Comparing the Effectiveness of Oral versus Intravenous Tranexamic Acid in Primary Total Hip and Knee Arthroplasty: A Randomized Trial

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INTRODUCTION:

As combined annual volume for total hip arthroplasty (THA) and total knee arthroplasty (TKA) is projected to reach about 4 million in the United States by 2030, reducing both the risk of complications and costs associated with these procedures should be a public health priority. Blood transfusion for acute blood loss in the setting of THA and TKA increases length-of-stay (LOS), cost of care, and adverse events rates, highlighting the importance of affordable and effective blood management tools and strategies. While the perioperative use of tranexamic acid (TXA) helps to reduce transfusion rates in THA and TKA and thereby reduce costs, it is not clear which formulation of the drug provides the optimal combination of effectiveness, cost, and ease of dosing.

The authors performed a randomized non-inferiority trial, hypothesizing that the use of one preoperative dose of 1,950 mg of oral TXA would be non-inferior to the use of 1,000 mg of IV TXA for patients undergoing primary THA or TKA, leading to similar calculated blood loss (CBL) and transfusion rates.

METHODS:

This was a single center, randomized non-inferiority trial comparing the use of oral TXA and IV TXA in THA and TKA. The study was designed as a non-inferiority trial (non-inferiority margin of 235 mL). Consecutive patients aged 18-80 years undergoing primary THA or TKA under regional anesthesia were enrolled. Those with prior history of venous thromboembolism, recent myocardial infarction or stroke, or prior major surgery on the joint of interest were excluded. Those on antiplatelelet or anticoagulant medications (other than aspirin 81mg daily) were excluded. For THA cases, only patients undergoing surgery with a posterolateral approach were included. All TKA approaches were performed with the use of a tourniquet and a medial parapatellar arthrotomy. Consenting patients were randomized according to a confidential list accessed by a research coordinator. The randomization sequences, which were separate for THA patients and TKA patients, were structured 1:1 with a block size of two. The trial was not blinded.

Preoperative laboratory data (within 1 month of surgery) were reviewed to determine baseline hematocrit for each patient. In the oral arm of the study, patients were to receive 1,950 mg of oral TXA (three 650 mg pills) in the holding area 2 hours prior to surgery. In the IV arm of the study, patients were to receive 1,000 mg of IV TXA in the operating room prior to and within 30 minutes of incision. A postoperative complete blood count (CBC) was sent upon arrival to the post-anesthesia care unit (PACU) and again on the morning of postoperative day (POD) 1 to measure hematocrit.

Calculated blood loss (CBL) was considered the primary outcome variable in this study and was calculated based on POD1 hematocrit using the Gross formula. Other outcomes included blood transfusions and complications such as DVT/PE.

RESULTS:

Four-hundred participants were randomized (200 THA and 200 TKA) between September 17, 2019 and November 10, 2021.

Oral TXA was dosed at a mean of 1.6 hours (+/- 0.6hr) prior to incision among patients undergoing THA and at a median of 2.0 hours (Q1: 1.0hr, Q3: 2.0hr) prior to incision among patients undergoing TKA. IV TXA was dosed at a median of 18 minutes (Q1: 12min, Q3: 27min) prior to incision among patients undergoing THA and at a mean of 19 min (+/- 9min) prior to incision among patients undergoing TKA.

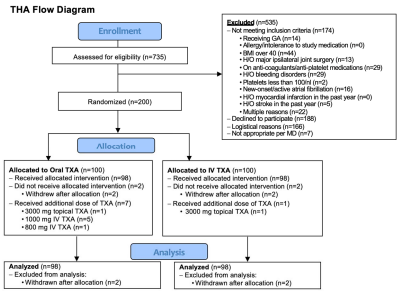
The final analysis included 196 THA patients (98 oral, 98 IV) and 191 TKA patients (93 oral, 98 IV). Oral TXA was non-inferior to IV TXA in terms of CBL for both THA (effect size -18.23 mL [95%CI -112.8-76.3]; $p<0.001$) and TKA (effect size -79.65 mL [95%CI -178.9-19.6]; $p<0.001$). There was one postoperative transfusion, which occurred in the IV TXA arm of the study. There was no difference in length-of-stay or complication rates between groups. No instances of venous thromboembolism were found.

DISCUSSION AND CONCLUSION:

This is the largest randomized trial showing that oral TXA is non-inferior to IV TXA in reducing blood loss and transfusions in the setting of THA and TKA. It also showed that oral TXA can be feasibly administered in the preoperative setting prior to THA or TKA. Switching from IV to oral TXA in this setting has the potential to improve patient safety and save hundreds of millions of dollars annually for national healthcare systems.

The authors believe that routine use of a single preoperative dose of 1,950 mg of oral TXA prior to primary THA or TKA in patients having no contraindications (with no routine repeat dosing) can potentially reduce costs and improve patient safety while maintaining the standard of care. IV and topical dosing should be retained as adjuncts for certain patients,

such as those with poor enteric drug absorption or intolerance of the oral tablets. Future work could determine more definitively the magnitude of cost savings expected with a switch to routine oral TXA dosing.



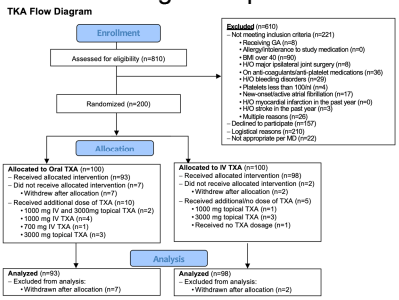


Table. Calculated Blood Loss at Postoperative Day 1

	Calculated Blood Loss (mL)		Effect Size (mL)	P-Value for Non-Inferiority
	Oral TXA	IV TXA		
Total Hip Arthroplasty	842.21 (327.52)	860.45 (313.37)	-18.23 [95%CI -112.8, 76.3]	<0.001*
Total Knee Arthroplasty	798.48 (334.37)	878.13 (347.51)	-79.65 [95%CI -178.9, 19.6]	<0.001*

CBL presented as mean (standard deviation).
Non-inferiority Margin = 235 ml, Alpha = 0.025.
*The null hypothesis was that CBL would be at least 235 mL higher for cases in which oral TXA was used compared to cases were IV TXA was used. These results indicate non-inferiority for oral TXA use.