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Efficacy of Tranexamic Acid in Reducing Blood Loss and Transfusion Requirements in Primary Total Knee Arthroplasty: A Prospective Comparative Study

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Learning Point of the Article:

Intravenous tranexamic acid significantly reduces perioperative blood loss and blood transfusion requirements in primary total knee arthroplasty without increasing thromboembolic complications, supporting its routine use in blood conservation protocols

Abstract

Introduction: Total knee arthroplasty (TKA) is associated with significant perioperative blood loss, often necessitating blood transfusion. Tranexamic acid (TXA), an antifibrinolytic agent, has been shown to reduce bleeding effectively. This study evaluated the efficacy and safety of intravenous TXA in reducing perioperative blood loss in patients undergoing primary unilateral TKA.

Materials and Methods: This prospective randomized controlled trial included 60 patients with Kellgren-Lawrence Grade 3 or 4 osteoarthritis undergoing primary unilateral TKA at a tertiary care center. Patients were randomized into two groups: The TXA group (n = 30) received 1g intravenous TXA before tourniquet release, while the control group (n = 30) received normal saline. Outcome measures included intraoperative blood loss, post-operative drain output, hemoglobin changes, and transfusion requirements.

Results: The TXA group demonstrated significantly lower intraoperative blood loss (205.33 vs. 305.67 mL, P < 0.001), total drain output (185.00 vs. 298.33 mL, P < 0.001), and proportional hemoglobin loss (14.19% vs. 19.98%, P < 0.001). Transfusion requirements were significantly reduced in the TXA group (6.67% vs. 26.67%, P = 0.039). No thromboembolic complications were observed in either group.

Conclusion: Intravenous TXA significantly reduces perioperative blood loss and transfusion requirements in TKA without increasing thromboembolic risk, supporting its routine use in blood conservation protocols.

Keywords: Tranexamic acid, total knee arthroplasty, blood loss, blood transfusion, antifibrinolytic.

Introduction

Total knee arthroplasty (TKA) is a well-established surgical procedure for end-stage osteoarthritis that significantly improves pain and functional outcomes. However, TKA is associated with substantial perioperative blood loss, typically ranging from 800 to 1800 mL, which frequently necessitates allogeneic blood transfusion [1,2]. Reported transfusion rates vary widely from 10% to 67% depending on patient factors, surgical technique, and institutional protocols [3,4]. Allogeneic blood transfusion carries inherent risks, including transfusion reactions, transmission of infectious diseases, immunomodulation, and increased post-operative infection rates [5,6]. These concerns have driven the development of various blood conservation strategies, including controlled hypotension, autologous blood donation, cell salvage, and pharmacological interventions [7].

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Table 1: Post-operative drain output			
Time Point	TXA group (mL)	Control group (mL)	*P*-value
24 h	115.00±28.45	178.33±42.67	<0.001
48 h	70.00±18.23	120.00±32.56	<0.001
Total drain output	185.00±38.92	298.33±62.45	<0.001
TXA: Tranexamic acid			

Tranexamic acid (TXA) is a synthetic derivative of lysine that competitively inhibits plasminogen activation, thereby preventing fibrin degradation and maintaining clot stability [8]. Multiple meta-analyses have demonstrated that TXA significantly reduces blood loss and transfusion requirements in TKA without increasing thromboembolic complications [9,10,11]. While TXA has been extensively studied in Western populations, there is relatively limited data from the Indian population, which may have different fibrinolytic profiles [12,13]. To assess the safety and effectiveness of intravenous TXA in reducing perioperative blood loss in patients receiving primary TKA at a tertiary care facility in India, a prospective randomized controlled trial was carried out.

Materials and Methods

This prospective randomized controlled trial was conducted at a tertiary care center from January 2023 to December 2023 after obtaining Institutional Ethics Committee approval. Written informed consent was obtained from all participants. Sixty patients aged 50–75 years with Kellgren-Lawrence Grade 3 or 4 primary osteoarthritis of the knee scheduled for primary unilateral TKA were enrolled. Exclusion criteria included revision surgery, inflammatory arthritis, bleeding disorders or anticoagulant therapy, history of thromboembolic disease, allergy to TXA, severe cardiovascular or renal impairment, and pre-operative hemoglobin <10 g/dL. The ethical clearance from the institution for the study was taken and the number is: VIEC/2023/APP/PG/035.

Patients were selected using randomized computer-generated random numbers into two groups of 30 patients each. The study followed single blinding technique where the patients of either group were not aware of the injection administered. The TXA group received 1 g (10 mL) of intravenous TXA administered 10 min before tourniquet release, while the control group received 10 mL of normal saline at the same time point. All surgeries were performed under spinal anesthesia using a standard medial parapatellar approach with pneumatic tourniquet application due to which the blood loss was minimal. Patients were managed with IV fluids for hypotension, and none of the patients in the study required a blood transfusion intraoperatively. A posterior-stabilized cemented prosthesis was implanted in all cases. A closed suction drain was placed in all patients and removed at 48 h postoperatively. Thromboprophylaxis with low molecular weight heparin was initiated 12 h postoperatively and continued for 2 weeks, as recommended in contemporary guidelines [14].

Outcome measures included intraoperative blood loss (estimated by weighing surgical mops), post-operative drain output at 24 and 48 h, hemoglobin levels (pre-operative, post-operative day 1 and day 3), proportional hemoglobin loss, and transfusion requirements. Blood transfusion was indicated when hemoglobin dropped below 8 g/dL or when symptomatic anemia occurred with hemoglobin between 8 and 10 g/dL. Patients were monitored for thromboembolic complications, including deep vein thrombosis (clinical assessment and Doppler ultrasonography if indicated) and pulmonary embolism. Sample size was calculated based on previous studies [12,15], estimating a mean difference of 200 mL in blood loss with a standard deviation of 250 mL, requiring 26 patients/group at 80% power and 5% significance level; 30 patients/group were enrolled to account for dropouts. Statistical analysis was performed using the Statistical Package for the Social Sciences version 25.0. Continuous variables were compared using independent t-tests and categorical variables using Chi-square or Fisher's exact test. A $P < 0.05$ was considered statistically significant.

Results

All 60 patients completed the study without any dropouts. Baseline demographic characteristics were comparable between the two groups. The mean age was 62.43 years in the TXA group and 63.47 years in the control group ($P = 0.515$). Gender distribution and baseline hemoglobin levels were similar between groups. (Chart 1).

Intraoperative blood loss was significantly lower in the TXA group compared to the control group (205.33 ± 52.41 mL vs. 305.67 ± 68.23 mL, $P < 0.001$). The mean reduction in intraoperative blood loss was 100.34 mL (32.8%) in the TXA

Table 2: Hemoglobin levels			
Parameter	TXA Group	Control group	*P*-value
Pre-operative (g/dL)	12.45±1.23	12.32±1.18	0.678
POD 1 (g/dL)	10.89±1.15	10.12±1.08	0.009
POD 3 (g/dL)	10.68±1.02	9.86±0.98	0.002
Proportional Hb loss (%)	14.19±3.45	19.98±4.12	<0.001
TXA: Tranexamic acid, Hb: Hemoglobin			

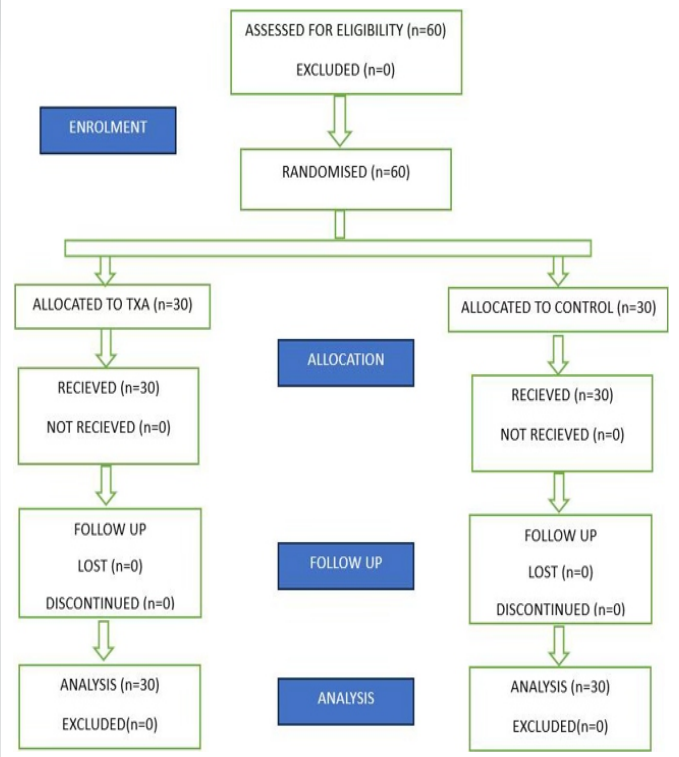

Chart 1: CONSORT flow diagram of patient enrollment, allocation, follow-up, and analysis.

group.

Post-operative drain output was significantly reduced in the TXA group at both 24 h (115.00 ± 28.45 mL vs. 178.33 ± 42.67 mL, P < 0.001) and 48 h (70.00 ± 18.23 mL vs. 120.00 ± 32.56 mL, P < 0.001). Total drain output was 185.00 ± 38.92 mL in the TXA group compared to 298.33 ± 62.45 mL in the control group (P < 0.001), representing a 37.9% reduction (Table 1).

Hemoglobin levels on post-operative day 1 and day 3 were significantly higher in the TXA group (Table 2). The proportional hemoglobin loss was 14.19 ± 3.45% in the TXA group compared to 19.98 ± 4.12% in the control group (P < 0.001). These findings are consistent with the blood-sparing effects reported in previous meta-analyses [9,10,11,16].

Blood transfusion was required in 2 patients (6.67%) in the TXA group compared to 8 patients (26.67%) in the control group (P = 0.039), representing a 75% reduction in transfusion rate. This significant reduction is clinically meaningful as it reduces exposure to transfusion-related risks [5,6]. No thromboembolic complications, including deep vein thrombosis or pulmonary embolism, were observed in either group during the study period, consistent with the safety profile reported in large meta-analyses [9,10,11,17].

Discussion

This study demonstrates that intravenous TXA significantly reduces perioperative blood loss and transfusion requirements in patients undergoing primary TKA. Our findings are consistent with the growing body of evidence supporting the efficacy and safety of TXA in joint arthroplasty surgery [9,10,11,16]. The 32.8% reduction in intraoperative blood loss and 37.9% reduction in post-operative drain output observed in our study are comparable to results reported in previous randomized controlled trials [1,12,13,15].

Gautam et al. [12] reported similar findings in the Indian population, with a mean post-operative blood loss of 272.5 mL in the TXA group compared to 685 mL in the placebo group. Kundu et al. [1] demonstrated a 40% reduction in blood loss with a single dose of TXA. Kumar et al. [15] also reported significant reductions in perioperative blood loss with TXA administration. The timing of TXA administration before tourniquet release is supported by Tanaka et al. [8], who demonstrated that maximum hemostatic effect occurs when TXA is given preoperatively and at tourniquet deflation. Dhillon et al. [13] confirmed the efficacy of TXA in bilateral TKA in the Indian population, reporting significant reductions in hemoglobin drop and transfusion requirements.

The transfusion rate in our control group (26.67%) is consistent with reported rates of 18–67% in TKA without TXA [3,4,7]. The 75% reduction in transfusion rate achieved with TXA has significant clinical and economic implications. Blood transfusion is associated with increased risk of post-operative infection, immunomodulation, and longer hospital stay [5,6]. Yang et al. [9] in their meta-analysis of 15 randomized controlled trials demonstrated that TXA reduces transfusion rates by approximately 50% without increasing thromboembolic complications. Alshryda et al. [10] in their systematic review of 19 trials reported a risk ratio of 2.56 for reduction in transfusion with TXA use. These findings have been incorporated into contemporary clinical practice guidelines recommending routine TXA use in TKA [17,18].

The safety of TXA regarding thromboembolic complications has been a concern given its antifibrinolytic mechanism. However, our study observed no thromboembolic events in either group. This is consistent with multiple large meta-analyses that have demonstrated no increased risk of deep vein thrombosis or pulmonary embolism with TXA use in TKA [9,10,11,16,17]. Poeran et al. [11] in a large retrospective analysis of over 872,000 patients undergoing joint arthroplasty found that TXA was associated with decreased odds of blood transfusion and complications without increased thromboembolic risk. The mechanism by which TXA reduces bleeding without increasing thrombosis may be related to its localized action on the fibrinolytic system activated during surgery rather than a systemic prothrombotic effect [8,18].

This study has several limitations, including its single-center design, relatively small sample size, and lack of long-term follow-up. The study did not compare different doses or routes of TXA administration, which have been evaluated in other studies [16,18]. Hidden blood loss was not calculated, which may underestimate total blood loss. Future studies with larger sample sizes and longer follow-up periods are warranted to further evaluate the safety profile of TXA in the Indian population.

Conclusion

Intravenous TXA administered before tourniquet release significantly reduces perioperative blood loss and transfusion requirements in patients undergoing primary TKA without increasing the risk of thromboembolic complications. These findings support the routine incorporation of TXA into blood conservation protocols for TKA.

Clinical Message

Intravenous tranexamic acid administered before tourniquet release is a safe and effective strategy to reduce perioperative blood loss and blood transfusion requirements in primary total knee arthroplasty without increasing thromboembolic complications.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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