Appendix 1 (as supplied by the authors): Protocol for intravenous administration of tranexamic acid during trauma resuscitation*

Introduction

Tranexamic acid has been shown to reduce overall mortality and death due to bleeding among severely injured patients, particularly if administered in the first 3 hours following injury. Trauma triggers fibrinolysis (clot breakdown) which in some circumstances may become pathological (hyper-fibrinolysis) and result in rapid consumption of fibrinogen and severe coagulopathy. Tranexamic acid is an anti-fibrinolytic agent that inhibits the conversion of plasminogen to plasmin and at the same time acts as a weak non-competitive inhibitor of plasmin thus arresting fibrinolysis. As a result, a stable clot can be formed and blood loss is reduced. One study has shown tranexamic acid reduces the risk of death due to bleeding without significantly increasing the risk of thrombotic complications in the setting of trauma (CRASH-2 Trial Collaborators, 2010).

Protocol

I. Restrictions/Persons authorized to implement this protocol:

This protocol is limited to acute trauma during the initial trauma resuscitation, which might occur in the ED, operating room, or in the ICU. It is expected that the RN will administer the medication using an infusion control device. A physician should be physically present during the administration of the loading dose.

II. Indications

Tranexamic acid should be administered to trauma patients with evidence of haemorrhage requiring transfusion within 3 hours and up to 8 hours from the time of injury. Tranexamic acid should be given as early as possible. Empiric administration of tranexamic acid should be considered in hemodynamically abnormal patients (e.g. systolic blood pressure< 100 mm Hg, HR > 110 bpm) at risk for haemorrhage who don't respond to initial crystalloid challenge (ie. who will likely be receiving transfusion).

III. Contraindications

Known hypersensitivity to tranexamic acid

IV. Precautions

Increased risk of thrombotic events if concurrent use of prothrombin complex concentrate (Octaplex or Beriplex) or rVIIa

While labelling indicates that tranexamic acid should not be used in those with active thromboembolic disease, disseminated intravascular coagulation (DIC), or a history or risk of thrombosis, the attending physician should balance the benefits versus risks of using tranexamic acid on an individual basis.
Suspected upper urinary tract bleeding (If the source of the bleed is from the renal parenchyma, tranexamic acid may aggravate the condition by causing intravascular precipitation of fibrin. Conversely, tranexamic acid does not pose the same risk if the source of the bleed is from the lower urinary tract, such as the bladder.)

Patients with acute non-traumatic SAH may be at increased risk for cerebral edema or infarction -consultation with the attending neurosurgeon is recommended.

V. Adverse Effects

Anaphylaxis
Thrombosis
Hypotension (with rapid infusion, such as rate of greater than 100 mg/min)
Nausea, vomiting, diarrhea
Visual disturbances (blurred vision, changes in color vision)

VI. Dosing and Administration

1. Loading Dose:
   a. Tranexamic acid is supplied in vials of 1000 mg / 10 mL. The standard loading dose of tranexamic acid is 1000 mg. Withdraw drug from the vial and inject into 100 mL sodium chloride 0.9%.
   b. Infuse tranexamic acid 1000 mg intravenously over 10 minutes.

2. Infusion:
   a. The standard IV infusion dose is 1000 mg. Withdraw drug from the vial and inject into 500 mL sodium chloride 0.9%.
   b. Infuse tranexamic acid 1000 mg intravenously over 8 hours.

Tranexamic acid may be administered peripherally or via central line using an infusion control device. Do not inject more rapidly than 100 mg/min to avoid hypotension.

VII. Stability/Compatibility

Compatible and stable for 24 hours at room temperature when diluted to 2 mg/mL with either 5% Dextrose or 0.9% sodium chloride

Tranexamic acid may be mixed with electrolyte solutions and carbohydrate solutions.

Do not mix with blood products or solutions containing penicillin.

VIII. Monitoring Requirements

Blood pressure and signs of allergic reaction at: baseline, 5 minutes into loading dose,
at the end of loading dose, every 2 hours during infusion
Clinical signs of thrombosis (ie. myocardial infarction, stroke, pulmonary embolism, deep vein thrombosis) - baseline, daily during hospital stay
CBC, INR, aPTT as per resuscitation and/or massive transfusion protocol

IX. Levels of responsibility

- **Physician**
  1. Familiarity with this protocol
  2. Assess the patient for indication and contraindications/precautions for using tranexamic acid.
  3. Be physically present during the administration of the loading dose.
  4. Monitor the patient in collaboration with the RN, as described in this protocol.

- **Nurse**
  1. Familiarity with this protocol
  2. Set up IV infusion device and administer the loading and maintenance dose of tranexamic acid.
  3. Monitor the patient in collaboration with the MD, as described in this protocol.
References


4. Compendium of Pharmaceuticals and Specialties 2010: Cyklokapron monograph (Pfizer)

5. Micromedex 2.0: Tranexamic acid

6. Lexi-Comp Online: Tranexamic acid

7. Sandoz Product Insert: Tranexamic acid injection BP

*Source: St. Michael's Hospital, Toronto, Ont.*