

Original Article

# Comparison of Intra-Articular and Intravenous Tranexamic Acid for Loss of Blood in Patients Undergoing Total Hip Replacement

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## ABSTRACT

**Background:** Tranexamic acid (TXA) is widely used in orthopedic surgeries to minimize blood loss, traditionally administered intravenously. Recent studies have explored intra-articular (IA) administration as a potentially more effective method due to its localized application and reduced systemic absorption.

**Objective:** To compare the effectiveness of IA and IV TXA in reducing blood loss in patients undergoing total hip replacement (THR).

**Methods:** This randomized controlled trial was conducted at Jinnah Hospital, Lahore, from August 30, 2019, to February 29, 2020, with approval from the Ethical Review Board. Seventy patients undergoing THR were enrolled and divided into two groups using a lottery system. Group A (n=35) received 1500 mg of IA TXA diluted in 100 ml of saline after implantation of THR components, while Group B (n=35) received 15 mg/kg of IV TXA five minutes before incision. Both groups were operated on using a lateral approach by the same surgeon. Postoperative blood loss was measured, and data were analyzed using SPSS version 20, with a p-value of <0.05 considered significant.

**Results:** The mean total blood loss in Group A was significantly lower at  $446.23 \pm 33.81$  ml compared to Group B, which had a mean of  $928.23 \pm 43.93$  ml (p-value = 0.0001). The results highlighted a marked reduction in blood loss with IA administration compared to IV.

**Conclusion:** IA administration of TXA during THR is more effective than IV administration in reducing total blood loss. This study supports the use of IA TXA as a safer, more efficient method for managing blood loss during hip replacement surgeries.

**Keywords:** Tranexamic acid, total hip replacement, intra-articular TXA, intravenous TXA, blood loss, orthopedic surgery, randomized controlled trial.

## INTRODUCTION

Arthritis, characterized by joint inflammation, commonly causes discomfort and swelling, particularly affecting the hips and knees. Among the various types of arthritis, osteoarthritis stands out as the most prevalent, often described as chronic joint degeneration or age-related arthritis, which tends to occur as individuals age. This condition arises when joint inflammation and damage lead to the deterioration of cartilage tissue, resulting in pain, swelling, and deformity. In healthy joints, cartilage—a hard, rubbery substance—serves as a cushion for the ends of bones and is composed primarily of fluids and proteins. Its main function is to reduce friction in the joints and act as a shock absorber, properties attributed to its high water content and ability to change shape under pressure. However, once damaged, the body's capacity to regenerate new cartilage is limited, typically leading to a gradual progression of osteoarthritis over many years, though there are exceptions (1,2).

Arthroplasty, or the surgical reshaping of a joint, aims to alleviate pain and preserve or restore mobility. Total hip arthroplasty, which involves replacing the acetabulum as well as the head and neck of the femur, is a particularly effective procedure for patients with severe degenerative hip conditions. The primary indication for this surgery in individuals with osteoarthritis is severe pain unresponsive to conservative treatments, followed by the goal of improving hip function. A successful joint replacement can transform a patient from a state of high dependency and poor function to one of near pain-free independence and enhanced locomotor function (3,4).

Tranexamic acid (TXA), a medication with anti-fibrinolytic effects that inhibits the conversion of plasminogen to plasmin, has been shown to reduce blood loss in various surgical scenarios, including total hip replacement (THR). Historically, the administration of TXA has primarily been through single or repeated intravenous (IV) injections, which have been demonstrated to reduce postoperative blood loss and the need for transfusions (5,6). However, the optimal method of TXA delivery remains a topic of debate (7,8). While IV administration ensures that a portion of TXA reaches the target area to prevent tissue fibrinolysis and stabilize the clot, it has been noted that this method reduces apparent hemorrhage but not covert bleeding. Consequently, alternative methods such as intra-articular (I/A) administration during surgery have been proposed as potentially safer and more straightforward, with comparable outcomes to IV treatment. Recent research suggests that I/A TXA could be superior due to the possible reduction of systemic side effects like deep vein thrombosis and pulmonary embolism. Additionally, I/A administration might decrease joint edema, enhance wound healing, and facilitate quicker recovery (9-11).

In clinical studies, the mean total blood loss was significantly lower in patients receiving intra-articular TXA ( $426 \pm 197$  ml) compared to those administered TXA intravenously ( $958.5 \pm 422.1$  ml) during THR (12,13). This underscores the importance of addressing hemorrhage in such extensive surgical procedures, as it is a major concern for both surgeons and anesthesiologists. Given the scarcity of data from our country and the mixed and controversial findings from international studies, it is imperative to determine the most effective route for TXA administration in these patients to minimize blood loss. Establishing a superior method could standardize the approach to hemorrhage control in patients undergoing THR, potentially leading to broader implementation in clinical practice.

## MATERIAL AND METHODS

This randomized controlled trial was conducted at the Orthopedics Department of Jinnah Hospital, Lahore, from August 30, 2019, to February 29, 2020. The study was approved by the Ethical Review Board, under approval reference CPSP/REU/OSG-2017-055-1787, dated August 5, 2020, and assigned REU No. 36891 by the Research Evaluation Unit of CPSP. The trial included 70 patients of both genders undergoing total hip replacement (THR), adhering to a non-probability, consecutive sampling method.

Exclusion criteria were set for patients with a history of previous surgery at the hip joint, a deranged coagulation profile (INR > 1.5), or known hypersensitivity to tranexamic acid (TXA) or its ingredients. Participants were randomly allocated into two groups using a lottery system. Group A received intra-articular TXA, while Group B was administered TXA intravenously (IV). Each participant underwent a comprehensive pre-operative evaluation where their name, age, gender, body mass index (BMI), and laterality were documented, and pre-operative hematocrit (HCT) levels were measured.

All surgical procedures were performed by a senior orthopedic surgeon with over five years of experience, using a lateral approach. In Group A, after making the incision, large bleeders were cauterized in the conventional manner. Subsequently, 1500 mg of TXA diluted in 100 milliliters of normal saline was irrigated into the operative area following the implantation of both components of the THR. The TXA solution was allowed to interact with the site for at least five minutes before being effectively suctioned out to facilitate the reconstruction of external rotators and the capsule. No drains were used in these procedures. Conversely, participants in Group B received 15 mg/kg of IV TXA five minutes prior to the incision. The remainder of the surgical procedure was identical across both groups. Post-operative care followed departmental protocols uniformly for all patients, and a second HCT blood sample was collected 24 hours post-operatively.

Data collection was standardized using a pre-designed proforma, capturing details pertinent to the study's outcome measures. The primary outcome measured was total blood loss, calculated and documented for each participant. Data analysis was conducted using SPSS version 20. Quantitative data such as age, BMI, and total blood loss were summarized using means and standard deviations, while qualitative characteristics like gender and side were analyzed using frequencies and percentages. The comparison of total blood loss between the two groups was made using a paired sample student's t-test, and further stratified by potential effect modifiers such as age, gender, BMI, and side. A p-value of less than 0.05 was considered statistically significant.

The study was conducted in compliance with the ethical principles of the Declaration of Helsinki, ensuring all participants' rights, safety, and well-being were safeguarded throughout the research process. This robust methodological framework aimed to provide reliable and valid results concerning the efficacy of intra-articular versus intravenous TXA in reducing blood loss during THR.

## RESULTS

In this study, a thorough examination of age distributions within the cohorts revealed significant insights. The overall sample consisted of 70 patients, split evenly between two groups, with each group comprising 35 participants. The age ranges were divided into two categories: 40-55 years and 56-70 years. In Group A, 15 participants (42.85%) were between the ages of 40 and 55, whereas Group B contained 12 individuals (34.28%) within the same age range. The older age category, 56-70 years, included 20 participants

(57.15%) in Group A and 23 participants (65.72%) in Group B. Collectively, the younger age group constituted 38.57% of the total sample, while the older group accounted for 61.43% (Table 1).

The mean age in Group A was 49.48 years with a standard deviation of 2.5, slightly higher than Group B, which had a mean age of 47.46 years with a standard deviation of 5.5. The total sample had a combined mean age of 48.67 years, with a variability of 7.41 years, reflecting a diverse age range among the participants (Table 1).

Table 1: Comparison of Age Distributions Between the Two Groups

Age Range (years)	Group A (n=35)		Group B (n=35)		Total (n=70)	
	No. of Patients	% Age	No. of Patients	% Age	No. of Patients	% Age
40-55	15	42.85	12	34.28	27	38.57
56-70	20	57.15	23	65.72	43	61.43
Mean $\pm$ SD	49.48 $\pm$ 2.5		47.46 $\pm$ 5.5		48.67 $\pm$ 7.41	

Table 2: Comparison of the Mean Total Loss of Blood Among Patients Undergoing THR

	Group A (n=35)		Group B (n=35)		P-value
Total Loss of Blood (ml)	Mean	SD	Mean	SD	
	446.23	33.81	928.23	43.93	0.0001

Table 3: Stratification of Total Loss of Blood (ml) With Respect to Age Groups, Gender, BMI, and Side of Patient

Characteristic	Age of Patients (years)	Group A (n=35)		Group B (n=35)		P-value
		Mean	SD	Mean	SD	
40-55	Total Loss of Blood (ml)	Mean	SD	Mean	SD	0.0001
		434.30	39.67	922.56	48.50	
56-70	Total Loss of Blood (ml)	452.20	29.79	930.67	42.86	0.0001
Gender	Male	436.85	34.94	944.50	34.70	0.0001
	Female	453.43	32.10	917.39	46.92	
BMI	$\leq$ 27	445.75	30.65	948.44	34.57	0.0001
	$>$ 27	446.56	36.64	919.57	45.36	
Sides	Right	463.64	14.84	922.15	47.57	0.0001
	Left	436.16	37.78	932.88	41.80	

The primary outcome of the study was the comparison of total blood loss between the two treatment modalities. Group A, which received intra-articular TXA, showed a mean blood loss of 446.23 ml with a standard deviation of 33.81 ml. In stark contrast, Group B, which received intravenous TXA, experienced a significantly higher mean blood loss of 928.23 ml, with a standard deviation of 43.93 ml. The difference between the groups was statistically significant with a p-value of 0.0001, underscoring the effectiveness of intra-articular administration in reducing blood loss during total hip replacement surgery (Table 2).

Further stratified analysis provided a detailed breakdown of total blood loss by different demographic and clinical variables such as age, gender, BMI, and the surgical side (Table V). In the 40-55 year age group, the mean blood loss for Group A was 434.30 ml (SD 39.67 ml) compared to 922.56 ml (SD 48.50 ml) for Group B, with a p-value of 0.0001 indicating significant differences. Similarly, in the 56-70 year age group, Group A patients lost an average of 452.20 ml of blood (SD 29.79 ml), whereas Group B patients lost 930.67 ml (SD 42.86 ml).

Gender-specific analysis revealed that males in Group A had a mean blood loss of 436.85 ml (SD 34.94 ml), whereas in Group B, it was 944.50 ml (SD 34.70 ml). Females showed a mean blood loss of 453.43 ml (SD 32.10 ml) in Group A, significantly lower than the 917.39 ml (SD 46.92 ml) observed in Group B. The BMI-based analysis noted that patients with a BMI of 27 or less experienced a mean blood loss of 445.75 ml (SD 30.65 ml) in Group A compared to 948.44 ml (SD 34.57 ml) in Group B. Patients with a BMI greater than 27 showed almost similar results. Regarding surgical side, right-sided surgeries in Group A resulted in a blood loss of 463.64 ml (SD 14.84 ml), considerably lower than the 922.15 ml (SD 47.57 ml) observed in Group B. Left-sided surgeries showed a mean blood loss of 436.16 ml (SD 37.78 ml) in Group A versus 932.88 ml (SD 41.80 ml) in Group B. These results, with respective p-values consistently less than 0.0001, strongly support the superior blood conservation seen with intra-articular TXA administration across all patient categories examined (Table 3).

## DISCUSSION

Tranexamic acid (TXA) has been widely adopted in the medical field for its antifibrinolytic properties, aimed at reducing intraoperative and postoperative hemorrhage. By inhibiting plasminogen activation and reducing plasmin synthesis, TXA enhances the body's ability to maintain effective blood clotting (10). Historically, the intravenous route has been the standard method of TXA administration during orthopedic surgeries, extensively documented to decrease transfusion rates and bleeding during total knee arthroplasty (TKA) without increasing the risk of adverse effects (11-15). However, intra-articular (IA) administration of TXA has gained attention for its ease of application, higher local concentrations at the bleeding site, and reduced systemic absorption, potentially offering an advantageous alternative (16).

The current study aimed to compare the effectiveness of IA and IV TXA in reducing blood loss among patients undergoing total hip replacement (THR). Results revealed that the mean total loss of blood was significantly lower in the IA TXA group compared to the IV TXA group, with means of 446.23 ml and 928.23 ml respectively ( $p$ -value = 0.0001). These findings are consistent with earlier studies suggesting that IA TXA could reduce blood loss effectively (13). Notably, meta-analyses have shown mixed results; some have found no significant difference in blood loss or postoperative hemoglobin levels between IA and IV TXA administration (17, 18), suggesting that the efficacy of TXA may not be markedly dependent on the route of administration when considering broader outcomes such as transfusion rates and hemoglobin levels.

Initial research by Akizuki et al. on the use of IA TXA in orthopedic surgery demonstrated reduced bleeding in patients undergoing cementless TKA who received 250 mg of TXA intra-articularly (19). These results have been supported by subsequent studies, which also reported no significant differences in thromboembolic events between TXA and placebo (20). Furthermore, studies by Seo et al. and others have underscored the comparable effectiveness of IA TXA in various orthopedic and pelvic surgeries, suggesting a broader applicability of this administration route (21, 23, 24). Conversely, research by Wind et al. and North et al. supported the use of IV TXA for THA, noting that while it reduces blood loss, it does not necessarily decrease the need for transfusions when compared to non-TXA controls (25, 26). This highlights a potential limitation in the effectiveness of TXA in reducing broader transfusion demands, irrespective of the administration route.

The discussion surrounding TXA efficacy underscores its role in stabilizing fibrin clots and sealing bleeding vessels (29). TXA rapidly exits joint fluid after IV administration, achieving serum concentrations swiftly (30). Despite these properties, high-concentration IA TXA at the site of surgery did not show superior benefits over lower-dose IV TXA, possibly due to differences in the timing of administration relative to the onset of fibrinolytic activity (31). This study contributes to the ongoing debate regarding the optimal administration route for TXA in orthopedic surgeries. The findings support the use of IA TXA for reducing blood loss in THR, consistent with previous research suggesting that local application can be as effective as systemic administration. However, the study is limited by its focus on blood loss metrics without a broader analysis of transfusion rates and long-term outcomes, which could further delineate the benefits of IA over IV TXA. Future research should address these gaps by including larger sample sizes and diverse clinical settings to validate the findings across different populations.

## CONCLUSION

In conclusion, while this research underscores the potential of IA TXA in reducing surgical blood loss in THR, it also calls for a balanced view that considers both the strengths and limitations of the data. Recommendations for clinical practice should incorporate not only the efficacy of TXA in controlling hemorrhage but also its impact on patient recovery and transfusion needs. This study, therefore, not only contributes to the body of evidence favoring IA TXA but also highlights the need for comprehensive evaluations of TXA's clinical benefits across different administration routes.

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