TRAUMA

TRANEXAMIC ACID

The CRASH-3 trial is an international, randomised, double blind, placebo controlled trial.

AIM

The CRASH-3 trial will provide reliable evidence about the effect of tranexamic acid on mortality and disability in patients with TBI. The effect of TXA on the risk of vascular occlusive events and seizures will also be assessed.

PRIMARY OUTCOME

Death in hospital within 28 days of injury (cause-specific mortality will also be recorded).

SECONDARY OUTCOMES

- Vascular occlusive events (myocardial infarction, pulmonary embolism, clinical evidence of deep vein thrombosis)
- Stroke
- Disability assessed using the Disability Rating Scale and Patient Orientated Outcome measures
- Seizures
- Neurosurgical intervention
- Days in intensive care
- Other adverse events

INCLUSION CRITERIA

Adults with traumatic brain injury

- Within 8 hours of injury
- With any intracranial bleeding on CT scan or GCS =<12, and
- With no significant extracranial bleeding (needing immediate blood transfusion)

INTERVENTIONAL TREATMENT

A loading dose of tranexamic acid (1 gram by intravenous injection) followed by a maintenance dose of 1g.

CONTROL TREATMENT

Placebo (sodium chloride 0.9%) bolus followed by maintenance dose.

PREVIOUS TRIALS

CRASH 2 (2010)

'Effects of tranexamic acid on death, vascular occlusive events and blood transfusion in trauma patients with significant haemorrhage: a randomised, placebo-controlled trial'

- DB MCRCT (274 hospitals, 40 countries)
- n = 20,211 adults within 8 hours of injury (blunt and penetrating) at risk of severe hemorrhage or in hemorrhagic shock
- Intervention: tranexamic acid 1g over 10 min then 1g over 8h IV
- Control: placebo
- Primary outcome: all cause mortality within 4 weeks of injury (bleeding, vascular occlusion – MI, CVA, PE, MOF, HI, other)
- Secondary outcomes: vascular occlusive events (MI, CVA, PE, DVT), surgical intervention (neurosurgery, thoracic, abdominal, pelvic), receipt of blood transfusion, units of blood products transfused, degree of dependency, FVIIa use and GI bleeding
- Results:
  - All cause mortality reduced in the TXA2 group
  - Decreased mortality due to bleeding (RR 0.85) (which was 35% of deaths)
  - Trend toward more vascular occlusive events in placebo group
  - No difference in transfusion and need for surgery
  - Trend towards early treatment being more effective
  - NNT 65, ARR 1.5%, RR 0.91
- Commentary and criticisms:
  - TXA2 group got more FVIIa
  - Most benefit appeared to be in the severe shock group
  - Many of the centers were in developing countries

CRASH 2 : A priori subgroup analysis (2011)

- Benefit for tranexamic acid was greater if given early
- NNT 125 (RR 0.68) for death from bleeding if given within 1 hour
- Benefit up to 3 hours post-injury
- Causes harm if given later than 3 hours