

TRANEXAMIC ACID IN ORTHOPAEDIC AND TRAUMA SURGERY: CURRENT EVIDENCE ON EFFICACY AND SAFETY

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Abstract. Tranexamic acid (TXA) has become a cornerstone of perioperative blood management. This review summarises the evidence on its efficacy and safety in trauma and orthopaedic surgery, including the CRASH-2 and CRASH-3 trials, meta-analyses and population-based studies in hip and knee arthroplasty, the 2018 multisociety clinical practice guidelines, and the POISE-3 trial in non-cardiac surgery. The data consistently show reduced blood loss and transfusion without a demonstrable increase in thromboembolic events, provided that the drug is given early and dosing is adjusted for renal function.

Keywords: tranexamic acid, antifibrinolytics, arthroplasty, trauma, blood loss, transfusion, patient blood management.

Introduction

Major orthopaedic and trauma surgery is frequently associated with substantial blood loss. Tissue injury activates fibrinolysis, which aggravates bleeding, while allogeneic transfusion carries risks of immunological reactions, infection, volume overload and higher costs. Tranexamic acid (TXA), a synthetic lysine analogue, competitively blocks lysine-binding sites on plasminogen and thereby inhibits fibrinolysis. Its low cost, wide availability and favourable safety profile have made it a key pharmacological component of patient blood management (PBM) programmes, which rest on three pillars: optimisation of red cell mass, minimisation of blood loss and a restrictive transfusion strategy [10].

Evidence in trauma

The CRASH-2 trial randomised 20,211 adult trauma patients with, or at risk of, significant haemorrhage to TXA (1 g over 10 min followed by 1 g over 8 h) or placebo within 8 h of injury. TXA reduced all-cause mortality (14.5% vs 16.0%) and death due to bleeding, with no increase in vascular occlusive events [1]. A

subsequent analysis showed that the benefit was greatest when treatment started within 1 h and that administration after 3 h was associated with an increased risk of death from bleeding [2]. This finding established the principle that TXA must be given as early as possible. In traumatic brain injury, the CRASH-3 trial demonstrated a reduction in head injury–related deaths among patients with mild-to-moderate injury treated within 3 h [3].

Evidence in elective arthroplasty

A cumulative meta-analysis by K. Ker et al., which included 129 randomised trials across surgical specialties, showed that TXA reduced the probability of blood transfusion by about one third, with the evidence for this effect regarded as conclusive [4]. In a population-based study of more than 870,000 patients undergoing total hip or knee arthroplasty in the United States, J. Poeran et al. found that TXA use was associated with a substantially lower transfusion rate and no increase in thromboembolic complications or acute renal failure [5].

The 2018 clinical practice guidelines endorsed by the American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons, the American Society of Regional Anesthesia and Pain Medicine and other societies concluded that intravenous, topical and oral TXA are all effective in reducing blood loss and transfusion in primary arthroplasty, without clear superiority of any route, and that available data do not show an increased risk of venous thromboembolism [6]. In hip fracture surgery, randomised trials and meta-analyses likewise report reduced blood loss and transfusion requirements; however, these frail patients have a high baseline thrombotic risk, and the data on safety are less robust than in elective arthroplasty.

Safety considerations

The largest perioperative safety trial, POISE-3, enrolled 9,535 patients undergoing non-cardiac surgery who received 1 g of TXA at the start and end of surgery or placebo. TXA reduced the composite bleeding outcome (9.1% vs 11.7%);

the composite cardiovascular outcome occurred in 14.2% and 13.9% of patients respectively, although the prespecified non-inferiority criterion was not formally met [7]. Seizures are a recognised dose-dependent adverse effect, described mainly after high-dose regimens in cardiac surgery [8]. Because TXA is excreted by the kidneys, the dose should be reduced in renal impairment. Relative contraindications include active thromboembolic disease and a history of seizures. Data from obstetric haemorrhage (WOMAN trial) further support the safety of the standard 1 g dose [9].

Place within patient blood management

TXA is most effective as part of a comprehensive PBM pathway that includes preoperative detection and treatment of anaemia, meticulous surgical haemostasis, controlled hypotension where appropriate, and restrictive transfusion thresholds. In elderly patients after hip surgery with cardiovascular risk factors, the FOCUS trial showed that a restrictive strategy (haemoglobin <8 g/dL or symptoms) was not inferior to a liberal one in terms of death or inability to walk independently [11].

Conclusion

Current evidence supports the routine use of TXA in arthroplasty and in bleeding trauma patients when administered early. It reduces blood loss and transfusion without a demonstrable increase in thromboembolic events in most surgical populations. Further research is needed to define optimal dosing regimens and the safety profile in high-risk groups, particularly frail patients with hip fractures and those with a history of thrombosis.

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