E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.48047/ijprt/16.01.56

Research Article

Comparative Evaluation of Single-Dose Intravenous vs. Dual-Route (Intravenous and Peri-articular) Tranexamic Acid in Total Knee Arthroplasty: A Randomized controlled trial study in a Tertiary Orthopaedic Centre

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Received Date: 20/01/2026 Accepted Date: 22/01/2026 Published Date: 16/02/2026

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ABSTRACT

Background: Minimizing perioperative haemorrhage is critical for enhancing recovery after total knee arthroplasty (TKA). While the efficacy of Tranexamic Acid (TXA) is well-documented, the clinical advantage of augmenting systemic administration with local joint infiltration remains a point of investigation. This study evaluates the haemostatic impact of supplementing a 500mg intravenous (IV) dose with a 750mg Peri-articular (PaI) dose. **Methods**: 60 patients (aged 50–70) undergoing primary Total Knee Arthroplasty will be randomized into Group A (IV only) and Group B (IV + PaI). Primary endpoints include 48-hour haemoglobin drop and total drain volume. **Results**: Preliminary data suggest that the dual-route strategy (Group B) yields a significantly more stable postoperative haemoglobin profile and a marked reduction in total measurable blood loss compared to the IV-only group (Group A). Clinical observations from this cohort indicate that the local application of 750mg TXA provides a synergistic effect without elevating the risk of thromboembolic complications. No instances of deep vein thrombosis were recorded during the study period at Sanjay Gandhi Institute of Trauma and Orthopaedics (SGITO). **Conclusion:** Utilizing a combination of 500mg IV and 750mg PaI TXA offers a superior blood-sparing effect compared to a standard 500mg IV dose alone. This protocol is recommended for optimization of patient outcomes and reduction of transfusion-related risks in institutional TKA procedures.
Total Knee Arthroplasty, Tranexamic Acid, Dual-route administration, Blood preservation, Peri-articular.

INTRODUCTION

Knee osteoarthritis (OA) is the most common type of arthritis and the major cause of chronic pain and disability worldwide. In 2021, there was 374 million prevalent instances of knee OA worldwide, a 132% rise from 1990. This escalation is being driven mostly by population aging and rising obesity rates, with both incidence and prevalence expected to rise further. [1]

The rise in knee OA has resulted in an increase in total knee arthroplasty (TKA) volumes. Between 2010 and 2023, TKA incidence rates increased by 150% to over 600% across national registries, with forecasts of another 130% increase by 2050.[2]
Although TKA efficiently recovers function and decreases discomfort, treatment is accompanied with significant perioperative blood loss (800-1500 mL). Tourniquets and post-deflation fibrinolysis enhance blood loss, resulting in both obvious and hidden components. Allogeneic transfusion is frequently required as a result of postoperative anaemia, which has been recorded in 10-40% of cases depending on institutional standards. [3]
Allogeneic transfusion involves major hazards, such as surgical infection, fluid overload, longer recovery, and increased mortality. Effective blood-conservation methods are thus required to improve outcomes following TKA. Blood-conservation techniques, including pharmaceutical assistance, are critical to improving TKA results and lowering morbidity.[4]
Tranexamic acid (TXA) is a synthetic lysine analogue that competes for lysine sites on plasminogen, limiting its activation to plasmin and therefore stabilizing fibrin clots. This antifibrinolytic activity targets surgery-induced hyperfibrinolysis while preserving normal coagulation.[5]
Intravenous (IV) TXA, at 10-20 mg/kg, has been widely verified in TKA. Meta-analyses consistently show a 30-50% reduction in total blood loss and transfusion rates with haemoglobin stability.[6]
Large observational cohorts demonstrate that these advantages are realized without increasing venous thromboembolism or other side effects. Some trials found no additional benefit over single IV TXA due to dosage thresholds, creating inconsistencies. [7]
Peri-articular injection has emerged as an alternate or supplementary treatment. Direct administration into peri-articular tissues results in high local concentrations at bleeding sites while minimizing systemic exposure. Randomized experiments have demonstrated that peri-articular TXA lowers postoperative drainage and concealed blood loss.[8]
Combining intravenous and peri-articular injection can enhance both systemic and local haemostasis. Prospective studies suggest that the dual-route regimen reduces haemoglobin decline and transfusion requirements compared to intravenous TXA alone. [9]
However, outcomes are variable. Some trials revealed that the combined strategy provided no additional benefit over single-dose intravenous TXA. These disparities are most likely due to variations in dose, timing, surgical technique, and patient groups. [10]
The majority of comparison evidence comes from high-volume locations in industrialized countries. There is still a scarcity of data from tertiary orthopaedic centres in high-OA locations.[11]
The current prospective study investigated the efficacy and safety of single-dose intravenous tranexamic acid against dual-route (intravenous plus peri-articular) administration in lowering perioperative blood loss in patients receiving primary TKA at a tertiary orthopaedic centre. This study aims to clarify existing disagreements and inform uniform perioperative blood-management methods in TKA.

OBJECTIVES

1. To compare the efficacy of combined intravenous (500mg) and peri-articular (750mg) Tranexamic Acid versus stand-alone intravenous (500mg) Tranexamic Acid in reducing total postoperative blood loss in patients aged 50–70 years undergoing primary Total Knee Arthroplasty

2. To measure and compare the total volume of wound drain output between the IV-only group and the combined IV+Pal group.

METHODOLGY

A prospective study was undertaken at the Sanjay Gandhi Institute of Trauma and Orthopaedics (SGITO), Bengaluru Tertiary Orthopaedic Center, from October 2025 to January 2026 on 60 patients undergoing total knee arthroplasty, with 30 patients in each group.

Pre-operative Preparation: All patients will undergo a standardized pre-anesthetic check-up. Baseline Hb, PT/INR, and Creatinine levels will be recorded.

Group A (Control - IV Only):

Administration: 500mg IV TXA diluted in 100ml Normal Saline.

Timing: Administered 15–20 minutes prior to tourniquet inflation.

Group B (Study - Combined IV + PaI):

Systemic Dose: 500mg IV TXA administered 15–20 minutes prior to inflation.

Local Dose: 750mg TXA (diluted in 15ml of Normal Saline) injected into the rectus femoris,

vastus medialis, patellar tendon, pes anserinus, and posterior capsule.

Timing: Injected after component implantation and thorough lavage, just prior to arthrotomy closure. The drain will be clamped for 2 hours post-injection.

Surgical technique and tranexamic injection protocol:

A single senior orthopaedic surgeon (CFC) performed all unilateral TKA procedures using a medial parapatellar approach under spinal anesthesia. The TKA prosthesis used were the Destiknee™ knee system & Freedom Total Knee® System (Meril, India) posterior-stabilized knee system with all components fixed using cement. A tourniquet (Pressure 350mmhg, site - Upper thigh) and a closed-suction drain (no 14) were used for every procedure.The PaI sites included the rectus femoris, vastus medialis, patellar tendon, pes anserinus, and posterior capsule. Surgical drains were inserted into the joints, clamped, and opened 1 h after the surgery. They were suctioned using full negative pressure and removed 48 h after surgery. The tourniquet was deflated after TXA administration via PaI. Standard wound closure was performed, and a sterile dressing was applied.

Postoperative care and blood transfusion criteria.

All patients received 1 gm of low-molecular-weight heparin 0.4 mg for postoperative days 0 and 1, Postoperative day 1 was overlapped with oral aspirin 75 mg OD, followed by oral aspirin 75 mg for 3 weeks postoperatively. Intravenous prophylactic antibiotics with cefaperazone salbactum 1.5gm was administered for 24 h after TKA unless there was evidence of infection. The Hb levels were measured on the same day. The criteria for blood transfusion were an Hb level < 9.0 mg/dL or a decrease in Hb level > 2.0 mg/dL if the patient exhibited intolerable symptoms or organ dysfunction due to anemia. These symptoms included, but were not limited to, malaise, dizziness, hypotension, or tachycardia. All patients began ambulation and rehabilitation protocols on postoperative day one and were discharged within five days after surgery.

Data collection & statistical analysis :

Primary Variables: Hemoglobin (Hb) Drop: Difference between pre-operative Hb and Hb at 24/48 hours post-op.

Drain Output: Total volume recorded in the suction drain over 48 hours.

Inclusion criteria: Age range: 50–70 years. The diagnosis is primary degenerative osteoarthritis of the knee. Procedure: Elective primary unilateral TKA; ASA grade: I–III.

Exclusion Criteria: Secondary OA refers to post-traumatic osteoarthritis or rheumatoid

arthritis. Hematological conditions include pre-operative anaemia (Hb < 11 g/dL), a history of DVT/PE, or coagulopathies. Pharmacological: An allergy to TXA or an inability to discontinue anticoagulants. Physiological: Severe kidney dysfunction.

Figure 1: Peri articular injection of TXA into quadriceps tendon

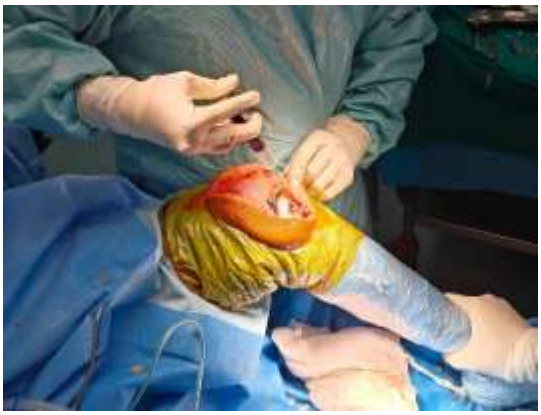


Figure 2: Peri articular injection of TXA into patellar tendon

Statistical Analysis

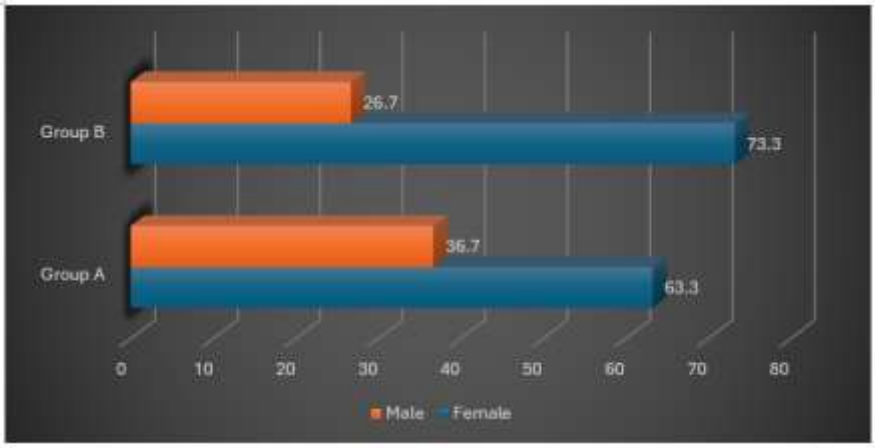
Continuous Data like Hb drop, Drain volume was analysed using the Independent Student's t-test. Categorical Data like Transfusion rates, DVT incidence was analysed using the Chi-Square test. A p-value < 0.05 will be considered statistically significant.

Ethical consideration: The study was conducted in accordance with the ICMR Ethical Guidelines. Informed written consent was obtained from all participants at SGITO.

RESULTS

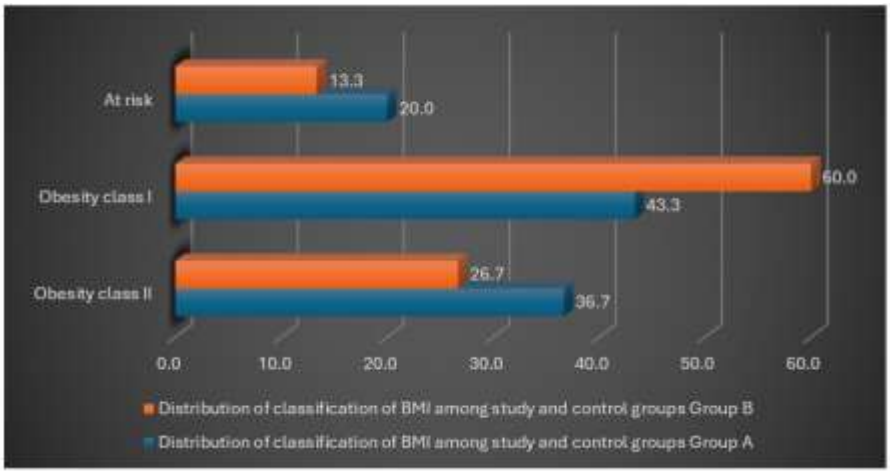
Group A- Control Group

Group B- Study Group



Graph No.1 Distribution of gender among study and control groups

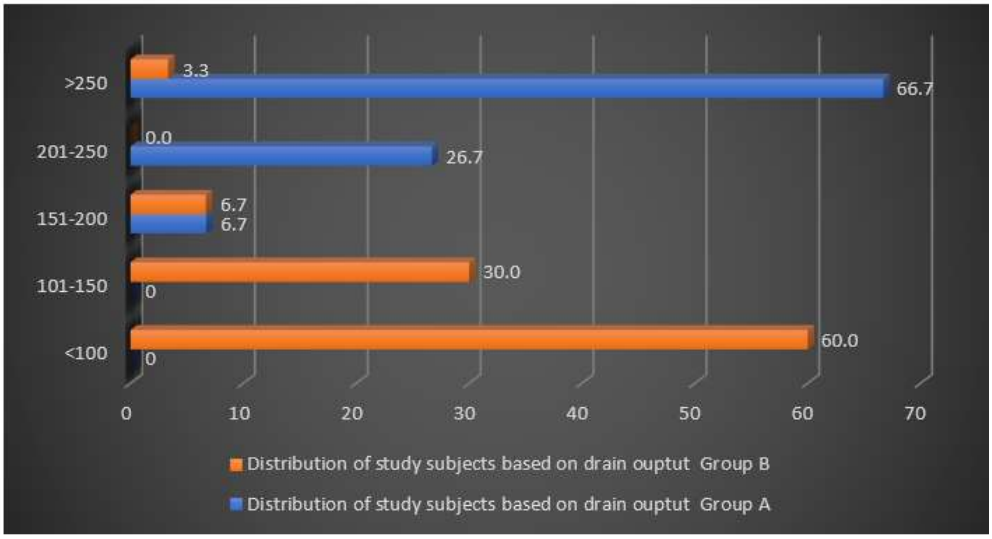
In the present study, majority of them were females in both group A 63.3% and in group B 73.3% shown in Graph no.1 based on Asian classification of BMI , in Group A 36.7% of them were classified under obesity class II followed by 43.3% under obesity class I and 20% of them were at risk. Among Group B majority of them were in obesity class I around 60% followed by 26.7% were obesity class I and only 13.3% were at risk.



Graph No.2 Distribution of classification of BMI among study and control groups

Table No.1 Distribution of study subjects based on drain ouptut

Volume (ml)	Group A(%)	Group B(%)
<100	00(0.0)	18(60.0)
101-150	00(0.0)	09(30.0)
151-200	02(6.7)	02(6.7)
201-250	08(26.7)	00(0.0)
>250	20(66.7)	01(3.3)
Total	30(100.0)	30(100.0)



Graph No.3 Distribution of study subjects based on drain ouptut

Based on the drain output over 24 hours, 66.7% of the patients under Group A had >250 ml followed by 26.7% who had 201-250 ml of drain output. Under Group B 30% of them had 101-150 ml drain output.

Table 1: The demographic data of the control and study groups

Variable	Group A(30)	Group B(30)	Mean difference	p Value
Age (yr) mean±SD	64±6.833	66.93±7.046	-2.93	0.107**
Comorbid conditions				
HTN	14(46.7)	18(60.0)		0.438
DM	15(50.0)	15(50.0)		1.000*
Hypothyroid	01(3.3)	03(10.0)		0.612*
Asthma	04(13.3)	01(3.3)		0.353*
NIL	10(33.3)	10(33.3)		1.000*
Deformity				
Varus knees	24(80.0)	22(73.3)		0.819*
Valgus	02(6.7)	03(10.0)		
Fixed flexion	04(13.3)	05(16.7)		
BMI(mean±SD)	28.13±3.256	27.47±2.700	0.667	0.392**
Drain Output (ml) (last 24 hrs)				
<100	00(0.0)	18(60.0)		0.000**
101-150	00(0.0)	09(30.0)		
151-200	02(6.7)	02(6.7)		
201-250	08(26.7)	00(0.0)		
>250	20(66.7)	01(3.3)		

Drain (last 24 hrs)	271.43±44.562	130.87±147.728	140.567	0.000**
Pre-operative Hb (g/Dl)	9.93±0.708	12.006±0.636	-2.073	0.000**
Post-operative Hb (g/Dl)	9.196±0.392	11.13±0.592	-1.940	0.000**

** - Independent t test was used.
* - chi Square test was used

The mean age was 64±6.833 in Group A and 66.93±7.046 in Group B.

Comorbidities like hypertension, diabetes, hypothyroid and asthma were present in both the groups. Diabetes was seen in 50% of the study group followed by hypertension whereas in control group hypertension was seen in 60% of them followed by diabetes.

An independent t test was performed to compare the baseline characteristics and outcome variables between the study and control group.

Variables like Age, BMI, comorbid conditions and deformity were found to have no significant association. However pre-operative hemoglobin (mean diff- -2.073, p <0.001) and post-operative hemoglobin (mean diff- -1.940, p <0.001) showed a statistically significant difference between the groups.

Regarding outcome measures, there was a highly significant difference in drain output at 24 hours between two groups (mean diff- 140.567. p>0.001).

DISCUSSION

The present study evaluated the hemostatic efficacy of a dual-route Tranexamic Acid (TXA) regimen, combining 500 mg intravenous (IV) and 750 mg peri-articular (PaI) administration, compared to a single 500 mg IV dose in patients undergoing primary Total Knee Arthroplasty (TKA). The most significant finding was a marked reduction in drain output in the combined group (Group B) compared to the IV-only group (Group A) (130.87 ± 147.72 ml vs. 271.43 ± 44.56 ml, $p < 0.001$). This suggests that supplementing systemic TXA with localized peri-articular infiltration provides a synergistic effect, effectively suppressing local fibrinolysis at the surgical site that systemic levels alone may not fully address. The statistical significance of these results reinforces the clinical utility of this multimodal protocol in minimizing observable blood loss in the immediate postoperative period.

A study done by Bi *et al.*, conducted a retrospective propensity-score matched study comparing intravenous, topical, and combined routes of TXA in primary TKA. Their results corroborated our findings, demonstrating that the combined group had significantly lower total blood loss (687.3 ± 160.8 ml) compared to the IV-only group (873.0 ± 241.1 ml) and the topical-only group. They concluded that the combined administration of IV and topical TXA is the most effective approach to decrease blood loss compared to single-route regimens, aligning with our observation that targeting both systemic and local pathways yields superior hemostasis.[12]

A study done by Jain *et al.*, performed a randomized controlled trial comparing combined IV and topical TXA against IV use alone in 119 patients. Their findings were consistent with ours, reporting that the combined group experienced significantly lower calculated total blood loss (385.68 ± 182.5 ml vs 590.69 ± 191.1 ml, $p < 0.001$). This study supports the premise that additional local administration acts synergistically with systemic prophylaxis to reduce postoperative bleeding more effectively than systemic administration alone.[13]

A study done by Paradeevisut, evaluated the effectiveness of combined IV and peri-articular TXA compared to IV TXA alone in simultaneous bilateral TKA. Although their study found a reduction in total blood loss and 24-hour drain output in the combined group, the difference did not reach statistical significance ($p = 0.773$) in their specific cohort. This contrast with our significant findings might be attributed to differences in surgical volume (bilateral vs. unilateral) or dosage protocols, but it highlights the ongoing need to optimize dosage to achieve statistical benefits.[14]

The present study observed that the dual-route strategy resulted in significantly better preservation of postoperative hemoglobin levels. Specifically, the decline in hemoglobin was significantly less pronounced in the combined group (Group B) compared to the IV-only group (mean difference -1.940 g/dL vs. postoperative drop in Group A, $p < 0.001$). This preservation of hemoglobin is clinically critical as it directly correlates with reduced postoperative anemia and faster functional recovery. The data indicates that the addition of 750 mg peri-articular TXA effectively mitigates the "hidden" blood loss that often persists despite systemic TXA administration.

A study done by Adravanti *et al.*, presented a prospective, randomized comparative study of intravenous alone versus combined intravenous and intra-articular administration. Their results mirrored our hemoglobin findings, showing significantly higher hemoglobin levels at postoperative day 4 in the combined group (11.1 ± 1.2 g/dL) compared to the IV-only group (10.4 ± 1.3 g/dL, $p = 0.0075$). They suggested that the combined regimen leads to higher postoperative hemoglobin levels without influencing drug safety, reinforcing the value of dual-route protocols in blood management.[9]

A study done by Wang *et al.*, performed a meta-analysis of seven clinical studies to illustrate the efficacy of combined topical and IV TXA. Their pooled analysis confirmed that, compared with IV TXA alone or control groups, combined TXA was associated with significantly less hemoglobin drop and a reduced need for transfusion ($p < 0.05$). This broad evidence base supports our single-center findings that combined regimens offer superior protection against postoperative anemia.[15]

The present study recorded no instances of deep vein thrombosis (DVT) or other thromboembolic events in either the combined Group B or the IV-only Group A. This safety profile was maintained despite the use of a combined dosing regimen, suggesting that the local application of 750 mg TXA does not elevate systemic thrombotic risk. These findings support the safety of using peri-articular TXA as an adjunct to systemic TXA in patients aged 50–70 years with standard comorbidities.

A study done by Pinsornsak *et al.*, conducted a randomized pilot study comparing peri-articular TXA injection versus IV TXA. Their investigation into local administration found no clinically detected venous thromboembolic events in patients receiving peri-articular injections. This aligns with our findings that depositing TXA directly into the soft tissues (medial/lateral capsules and quadriceps tendon) remains a safe intervention with no observable increase in systemic toxicity.[16]

A study done by Abdulwahab *et al.*, compared intra-articular alone versus combined IV and intra-articular TXA in a Middle Eastern population. They also reported no patients with postoperative complications such as symptomatic deep vein thrombosis or pulmonary embolism in either group. This reinforces the consensus across multiple studies that combined and local

TXA regimens possess a favorable safety profile comparable to single-route administration.[17]

The present study utilized a peri-articular injection technique, infiltrating the rectus femoris, vastus medialis, patellar tendon, pes anserinus, and posterior capsule. This method was chosen to maximize tissue concentration at the source of bleeding while minimizing rapid clearance. The superior results in Group B suggest that this specific infiltration technique is highly effective in sealing the surgical envelope and reducing drain output.

A study done by Pinsornsak *et al.*, conducted a randomized controlled trial comparing combined peri-articular and intra-articular injection versus combined intravenous and intra-articular injection. Their results indicated that the peri-articular combination group displayed significantly less soft tissue swelling (thigh swelling 2.15 cm vs 2.79 cm, $p = 0.04$) compared to the IV combination group, while maintaining similar efficacy in blood loss reduction. This supports the rationale of our study that peri-articular administration is not only effective for hemostasis but may also offer advantages in localized tissue recovery compared to systemic routes.[18]

The combined route of IV and IA-TXA, compared with only IA or IV TXAalone, offered lower total blood loss ($p<0.001$), lower postoperative blood draining ($p=0.009$), and lower hemoglobin drop ($p<0.001$) than IV alone, according to the updated meta-analysis by Ling *et al.*[19]., which examined the safety and efficacy of combined IV and IA-TXA in TKA in 2022 with 1,306 patients in ten RCTs. The results were found to be similar in the present study.

CONCLUSION

This study supports data that administering IV and IA TXA together has a synergistic impact that reduces blood loss in TKA patients without compromising drug safety when compared to IV TXA alone. This impact was observed at POD 4, with the group that received combined IV and IA administration of TXA showing a positive tendency for less blood being drained in the first 24 hours and less blood loss overall.

Declaration of conflict of interest: The authors do NOT have any potential conflicts of interest for this manuscript.

Declaration of funding: The authors received NO financial support for the preparation, research, authorship, and publication of this manuscript.

Declaration of informed consent: There is no information (names, initials, hospital identification numbers, or photographs) in the submitted manuscript that can be used to identify patients.

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