Halt it
Haemorrhage alleviation with tranexamic acid - Intestinal system
Gastrointestinal haemorrhage

➢ A common emergency
➢ Important cause of mortality and morbidity
➢ Case fatality is high (10–20% in the UK)

Most common causes

➢ Cause varies by country, but in general:

➢ **Upper GI haemorrhage:**
  • Peptic ulcer
  • Oesophageal varices

➢ **Lower GI haemorrhage:**
  • Diverticular disease
  • Colitis
  • Cancer
TXA in upper GI bleeding

TXA may reduce death in GI bleeding but the quality of the trials is poor

Risk ratio, M-H, Fixed, 95% CI

- Bagnenko 2011: 0.38 (0.04–3.38)
- Barer 1983: 0.46 (0.26–0.82)
- Bergqvist 1980: 0.63 (0.17–2.31)
- Biggs 1976: 0.47 (0.09–2.51)
- Cormack 1973: 0.97 (0.20–4.67)
- Engqvist 1979: 0.88 (0.41–1.87)
- Hawkey 2001a: 0.80 (0.22–2.63)
- Hawkey 2001b: 2.41 (0.48–12.12)
- Staël von Holstein 1987: 0.77 (0.22–2.63)
- Pooled: 0.66 (0.47–0.93)

χ²=5.29 (P=0.73); I²=0%
Z=2.37 (P=0.02)

Manno D et al. BMJ 2014; 348:g1421
TXA in upper GI bleeding (2)

Trials are too small to assess the effect of TXA on thromboembolic events.

<table>
<thead>
<tr>
<th></th>
<th>TXA Events</th>
<th>TXA Total</th>
<th>Placebo Events</th>
<th>Placebo Total</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engquist 1979</td>
<td>5</td>
<td>102</td>
<td>2</td>
<td>102</td>
<td></td>
</tr>
<tr>
<td>Barer 1983</td>
<td>5</td>
<td>256</td>
<td>2</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>von Holstein 1987</td>
<td>1</td>
<td>164</td>
<td>2</td>
<td>164</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>11</strong></td>
<td><strong>522</strong></td>
<td><strong>6</strong></td>
<td><strong>526</strong></td>
<td><strong>1.86 (0.66, 5.24)</strong></td>
</tr>
</tbody>
</table>

Favours TXA  Favours placebo
GI bleeding is an important cause of death

TXA reduces bleeding in surgery

TXA reduces death due to bleeding in trauma patients

TXA may reduce deaths in GI bleeding but the evidence is poor

TXA could reduce death and morbidity in GI bleeding
➢ The HALT-IT trial will provide reliable evidence about the effect of tranexamic acid on mortality and morbidity in patients with significant gastrointestinal bleeding.

➢ The effect of TXA on the risk of thromboembolic events will also be assessed.
Study characteristics

➢ **Trial design:** randomised, double blind, placebo controlled

➢ **Target sample size:** 8,000 adults with acute significant upper or lower GI bleeding

➢ **Where?** Worldwide: Egypt, Georgia, Malaysia, Nigeria, Pakistan, Papua New Guinea, Romania, United Kingdom
Aims

To quantify the effect of TXA on mortality and morbidity

➢ Primary outcome: death in hospital within 28 days of randomisation (cause-specific mortality will also be recorded)

➢ Secondary outcomes:
  • Re-bleeding
  • Need for surgery or radiological intervention
  • Blood product transfusion
  • Thromboembolic events
  • Other adverse medical events
  • Patient’s selfcare capacity
  • Days spent in ICU or HDU
  • Patient status (death, hospital readmission) at 12 months*

* England and Wales only
Overview

**ELIGIBILITY** (data collected on entry form)
- Adults with significant acute upper or lower gastrointestinal bleeding
- Responsible clinician is substantially uncertain as to the appropriateness of tranexamic acid in a patient

Appropriate **CONSENT PROCESS**
(patient, representative or waiver)

**RANDOMISE** (tranexamic acid or placebo)
Entry form completed

**LOADING DOSE** (1g) over 10 minutes

**MAINTENANCE DOSE** (3g) over 24 hours

Complete **OUTCOME FORM** at discharge, death or day 28 whichever is earlier

All clinically indicated treatment is given in addition to trial enrolment

Adverse events are reported up to day 28

If prior consent waiver used, consent from patient or relative required after emergency is over
**ENTRY**

**PLEASE COMPLETE 1–19 BEFORE RANDOMISING THE PATIENT**

**ABOUT THE HOSPITAL**

1. Country
2. Hospital code (if not locally held)

**ABOUT THE PATIENT** (please ensure all information below is contained in the medical records)

3. Patient's initials
4. Sex (male/female)
5. Do you know the date of birth? YES / NO
   - day
   - month
   - year
   - approximate age
6. Time since onset of GI bleed symptoms
   - hours
   - in relation to this acute episode only
7. Suspected location of GI bleed
   - Uppper
   - Lower
8. Hemeatemesis or coffee-ground vomitus? YES / NO
   - Ask: are you passing blood in one or all of these forms?
9. Nocturnal fresh blood per rectum? YES / NO
   - Ask: does the patient have blood present on rectal examination?
10. Suspected variceal bleed? YES / NO
11. Systolic blood pressure
12. Heart rate
13. Signs of shock present? YES / NO
   - Ask: are the patient's blood pressure and pulse low?
14. Suspected current active bleeding? YES / NO
15. Other co-morbidities? YES / NO
   - Carbohydrates
   - Renal
   - Liver
   - Respiratory
   - QLD / Meningoencephalitis
   - Other red blood cell requirement
   - Misc
16. On anti-coagulant therapy? YES / NO
17. Emergency admission? YES / NO

**RANDOMISATION INFORMATION** (fully eligible if yes, significant upper or lower GI bleed, ABO uncertainty about the use of an emergency blood transfusion on a particular patient)

18. Eligible? YES / NO
19. Consent for entry obtained from: YES / NO
   - Waiver
   - Relative
   - Other
   - Unwilling
20. Treatment pack number
21. Date of randomisation
22. Time of randomisation
23. a) Name of person randomising patient
    - Firstname
    - Last name

**PLEASE SEND THESE DATA TO THE COORDINATING CENTRE IMMEDIATELY AFTER RANDOMISATION — SEE GUIDELINES OVERLEAF**

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**Entry form**

- Complete questions 1–18 to assess eligibility
- If eligible, follow appropriate consent process – complete 19
- **RANDOMISE:** Use next lowest available pack number

**STRICT NUMERICAL ORDER**
No extra tests required – a short single page Outcome form completed 4 weeks (28 days) after randomisation, at discharge, or at death (whichever occurs first)

Outcome to be collected even if the trial treatment is interrupted or is not actually given

Form to be sent to the TCC as soon as possible
Adult with significant upper or lower GI bleeding

Uncertainty principle: the responsible clinician is substantially uncertain as to whether or not to use TXA

If the clinician believes there is a clear indication for, or clear contraindication to, tranexamic acid use, the patient should not be randomised.
JOIN THE GLOBAL COLLABORATION OR
REGISTER FOR THE TRIAL RESULTS

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