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Role of Tranexamic Acid in Reducing Perioperative Bleeding in Patients Undergoing Percutaneous Nephrolithotomy for Complex Renal Stones – a Prospective, Randomized Study

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ABSTRACT:

Background: Complex renal calculi correspond to grades III and IV of the Guy's stone score. Percutaneous nephrolithotomy (PCNL) is considered the optimal treatment for such cases. However, bleeding and the need for blood transfusions are common complications associated with this procedure.

Objective: To evaluate the effectiveness of TXA in reducing intraoperative and postoperative bleeding as well as the rate of blood transfusions in patients undergoing PCNL for complex renal calculi. Secondary objectives included comparing operative time, complication rates, duration of hospital stay, and the complete stone-free or success rate between the two groups.

Methods: This study was a randomized, prospective, single-center investigation conducted over a 12-month period. A total of 46 patients with complex renal calculi were randomly assigned in a 1:1 ratio to either the TXA group or the control group. Patients in the TXA group received a single dose of 1 g TXA at the time of anesthesia induction during PCNL.

Results: Patients in the TXA group experienced a smaller decline in hemoglobin levels compared to the control group, both immediately after PCNL (1.27 g/dL vs. 1.6 g/dL) and 24 hours post-procedure (1.62 g/dL vs. 2.15 g/dL). The postoperative blood transfusion rate was significantly lower in the TXA group compared to the control group (4.3% vs. 21.74%). There was no statistically significant difference in operative duration, measured from calyx puncture to nephrostomy tube placement, between the two groups (71.39 minutes vs. 74.34 minutes). Similarly, no significant differences were observed in complication rates (13% vs. 17.4%) or the length of hospital stay (4.52 days vs. 4.87 days). However, the TXA group demonstrated a significantly higher overall success rate (87% vs. 52.2%) and a higher complete stone-free rate (26.08% vs. 13.04%) compared to the control group.

Conclusion: The administration of TXA in patients undergoing PCNL for complex renal calculi significantly reduces perioperative blood loss and the need for blood transfusions, without increasing the incidence of complications. It does not appear to affect operative time, or the duration of hospital stay. Furthermore, TXA use is associated with higher rates of complete stone clearance and overall success.

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Introduction

Lifetime prevalence of renal calculus disease is 1% to 15%. Its prevalence rate in Asia is 1% to 5%.(1) In developing countries like India, 10 to 15% are complex renal calculi and women are twice more frequently affected compared to men.(2) Renal calculus which extends from renal pelvis to one or more renal calyx(s) is considered as staghorn calculus. There are no standard definitions for either complete or partial staghorn calculi, however, it is considered that complete staghorn calculi involve entire renal collecting system, whereas partial staghorn stones involve less.(3, 4)

Complex renal calculi constitute Guys stone score (GSS) grades III and IV. GSS grade III includes partial staghorn calculus, multiple renal stones in kidney with abnormal anatomy, and stones in calyceal diverticulum. GSS grade IV includes complete staghorn calculus, calculus in spinal injury patients.(5-7) The ideal management for complex renal calculi is percutaneous nephrolithotomy (PCNL), according to EUA & AUA guidelines.(8) Bleeding and blood transfusion requirement are frequent complications of PCNL.(9) Risk of bleeding during PCNL is related to complexity of the calculi as well.(10, 11)

Tranexamic acid (TXA) use in reducing intraoperative and postoperative bleeding has increased in the recent times.(12) It binds to lysine receptors on plasminogen reversibly, preventing breakdown of fibrin.(13) It prevents clots lysis in the urinary system by inhibiting urokinase.(14) Half-life of TXA is 1.5 to 2 hours. It is eliminated by kidneys and urinary recovery is >95%. Its therapeutic dosage is 1 to 1.5gm orally every 6^{th} or 8^{th} hourly, 500mg to 1gm IV every 8^{th} hourly. Its adverse effects are headache, nasal stuffiness, fatigue, nausea, vomiting, diarrhea, dyspepsia, hypersensitivity reaction, and thromboembolic events.(15-17) Till date, some authors have studied the role of TXA in PCNL, and inconsistent results were reported regarding the perioperative bleeding, need of blood transfusion, operative time, over-all complications rate, duration of stay in the hospital, and complete stone free rate or success rate.

Materials and Methods

This study was a randomized, prospective, single-center investigation conducted over a 12-month period, from August 2023 to July 2024, in the Department of Urology at JSS Academy of Higher Education and Research, Mysuru, Karnataka, India. The primary objective was to evaluate the effectiveness of tranexamic acid (TXA) in reducing intraoperative and postoperative bleeding as well as the need for blood transfusions in patients with complex renal calculi undergoing percutaneous nephrolithotomy (PCNL). Secondary objectives included assessing differences in operative time, complication rates, duration of hospital stay, and the complete stone-free or overall success rate.

The study population included patients with complex renal calculi classified as Guy's Stone Score (GSS) grades III and IV who required PCNL. Exclusion criteria included patients with a history of allergy to TXA, those receiving antiplatelets or anticoagulants, patients with a history of thromboembolic events, known coagulopathies, chronic kidney disease, or concomitant hormonal contraceptive use.

Participants were alternately assigned in a 1:1 ratio to either the TXA group or the control group. In the TXA group, a single dose of 1 g TXA diluted in 250 ml normal saline was administered intravenously over 10–30 minutes at the time of anesthesia induction. All procedures were performed under general anesthesia. Ureteric catheters were placed with the patient in the lithotomy position, followed by percutaneous renal access to the desired calyx or calyces under fluoroscopic guidance in the prone position. Tract dilations were carried out using Alkem dilators, and Amplatz sheaths of variable sizes were deployed based on stone volume. Pneumatic lithotripters were used to fragment the calculi, and double-J stents were placed antegradely in all cases. At the conclusion of the procedure, nephrostomy tubes of appropriate size were positioned in all patients. Hemoglobin and packed cell volume levels were measured immediately after the procedure and 24 hours postoperatively. Stone clearance was assessed by non-contrast computed tomography of the kidney, ureter, and bladder (NCCT KUB) during follow-up one week after the procedure.

Purposive sampling was used for participant selection, and the sample size was calculated using the formula (S=Z^2PQ/D^2), where (S) represents the sample size, (Z) is the standard normal value at the 95% confidence level, (P) is the prevalence of the condition, (Q=1-P), and (D) is the margin of error. A total of 46 participants were

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included, with 23 allocated to each group. Data analysis was performed using statistical methods, including Pearson's Chi-Square, Fisher's Exact Test, Linear-by-Linear Association, and Likelihood Ratio tests.

Results

In our study, 73.9% of participants in the TXA group and 60.9% in the control group were male. The average age of participants was comparable between the two groups, with a mean age of 48.08 years in the TXA group and 48.26 years in the control group. The majority of participants in both groups were symptomatic, with 91.3% in the TXA group and 87% in the control group reporting symptoms (Table 1).

Comorbidities were present in 60.8% of participants in the TXA group, with diabetes mellitus being the most common, followed by hypertension. In the control group, 39.1% had comorbidities, predominantly hypertension followed by diabetes mellitus (Table 1). In both groups, 60.86% of participants had right-sided renal calculi. The mean stone size and density in the TXA group were 2.71 cm and 971.3 Hounsfield Units (HU), respectively, compared to 2.62 cm and 968 HU in the control group. In terms of stone complexity, 82.6% of participants in the TXA group had GSS III stones, and 17.45% had GSS IV stones, compared to 78.3% with GSS III stones and 21.7% with GSS IV stones in the control group (Table 2).

Renal stones were accessed via a single tract in the majority of cases, with 91.3% in the TXA group and 82.6% in the control group. The remaining patients required access through two tracts (Table 2). There was no statistically significant difference in the duration of surgery between the two groups, whether measured from cystoscopy to ureteric catheter placement (10.21 vs. 10.43 minutes, $p = 0.62$) or from calyx puncture to nephrostomy tube placement (71.39 vs. 74.34 minutes, $p = 0.53$) (Table 2).

Hemoglobin levels decreased less in the TXA group compared to the control group. The mean hemoglobin drop immediately after PCNL was 1.27 g/dL in the TXA group versus 1.6 g/dL in the control group ($p = 0.04$), and 24 hours post-procedure, it was 1.62 g/dL in the TXA group versus 2.15 g/dL in the control group ($p = 0.03$) (Table 3). Similarly, the mean packed cell volume (PCV) drop was lower in the TXA group. Immediately after PCNL, the PCV drop was 4.87% in the TXA group compared to 6.55% in the control group ($p = 0.04$), and 24 hours post-procedure, it was 5.79% in the TXA group versus 7.82% in the control group ($p = 0.03$) (Table 3).

Only one patient in the TXA group required a postoperative blood transfusion, compared to five patients in the control group, representing a statistically significant difference ($p = 0.04$) (Table 4). Additionally, patients in the TXA group had significantly higher success rates (87% vs. 52.2%, $p = 0.02$) and complete stone-free rates (26.08% vs. 13.04%, $p = 0.04$) compared to the control group (Table 4). Complications were comparable between the groups. Acute kidney injury occurred in 8.6% of participants in both groups, while sepsis was observed in 8.6% of participants in the control group and 4.3% in the TXA group, with no statistically significant difference in the overall complication rates ($p = 0.33$) (Table 4). The duration of hospital stay was also similar between the two groups, averaging 4.52 days in the TXA group and 4.87 days in the control group ($p = 0.10$) (Table 4).

Discussion

Between August 2023 and July 2024, 46 eligible patients at our institution were included in the study based on predefined inclusion criteria. These patients were randomized and allocated equally into either the TXA group ($n = 23$) or the control group ($n = 23$). Full recruitment was achieved, and complete data were collected for all participants. Randomization was performed in a 1:1 alternating manner, resulting in 23 patients receiving TXA and 23 patients not receiving the drug. All participants successfully completed the follow-up process.

The dosage and mode of TXA administration were selected based on prior research. Due to its half-life, a single dose of 1 g TXA was determined to be optimal for achieving its efficacy.(18) Preoperative infection screening was performed for all participants, including urine culture. In cases where microbial growth was detected, appropriate antibiotics were initiated at least seven days before the procedure. In this study, hemoglobin and packed cell volume (PCV) drops were significantly lower in the TXA group compared to the control group, both immediately after PCNL and 24 hours post-procedure. Only one patient in the TXA group required a blood transfusion, whereas five patients in the control group underwent transfusion, indicating that the

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administration of TXA substantially reduced the likelihood of perioperative blood transfusions.

These findings align with the results reported by Kumar et al.(19) (2013), who demonstrated that TXA reduced perioperative bleeding and the need for blood product transfusions. However, their study did not categorize participants based on the complexity of calculi. In contrast, Mohammadi et al.(20) (2018) suggested reconsidering the use of TXA in PCNL, as their study reported no significant differences in hemoglobin reduction or transfusion requirements. More recently, Batagello et al.(16) (2022) observed a five-fold reduction in blood transfusion requirements among patients with complex renal calculi who received TXA during PCNL.

In the present study, there was no statistically significant difference between the groups in terms of surgery duration, length of hospital stays, or complication rates. These findings are consistent with the results reported by Batagello et al.(16) and Kumar et al.(19) Non-contrast CT (NCCT) of the kidney, ureter, and bladder (KUB) was used to evaluate both the complete stone-free rate and success rate. In this study, success was defined as the presence of residual stone fragments ≤4 mm or no residual fragments, as per established guidelines. However, the optimal residual stone size for reporting successful outcomes after PCNL continues to be explored. It was hypothesized that reducing intraoperative bleeding improves visualization of the pelvicalyceal system, facilitating the identification of residual fragments and minimizing the need to abort the procedure.

This study demonstrated a success rate of 87% in the TXA group, which is consistent with findings from the CROES PCNL Global Study involving 5,803 patients, where a success rate of 75.7% was reported. These results further underscore the potential benefits of TXA in enhancing outcomes for patients undergoing PCNL for complex renal calculi.(21)

Conclusion

In conclusion, administration of TXA in patients undergoing PCNL for complex renal stones significantly reduces the perioperative blood loss, and need for blood transfusions, without increasing the overall complication rates. Moreover, patients who receive TXA show higher rates of complete stone clearance and overall success rate. However, TXA may not affect the duration of surgery and duration of stay in the hospital. Further research with larger sample sizes is required to confirm these findings and better define the TXA's role in this setting.

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Table 1: Characteristics of the study groups

Characteristics	Control Group	TXA Group	P value
Age, in years (mean)	48.26	48.08	0.96
Male, n (%)	14 (60.9)	17 (73.9)	0.53
Symptomatic, n (%)	20 (87)	21 (91.3)	0.50
Positive baseline urine culture (%)	2 (8.7)	2 (8.7)	1.00
Comorbidities			

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No Comorbidities, n (%)	14 (60.9)	9 (39.1)	0.17
DM, n (%)	3 (13)	6 (26)	
HTN, n (%)	6 (26)	8 (34.8)	

Table 2: Comparison of study groups by clinical characteristics

Characteristics	**Control Group**	**TXA Group**	**'p' value**
Stone features			
Right laterality (%)	14 (60.9)	14 (60.9)	1.00
Size, mm (mean)	26.2	27.1	0.72
Density, HU (mean)	968	971.3	0.97
Guy's Stone score (%)			
III	18 (78.3)	19 (82.6)	0.50
IV	5 (21.7)	4 (17.4)	
Number of tracts, n (%)			
1	19 (82.6)	21 (91.3)	0.38
2	4 (17.4)	2 (8.7)	
Duration of surgery, min (mean)			
Cystoscopy to Ureteric catheter placement	10.43	10.21	0.62
Calyceal puncture to Nephrostomy placement	74.34	71.39	0.53

Table 3: Comparison of study groups by laboratory characteristics

Characteristics	**Control Group**	**TXA Group**	**'p' value**
Hemoglobin, gm/dl (mean)			
Baseline	12.98	13.14	0.20
Immediately at the end of PCNL	11.38	11.87	0.04
24hr post-PCNL	10.83	11.52	0.03
Hemoglobin Drop (%)			

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Immediately at the end of PCNL	1.6	1.27	0.04
24hr post-PCNL	2.15	1.62	0.03
PCV, % (mean)			
Baseline	39.19	39.12	0.38
Immediately at the end of PCNL	32.64	34.25	0.04
24hr post-PCNL	31.37	33.33	0.03
PCV Drop (%)			
Immediately at the end of PCNL	6.55	4.87	0.04
24hr post-PCNL	7.82	5.79	0.03

Table 4: Comparison of study groups by outcomes of interest

Characteristics	**Control Group**	**TXA Group**	**'p' value**
Blood transfusion, n (%)	5 (21.74)	1 (4.3)	0.04
Complete Stone free rate, n(%)	3 (13.04)	6 (26.08)	0.046
Success rate, n(%)	12 (52.2)	20 (87)	0.023
Duration of hospital stay, days (mean)	4.87	4.52	0.104
Postoperative complications, n (%)			
AKI	2 (8.7)	2 (8.7)	0.330
Sepsis	2 (8.7)	1 (4.3)	
Pleural effusion/ Pulmonary embolism/Bowel injury/Ureteric clots	0	0	