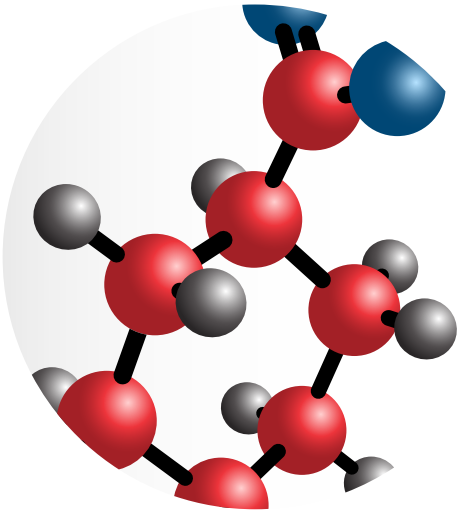
NHS
Blood and Transplant



Information for clinicians

Tranexamic acid use in the management and prevention of blood loss

Minimising blood loss is one of the 3 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. the likelihood of needing a transfusion of blood components and the risks associated with transfusion are reduced [1,2].

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Patient Blood Management

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)[3].

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)[4].

Dosing guidance for general fibrinolysis should be applied.

Orthopaedic surgery

Fillingham et al (2018) conducted a review of relevant literature for the use of TXA in joint arthroplasty. The analysis demonstrated that use of TXA had a direct impact on reducing calculated blood loss and transfusion requirements and recommended IV TXA pre-incision, as it demonstrated superior outcomes. There was no associated increased risk of thrombotic events with any formulation[5].

Summary of recommendations[5]

Administration of intravenous (IV), topical, and oral TXA as well as combinations of individual formulations of TXA are all effective strategies when compared to placebo for reducing calculated blood loss and the need for transfusion during the perioperative episode of a primary TJA (total joint arthroplasty).

The analysis of studies did not identify a clearly superior method, or combinations of methods, for the administration of TXA. All methods of administration effectively demonstrate equivalent efficacy at reducing calculated blood loss and the risk of transfusion during the perioperative episode of a primary TJA.

Within the context of the TXA doses used in primary TJA, the dose amount of TXA was not found to significantly affect its reduction of calculated blood loss or the need for transfusion during the perioperative episode of a primary TJA.

Administration of multiple doses of IV or oral TXA compared to a single dose of IV or oral TXA does not significantly alter the amount of calculated blood loss and need for transfusion during the perioperative episode of a primary TJA.

In primary TJA, administration of IV TXA before the incision potentially reduces blood loss and the need for transfusion compared to its administration after incision.

Administration of IV, topical, and oral TXA in patients without a known history of a venous thromboembolism (VTE) does not increase the risk of developing a VTE compared to placebo during the perioperative episode of a primary TJA.

There is a paucity of randomized clinical trials on the risk of adverse effects of IV, topical, and oral TXA in patients with known history of a VTE, MI, CVA, TIA, and/or vascular stent placement. The existing high quality literature regarding administration of TXA in patients of generally higher comorbidity burden does not suggest increased risk of adverse thromboembolic events during the perioperative episode of a primary TJA.

There is a paucity of randomized clinical trials on the risk of arterial thromboembolism (ATE) due to the administration of TXA intravenously, topically, and orally. However, the existing evidence does not suggest that TXA increases the risk of developing an ATE compared to placebo during the perioperative episode of a primary TJA.

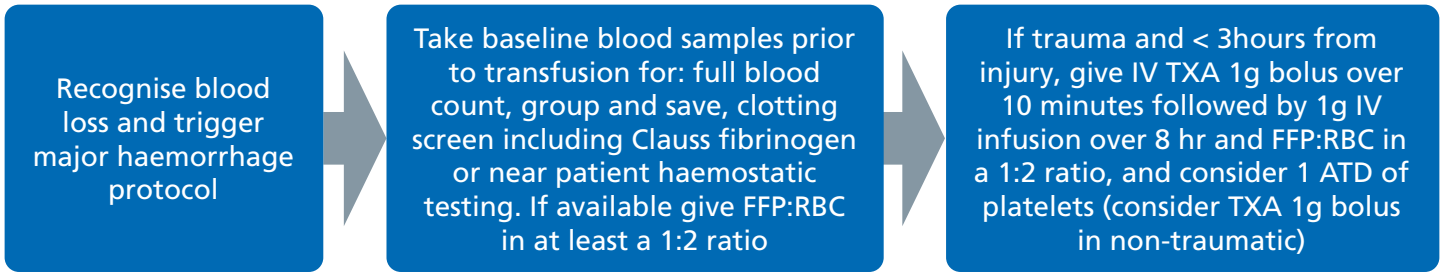
Trauma

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[6,7].

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[8]. However, it was found in the HALT-IT trial that tranexamic acid did not reduce death from gastrointestinal bleeding[9].



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[10].

Menorrhagia

Oral TXA is indicated for use in managing menorrhagia independently or as part of a surgical plan[11].

Paediatrics

NICE Guideline NG 24 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 in accordance with Royal College of Paediatrics and Child Health recommendations (2012)[12]. Use of antifibrinolytic therapy should be considered for neonates and children undergoing cardiac surgery at high risk of significant bleeding[12].

Dosing

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

Published dosing regimens

Adult cardiac surgery	10 mg/kg intravenously (IV) immediately pre-op followed by IV infusion of 1 mg/kg/h
Adult trauma	1g IV within 3 hours of the event followed by 1g infused over 8 hours
Paediatric trauma	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
PPH	1g IV followed by a further 1g if bleeding continues or recurs

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 cardio-pulmonary bypass may also effect dosing requirements[13].

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NHS Blood and Transplant

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