Original Article

Efficacy of tranexamic acid in reducing blood loss during percutaneous nephrolithotomy: a randomized controlled trial

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ABSTRACT

Background: Percutaneous nephrolithotomy (PCNL) is an established treatment for large renal stones, but perioperative bleeding and transfusion remain important concerns. Tranexamic acid (TXA) may reduce bleeding by inhibiting fibrinolysis. This study evaluated the effect of prophylactic intravenous TXA on hemoglobin decline and blood loss during PCNL.

Materials and Methods: This single-blind randomized controlled trial included 36 adults undergoing PCNL at the Institute of Kidney Diseases, Peshawar from May 2026 to August 2026. Eighteen patients received 1 g intravenous TXA at induction and 18 received placebo. Preoperative and 24-hour postoperative hemoglobin, hemoglobin decline, intraoperative blood loss, procedure duration, and transfusion requirement were recorded. Continuous variables were compared with independent-samples t tests and transfusion frequency with Fisher's exact test; $p<0.05$ was considered significant.

Results: Baseline characteristics were comparable. Mean hemoglobin decline was 1.39 ± 0.11 g/dL in the TXA group versus 1.85 ± 0.13 g/dL in controls ($p<0.001$). Mean blood loss was 259.17 ± 86.93 mL versus 355.00 ± 106.45 mL, respectively ($p=0.006$). Postoperative hemoglobin was 11.91 ± 1.00 versus 11.26 ± 0.98 g/dL ($p=0.055$). No TXA-treated patient required transfusion compared with 5 (27.8%) controls ($p=0.045$, Fisher's exact test).

Conclusion: In this 36-patient randomized trial, prophylactic TXA was associated with significantly lower hemoglobin decline and intraoperative blood loss during PCNL. The observed reduction in transfusion requirement was not statistically definitive despite all transfusions occurring in the control group.

Keywords: tranexamic acid; percutaneous nephrolithotomy; PCNL; blood loss; hemoglobin; blood transfusion; renal calculi.

INTRODUCTION

Urolithiasis is a common clinical problem with substantial recurrence, and renal calculi frequently require intervention when they are large, complex, or unsuitable for less invasive treatment. The supplied study synopsis describes PCNL as an established minimally invasive treatment for large renal and upper ureteric stones (1,2).

Although PCNL is less invasive than open renal surgery, hemorrhage remains one of its most important complications. Bleeding may arise from renal parenchymal trauma, vascular injury during access, tract formation, surgical instrumentation, or postoperative vascular lesions. Larger stones, staghorn configuration, multiple punctures, larger access tracts, and longer procedures have been described as factors associated with greater bleeding risk (2,11-13).

Strategies to reduce bleeding include tract miniaturization, careful calyceal access, avoidance of vascular structures, and techniques that tamponade the nephrostomy tract. Pharmacological reduction of fibrinolysis provides another potential approach. Tranexamic acid (TXA) is a synthetic antifibrinolytic that competitively inhibits plasminogen activation at lysine-binding sites, thereby stabilizing fibrin clots (3,4,16,17).

Evidence from PCNL studies and systematic reviews indicates that TXA can reduce perioperative bleeding, hemoglobin decline, and/or transfusion requirements, although the magnitude of benefit varies among studies (3,5-8,18-20). More recent reports have also evaluated TXA specifically in complex renal stones undergoing PCNL (9,10). Broader surgical evidence further supports TXA as an effective antifibrinolytic blood-conservation strategy (21-23).

The present randomized controlled trial was therefore designed to determine whether prophylactic intravenous TXA reduces blood loss during PCNL. The primary outcome was postoperative hemoglobin decline, while intraoperative blood loss and transfusion requirement were also evaluated (18-20).

MATERIALS AND METHODS

This single-blind randomized controlled trial was conducted in the Department of Urology & Renal Transplant, Institute of Kidney Diseases, Peshawar from May 2026 to August 2026. The study protocol specified a sample of 36 patients, with 18 participants allocated to each treatment arm, based on a 95% confidence level and 90% study power using previously reported mean hemoglobin declines of 1.38 ± 0.42 g/dL with TXA and 1.85 ± 0.39 g/dL with placebo (10). Consecutive sampling was planned until the required sample size was reached. The protocol describes computer-generated randomization in a 1:1 ratio, allocation

concealment using sealed opaque envelopes, and a single-blind design in which the operating surgeon was unaware of treatment assignment (source protocol, pp. 4-5). The sample-size assumptions were based on previously reported PCNL TXA findings cited in the protocol (10).

Adults aged 20-60 years with renal stones larger than 20 mm, including non-staghorn and staghorn stones, and a history of stone disease for more than one month were eligible. Both sexes were included. Patients with coagulopathy, active urinary tract infection, renal structural anomalies, pelvi-ureteric junction obstruction, sepsis, pyonephrosis, bilateral renal stones, inability to undergo general anesthesia, chronic liver disease with bilirubin >2.0 mg/dL, or chronic renal failure with serum creatinine >1.5 mg/dL were excluded. Hypertension was also listed as an exclusion criterion in the study protocol (source protocol, pp. 4-5).

After consent and randomization, Group A received 1 g intravenous TXA during induction of anesthesia, whereas Group B received normal saline placebo. The study medication was supplied by the hospital. PCNL was performed by surgeons with at least one year of post-fellowship experience. Standard postoperative care included diclofenac sodium and ceftriaxone as specified in the protocol. Preoperative hemoglobin and hemoglobin 24 hours after surgery were recorded, and hemoglobin decline was calculated as preoperative hemoglobin minus postoperative hemoglobin. Intraoperative blood loss and the need for blood transfusion were also documented. The selected dose and timing are consistent with the PCNL TXA literature summarized in the protocol (5,7,10).

The final analysis was performed on the 36 individual patient records supplied for this manuscript, comprising 18 patients in each randomized group. Variables included age, sex, BMI, stone size, diabetes status, affected side, stone number/configuration, puncture site, number of punctures, procedure duration, preoperative and postoperative hemoglobin, calculated hemoglobin decline, percentage hemoglobin decline, transfusion, and estimated intraoperative blood loss. The supplied corrected dataset contained no hypertension variable, consistent with hypertension being an exclusion criterion in the protocol.

Continuous variables were summarized as mean ± standard deviation. Between-group comparisons of continuous variables were performed using independent-samples t tests, consistent with the statistical plan in the protocol. Transfusion frequency was compared using Fisher's exact test because of the small cell counts. A two-sided p value <0.05 was considered statistically significant. The analysis was conducted from the individual-level data, and no missing outcome values were present in the supplied 36 records.

The protocol states that institutional ethical approval was obtained and that informed consent was required before participation. The participant information and consent document identifies the study as a randomized controlled trial at the Institute of Kidney Diseases, Peshawar and states that ethical approval was obtained from the HMC Ethical Review Committee and that the study was registered with the Clinical Trial Unit of Khyber Medical University, Peshawar (source protocol, pp. 9-12).

RESULTS

Thirty-six patients were analyzed, with 18 participants in each group. The demographic and preoperative clinical characteristics were closely comparable between the TXA and control groups. Mean age was 42.33 ± 9.93 years in the TXA group and 43.11 ± 10.08 years in the control group (p=0.817). Mean BMI was 26.90 ± 2.82 versus 27.02 ± 2.74 kg/m² (p=0.896), and mean stone size was 34.67 ± 7.58 versus 35.56 ± 7.72 mm (p=0.730). Preoperative hemoglobin was also similar (13.30 ± 1.09 vs 13.11 ± 1.10 g/dL; p=0.598).

Variable	TXA (n=18)	Control (n=18)	p-value
Age, years	42.33 ± 9.93	43.11 ± 10.08	0.817
BMI, kg/m²	26.90 ± 2.82	27.02 ± 2.74	0.896
Stone size, mm	34.67 ± 7.58	35.56 ± 7.72	0.730
Procedure duration, min	116.28 ± 34.17	118.56 ± 34.22	0.843
Preoperative Hb, g/dL	13.30 ± 1.09	13.11 ± 1.10	0.598

Table 1. Baseline and procedural continuous characteristics. Values are mean ± SD.

The distribution of sex, diabetes status, affected side, stone category, puncture site, and number of punctures was identical between groups. Nine patients in each group were male and nine were female. Diabetes was present in 7 patients in each group. Each group included 8 single, 5 multiple, and 5 staghorn stone cases. Puncture characteristics were likewise identical, with 7 lower-calyx, 6 middle-calyx, and 5 upper-calyx access sites in each group; 8 patients had a single puncture and 10 had multiple punctures in each arm.

Categorical variable	TXA (n=18), n (%)	Control (n=18), n (%)
Male sex	9 (50.0)	9 (50.0)
Female sex	9 (50.0)	9 (50.0)

Diabetes mellitus: Yes	7 (38.9)	7 (38.9)
Right-sided stone	9 (50.0)	9 (50.0)
Left-sided stone	9 (50.0)	9 (50.0)
Single stone	8 (44.4)	8 (44.4)
Multiple stones	5 (27.8)	5 (27.8)
Staghorn stone	5 (27.8)	5 (27.8)
Lower calyx puncture	7 (38.9)	7 (38.9)
Middle calyx puncture	6 (33.3)	6 (33.3)
Upper calyx puncture	5 (27.8)	5 (27.8)
Single puncture	8 (44.4)	8 (44.4)
Multiple punctures	10 (55.6)	10 (55.6)

Table 2. Distribution of categorical baseline and operative characteristics.

The principal hematological outcomes favored TXA. Postoperative hemoglobin was 11.91 ± 1.00 g/dL in the TXA group and 11.26 ± 0.98 g/dL in controls; this difference approached but did not reach statistical significance (p=0.055). In contrast, mean hemoglobin decline was significantly lower with TXA: 1.39 ± 0.11 g/dL versus 1.85 ± 0.13 g/dL (p<0.001). The corresponding percentage decline was 10.44 ± 0.40% versus 14.14 ± 0.45%.

Outcome	**TXA (n=18)**	**Control (n=18)**	**p-value**
Postoperative Hb, g/dL	11.91 ± 1.00	11.26 ± 0.98	0.055
Hb drop, g/dL	1.39 ± 0.11	1.85 ± 0.13	<0.001
Hb drop, %	10.44 ± 0.40	14.14 ± 0.45	<0.001
Blood loss, mL	259.17 ± 86.93	355.00 ± 106.45	0.006

Table 3. Hematological and blood-loss outcomes. Values are mean ± SD.

Mean intraoperative blood loss was 259.17 ± 86.93 mL with TXA compared with 355.00 ± 106.45 mL in the control group, an absolute between-group difference of 95.83 mL (p=0.006). Five control patients (27.8%) received transfusion compared with none in the TXA group. Fisher's exact test produced p=0.045; although this meets the prespecified 0.05 threshold, the small sample and zero events in one arm warrant cautious interpretation.

Measure	TXA	Control	Statistical result
No transfusion	18 (100.0)	13 (72.2)	—
Transfusion required	0 (0.0)	5 (27.8)	0.045†
Mean Hb-drop difference (TXA − control)	−0.46 g/dL	—	95% CI −0.54 to −0.38
Mean blood-loss difference (TXA − control)	−95.83 mL	—	95% CI −161.76 to −29.90

Table 4. Between-group differences in principal outcomes. †Fisher's exact test.

DISCUSSION

This randomized controlled trial found that administration of 1 g intravenous TXA at induction was associated with a significantly smaller postoperative hemoglobin decline and lower intraoperative blood loss during PCNL. The mean Hb decline was 1.39 g/dL with TXA compared with 1.85 g/dL with placebo, while estimated blood loss was approximately 96 mL lower in the TXA arm. These findings are directionally consistent with randomized and systematic-review evidence reporting reductions in blood loss or hemoglobin decline with TXA during PCNL (14-18).

The magnitude of hemoglobin preservation is clinically relevant in the context of PCNL because bleeding can increase the need for transfusion and may complicate postoperative recovery. The mechanism is biologically plausible: TXA competitively inhibits activation of plasminogen to plasmin and consequently reduces fibrin degradation, allowing formed clots to remain more stable (16-18,21). In a procedure involving renal parenchymal access and tract formation, stabilization of clot formation may reduce ongoing bleeding from the access tract and injured renal tissue (11-13).

The present findings are consistent with the PCNL-specific literature summarized in the protocol. Previous randomized and systematic-review evidence has reported reductions in blood loss, hemoglobin decline, or transfusion requirements with TXA during PCNL (14-18). The direction of effect is also compatible with broader surgical evidence demonstrating reduced perioperative bleeding with antifibrinolytic therapy (18,21-24). Differences in TXA dose, timing, stone complexity, operative technique, and outcome measurement can nevertheless influence the observed effect size.

The lack of a statistically significant difference in postoperative hemoglobin deserves consideration. Although postoperative hemoglobin was

numerically higher with TXA (11.91 vs 11.26 g/dL), the p value was 0.055. The stronger separation in calculated hemoglobin decline is likely more directly informative for the study question because it incorporates each participant's preoperative hemoglobin. Similar Hb-drop outcomes have been used in previous PCNL studies evaluating TXA (14-18).

The present data also showed fewer transfusions in the TXA group: no patient receiving TXA was transfused compared with five patients receiving placebo. Fisher's exact test gave p=0.045. This finding meets the conventional statistical threshold, but it should be interpreted cautiously because only 36 participants were enrolled and all transfusion events occurred in one arm. Previous PCNL trials and reviews have also examined transfusion as an important secondary outcome (14-18,25).

Baseline comparability strengthens interpretation of these findings. Age, BMI, stone size, procedure duration, and preoperative hemoglobin did not differ significantly between groups. In addition, the corrected dataset showed identical distributions of sex, diabetes, affected side, stone category, puncture site, and number of punctures. This balance reduces concern that the observed difference in blood loss was driven by an obvious imbalance in measured baseline or procedural factors. PCNL literature recognizes stone burden, access characteristics, and operative duration as relevant determinants of bleeding risk (11-15).

Stone complexity and operative access are important because staghorn stones and multiple punctures can increase bleeding risk. In this dataset, both groups contained five staghorn cases, five multiple-stone cases, and ten patients requiring multiple punctures. The equal distribution of these characteristics is particularly useful because they are clinically relevant determinants of procedural blood loss (11-15).

The findings are also consistent with the local rationale presented in the synopsis, which emphasizes the importance of preventing blood loss in settings where anemia and access to transfusion may create additional clinical challenges. Earlier PCNL literature and more recent reports have described potentially favorable effects of TXA, including reductions in hemoglobin decline and blood loss (14-20). Broader perioperative evidence likewise supports TXA as a blood-conservation intervention across surgical specialties (18,21-24).

Safety is an important component of any prophylactic antifibrinolytic strategy. Published randomized and systematic-review evidence has evaluated TXA safety across surgical settings, while PCNL-specific reviews have not identified a consistent signal of clinically important excess thromboembolic events attributable to standard perioperative TXA use (3,7,18,21-24). The present

dataset did not contain detailed postoperative thromboembolic or other adverse-event outcomes, so no independent safety conclusion can be drawn from this study.

Several limitations should be considered. First, the sample size was small and was based on the protocol's calculation for the Hb-drop outcome; therefore, the study has limited precision for uncommon outcomes such as transfusion. Second, the dataset did not include detailed postoperative adverse events, length of hospital stay, stone-free status, or longer-term thromboembolic outcomes, so no conclusion can be drawn regarding these endpoints. Third, blood loss was recorded as an operative estimate rather than by a more comprehensive quantitative method. Finally, the analysis was based on the supplied individual-level dataset, and the manuscript cannot independently verify source-record accuracy. These limitations are particularly relevant when interpreting findings from a small single-center PCNL trial (14,18,25).

Despite these limitations, the randomized design, balanced groups, standardized TXA dose, and prespecified hemoglobin outcome provide a coherent basis for the observed association between TXA administration and reduced perioperative bleeding. Larger multicenter randomized trials would be useful to determine the effect on transfusion, safety, and other patient-centered outcomes and to establish the most effective dose and timing of TXA for PCNL (14-20,24-30).

FUNDING

The participant information sheet states that study-related investigations were provided free of charge and that the study drug was covered by the hospital. No separate external funding source is specified in the supplied protocol. □filecite□turn2file0□L290-L294□

CONFLICT OF INTEREST

No conflict-of-interest statement was provided in the supplied study materials. The authors should confirm and insert the final declaration before submission.

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