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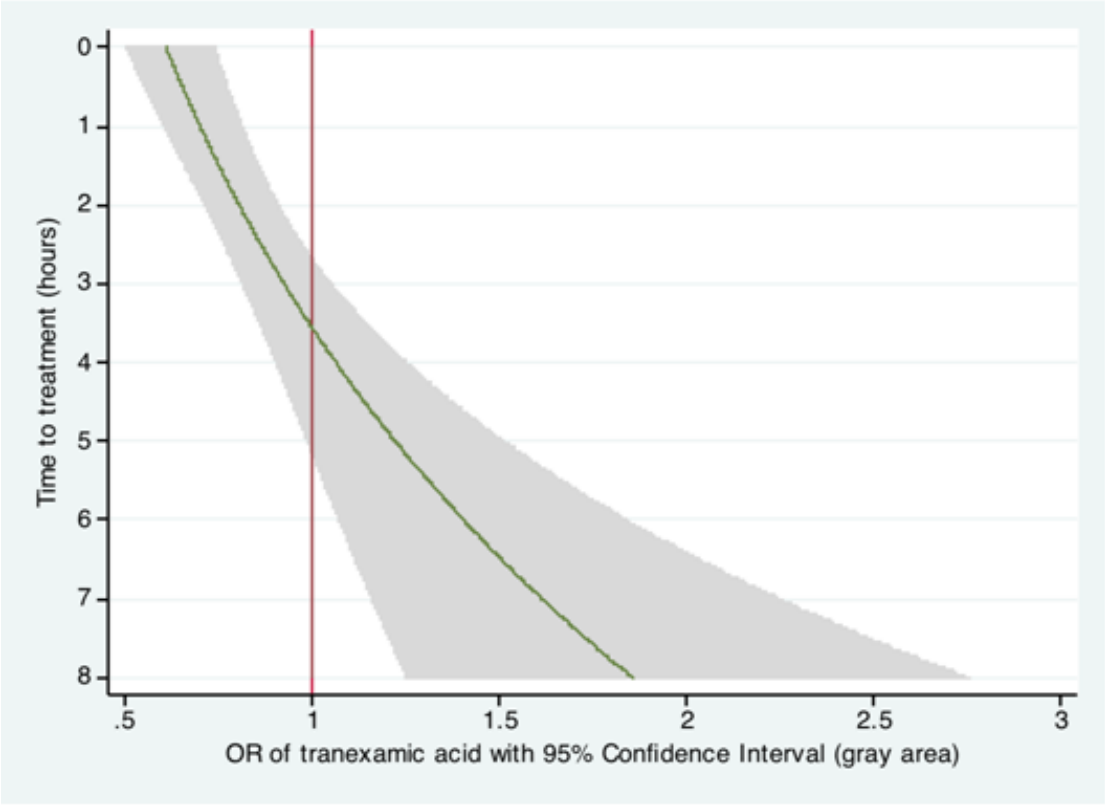
Briefing Document – Use of Tranexamic Acid in trauma care

Evidence from the CRASH2 trial

- TXA safely reduces all-cause mortality in bleeding trauma patients.
- There is no evidence of harmful side effects (in fact thrombotic complications are actually reduced).
- Early treatment is much more effective than later treatment (see below).



- If given within the first hour, TXA reduces the risk of death due to bleeding by around one third.
- There is evidence that the large majority of death due to bleeding will occur in patients with lower probability of death (as they represent a larger group of patients).
- There is evidence of benefit from TXA in the patients with lower probability of death as well as high probability of death – in other words it is not only the most severely injured patients who benefit (in fact about half the lives saved are in patients with a lower probability of death).
- There is no evidence of complications if patients with a lower probability of death are treated – in fact thrombo-embolic complications are reduced.
- Modeling from the CRASH2 data shows that if the Step 1 trauma transfer criteria were applied to the CRASH2 patients and TXA was given to all of them, about 90% of the total lives saved would be achieved (approx 400 lives a year in the UK – as much benefit as prehospital thrombolysis).

Conclusions from the evidence

1. We should give TXA to all bleeding or potentially bleeding injured patients, not just those with obvious severe haemorrhage or obvious high risk of death.
2. We should aim to give TXA early – within the first hour.
3. In the UK trauma system this means that TXA should be given in the prehospital phase .
4. We can use broad indications for TXA therapy as there is good evidence of benefit and no evidence of harm with early treatment.

Treatment strategy

In the CRASH2 study a 1 gram bolus of TXA was followed by an 8 hour infusion. It is not realistic to use an infusion pump in the prehospital phase., however as TXA has a relatively long half life (3 to 4 hrs) a 'bolus-move-infusion' strategy would give effective drug levels. The bolus is 1 gram in 10mls and needs to be given over 10 minutes (not continuous).

The drug is temperature stable, has a long shelf life and costs approx £16 for a box containing 5 doses (1 dose required per patient).

Paediatric dose has not been trialed in trauma. In paediatric cardiac surgery a weight adjusted adult dose is given (of 10mg/kg) and we would suggest the same for paediatric trauma.

Indications

The CRASH2 indication for treatment (the clinician thinking that the trauma patient was bleeding or at significant risk of bleeding) is not directly applicable to prehospital practice, as less information is available. We have modeled various prehospital indications based on key trigger points within the major trauma triage protocol and the NICE prehospital fluid protocol.

If all patients with trauma and significant bleeding would be treated with TXA within 3 hours of injury 400 lives would be saved every year in the UK (100%).

Below we present the proportion of the total potential benefit of TXA that would be achieved using different indications:

Major trauma triage Stage 1	90% (360 lives per year)
SBP < 90mmHg	72% (288 lives per year)
SBP<90 AND HR>110	87% (348 lives per year)
SBP<100 AND HR>110	94% (376 lives per year)

I would suggest that relating TXA use to three existing JRCALC Guidelines would be the simplest method of patient identification for TXA therapy in prehospital care, so Indications would be:

1) Patients with time critical injury (see Trauma Emergencies in Adults Overview).

2) All injured patients who require IV fluid therapy (see Intravascular Fluid Therapy Guideline).

3) Injured patient fulfilling local Step1 or Step 2 trauma triage protocol (see Trauma Emergencies in Adults Overview).

The other few percent of patients would still get some benefit if the TXA was given on arrival in the Emergency Department.

Contraindications

Isolated head injury.

Age < 5 years.

Critical interventions required (if critical interventions leave insufficient time for TXA administration).

Bleeding now stopped.

Implementation

This would require modifications to the Major Trauma Triage as in Appendix 1 and modification of the JRCALC Trauma Guideline as in Appendix 2. The start of a Prehospital Guide is in Appendix 3.

Appendix 1 – Place of TXA in Major Trauma Triage Protocol

As this protocol does not have interventions specified this is included to illustrate where the trigger for TXA might come in the prehospital patient assessment process.

Entry criteria for use of triage is a judgment that the patient may have suffered significant trauma

Step 1

• Physiological:
– GCS < 14
– SBP < 90 mmHg
– RR < 10 bpm (20 bpm in infant) or > 29 bpm

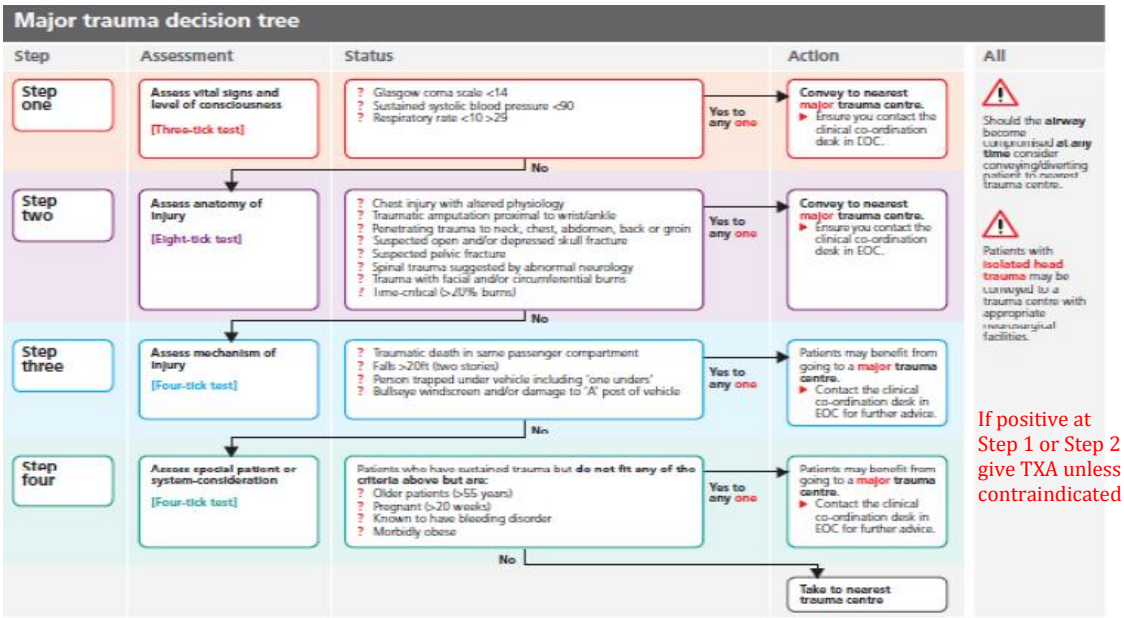
If any of the above factors are present, activate Major Trauma Alert and definitive care to be from Major Trauma Centre and give TXA unless contraindicated, otherwise proceed to Step 2

Step 2

• Anatomical:
– Penetrating to head/neck/torso/ limbs proximal to elbow/knee
– Chest injury with altered physiology
– 2 proximal long bone fractures
– Crushed/degloved/mangled extremity
– Amputation proximal to wrist/ankle
– Pelvic fractures
– Open or depressed skull fracture
– Sensory or motor deficit (new onset following trauma)

If any of the above factors are present activate a Major Trauma Alert and definitive care to be from

Major Trauma Centre and give TXA unless contraindicated, otherwise proceed to Step 3……



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Appendix 2 – Place of TXA in JRCALC Major Trauma Guideline

See modified JRCALC draft (not circulated).

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Appendix 3 – Tranexamic Acid (TXA) – Prehospital guide

To be circulated separately by JRCALC Guidelines Group.