding (HR>110, SBP<90, clinical judgment) were randomized to either TXA or placebo administered as a loading dose of 1 gram over 10 minutes followed by an infusion of 1 gram over 8 hours. The overall mortality rate in the cohort studied was 15.3%, of whom 35.3% died on the day of randomization. A total of 1063 died due to hemorrhage, of whom 59.9% died on the day of randomization. The authors reported that TXA use resulted in a statistically significant reduction in the relative risk of all-cause mortality of 9% (14.5% vs. 16.0%, RR 0.91, CI 0.85-0.97; p = 0.0035). A recent post-hoc analysis of the CRASH-2 data shows that the greatest benefit of TXA administration is likely to occur when patients receive the medication soon after injury. In this analysis, TXA given between 1 and 3 hours post-trauma reduced the risk of death due to bleeding by 21% (147/3037 [4.8%] vs. 184/2996 [6.1%], RR 0.79, CI 0.64-0.97; p=0.03). Treatment given after 3 hours increased the risk of death due to bleeding (144/3272 [4.4%] vs. 103/3362 [3.1%], RR 1.44, CI 1.12-1.84; p=0.004). Finally, a recent meta-analysis reported that TXA is effective for preventing blood loss in surgery and reducing transfusion, and was not associated with increased vascular occlusive events.

A recently completed retrospective review of our local experience with infusing TXA for trauma patients that meet the above criteria has been performed. In the 98 of 1032 patients that received TXA there was no effect on mortality. Most patients corrected their LY30 to normal. There did not appear to be any morbidity associated with using TXA. There are two planned prospective and randomized trials of TXA that are starting. We await those results.

Adverse events associated with TXA use have been reported. These include acute gastrointestinal disturbances (nausea, vomiting and diarrhea, generally dose-related), visual disturbances (blurry vision and changes in color perception, especially with prolonged use), and occasional thromboembolic events (e.g., deep venous thrombosis, pulmonary embolism, generally observed in the setting of active intravascular clotting such as thrombotic DIC). Its use is thus contraindicated in the settings of acquired defective color vision and active intravascular clotting. TXA should be used with caution in the setting of urinary tract bleeding as ureteral obstruction due to clotting has been reported. TXA is contraindicated in patients with aneurysmal SAH, however there have been no reported complications associated with intra or extra cranial hemorrhage associated with trauma. TXA should not be given with activated prothrombin complex concentrate or factor IX complex concentrates as this may increase the risk of thrombosis.

TXA is an anti-fibrinolytic that inhibits both plasminogen activation and plasmin activity, thus preventing clot break-down rather than promoting new clot formation. TXA is a small molecule (MW 157.2) inhibitor of plasminogen activation, and inhibitor of plasmin activity. It occupies the lysine binding sites on plasminogen thus preventing its binding to lysine residues on fibrin. This reduces plasminogen activation to plasmin. Similarly, blockade of lysine-binding sites on circulating plasmin prevents binding to fibrin, and thus prevents clot break-down. TXA is 10 times more potent in vitro than an older drug of the same class, aminocaproic acid. At therapeutically relevant concentrations, TXA does not affect platelet count or aggregation or coagulation parameters. It is excreted largely unchanged in urine and has a half-life of about 2 hours in circulation. While prolonged use requires that dosing be adjusted for renal impairment, use in the acute trauma situation does not appear to require adjustment. No adjustment is needed for hepatic impairment. TXA (intravenous trade name: cyklokapron) is supplied in ampoules of 1000 mg in 10 ml water for injection.

The early use of TXA should be considered for any patient with an elevated LY30 ≥ 3% and with ongoing transfusion requirement that indicates substantial bleeding. Importantly, early use of tranexamic acid within 3 hours of injury is associated with the greatest likelihood of clinical benefit.
TXA (intravenous trade name: cyklokapron) is supplied in ampoules of 1000 mg in 10 ml water for injection.

References