Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P36
March 20th, 2025

Tranexamic Acid Use in Neurosurgery and Spinal Surgery

J.H. Ng,[1] M. Moore[1].

Department of Anaesthesiology and Critical Care Medicine, Beaumont Hospital, Beaumont Rd., Dublin 9, Ireland.

Abstract

Introduction

Tranexamic acid (TXA) effectively reduces intraoperative blood loss, yet its utilization in neurosurgery is underexplored. Our study evaluated the current practice of TXA administration in neurosurgical and spinal procedures.

Methods

A prospective observational design was used, encompassing neurosurgery and spinal surgery conducted at a tertiary neurosurgical centre in November and December 2023. Data on patient comorbidities, surgical procedures, TXA dosage, and blood loss were collected and analysed.

Results

212 cases were recorded – 162 (76%) neurosurgery, 50 (24%) spinal surgery. TXA was used in 43 cases (20.3%), with 34 (16%) cases in neurosurgery and 9 (4.2%) cases in spinal surgery. TXA was predominantly utilized in intracranial hematoma evacuation (43.5%) and infrequently in other procedures including decompressive craniectomy (33.3%), neurovascular interventions (33.3%) and excision of intracranial tumours (23.3%). TXA saw no utilization in deep brain stimulation (DBS) surgery, vagal nerve stimulation (VNS) surgery, or wound washouts. In spinal surgery, TXA was mainly used in tumour excision (40%), with limited use in spinal fusion (1 out of 3 patients). TXA was administered at the start of surgery in 65.1% of cases, at a dosage of 1000mg. Only 1 out of 20 patients with seizure disorders received TXA (5%). 3 patients experienced seizures postoperatively, none of which had received TXA during their procedures. 2 patients developed pulmonary embolism (PE) post-operatively, with 1 having received TXA.

Discussion

This study highlights the infrequent use of TXA in neurosurgery despite its potential benefits. Further research is needed to determine the role of TXA in neurosurgery, in particular to

optimise its use, especially in patient following haemorrhage or those at risk of intraoperative bleeding.

Introduction

Tranexamic acid (TXA), a synthetic antifibrinolytic drug, is used in surgery to reduce intraoperative blood loss. Owing to its competitive action at the lysine receptor, it helps inhibit the conversion of plasminogen to plasmin, thereby preventing the breakdown of fibrin.[1] Its use has seen widespread adoption in surgery in the last decade due to its demonstrated efficacy coupled with a relatively low risk profile. The Joint Royal Colleges Tranexamic Acid in Surgery Implementation Group, formed by three royal colleges in the UK, had recently advocated for the increased use of TXA, recommending that TXA be considered in all adults undergoing inpatient surgery. [2]

Despite growing evidence in favour of TXA, concerns persist, especially regarding the potential risks such as thromboembolism and seizure. However, landmark trials, including POISE-3 (Peri-Operative Ischemic Evaluation-3) and CRASH-3 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 3), have consistently failed to demonstrate an increased risk of thrombosis with TXA.[3,4] Recent meta-analyses of randomised trials have also found no evidence of increased risk of seizure with recommended dose of TXA.[5,6]

While TXA's benefits are recognized in various surgical contexts, its application in neurosurgery is not well-explored.[7] Recent studies have suggested that TXA can be effective in reducing intraoperative blood loss in neurosurgical procedures, such as craniotomy for tumour resection, where bleeding risks are significant. However, its use in this field is still not universally adopted, and concerns about its safety profile, particularly regarding seizures, persist.[8,9] We carried out a study to investigate the intraoperative application of tranexamic acid in our neuro-anaesthesia practice, analyzing current practices and evaluating adherence to guidelines.

Methods

This study employed a prospective observational design, encompassing all intracranial and spinal procedures conducted at Beaumont Hospital, Dublin, from November 1 to December 2023. Patient data was collected using a standardized proforma, completed by doctors or nurses after each operation. Variables collected include patient comorbidities, details of surgical procedures performed, dosage of TXA administered, and estimated blood loss. The collected data were then entered into an Excel spreadsheet for analysis.

Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P36
March 20th, 2025

Results

A total of 212 neurosurgical procedures were captured. These procedures included intracranial, extracranial and spinal surgeries as shown in the charts below: (Figure 1, 2)

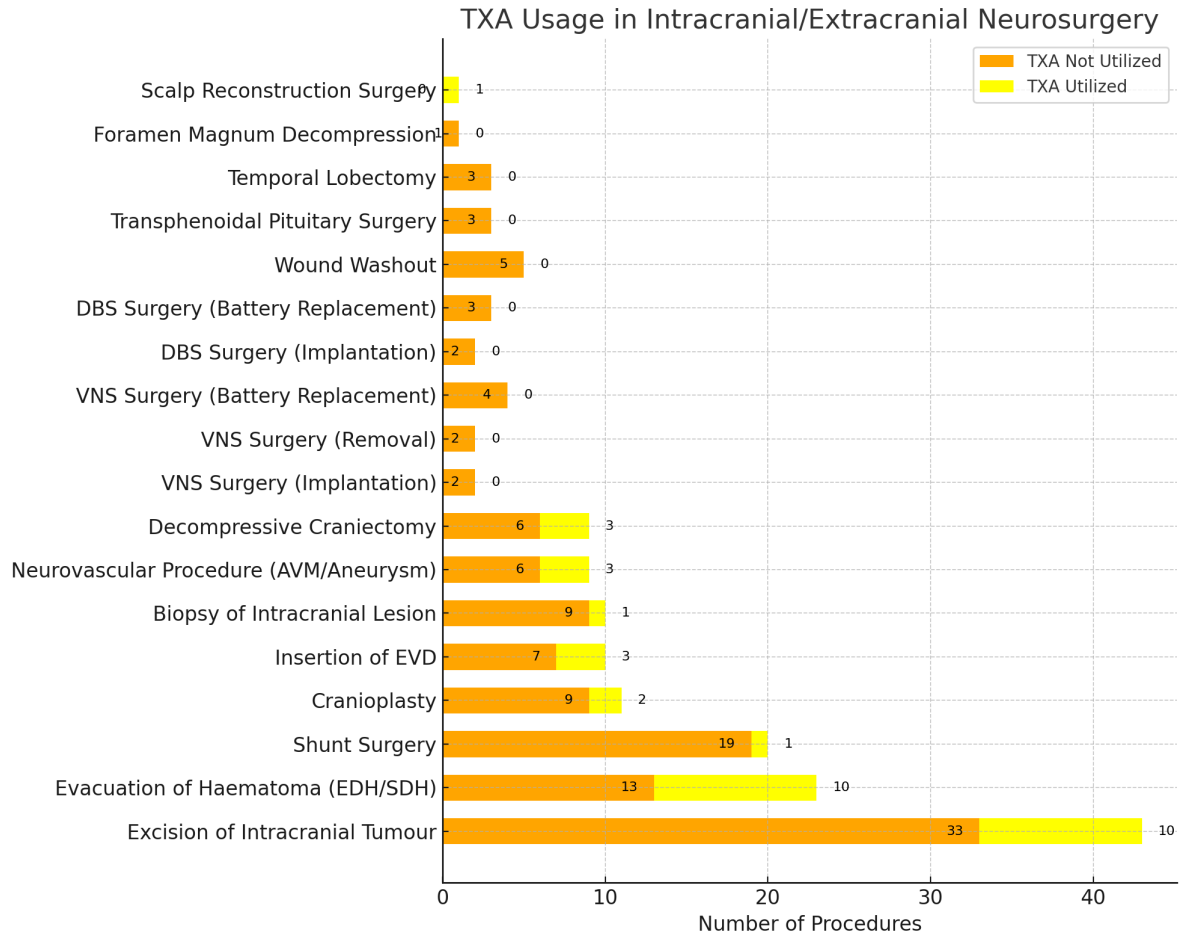

Figure 1: TXA Usage in Intracranial/Extracranial Neurosurgery
Orange: TXA Not Utilized
Yellow: TXA Utilized

IMJ Official Journal of the Irish Medical Organisation

Ir Med J; March 2025; Vol 118; No. 3; P36
March 20th, 2025

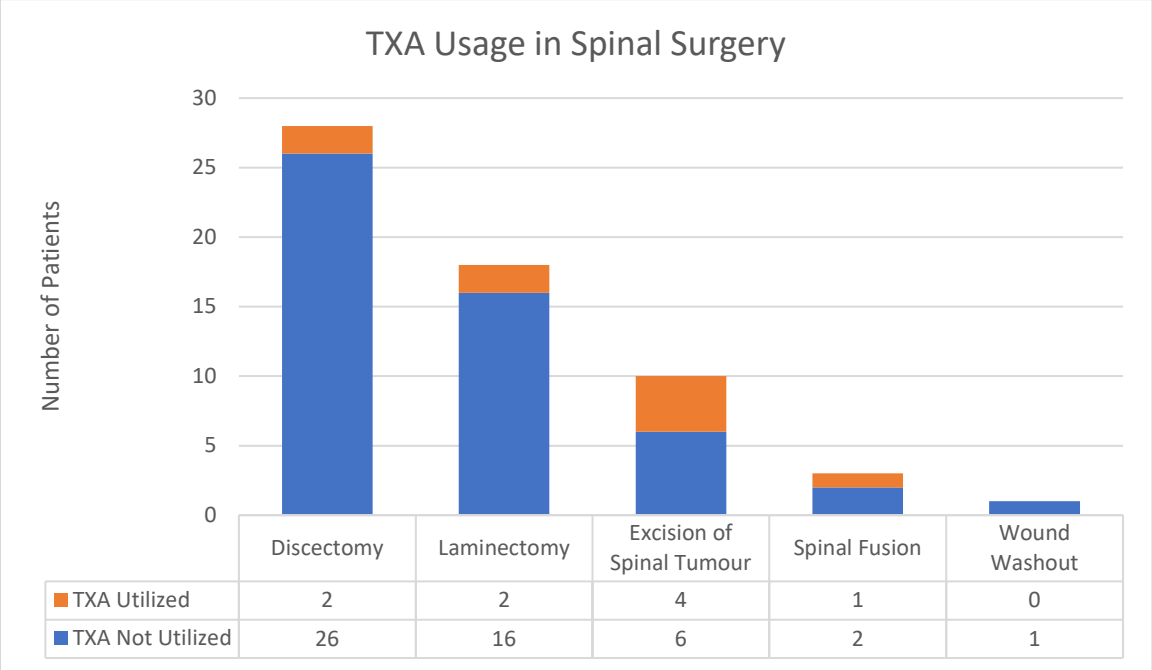

Figure 2: TXA Usage in Spinal Surgery
Blue: TXA Not Utilized
Orange: TXA Utilized

TXA was used in 43 of our 212 neurosurgical procedures. There were 162 intracranial/extracranial neurosurgical procedures carried out in the 2-month period. Of these 162 procedures 34 received TXA. 79 craniotomies were performed and only 23 of these received TXA. These craniotomies included procedures such as brain tumour excision, AVM excision, evacuation of haematoma and temporal lobectomy. 9 decompressive craniectomy were performed with only 3 receiving TXA. None of the patients undergoing deep brain stimulation (DBS) procedures, which encompassed both battery replacement and lead implantations, received TXA.

Transphenoidal pituitary surgery, which can entail significant intraoperative and postoperative bleeding risks, did not involve the use of TXA in any of our cases.
Among the remaining procedures, which included scalp reconstruction, wound washout, vagus nerve stimulation (VNS) surgery, burrhole biopsy of intracranial lesions, insertion of extra-ventricular drain (EVD), cranioplasty and VP shunt insertion, TXA was administered in only 8 out of 65 cases.

50 spinal surgical procedures were recorded in our study. There were 28 lumbar discectomy, 18 lumbar laminectomy, 10 spinal cord tumour excision, 1 lumbar spinal fusion, 2 cervical spinal fusion and 1 wound washout. Of these 50 procedures 8 received TXA.

A total of 43 patients received TXA. The majority (28) received it during the induction of anaesthesia, while 8 patients received it in response to intraoperative bleeding. 4 cases involved patients receiving two doses, one at the start of surgery and a second dose at the conclusion of surgery. Among those receiving a single dose, 1g was administered in 37 cases, with one patient receiving 500mg. For patients receiving two doses, a total of 2g was administered.

Blood loss during neurosurgical procedures varied across different types of interventions. (Figure 3) The mean blood loss was highest in temporal lobectomy procedures at 316.6ml, followed by craniotomies for neurovascular procedures (277ml), evacuation of hematoma (264.2ml), and tumour excision (238.7ml). Scalp reconstruction procedures and foramen magnum decompression each involved only one patient, with recorded blood losses of 1300ml and 100ml, respectively. Transphenoidal pituitary surgeries and wound washouts averaged 100ml of blood loss. Conversely, procedures such as VNS surgery, DBS surgery, and burr hole biopsies of intracranial lesions showed relatively lower mean blood losses of 50ml. Among the 212 procedures audited, 13 patients experienced moderate blood loss, with EBL >500ml. Of these, 9 received TXA.

20 patients were identified with seizure disorders, out of these 20 patients, 11 were undergoing procedures specifically indicated for their condition. Among these, 8 patients were scheduled for VNS surgery, and another 3 were undergoing temporal lobectomy. The remaining patients underwent various other procedures, including craniotomies for evacuation of hematoma (2 cases), tumour excision (2 cases), wound washout (1 case), cranioplasty (2 cases), burr hole biopsy (1 case), and VP shunt insertion (1 case). Among these 20 patients, only 1 received TXA.

3 patients experienced seizures postoperatively, none of which had received TXA. 2 patients developed pulmonary embolism (PE) post operatively, with only one receiving TXA. Both patients had craniotomy for tumour excision, neither patient suffered any adverse consequences of the PE.

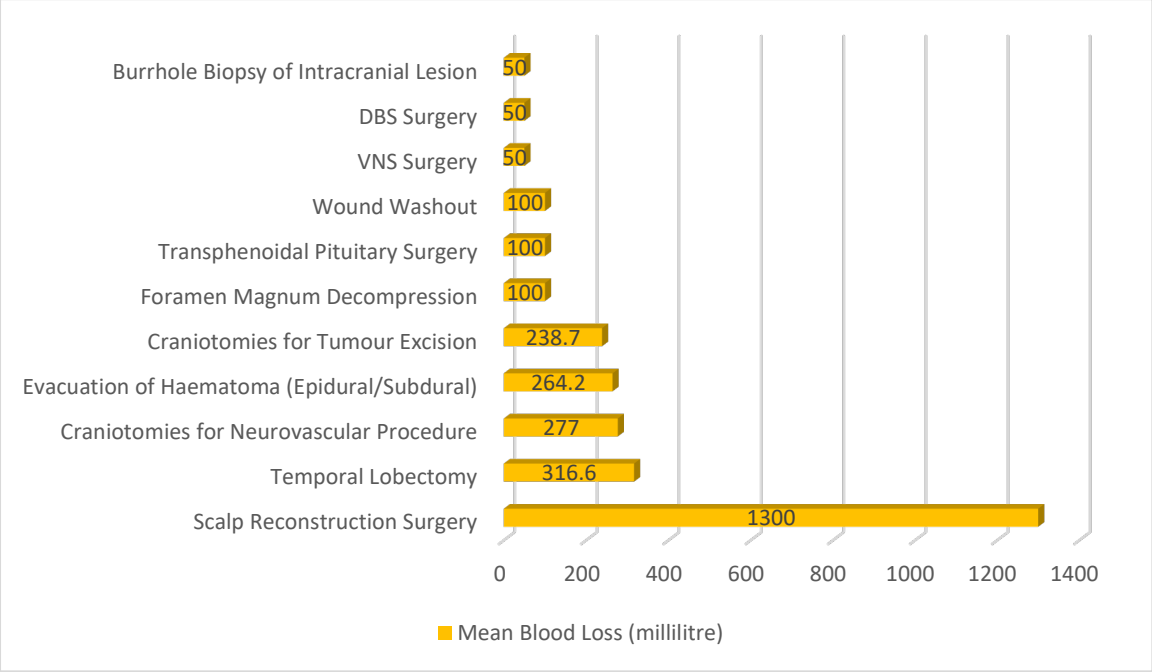

Figure 3: Mean Blood Loss in Different Neurosurgical/Spinal Surgery

Discussion

TXA serves as a chemical haemostatic agent that can effectively reduce intraoperative blood loss and minimize the need for perioperative transfusions.[7] Despite its efficacy, reservations persist within neurosurgery due to its controversial risk-benefit profile.[10] Our study highlights a minimal utilization of TXA in both intracranial and spinal surgery within our standard practice.

Neurosurgeries often involve procedures with heightened bleeding risks. Intracranial tumours, which constitute a significant majority of neurosurgical cases, as indicated in our study, are frequently associated with haemostatic dysfunction, particularly meningiomas, which are known to have the effect of local tissue plasminogen activator (tPA) activation.[11] Spinal surgeries pose similar challenges with excessive blood loss, as they typically involve stripping paraspinal muscles off the lamina causing bleeding from raw muscle edges and periosteum.[7] This is more pronounced if instrumentation is involved. A study investigating spinal fusion surgery has reported blood loss to be typically ranging from 800 ml to 1500 ml.[12]

The reserve with TXA in the context of neurosurgery stems primarily from concerns about its potential side effects. From its effect on fibrinolytic inhibition, TXA can theoretically induce a pro-thrombotic state leading to increased risks of thrombotic events such as venous

thromboembolism (VTE), myocardial infarction (MI), or stroke. While there are instances documented in case reports and series, larger trials have refuted this concern.[3,4]

Another apprehension linked with its usage is the potential for seizures. This is believed to stem from the structural similarity between TXA and neurotransmitters like gamma-aminobutyric acid type A (GABA-A) and glycine. By binding to these receptors, TXA can potentially disrupt GABA-mediated inhibition of the central nervous system (CNS). This is particularly relevant in neurosurgery, where seizures are common. Concerns regarding these adverse effects, coupled with the lack of strong consensus or guidelines advocating its use in neurosurgery, might lead clinicians to err on the side of caution and avoid TXA.

Studies by Takagi and Myles et al have explored this concern among cardiac patients, finding the incidence rate of TXA-induced seizures to be dose dependent, with a higher rate in the high-dose group.[13,14] However, a recent systematic review, meta-analysis, and trial sequential analysis by Tsan et al involving 191 RCTs, found no correlation between TXA and the incidence of seizures.[6] The study also indicated that the occurrence of seizures with TXA is rare and is not significantly increased when used at typical perioperative doses.[6] In our study, TXA was administered to only one patient with seizure disorders. This limited usage could be attributed to the inherently low bleeding risks associated with the procedures undergone by this patient cohort, such as VNS surgery, rendering the use of TXA unnecessary. Alternatively, clinicians may have deemed the potential risks to outweigh the benefits and consequently opted against its administration. Among the study population, we also found that three patients experienced seizures in the post-operative period, none of whom received TXA. Given the frequent occurrence of seizures in neurosurgery, distinguishing whether perioperative seizures stem from the underlying pathology or represent a side effect of TXA would be a challenging task. This highlights the complexity of balancing the potential benefits of TXA in reducing blood loss with its theoretical and observed risks in neurosurgery.

Our institutional protocol involves administering 1 gram of TXA at the start of surgery, which aligns with recommendations from the Joint Royal Colleges Tranexamic Acid in Surgery Implementation Group, stating that “1 gram of tranexamic acid should be given by slow intravenous injection at the start and end of surgery.”[2] A model-based meta-analysis also supports a cumulative dose of approximately 20 mg/kg as optimal for reducing blood loss while minimizing seizure risk, a strategy endorsed by the European Society of Anaesthesiology and Intensive Care guidelines.[15,16] While these recommendations are based on other surgical specialties, they offer a potential framework for optimizing TXA dosing in neurosurgery, where clear guidelines remain lacking.

Despite the reservations and minimal use within our routine practice, TXA consistently finds application in case of significant blood loss, such as decompressive craniectomy and instances of intracranial haemorrhage. Notably, TXA sees more frequent use in neurosurgeries compared to spinal surgeries. It was also noted that the dosage used were consistent at 1000 mg, aligning with recommendation by evidentiary body.[2]

This study highlights the infrequent use of TXA in neurosurgery despite its potential benefits. Further research is needed to determine the role of TXA in neurosurgery, in particular to optimise its use, especially in patient following haemorrhage or those at risk of intraoperative bleeding.

Declarations of Conflicts of Interest:
None declared.

Corresponding author:
Jun Hui Ng,
Department of Anaesthesiology and Critical Care Medicine,
Beaumont Hospital,
Beaumont Rd.,
Dublin 9,
Ireland.
E-Mail: junhuing@gmail.com

References:

1. Peck TE, Hill SA. *Pharmacology for Anaesthesia and Intensive Care*. 4th ed. Cambridge: Cambridge University Press; 2014.
2. UK Royal Colleges Tranexamic Acid in Surgery Implementation Group; Grocott MPW, Murphy M, Roberts I, Sayers R, Toh CH. Tranexamic acid for safer surgery: the time is now. *Br J Anaesth*. 2022 Oct;129(4):459-461.
3. Devereaux PJ, Marcucci M, Painter TW, Conen D, Lomivorotov V, Sessler DI et al; POISE-3 Investigators. Tranexamic Acid in Patients Undergoing Noncardiac Surgery. N Engl J Med. 2022 May 26;386(21):1986-1997.
4. CRASH-3 trial collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. *Lancet*. 2019 Nov 9;394(10210):1712.
5. Murao S, Nakata H, Roberts I, Yamakawa K. Effect of tranexamic acid on thrombotic events and seizures in bleeding patients: a systematic review and meta-analysis. Crit Care 2021;25:380.

6. Tsan SEH, Viknaswaran NL, Cheong CC, Cheah S, Ng KT, Mong SXY et al. Prophylactic intravenous tranexamic acid and thromboembolism in non-cardiac surgery: a systematic review, meta-analysis and trial sequential analysis. Anaesthesia. 2023 Sep;78(9):1153-1161.
7. Hooda B, Muthuchellappan R. Tranexamic acid in neuroanesthesia and neurocritical care: Time for its critical appraisal. *J Neuroanaesth Crit Care.* 2019;6:257–66.
8. Ahmed, A. S., et al. "The Use of Tranexamic Acid in Neurosurgical Procedures: A Review of Safety and Efficacy." *Neurosurgical Review*, vol. 40, 2019, pp. 249-257.
9. Dinh, A., et al. "Tranexamic Acid and Seizure Risk in Neurosurgery: A Systematic Review." *Journal of Clinical Neuroscience*, vol. 71, 2020, pp. 25-31.
10. de Faria JL, da Silva Brito J, Costa E Silva LT, Kilesse CTSM, de Souza NB, Pereira CU et al. Tranexamic acid in Neurosurgery: a controversy indication-review. Neurosurg Rev. 2021 Jun;44(3):1287-1298.
11. Tsuda H, Oka K, Noutsuka Y, Sueishi K. Tissue-type plasminogen activator in patients with intracranial meningiomas. *Thromb Haemost* 1988;60(3):508–513
12. Möller H, Hedlund R. Instrumented and noninstrumented posterolateral fusion in adult spondylolisthesis–a prospective randomized study: part 2. Spine 2000;25(13):1716–1721
13. Takagi H, Ando T, Umemoto T; All-Literature Investigation of Cardiovascular Evidence (ALICE) group. Seizures associated with tranexamic acid for cardiac surgery: a meta-analysis of randomized and non-randomized studies. J Cardiovasc Surg (Torino) 2017;58(4):633–641
14. Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T et al; ATACAS Investigators of the ANZCA Clinical Trials Network. Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery. N Engl J Med. 2017 Jan 12;376(2):136-148.
15. Kietaibl S, Ahmed A, Afshari A et al. Management of severe peri-operative bleeding: guidelines from the European society of Anaesthesiology and intensive care: second update 2022. Eur J Anaesthesiol 2023;40(4):226–304.
16. Zufferey PJ, Lanoiselee J, Graouch B, Vieille B, Delavenne X, Ollier E. Exposure-response relationship of tranexamic acid in cardiac surgery. Anesthesiology 2021;134(2):165–78.