The Effectiveness and Safety of High and Low Dosages of Intraoperative Intravenous Tranexamic Acid During Surgical Treatment of Adult Spinal Deformity: A Network Meta-Analysis

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INTRODUCTION:

Intraoperative intravenous tranexamic acid (TXA) is increasingly used to reduce blood loss during adult spinal deformity (ASD) surgery, where excessive bleeding is linked to higher perioperative complications. TXA, an antifibrinolytic agent, inhibits fibrin degradation by binding plasminogen, thereby reducing surgical bleeding. Its use in ASD surgery rose from 13.3% in 2009 to 48.6% in 2016 and is considered cost-effective. Despite growing interest and multiple studies, optimal TXA dosing remains unclear. A 2019 meta-analysis by Hariharan et al. showed TXA reduces blood loss without increasing venous thromboembolism risk but combined varied dosing regimens and assessed only VTE as a safety outcome. Other complications, like cardiac events and stroke, are also important but understudied. Recent trials have compared high- and low-dose TXA, suggesting high doses may be safe and effective, but consensus is lacking. Given these gaps and new comparative studies, a network meta-analysis (NMA) is needed to evaluate the effectiveness and safety of different TXA dosing strategies in ASD surgery. This study aims to fill that gap to guide optimal TXA use in complex ASD procedures.

METHODS:

A pre-registered network meta-analysis (PROSPERO: CRD420251035431) used PubMed, Embase, and CINAHL with a corresponding full reference search and grey literature search. Inclusion criteria were articles that reported on specific intraoperative IV TXA doses used in surgery for ASD. We compared three different groups based on TXA dosage: the High TXA group (30-50 mg/kg loading dose with 3.0-10.0 mg/kg/hr maintenance dose), the Low TXA group (10-20 mg/kg loading dose with 0.5-2 mg/kg/hr maintenance dose), and the No TXA group (placebo of saline or no TXA given). A Bayesian network meta-analysis was conducted with mean difference (MD) or risk ratio (RR) with 95% confidence intervals (CI). We also assessed the certainty of the data, included article quality, and network model transitivity.

RESULTS:

Eight articles (three randomized studies and five observational studies) were included. Patients (n=1,016; mean age=59 years; mean operated levels =12.2; mean operative time=384 minutes) were divided into the High TXA group (n=223), Low TXA group (n=539), or No TXA group (n=254) based on TXA dosage with sufficient transitivity. For effectiveness, the High TXA group had a high probability of being the best treatment (>90%) and the No TXA group had a high probability of being the worst treatment (>90%) for minimizing total intraoperative EBL and EBL per vertebral level. Compared to the No TXA group, there was a statistically significant decrease in EBL per vertebral level and total EBL for the High TXA group (MD= -60.9 mL and -602.0 mL) with no statistically significant difference for the Low TXA group (MD= -31.3 mL and -387.0 mL). There was no statistically significant difference in EBL per vertebral level or total EBL between the High TXA group and the Low TXA group. For safety, none of the groups had a high probability of the best or worst treatment for minimizing TXA-related complications with no statistically significance difference in risk between groups. The total TXA-related complication rate was 10.8% for the High TXA group, 8.6% for the Low TXA group, and 12.7% for the No TXA group, suggesting similar risk. Rates for venous thromboembolism (2.4%-3.6%), stroke (0.4%-0.5%), and cardiac complications (4.2%-6.7%) were similar between groups. Certainty of evidence was very low.

DISCUSSION AND CONCLUSION:

Intraoperative high dose IV TXA during surgery for ASD may be associated with greater effectiveness in reducing total EBL (MD=-602.0 mL) and EBL per level (MD=-60.9 mL) without a concomitant increase in total TXA-related complications compared to no TXA, but not compared to low dose IV TXA, based on very low certainty of evidence derived from eight comparative studies. Additionally, this study found that specific complication rates for VTE (2.4%-3.6%), stroke (0.4%-0.5%), and cardiac complications (4.2%-6.7%) were similar between groups, potentially indicating similar risk profiles between high-dose TXA, low-dose TXA, and no TXA during surgery for ASD. Surgeons should cautiously incorporate this evidence on a case-by-case basis while considering the unique risk-benefit profile for each patient. These results for ASD appear consistent with the wider literature for all-type spine surgery for high-dose TXA.

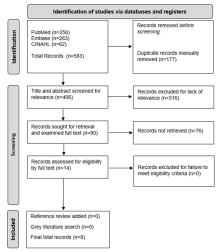

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

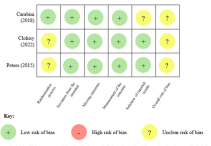

Figure 2: Risk of bias as assessed by the Cochrane Collaboration's Tool for randomized controlled trials.

Figure 3: Measure of between-study transitivity by mean age (upper), mean number of operated levels (middle), and mean operative time (lower). Abbreviations: N (No TXA), L (Low TXA), H (High TXA).

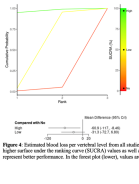

Figure 4: Estimated blood loss per vertebral level from all studies. In the Litmus Rank-O-Gram (upper), higher surface under the ranking curve (SUCRA) values as well as higher cumulative probability curves represent better performance. In the forest plot (lower), values are in milliliters (mL) for each group.

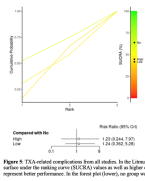

Figure 5: TXA-related complications from all studies. In the Litmus Rank-O-Gram (upper), higher surface under the ranking curve (SUCRA) values as well as higher cumulative probability curves represent better performance. In the forest plot (lower), no group was statistically significantly different.