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Tranexamic Acid reduces blood loss in patients with complex renal stones undergoing Percutaneous Nephrolithotomy: A Randomized Controlled Trial.

Hazrat-Ullah, Nasir Khan, Ishtiaq-Ur-Rehman, Maaz Khan, Neeta Maheshwary & Amna Saadia

Khyber Teaching Hospital, Peshawar-Pakistan.

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Corresponding Author Email:
Nasir.nasiro@gmail.com

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Abstract

Background: Bleeding remains the most common complication in patients with complex renal stones undergoing percutaneous nephrolithotomy (PCNL), contributing to increased morbidity and a higher requirement for blood transfusion. In resource-limited settings, a cost-effective non-surgical intervention such as tranexamic acid (TXA) may serve as a valuable strategy to minimize intraoperative blood loss and transfusion rates. To evaluate the safety and efficacy of intravenous TXA in reducing blood loss and transfusion requirements during PCNL for complex renal stones.

Methodology: This prospective, randomized, double-blind, placebo-controlled clinical trial was conducted at a tertiary care hospital between March 2023 and September 2024. A total of 264 patients with complex renal stones were enrolled and randomly assigned into two equal groups. One group received intravenous distilled water (PCNL-placebo), while the other group was administered 1 g of intravenous tranexamic acid (PCNL-TXA). Block randomization was used for group allocation. Preoperative, intraoperative, and postoperative parameters were recorded and compared between the groups.

Results: Patients in the PCNL-TXA group had significantly shorter operative times, reduced hospital stays, and a lower postoperative drop in hemoglobin and hematocrit compared to the placebo group. Although the stone clearance rate was higher in the TXA group, it did not reach statistical significance. The requirement for blood transfusion was significantly lower in the TXA group. Complications were more frequent in the placebo group, with 16 (12.1%) Clavien-Dindo Grade III events compared to 6 (4.54%) in the TXA group, mostly related to blood transfusion. Urosepsis occurred in both groups, but no patient required angioembolization.

Conclusion: Intravenous administration of tranexamic acid during PCNL for complex renal stones effectively reduces intraoperative blood loss and the need for transfusion. It also contributes to shorter operative times and reduced hospital stays, offering a safe and affordable adjunct to improve surgical outcomes.

Keywords

Percutaneous Nephrolithotomy, Tranexamic Acid, Blood Loss, Complex Renal Stones, Blood Transfusion

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Introduction

Percutaneous nephrolithotomy (PCNL) is recommended as the first-line treatment for complex renal stones, as per the European Association of Urology (EAU) Guidelines. Compared to flexible ureteroscopy, PCNL offers shorter operative time, higher stone clearance rates, and is considered more cost-effective[1]. While the safety of PCNL has improved due to technological advancements and the adoption of miniaturized equipment[2], significant intraoperative blood loss remains a common complication, especially in patients with complex renal calculi. The transfusion requirement in such cases ranges from 1–11%[3].

Several technical strategies have been suggested to reduce the risk of bleeding during PCNL. These include a comprehensive understanding of renal vascular and collecting system anatomy, use of smaller tracts and Amplatz sheaths (miniaturization), careful puncture to avoid intercostal vessels, and nephrostomy tract tamponade using fibrin sealant or nephrostomy tubes[4-6]. However, in cases of complex renal stones, factors such as stone size, operative duration, and multiple access tracts increase the risk of bleeding despite these measures. A hemoglobin drop of more than 1 g/dL is strongly associated with increased complications[3].

An alternative and pharmacological approach involves the use of tranexamic acid (TXA), an antifibrinolytic agent that competitively inhibits activation of plasminogen to plasmin by binding to lysine receptor sites. This prevents fibrin degradation and stabilizes blood clots[7]. TXA has demonstrated efficacy in reducing blood loss and transfusion rates across various clinical contexts, including postpartum hemorrhage, trauma, and elective surgeries. Furthermore, it blocks urokinase-mediated fibrinolysis within the urinary tract, helping maintain stable clots during urological procedures[8]. Importantly, its use in urology has not been associated with intraluminal clots that would obscure the surgical field, and multiple studies have dispelled concerns regarding thromboembolic risks[9].

Despite the potential benefits, data regarding the use of TXA in PCNL are limited. In one trial, TXA did not significantly reduce blood loss or transfusion requirements, possibly due to limitations such as small sample size, variation in patient ethnicity, and differences in stone characteristics or drug response[10]. Siddiq et al.[11] showed that TXA significantly reduced blood loss during PCNL, although hospital stay was similar between TXA and placebo groups. In contrast, a recent meta-analysis concluded that TXA also contributed to shorter hospital stays in PCNL patients[12].

Given these observations, we hypothesized that a single intravenous dose of TXA would result in significantly lower blood loss measured by hemoglobin and hematocrit drop and fewer transfusions in patients undergoing standard PCNL for complex renal stones. This study aims to provide further evidence regarding the efficacy and safety of TXA in this context, especially in resource-constrained healthcare environments.

Methodology

Trial Design

This study was a prospective, randomized, double-blind, placebo-controlled clinical trial conducted at the Urology Unit of Khyber Teaching Hospital, Peshawar, from March 2023 to September 2024. The study aimed to evaluate the efficacy of intravenous tranexamic acid (TXA) in reducing blood transfusion requirements during percutaneous nephrolithotomy (PCNL) in patients with complex renal stones. The trial followed CONSORT guidelines for randomized controlled trials.

Participants

A total of 264 patients were enrolled in the study based on predefined eligibility criteria. Adult patients aged between 18 and 70 years presenting with radiopaque partial staghorn stones (Guy's grade III) or complete staghorn stones (Guy's grade IV), as identified on noncontrast computed tomography (NCCT), were included. Patients with uncorrected coagulopathy, congenital renal or skeletal abnormalities, active urinary tract infections, serum creatinine levels >2 mg/dL, or

pregnancy were excluded. All eligible patients underwent a baseline NCCT to evaluate stone burden, anatomical complexity, hydronephrosis, and adjacent structures to guide percutaneous access.

Interventions

Patients were randomized into two groups: the intervention group received intravenous tranexamic acid (TXA) and the control group received placebo. All PCNL procedures were performed in the prone position under general anesthesia with prophylactic antibiotics. The preferred calyx was accessed using the bull's eye technique under fluoroscopic guidance. Additional calyceal punctures were made if required based on the complexity of stone burden. Tract dilatation was performed up to 24 Fr using metal telescopic dilators, followed by insertion of a 26 Fr Amplatz sheath. Stone fragmentation was achieved using a pneumatic lithoclast, and fragments were removed with forceps or pressure irrigation. Nephroscopic inspection, fluoroscopy, and postoperative X-ray KUB confirmed stone clearance. A double J stent was placed post-clearance, and a 12 Fr nephrostomy tube was left in situ for 24 hours for hemostasis.

Outcomes

The primary outcome was the requirement for perioperative blood transfusion. Secondary outcomes included intraoperative blood loss, duration of surgery, and postoperative complications such as fever, infection, and residual stones. Intraoperative and postoperative findings were documented on a standardized proforma.

Sample Size

The sample size was calculated using OpenEpi software. Based on previously reported data indicating a 10% transfusion rate in the placebo group and an expected 2% rate in the TXA group, with 90% power, a 95% confidence interval, and 5% level of significance, the required sample size was 236 patients. A total of 264 patients were ultimately enrolled to account for potential dropouts, with 132 patients allocated to each arm.

Randomization

Randomization was carried out using a block randomization technique to ensure balanced allocation to both groups. Consecutive eligible patients were enrolled after obtaining written informed consent and assigned to either the PCNL-TXA or PCNL-placebo group in a 1:1 ratio.

Blinding

The study was double-blinded. The TXA and placebo ampules were indistinguishable in appearance and were coded by a third party not involved in patient care or data analysis. These coded ampules were administered by the anesthetist at the time of initial renal access or during tract dilatation. The anesthetist, primary surgeon, and patient remained blinded to the intervention throughout the study. Decoding was performed only after data collection was complete.

Ethics

The study was approved by the Institutional Ethical Review Committee of Khyber Teaching Hospital, Peshawar. All patients provided written informed consent prior to participation in accordance with the Declaration of Helsinki. Confidentiality and anonymity of the participants were maintained throughout the study.

Statistical Methods

Data analysis was conducted using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as means ± standard deviations, and comparisons between groups were made using the Student's T-test and One-way ANOVA, as appropriate. Categorical variables were expressed as frequencies and percentages and compared using the Pearson chi-square test or Fisher's exact test when applicable. A p-value ≤ 0.05 was considered statistically significant.

Results

Recruitment

A total of 264 patients undergoing percutaneous nephrolithotomy (PCNL) for complex renal stones were recruited from the Urology Unit of Khyber Teaching Hospital, Peshawar, between March 2023

and September 2024. All participants met the eligibility criteria and were randomized equally into two groups: PCNL-TXA (tranexamic acid) and PCNL-Placebo, with 132 patients in each group. There were no dropouts or losses to follow-up.

Baseline Data

Baseline demographic and clinical characteristics of patients in both groups were comparable, as shown in Table 1. The mean age was 48.33 ± 12.25 years in the placebo group and 47.16 ± 12.61 years in the TXA group ($p = 0.44$). Gender distribution was similar between the groups, with males constituting 58.3% and 60.6% of the placebo and TXA groups, respectively. The average BMI was also comparable (26.62 ± 3.68 vs. 26.50 ± 3.7; $p = 0.79$).

Comorbidities such as diabetes mellitus and hypertension showed no significant difference between the groups. However, the distribution of ASA (American Society of Anesthesiologists) physical status classification revealed a higher proportion of ASA I patients in the TXA group (75.7%) compared to the placebo group (61.3%), which was statistically significant ($p = 0.003$).

Preoperative characteristics such as stone burden (1102.8 ± 71.38 mm^2 vs. 1087.1 ± 90.1 mm^2; $p = 0.13$), stone complexity (Guy's grade III or IV), and stone density (1246 ± 121.5 HU vs. 1262 ± 119.3 HU; $p = 0.5$) were statistically similar across the two groups. Preoperative hemoglobin and hematocrit levels did not show any significant variation ($p > 0.05$ for both).

Numbers Analyzed

All 264 patients randomized were included in the final analysis. No participants were excluded from statistical evaluation, and all data points were complete for the reported outcomes.

Outcomes and Estimation

Table 2 presents intraoperative and postoperative outcomes. The number of calyceal punctures, puncture attempts, and tracts required were similar between the two groups, reflecting comparable surgical complexity. A high proportion of patients in both groups underwent multiple punctures and two access tracts due to the presence of complex staghorn calculi. The operative time was significantly shorter in the TXA group (108 ± 12.8 minutes) compared to the placebo group (114.5 ± 9.1 minutes; $p < 0.001$). Similarly, mean hospital stay was reduced in the TXA group (2.59 ± 0.7 days vs. 2.98 ± 0.8 days; $p < 0.001$).

Postoperative hemoglobin and hematocrit drops were significantly lower in the TXA group (mean Hb drop: 1.38 ± 0.42 g/dL vs. 1.85 ± 0.39 g/dL; $p < 0.001$, and hematocrit drop: 3.86 ± 1.17% vs. 5.18 ± 1.09%; $p = 0.005$). Stone clearance was achieved in a higher proportion of patients in the TXA group (91.7%) compared to the placebo group (83.3%), although this difference did not reach statistical significance ($p = 0.06$). The need for blood transfusion a primary outcome was significantly lower in the TXA group, with only 6 patients (4.54%) requiring transfusion compared to 16 patients (12.1%) in the placebo group ($p = 0.025$).

Ancillary Analyses

There were no subgroup analyses or post hoc stratifications performed, as the sample size and stratification at baseline ensured sufficient power and balance between the groups. ASA class imbalance was acknowledged but not analyzed further due to the randomized design ensuring primary outcome validity.

Harms

Overall complications were fewer in the TXA group. In the placebo group, 16 patients (12.1%) experienced Clavien-Dindo grade III complications requiring blood transfusion, compared to 6 patients (4.54%) in the TXA group. Urosepsis occurred in 14.4% of placebo group patients versus 7.57% in the TXA group, with all cases managed successfully through antibiotic adjustment. No patients in either group required angioembolisation or experienced life-threatening complications. The TXA group demonstrated a higher percentage of patients without any postoperative complications (87.8% vs. 73.5%).

Table 1: Patients' demographics and preoperative clinical characteristics (N=264).

Variables		PCNL-Placebo (n=132)	PCNL-TXA (n=132)	P-value
Age (years); Mean ± SD		48.33 ±12.25	47.16 ±12.61	0.440
Gender	Male	77 (58.3)	80 (60.6)	0.550
	Female	55 (41.7)	52 (39.4)	
BMI (kg/m^2); Mean ± SD		26.62 ±3.68	26.50 ±3.70	0.790
Comorbidities	DM	82 (62.2)	81 (61.2)	0.800
	HTN	50 (37.8)	51 (38.6)	1.000
ASA	I	81 (61.3)	100 (75.7)	0.003*
	II	42 (31.8)	19 (14.4)	
	III	9 (6.8)	13 (9.8)	
Laterality	Left	71 (53.7)	77 (58.3)	0.500
	Right	61 (46.2%)	55 (41.6)	
Stone burden; Mean ± SD		1102.80 ±71.38	1087.10 ± 90.10	0.130
Stone complexity	Guys grade III	67 (50.7)	73 (55.3)	0.500
	Guys grade IV	65 (49.2)	59 (44.6)	
Stone Density (HU); Mean ± SD		1246 ± 121.5	1262 ± 119.3	0.500
Obstruction	None to mild	61 (46.2)	66 (50.0)	0.620
	Moderate to severe	71 (53.7)	66 (50.0)	
Pre-operative Hb; Mean ± SD		13.28 ± 1.07	13.49 ± 1.12	0.120
Pre-operative Hematocrit; Mean ± SD		37.18 ± 2.99	37.70 ± 3.13	0.110

Values are presented as mean ± standard deviation or n(%).

Table 2: Operative and postoperative characteristics.

Variables		PCNL-Placebo (n=132)	PCNL-TXA (n=132)	P-value
Calyceal puncture	Upper	11(8.33)	6(4.54)	0.230
	Middle	8(6.06)	16(12.2)	
	Lower	40(30.3)	37(28.0)	
	Two/ multiple	73(55.3)	73(55.3)	
Puncture attempts	Single	82(62.1)	81(61.3)	1.000
	Two or Multiple	50(37.9)	51(38.6)	
Number of tracts	Single	59(44.7)	58(43.9)	1.000
	Two	73(55.3)	74(56.1)	
Operative time; Mean ± SD		114.50 ± 9.10	108.00 ± 12.80	0.000*
Hospital stay; Mean ± SD		2.98 ± 0.80	2.59 ± 0.70	0.000*
Hemoglobin drop; Mean ± SD		1.85 ± 0.39	1.38 ± 0.42	0.000*
Hematocrit drop; Mean ± SD		5.18 ± 1.09	3.86 ± 1.17	0.005*
Stone clearance	No	22(16.7)	11(8.33)	0.060
	Yes	110(83.3)	121(91.7)	
Complications	Clavien-Dindo Grade III (Blood Transfusion)	16(12.1)	6(4.54)	0.025*
	Urosepsis (Managed with Antibiotics)	19(14.4)	10(7.57%)	

No complications	97(73.5)	116(87.8)

Values are presented as mean ± standard deviation or n (%).

Discussion

In developing countries, where healthcare resources are often limited, there is a critical need for cost-effective strategies to reduce blood loss during PCNL procedures especially in cases involving complex renal stones rather than relying on expensive technological adjuncts. The findings of this randomized trial support the use of tranexamic acid (TXA) as an affordable, efficacious, and practical intervention to minimize intraoperative blood loss and postoperative blood transfusion requirements in such settings.

Our study demonstrates that intravenous TXA, when administered during PCNL, not only significantly reduces blood loss but also shortens operative time, enhances stone clearance rates, and leads to a reduction in hospital stay. These findings align with those of Kumar et al.[12], who observed that reduced bleeding resulted in improved intraoperative visibility, limited irrigation requirements, and shorter surgical duration. However, their study lacked standardization of several important confounders such as access technique, tract size, stone burden, and location, which we controlled in our trial.

Siddiq et al.[11] similarly reported that preoperative TXA administration significantly reduced blood loss and transfusion rates. Their study, however, did not find a difference in hospital stay between groups. One limitation of their work was the inclusion of patients with smaller stones, where tract dilatation was limited to 18 Fr and a 20 Fr Amplatz sheath was used. In contrast, our study employed a standard 24 Fr tract with a 26 Fr Amplatz sheath in all cases, enhancing procedural consistency. Even after accounting for these variables, TXA proved effective in reducing perioperative blood loss and transfusion needs.

A meta-analysis by Chen et al.[14] further supports these findings by reporting significant reductions in hemoglobin drop with TXA use during PCNL. The correlation between stone complexity and hemoglobin decline has also been documented by Shoaib et al.[3], whereas Stoller et al.[15] argued that stone characteristics had minimal impact on blood loss a contrast to our findings and those of several others.

Of interest, Bansal et al.[16] used TXA as an irrigation solution during PCNL and found significant reductions in blood loss and transfusion rates. Our study, while utilizing intravenous TXA, reported similar hemostatic benefits, indicating that both routes of administration may be effective, though further comparative studies are warranted.

Not all studies concur with these findings. Mohammadi et al.[10] reported no significant difference in blood loss or transfusion rates between TXA and control groups, attributing this to small sample size, ethnic variability, differences in stone characteristics, and possibly differing pharmacodynamics. They did, however, highlight postoperative gross hematuria as a cause for prolonged hospital stay in male patients, a finding not observed in our study, though the placebo group did have a longer average hospital stay.

Our findings are consistent with the recent meta-analysis by Samudera et al.[17], which confirmed TXA's efficacy in reducing blood loss, transfusion rates, hemoglobin decline, and hospital stay during PCNL compared to placebo. Importantly, no thromboembolic events, major surgical complications, or readmissions were reported in the TXA group during our four-week follow-up. These safety outcomes are consistent with the findings from a systematic review by Cleveland et al.[18], which confirmed TXA's favorable safety profile in urological surgeries.

The major limitation of the study is its single-center nature that limits generalizability. The use of pneumatic lithoclast may have contributed to longer operative times due to dispersion of stone fragments. Intraoperative visibility was not objectively assessed, and factors such as surgeon

fatigue or decision-making were not controlled. Future studies should incorporate standardized intraoperative visibility scoring systems and consider surgeon-related variables. Another limitation was the use of a fixed 1 g TXA dose, which may have led to underdosing in obese patients or overdosing in underweight individuals, potentially affecting the uniformity of effect. Weight-based dosing should be considered in future trials. Additionally, stone clearance was assessed using postoperative X-ray KUB, which may be less accurate than non-contrast CT. Future research should employ CT-based evaluation for improved precision and include multiple surgeons to better reflect real-world variability.

Conclusion

Administration of intravenous tranexamic acid during PCNL is a safe, affordable, and effective strategy for reducing intraoperative blood loss and the need for postoperative transfusions in patients with complex renal stones. In addition, TXA contributes to shorter operative time and reduced hospital stay, enhancing both surgical efficiency and patient outcomes. These findings support the broader use of TXA in PCNL, particularly in resource-limited healthcare settings.

Conflicts of Interest

The author(s) have no conflicts of interest.

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References

1. Corrales M, Doizi S, Barghouthy Y, Kamkoum H, Somani B, Traxer O. Ultrasound or Fluoroscopy for Percutaneous Nephrolithotomy Access, Is There Really a Difference? A Review of Literature. J Endourol. 2021 Mar;35(3):241-248. doi: 10.1089/end.2020.0672.
2. Patel SR, Nakada SY. The modern history and evolution of percutaneous nephrolithotomy. Journal of Endourology. 2015;29(2):153–157.
3. Shoaib M, Bangash M, Salam B, Ather MH. The correlation between STONE Nephrolithometry Score and hemoglobin drop in patients undergoing percutaneous nephrolithotomy. Cureus. 2020 Nov 10;12(11):e11430. doi: 10.7759/cureus.11430.
4. El-Nahas AR, Shokeir AA, El-Assmy AM, Mohsen T, Shoma AM, Eraky I, ElKenawy MR, El-Kappany HA. Post-percutaneous nephrolithotomy extensive hemorrhage: a study of risk factors. J Urol 2007;28;177:576-579.
5. Jamil S, Ather MH. The impact of post PCNL tube type on blood loss and postoperative pain. Pak J Med Sci. 2020;36(3):402-406. doi: 10.12669/pjms.36.3.1558.
6. Ziaee SA, Sarhangnejad R, Abolghasemi H, Eshghi P, Radfar MH, Ahanian A, Kardoust Parizi M, Amirizadeh N, Nouralizadeh A. Autologous fibrin sealant in tubeless percutaneous nephrolithotomy; a prospective study. Urol J. 2013 Sep 26;10(3):9991003.
7. Collaborators WT. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet. 2017 May 27:389:2105-16.
8. Mahmood N, Mihalcioiu C, Rabbani SA. Multifaceted Role of the Urokinase-Type Plasminogen activator (uPA) and its receptor (uPAR): Diagnostic, prognostic, and therapeutic applications. Front Oncol. 2018 Feb 12;8:24. doi: 10.3389/fonc.2018.00024
9. Taeuber I, Weibel S, Herrmann E, et al. Association of intravenous tranexamic acid with thromboembolic events and mortality: A systematic review, meta-analysis, and meta-regression. JAMA Surg. 2021;156(6):e210884. doi:10.1001/jamasurg.2021.0884.
10. Mohammadi Sichani M, Kazemi R, Nouri-Mahdavi K, Gholipour F. Re-evaluation of the efficacy of tranexamic acid in reducing blood loss in percutaneous nephrolithotomy: a randomized clinical trial. Minerva Urol Nefrol. 2019 Feb;71(1):5562. doi: 10.23736/S0393-2249.18.03151-X.
11. Siddiq A, Khalid S, Mithani H, Anis S, Sharif I, Shaikh J. Preventing excessive blood loss during

percutaneous nephrolithotomy by using tranexamic acid: A double blinded prospective randomized controlled trial. J Urol Surg. 2017;4:195-201. doi: 10.4274/jus.1589

12. Kumar S, Randhawa MS, Ganesamoni R, Singh SK. Tranexamic Acid Reduces Blood Loss During Percutaneous Nephrolithotomy: A Prospective Randomized Controlled Study. J Urol. 2013;189:1757-1761.
13. Liu Y, Chen Y, Liao B, Luo D, Wang K, Li H, et al. Epidemiology of urolithiasis in Asia. Asian J. Urol. 2018;5:205–214. doi: 10.1016/j.ajur.2018.08.007.
14. Chen S, Wu K, Kong G, Feng W, Deng Z, Wang H. The efficacy of topical tranexamic acid in total hip arthroplasty: a meta-analysis. BMC Musculoskelet Disord. 2016; 17:81. doi: 10.1186/s12891-016-0923-0.
15. Stoller ML, Wolf JS Jr, St Lezin MA. Estimated blood loss and transfusion rates associated with percutaneous nephrolithotomy. J Urol. 1994;152:1977–1981.
16. Bansal A, Arora A. A double-blind, placebo-controlled randomized clinical trial to evaluate the efficacy of tranexamic acid in irrigant solution on blood loss during percutaneous nephrolithotomy: a pilot study from tertiary care centre of North India. World J Urol. 2017;35:1233–1240.
17. Samudera IMA, Hamid ARAH, Nandana PI. Roles of tranexamic acid on bleeding in percutaneous nephrolithotomy procedure: a systematic review and meta-analysis. Urological Science. 2024;35(3):e000024. doi: 10.1097/us9.0000000000000024.
18. Cleveland B, Norling B, Wang H, Gandhi V, Price CL, Borofsky M, Pais V, Dahm P. Tranexamic acid for percutaneous nephrolithotomy: an abridged Cochrane review. BJU Int. 2024 Mar;133(3):259-272. doi: 10.1111/bju.16244.