Drug Guideline: Tranexamic Acid (Cyklokapron)

Summary: Tranexamic Acid (TXA) is a synthetic lysine derivative that inhibits fibrinolysis by blocking the lysine binding sites on plasminogen, an inactive form of plasmin which acts to dissolve fibrin clots. Plasmin also has inflammatory and neurotoxic effects. The observed reduction in bleeding is likely due to reduced fibrinolysis, and therefore reduced clot breakdown. TXA has been used to control haemorrhage in patients undergoing surgery and to manage other conditions such as gastrointestinal and heavy menstrual bleeding.

Approved by: ICU Director Prof Michael Parr

Publication (Issue) Date: July 2015

Next Review Date: July 2018

Replaces Existing Guideline: Tranexamic Acid_2011

1. Introduction:
The risk addressed by this policy:

Patient Safety

The Aims / Expected Outcome of this policy:

Tranexamic acid should be administered safely and without any adverse side effects

Related Standards or Legislation

NSQHS Standard 1 Governance

National Standard 4 Medication Safety

Related Policies

<table>
<thead>
<tr>
<th>LH_PD2013_C03.12</th>
<th>Administration of Intravenous (IV) Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH_PD2013_C03.01</td>
<td>Drug Administration</td>
</tr>
<tr>
<td>LH_PD2013_C03.00</td>
<td>Drug Prescribing</td>
</tr>
</tbody>
</table>

2. Policy Statement:
- All care provided within Liverpool Hospital will be in accordance with infection prevention/control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer unless required during an emergency.
• Medications are to be given at the time prescribed and are to be signed by the administering registered nurse.
• Parenteral medication prescriptions and the drug are to be checked with a second registered nurse prior to administration.
• Infection Control guidelines are to be followed.
• All drugs administered during an emergency (under the direction of a medical officer) are to be documented during the event, then prescribed and signed following the event.
• Adverse drug reactions are to be documented and reported to a medical officer.
• Medication errors are to be reported using the hospital electronic IIMS reporting system.
• Guidelines are for adult patients unless otherwise stated.

3. Principles / Guidelines

Actions: 1, 2, 3
Tranexamic acid forms a reversible complex that displaces plasminogen from fibrin resulting in inhibition of fibrinolysis. It also inhibits the proteolytic activity of plasmin. With reduction in plasmin activity, tranexamic acid also reduces activation of complement and consumption of C1 esterase inhibitor (C1-INH), thereby decreasing inflammation associated with hereditary angio oedema.

Indications: 1, 2, 3
• Reduction of peri and post operative blood loss and the need for blood transfusion in patients undergoing cardiac surgery, total knee and total hip surgery.
• Major trauma patients at risk of major bleeding, Treatment commenced in ED or operating theatres within 3 hours of injury and infusion completed in ICU if indicated.

Contraindications: 1, 2, 3
• History or risk of thrombosis, unless at the same time it is possible to give treatment with anticoagulants.
• Active thromboembolic disease such as deep vein thrombosis (DVT), pulmonary embolism and cerebral thrombosis.
• Acquired disturbances of colour vision. If disturbances of colour vision arise during the course of treatment, the administration of the preparation should be discontinued.
• Subarachnoid haemorrhage, as anecdotal experience indicates that cerebral oedema and cerebral infarction may be caused in such cases.
• Hypersensitivity to tranexamic acid.

Precautions1, 2, 3
• The dose of tranexamic acid should be reduced in patients with renal impairment because of the risk of accumulation of tranexamic acid.
• Rapid intravenous injection of tranexamic acid solution for injection may cause dizziness and/or hypotension.
• Venous and arterial thrombosis or thromboembolism has been reported.
• Patients with a high risk for thrombosis (a previous thromboembolic event and a family history of thromboembolic disease) should use tranexamic acid only if there is a strong medical indication and under strict medical supervision.
• Tranexamic acid should not be administered concomitantly with factor IX complex concentrates or anti-inhibitor coagulant concentrates, as the risk of thrombosis may be increased.
• Blood in body cavities such as the pleural space, joint spaces and the urinary tract (e.g. renal pelvis, bladder) may develop indissoluble clots in these cavities due to extravascular blood clots which may be resistant to physiological fibrinolysis.
• Patients with disseminated intravascular coagulation (DIC) must be under the strict supervision of a doctor experienced in treating this disorder.
• Should not be used during pregnancy unless clearly indicated as it is known to cross the placenta and appears in cord blood at concentrations approximately equal to maternal concentration.
Ocular effects: Visual defects (e.g. colour vision change, visual loss) and retinal venous and arterial occlusions have been reported.

Seizures have been reported with use; most often with intra-operative use (e.g. open chamber cardiac surgery) and in older patients.

**Interactions**

- Anti-inhibitor Coagulant Complex: Antifibrinolytic Agents may enhance the thrombogenic effect of Anti-inhibitor Coagulant Complex
- Contraceptives may enhance the thrombogenic effect of tranexamic acid
- Tranexamic acid solution for injection should not be mixed with blood for transfusion or infusion solutions containing penicillin.

**Adverse Effects**

1. Cardiovascular: Hypotension (with rapid I.V. injection)
2. Central nervous system: Giddiness
3. Dermatologic: Allergic dermatitis
4. Endocrine & metabolic: Unusual menstrual discomfort
5. Gastrointestinal: Diarrhoea, nausea, vomiting
6. Ocular: Blurred vision
7. Renal cortical necrosis (rarely)
8. Anaphylaxis
9. Thromboembolic disorder (rarely)

**Overdosage**

Overdose data is limited. There is one report of over dosage in which a 17 year old ingested tranexamic acid 37g and, after receiving treatment with gastric lavage, mild intoxication was reported.

Symptoms of overdose may include dizziness, headache, nausea, vomiting, diarrhoea, orthostatic symptoms, hypotension and convulsions.

There is no known antidote for tranexamic acid overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures should be instituted as required.

**Presentation**

- Tranexamic acid solution for injection is a sterile, clear, colourless solution.
- Tranexamic acid 100 mg /ml, (1000mg/10ml ampoule)
- 5ml ampoules contains 500mg tranexamic acid

**Administration Guidelines**

- Can be mixed with the following solutions:
  - 0.9% sodium chloride solution;
  - 5% glucose solution;
  - Dextran 40; Dextran 70;
  - Ringer's solution (compound sodium chloride).

- Mixture should be used immediately after preparation.
- If storage is necessary, the mixture should be stored at 2-8 degrees celsius for a maximum of 24 hours.
- Mixture should be discarded after 24 hours of preparation.

- The recommended rate of administration is 50 mg/min.
- Undiluted tranexamic acid solution for injection (100 mg/mL) may be administered at 0.5 mL/min by intravenous infusion or intravenous injection.
- Solutions diluted to 1% tranexamic acid (i.e. 1 g in 100 mL or 10 mg/mL), may be administered at 5 mL/min
- Solutions diluted to 2% tranexamic acid, may be administered at 2.5 mL/min by intravenous infusion.
- In general, tranexamic acid loading doses are diluted in 50 to 250 mL of Glucose or 0.9% sodium chloride and are administered over 5 to 30 minutes. \(^1\)
- The required volume of tranexamic acid solution for injection may be added to the chosen infusion solution to achieve final concentrations of 1 or 2 g in 100 mLs (10 or 20 mg/mL, 1% or 2%) \(^3\)

**Trauma associated haemorrhage** \(^1\)
- IV loading dose: 1000mg in 100mls 0.9% sodium chloride over 10 minutes which will be commenced within 3 hours of injury usually in ED or operating theatres followed by 1000mg over the next 8 hours
  - **Note:** The CRASH 2 clinical trial included patients with significant haemorrhage (SBP<90mmHg, heart rate>110bpm or both or those at risk of significant haemorrhage.

**Adult cardiac surgery.**
- After induction of anaesthesia and prior to skin incision, administer a pre-surgical loading dose of 15 mg/kg tranexamic acid followed by infusion of 4.5 mg/kg/h for the duration of surgery. 0.6 mg/kg of this infusion dose may be added in the priming volume of the heart-lung machine
- **For patients with renal impairment the dose should be reduced:** \(^3\) (see below)

### Adult cardiac surgery

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Loading</th>
<th>Prime</th>
<th>Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-89</td>
<td>15 mg/kg</td>
<td>0.6 mg/kg</td>
<td>3.75 mg/kg/h</td>
</tr>
<tr>
<td>30-59</td>
<td>15 mg/kg</td>
<td>0.6 mg/kg</td>
<td>2.5 mg/kg/h</td>
</tr>
<tr>
<td>&lt;29</td>
<td>15 mg/kg</td>
<td>0.6 mg/kg</td>
<td>1.25 mg/kg/h</td>
</tr>
</tbody>
</table>

**Adult Total KNEE Arthroplasty** \(^3\)
- Administration of 15 mg/kg tranexamic acid prior to release of the tourniquet followed by repeat bolus injection of 15 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.

<table>
<thead>
<tr>
<th>Prior to release of tourniquet</th>
<th>8hrs after initial dose</th>
<th>8hrs after second dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>15mg/kg : 1st dose</td>
<td>15mg/kg: 2nd dose</td>
<td>15mg/kg: 3rd dose</td>
</tr>
</tbody>
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**Dosage of tranexamic acid for Knee Arthroplasty:** MIMS online. Accessed June 2015

- **Dose should be adjusted for patients with renal impairment. See table below**

### Adult total knee arthroplasty

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<td>30-59</td>
<td>Administration of 15 mg/kg tranexamic acid immediately prior to tourniquet release followed by a repeat bolus of 8.4 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.</td>
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<td>Administration of 15 mg/kg tranexamic acid immediately prior to tourniquet release followed by a repeat bolus of 6.3 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.</td>
</tr>
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</table>

**Dosage of tranexamic acid for renal impairment,** MIMS online. Accessed November 2015
**Adult Total HIP Arthroplasty**

- Administration of 15mg/kg tranexamic acid immediately prior to skin incision, followed by a repeat bolus of 15 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.

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<td>15mg/kg: 3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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*Dosage of tranexamic acid for Total hip Arthroplasty: MIMS online. Accessed November 2015*

- Dose should be adjusted for patients with renal impairment. See table below

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<th>Adult total hip arthroplasty</th>
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<tr>
<td><strong>eGFR (mL/min/1.73 m&lt;sup&gt;2&lt;/sup&gt;)</strong></td>
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*Dosage of tranexamic acid for renal impairment: MIMS online. Accessed November 2015*

4. **Performance Measures**

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. **Clinical Considerations**

- Monitor blood pressure, heart rate and oxygen saturation continuously
- Don’t run infusion via the same lumen with blood products or penicillin
- Anti-thrombolytic precautions should be utilised as per the units DVT prophylaxis i.e. anti thrombolytic stockings, calf compressors, and subcutaneous heparin.

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**Reviewers:** NM, ICU CNC, CNE’s, NUM’s, CNS’s & Staff Specialists, Pharmacist

**Endorsed by:** ICU Medical Director – Prof. Michael Parr
6. References / Links


7. Pre-hospital Tranexamic Acid (TXA) in Trauma. Briefing document. July 2012. Prof Russell Gruen, MBBS, PhD, FRACS, Professor of Surgery and Public Health. The Alfred and Monash University: Director, National Trauma Research Institute: Melbourne, Australia


9. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: retrospective analysis of effectiveness and safety BMJ 2014; 349 doi: http://dx.doi.org/10.1136/bmj.g4829 (Published 12 August 2014)