

A STUDY ON THE USE OF TOPICAL VERSUS INTRAVENOUS TRANEXAMIC ACID IN MINIMIZING BLOOD LOSS IN PRIMARY TOTAL KNEE REPLACEMENT IN A TERTIARY CARE HOSPITAL

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Abstract: Significant blood loss during total knee replacement (TKR) surgery is a major concern, with tranexamic acid (TXA) commonly used to reduce it. This study compares the efficacy of topical versus intravenous TXA in minimizing blood loss in primary TKR. **Objective:** To compare the efficacy of topical versus intravenous tranexamic acid in minimizing blood loss in primary total knee replacement surgery. **Methods:** This prospective randomized controlled trial was conducted at the Department of Orthopedics, CMH Rawalpindi, Pakistan in the duration from December 2023 to May 2024 to compare the efficacy of intravenous and intra-articular Tranexamic Acid (TXA) in primary total knee replacement (TKR) patients. 120 adult patients with primary knee osteoarthritis were randomly assigned to two groups: Group A (IV TXA) received 15 mg/kg TXA intravenously twice, and Group B (IA TXA) received 2 grams of TXA intra-articularly. Exclusion criteria included conditions like hepatitis B or C, TXA allergy, and severe medical histories such as thromboembolic events. Surgeries were performed by a single consultant orthopedic surgeon using a mid-vastus approach and cemented prosthesis, with standardized postoperative care, including drain management and rehabilitation exercises. Data on drain output, hemoglobin levels, and transfusion requirements were collected and analyzed using SPSS version 23, with statistical significance set at $p < 0.05$. Ethical approval and informed consent were obtained before the study. **Results:** In this study involving 120 patients undergoing total knee replacement (TKR), participants were evenly divided into Group A (Intravenous TXA) and Group B (Topical TXA). Both groups were comparable in demographics, procedural characteristics, and co-morbidities, ensuring balanced baseline conditions. Results showed that while Group B exhibited significantly less blood loss on Day 1 post-surgery ($p = 0.15$), there were no significant differences in immediate post-surgery blood loss, hemoglobin levels, or the need for transfusions. Postoperative complications, hospital stay length, and patient satisfaction were similar between the groups. Group B showed a trend towards a shorter hospital stay and better range of motion at six weeks. **Conclusion:** Our research demonstrates that topical and intravenous Tranexamic Acid (TXA) is equally effective in reducing intraoperative and postoperative blood loss in primary total knee replacement (TKR). No significant differences were observed between the two methods regarding hemoglobin level changes, transfusion rates, blood loss, complications, hospital stay duration, patient satisfaction, or functional outcomes. However, topical TXA offers advantages such as local application, enhanced safety, and ease of administration. These findings support the TXA delivery method based on patient preferences and characteristics, providing flexibility in clinical practice for managing blood loss in TKR.

Keywords: Total knee replacement, topical tranexamic acid, intravenous tranexamic acid, blood loss.

Introduction

In recent years, the global rise in life expectancy has resulted in a significant increase in osteoarthritis cases, with the knee joint being the most frequently affected. (1) Patients suffering from osteoarthritis experience severe disruptions in daily life due to joint pain that worsens with activity, stiffness, and reduced functional capacity. (2) For people with severe knee osteoarthritis, total knee replacement (TKR) is generally considered an effective way to improve mobility and relieve pain. (3) Nevertheless, there are significant drawbacks to TKR, most notably the potential for significant perioperative blood loss (up to 1800 ml). This level of blood loss can significantly impact patient morbidity and mortality, especially since most TKR patients are elderly. (4, 5)

Blood transfusions are commonly required to compensate for this blood loss. Still, they carry risks such as allergic reactions, cardiovascular strain, and the potential transmission of infections like HIV. (6) To address these concerns, various strategies have been investigated to minimize intraoperative and postoperative bleeding, with

Tranexamic Acid (TXA) emerging as a promising agent. TXA, a synthetic lysine derivative, works by inhibiting fibrinolysis, which breaks down blood clots, thereby promoting clot stability and reducing blood loss. (7)

Extensive research has evaluated intravenous (IV) and intra-articular (topical) administration of TXA in TKR procedures. (8) IV TXA is often favored due to its proven efficacy in minimizing blood loss and the necessity for transfusions while maintaining a good safety profile without increasing the risk of infections or thromboembolic events. (9)

Intra-articular TXA, administered directly at the surgical site, has proven to be even more effective in lowering postoperative blood loss due to its higher localized concentration and reduced systemic absorption, which decreases the risk of thromboembolic complications. (10)

Despite the demonstrated benefits of TXA, there remains ongoing debate regarding the optimal dosage and administration regimen. The challenge lies in balancing the reduction of transfusion requirements with the risk of thrombotic events, particularly in patients with pre-existing cardiovascular conditions. This study aims to compare the

effectiveness of intravenous and intra-articular TXA in primary TKR patients, evaluating outcomes such as hemoglobin levels, transfusion needs, and drain output to optimize TXA use and improve patient safety and outcomes in TKR procedures.

OBJECTIVE

To compare the efficacy of topical versus intravenous tranexamic acid in minimizing blood loss in primary total knee replacement surgery.

Methodology

Study Design and Setting

This prospective randomized controlled trial was carried out at the Department of Orthopedics, CMH Rawalpindi, Pakistan, from December 2023 to May 2024, after obtaining approval from the hospital's ethical committee.

Participant Selection Criteria

Participants in the trial had to be adults (18 years of age and older) with primary knee osteoarthritis that required complete knee replacement. Conditions including hepatitis B or C, a history of knee replacement surgery, a TXA allergy, a history of antiplatelet consumption, and severe medical histories such as thromboembolic events or cardiovascular diseases were among the exclusion criteria.

Sample Size Calculation and Randomization

One hundred twenty patients made up the sample size with a 95% confidence interval and 80% study power, estimated with Open Epi version 3.04. A software-generated random number list was used to randomly assign participants who met the inclusion criteria into groups A and B, each with 60 participants.

Surgical Procedures

Under spinal anesthesia, a single consultant orthopedic surgeon undertook all procedures utilizing a mid-vastus route and total knee cemented prosthesis substituting the posterior cruciate ligament. Surgical procedures included limb exsanguination with an Esmarch bandage followed by tourniquet application at 350 mmHg pressure.

Intervention Methods

Group A (Intravenous TXA):

TXA was given intravenously to the patients twice at a dose of 15 mg per kg body weight, diluted in 10 ml of normal saline. Two doses were given: one 15 minutes before

tourniquet inflation and the other 15 minutes following deflation.

Group B (Intra-articular TXA):

Patients received 2 grams of TXA diluted in 100ml normal saline via intra-articular injection immediately after wound closure.

Postoperative Management

A 12-gauge drain was placed in each wound postoperatively and removed after 48 hours, with drain output recorded at 12-hour intervals. Blood transfusion was initiated if postoperative hemoglobin levels fell below 8.0g/dl. Standardized rehabilitation included ankle pump exercises starting immediately after surgery and continuous passive motion exercises from the second postoperative day, with discharge planned for the seventh postoperative day.

Data Collection and Statistical Analysis

SPSS version 23 was used to analyze the data gathered using a pre-formed proforma. Descriptive statistics were used to summarize baseline characteristics. Baseline homogeneity was evaluated using chi-square and independent samples t-tests; non-parametric tests, such as the Mann-Whitney U test, were used for variables that were not normally distributed ($p < 0.05$ was deemed statistically significant).

Ethical Considerations

Informed consent was obtained from all participants in compliance with ethical principles, while ethical approval was also obtained for this study beforehand.

Results

An overall 120 participants were included in this study, categorized into Group A (Intravenous TXA) and Group B (Topical TXA), each comprising 60 patients. Table 1 shows the demographic and procedural characteristics of both groups. There were no statistically significant differences observed in mean age (62.1 years in Group A vs. 61.5 years in Group B, $p = 0.68$), mean body mass index (26.1 kg/m² vs. 25.8 kg/m², $p = 0.54$), and mean duration of surgery (82.5 minutes vs. 83.2 minutes, $p = 0.49$) between the two groups. These findings suggest that at baseline, both groups were comparable in age, body mass index, and duration of surgery, minimizing potential confounding factors in the study.

Table 1: Demographic Characteristics at Baseline

Variable	Group A (Intravenous TXA) N=60	Group B (Topical TXA) N=60	p-value
Mean Age ± SD (years)	62.1 ± 6.9	61.5 ± 7.2	0.68
Mean Body Mass Index ± SD (kg/m ²)	26.1 ± 2.7	25.8 ± 2.5	0.54
The mean duration of surgery ± SD (minutes)	82.5 ± 3.8	83.2 ± 4.1	0.49

Furthermore, Table 2 compares the gender distribution and the operated knee side between the groups. There were 52 males and 68 females overall, with 27 males and 33 females in Group A and 25 males and 35 females in Group B. The distribution of operated sides showed 31 cases on the right knee and 29 on the left knee in Group A, whereas 29 cases on the left knee and 31 cases on the right knee in Group B. Statistical analysis indicated no significant differences in gender distribution ($p = 0.92$) or operated knee side ($p = 0.71$) between both the groups. This balance in demographic and surgical characteristics helps ensure that any observed

differences in treatment outcomes can be attributed more reliably to the type of TXA administration rather than demographic or procedural factors. This graphical presentation, depicted in Figure 1, shows the prevalence of diabetes, hypertension, and cardiac disease among patients in both study groups. In Group A, 30% had diabetes, 41% had hypertension, and 6% had cardiac disease. Group B's figures were 32%, 39%, and 9%, respectively. The similarity in co-morbidity percentages between the groups suggests a balanced distribution of underlying health conditions relevant to surgical outcomes.

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Table 2: Distribution of Cases according to Gender and Operated Knee Side

Variable	Subsets	Group A (Intravenous TXA) N=60	Group B (Topical TXA) N=60	Total (N=120)	p-value
Gender	Male	27	25	52	0.92
	Female	33	35	68	
Operated Side	Right Knee	31 (51.7%)	29 (48.3%)	60 (100%)	0.71
	Left Knee	29 (48.3%)	31 (51.7%)	60 (100%)	

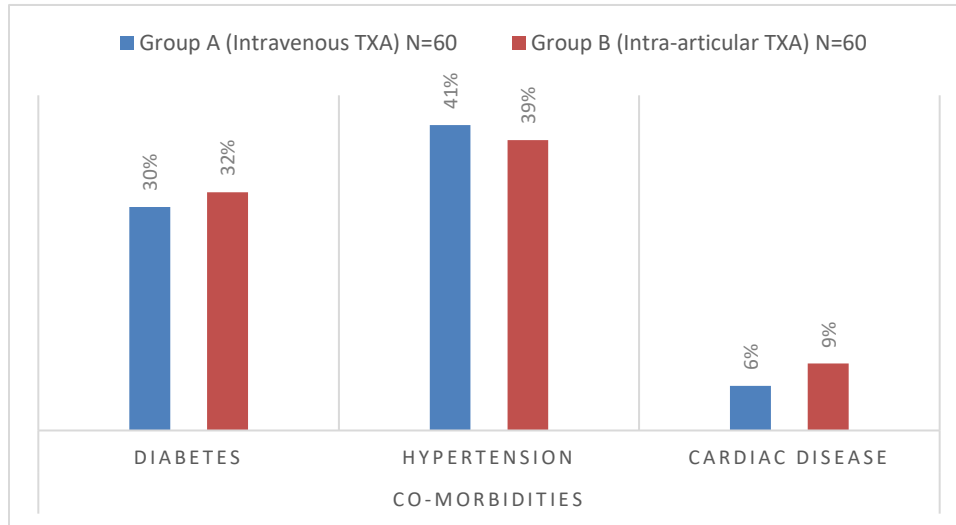


Figure 1: Distribution of Co-morbid conditions within study groups

Table 3 presents the comparison focused on various measures related to surgical recovery and outcomes. In terms of blood loss, Group B showed significantly less blood loss at Day 1 post-surgery compared to Group A (p = 0.15). However, there was no significant difference immediately post-surgery (p = 0.72). Hemoglobin levels preoperatively and at Day 1 postoperatively did not differ significantly between the groups (p = 0.82 and p = 0.49, respectively). The need for blood transfusion also showed no significant difference (p = 0.30), indicating similar management of perioperative blood loss between the groups.

Regarding postoperative complications, rates of thromboembolic events (p = 0.36) and infections (p = 0.63) were comparable between Group A and Group B. Length of hospital stay was slightly shorter in Group B (p = 0.09), suggesting a potential benefit of Topical TXA in reducing hospitalization duration. Functional outcomes at six weeks showed a trend towards better range of motion in Group B (p = 0.08), while pain scores were similar between the groups (p = 0.57). Patient satisfaction did not significantly differ (p = 0.41), indicating comparable overall satisfaction with the surgical outcomes.

Table-3: Postoperative Outcomes

Outcome Measure	Subsets	Group A (Intravenous TXA) N= 60	Group B (Topical TXA) N=60	p-value
Blood Loss (Mean ± SD)	Intraoperative (mL), Immediate	42.55 ± 24.32	44.86 ± 27.65	0.72
	Postoperative (mL), on Day-1	200.94 ± 40.77	180.66 ± 65.25	0.15
Hemoglobin Levels (g/dL)	Preoperative	13.5 ± 1.75	13.4 ± 1.81	0.82
	Postoperative, at Day-1	11.8 ± 0.97	11.6 ± 0.93	0.49
Need for Blood Transfusion		1 (1.66%)	3 (5%)	0.30
Postoperative Complications	Thromboembolic Events	1 (1.66%)	0 (0%)	0.36
	Infections	2 (3.33%)	1 (1.66%)	0.63
Length of Hospital Stay, Mean (Range)		4 (3-6) days	3.5 (3-5) days	0.09
Functional Outcomes	Range of Motion (degrees) at six weeks	110 ± 5.5	115 ± 3.8	0.08
	Pain Scores (VAS*) at six weeks	2.5 ± 0.7	2.3 ± 1.0	0.57
	Patient Satisfaction (%)	85%	90%	0.41

*VAS= visual analog scale (0-10)

Discussion

Our study provides an in-depth analysis of the effectiveness of intravenous and topical Tranexamic Acid (TXA) in minimizing blood loss and improving outcomes in patients undergoing total knee replacement (TKR). The findings from our research align with several established studies while also contributing new insights into the comparative effectiveness of these two TXA administration routes.

One of the primary concerns in TKR is the perioperative and postoperative blood loss, typically ranging from 800 to 1800 ml, as highlighted by Maniar et al., Kim et al. and Park et al. (11-13). In our study, the mean intraoperative blood loss was slightly lower in the topical TXA group compared to the intravenous group (44.86 ± 27.65 ml vs. 42.55 ± 24.32 ml, $p = 0.72$), though not statistically significant. Similarly, postoperative blood loss on Day 1 was less in the topical TXA group (180.66 ± 65.25 ml vs. 200.94 ± 40.77 ml, $p = 0.15$). These results are consistent with findings by Gomez-Barrena et al., where no significant difference was observed between intra-articular and intravenous TXA regarding drain output. (14) Furthermore, the hemoglobin levels preoperatively and postoperatively (Day 1) showed no significant difference between the groups ($p = 0.82$ and $p = 0.49$, respectively), paralleling the findings by Fu et al., who also reported no significant difference in hemoglobin drop between the two TXA administration routes. (15) This consistency across studies reinforces the efficacy of both TXA routes in managing blood loss without a significant difference in hemoglobin reduction.

Our study found that 1.66% of patients in the intravenous TXA group required blood transfusion compared to 5% in the topical TXA group ($p = 0.30$). This result aligns with studies by Chen et al. and Pispati et al., which also reported no significant difference in transfusion rates between the two groups. (16, 17) However, contrasting results were noted in the study by Balasubramanian et al., where the intravenous TXA group required more transfusions than the intra-articular group. (18) This discrepancy may be attributed to differences in study design, patient demographics, and perioperative management protocols.

Our results indicated comparable rates of postoperative complications between the two groups, with thromboembolic events occurring in 1.66% of the intravenous TXA group and none in the topical TXA group ($p = 0.36$). Infections were slightly higher in the intravenous TXA group (3.33% vs. 1.66%, $p = 0.63$). The literature suggests that intra-articular TXA may have a lower risk of systemic complications due to reduced systemic absorption. This aligns with our findings of a slightly lower complication rate in the topical group. (19)

Functional outcomes, including range of motion and pain scores at six weeks, showed a trend towards better results in the topical TXA group, though not statistically significant. The range of motion was slightly higher in the topical group (115 ± 3.8 degrees vs. 110 ± 5.5 degrees, $p = 0.08$), and pain scores were marginally lower (2.3 ± 1.0 vs. 2.5 ± 0.7 , $p = 0.57$). Patient satisfaction was also higher in the topical TXA group (90% vs. 85%, $p = 0.41$), suggesting a preference towards topical administration despite the lack of significant differences. The mean length of hospital stay was shorter for the topical TXA group (3.5 days vs. four days, $p = 0.09$), indicating a potential benefit of topical TXA in reducing hospital stay duration. This result is in line with

other research that found fewer days of stay in the hospital and reduced costs linked to fewer complications and requirements for blood transfusions. (20)

Our research validates the conclusion that topical and intravenous TXA are equally efficient in lowering the loss of blood and rates of blood transfusions among TKR patients without appreciable variations in hemoglobin levels or severe side effects, based on a comparison of our results with previous research. However, the topical TXA group's marginally better results in functional assessments and length of hospital stay indicate that this approach might provide slightly improved patient recovery experiences. This aligns with the findings of the Fu et al. meta-analysis and the Seo et al. study, which emphasized the effectiveness of topical TXA. (15, 21)

Thus, this work contributes to the increasing amount of data that supports TXA utilization in TKR. Both topical and intravenous TXA are helpful in minimizing blood loss and preserving hemoglobin levels; however, topical TXA appears to provide a minor benefit in shortening hospital stays and enhancing functional outcomes. These results emphasize how crucial it is to consider co-morbidities and patient-specific factors when deciding how best to administer TXA to maximize surgical success and patient satisfaction. More research with more significant sample numbers and longer follow-up times is necessary to clarify the relative advantages of different delivery methods.

Conclusion

According to our research, topical and intravenous Tranexamic Acid (TXA) are equivalently useful in minimizing intraoperative and postoperative blood loss in primary total knee replacement (TKR). Between the two ways, there was no discernible difference in hemoglobin level variations, transfusion rates, intraoperative and postoperative blood losses, or complications. There were similarities in the duration of stay in the hospital, satisfaction among patients, and functional outcomes across the two cohorts. Topical (intra-articular) TXA, on the other hand, has the advantages of local application, enhanced safety profile, and easy administration. Based on patient preferences and characteristics, these results suggest that both TXA delivery methods are practical options for controlling blood loss in TKR, allowing clinical practice flexibility.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

It is approved by the department concerned. (IRB-CMH-09374/22)

Consent for publication

Approved

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Conflict of interest

The authors declared an absence of conflict of interest.

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Concept & Design of Study

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