Minimising blood loss is one of the three founding pillars of patient blood management. Pharmacological measures are a key tool to achieve this in clinical practice. Tranexamic acid (TXA) is a synthetic antifibrinolytic drug and a lysine analogue. Its mode of action is to bind to the lysine receptor of plasminogen, preventing its activation to plasmin (a factor essential for fibrinolysis causing the dissolution of blood clots). By inhibiting fibrinolysis, breakdown of clots is reduced and the likelihood of needing a transfusion of blood components and the risks associated with transfusion are reduced\textsuperscript{1,2}.
Indications for use:

Surgery

NICE Quality Standard QS138 – Statement 2:
Recommends the use of TXA in patients undergoing surgery where there is expected moderate blood loss (>500mls in line with WHO surgical checklist). NB: For children over 1 year old the recommended threshold is 10% blood volume.

NICE Guideline NG24:
Recommends TXA is used concomitantly where perioperative cell salvage is used. Specifically suggests considering intraoperative cell salvage with TXA for patients who are expected to lose a very high volume of blood (cardiac and complex vascular surgery, major obstetric procedures, pelvic reconstruction, and scoliosis surgery).

Dosing guidance for general fibrinolysis should be applied.

Orthopaedic surgery

NICE Guideline NG157:
Primary elective hip or knee replacement: Recommends IV TXA with additional topical (intra-articular) TXA diluted with saline before wound closure. Total dose should not exceed 3g. NB: For patients with renal impairment, a reduced IV dose should be given on its own.

Primary elective shoulder replacement: Recommends considering IV TXA with additional topical (intra-articular) TXA diluted with saline before wound closure. Total dose should not exceed 3g. NB: For patients with renal impairment, if used, a reduced IV dose should be given on its own.

Trauma

CRASH 2 & 3:
CRASH 2 demonstrated TXA is effective and safe in bleeding trauma patients, significantly reducing the risk of mortality. CRASH 3 established a reduction in head injury-associated mortality in patients with mild to moderate traumatic brain injury. Both studies showed no apparent thrombotic side effects or increase of vascular occlusive events. Efficacy is greatly improved the closer to time of injury TXA is administered, the studies therefore recommended administration <3 hours post injury.
Major haemorrhage
The British Society for Haematology (BSH) guidelines (Hunt et al, 2015) recommend the use of TXA for management of non-traumatic major haemorrhage to reduce blood loss and reduce the need for blood component use. However, it was found in the HALT-IT trial that tranexamic acid did not reduce death from gastrointestinal bleeding.

Obstetrics and gynaecology

Post-partum haemorrhage
The WOMAN trial demonstrated a reduction in death due to bleeding in women with post-partum haemorrhage without significant increase in adverse effects. The benefit was most notable when TXA was given within 3 hours of birth and the authors recommended it should be given as soon as possible after bleeding commenced.

Menorrhagia
Oral TXA is indicated for use in managing menorrhagia independently or as part of a surgical plan.

Paediatrics
NICE Guideline NG24 recommends the use of TXA in paediatric surgery where blood loss of 10% blood volume is expected.

BSH Guideline: Transfusion for Fetuses, Neonates and Older Children (2016) suggests TXA is used where massive blood loss is expected in children presenting with major traumatic injuries. Dosing and timing should be in accordance with Royal College of Paediatrics and Child Health recommendations (2012). Use of antifibrinolytic therapy should be considered for neonates and children undergoing cardiac surgery at high risk of significant bleeding.

Dosing
Dosing regimens vary. Below is a summary of some of the dosing recommendations from the above publication and BNF advice.
Published dosing regimens

<table>
<thead>
<tr>
<th>Adult cardiac surgery</th>
<th>10 mg/kg intravenously (IV) immediately pre-op followed by IV infusion of 1 mg/kg/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult trauma</td>
<td>1g IV within 3 hours of the event followed by 1g infused over 8 hours</td>
</tr>
<tr>
<td>Paediatric trauma</td>
<td>15 mL/kg (maximum 1000 mg) IV over 10 minutes followed by 2 mg/kg/h (max 125 mg/h) by IV infusion until haemorrhage is controlled</td>
</tr>
<tr>
<td>PPH</td>
<td>1g IV followed by a further 1g if bleeding continues or recurs</td>
</tr>
</tbody>
</table>

NB: BSH (2016)⁶ recognises a lack of evidence to guide dosing for TXA in paediatric cardiac surgery but acknowledges the findings by Wesley et al. (2015) that a bolus dose followed by an infusion may be the most effective method, that age may be a better determining factor than weight for dosing, and the use of cardiopulmonary bypass may also affect dosing requirements¹³.

References


6. CRASH-2 Trial: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4576020/

7. CRASH-3 Trial: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32233-0/fulltext


Effective: 01/12/2021


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This leaflet was prepared by NHS Blood and Transplant in collaboration with the National Blood Transfusion Committee.

Individual copies of this leaflet can be obtained by calling 01865 381010

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