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The effects of antifibrinolytic drug use in decreasing hemoglobin drop following Percutaneous Nephrolithotomy in Al-Hillah Province

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Abstract

Introduction: Objective: To assess the effectiveness and safety of tranexamic acid in lowering postoperative haemoglobin and hematocrit decline, operational time, postoperative complications, and hospitalisation in percutaneous nephrolithotomy patients.

Methods: A 40-patient Al-Hilla Teaching Hospital randomised controlled clinical trial ran from January 2020 through July 2022. All ultrasound-guided PCNL patients with renal stones were randomised into two groups. Group A consisted of 20 patients (13 males and 7 females) with a mean age of (45.05 ±12.23) years who received tranexamic acid (1gm slow intravenous infusion diluted in 100 cc normal saline over 10 minutes) on call to surgery and then (0.5 gm infusion every 8 hours for the first 24 hours postoperatively). Group B included 20 non-tranexamic acid-treated patients (9 males and 11 females) with a mean age of 42.15 ± 10.64 years. We are comparing haemoglobin and hematocrit decline, operational time, postoperative complications, and hospitalisation between two groups.

Results: Group A had a much lower postoperative haemoglobin decline than group B, 12.97 ±1.21 g/dl vs 11.82 ±1.44 (p = 0.010). Group A had a much lower postoperative hematocrit decline (39.11 ±3.95%) than group B (34.86 ±3.73%) (p = 0.001). 63.25 ±10.79 minutes against 73.50 ±16.31 minutes (p = 0.024). Group A had a significantly shorter hospital stay than group B (54.00 ±10.66 hours vs. 60.60 ±11.74 hours, p = 0.021). All patients in two groups had postoperative moderate hematuria, however group B had 4 (20.0%) instances of severe hematuria, whereas group A had just one (5%) case (p = 0.047). Four (20.0%) group B patients and one (5%) group A case required blood transfusion, a statistically significant difference (p = 0.047).

Conclusions: TXA reduces postoperative haemoglobin and hematocrit drops and blood transfusions in PCNL with minimal side effects and a shorter operational time and hospital stay.

Keywords: Percutaneous nephrolithotomy, tranexamic acid, bleeding

Introduction

The lifetime prevalence of kidney stone disease is estimated at 1% to 15%, varying according to age, gender, race, and geographic location. Around the world prevalence rates vary ranging from 7% to 13% in North America, 5% to 9% in Europe, and 1% to 5% in Asia [1]. The most recent prevalence estimate of 8.8% for the period 2007 to 2010 [2]. It has been suggested that the rise in stone incidence and prevalence seen in the United States and worldwide can be attributed in part to a rise in the detection of asymptomatic calculi through increased use of radiographic imaging, particularly computed tomography (CT) [3]. In both the European and U.S. Urological Association guidelines, percutaneous nephrolithotomy (PCNL) is the first-line therapy for patients presenting with large and complex kidney stones >2 cm [4]. Indications to perform a PCNL including the following: stone larger than 2 cm; inferior polar stone larger than 1.5cm; failed FURS for the treatment of calyceal diverticula calculi; partial or complete staghorn calculi; and some cases of ureteral calculi [5]. There are different ways to extract the stones. The stones smaller than 1 cm are usually removed immediately in one piece with a basket or grasper. Calculi larger than 1 cm require fragmentation first. Many types of lithotripters are used during a PCNL; the ballistic lithotripsy, ultrasonic lithotripsy, the combined ballistic and ultrasonic devices are significantly better for the stone clearance, Holmium: YAG laser for small residual fragments [6].

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Overall significant complications associated with PNL, including acute loss of kidney, colon injury, hydrothorax, perforation, pneumothorax, prolonged leak, sepsis, ureteral stone, and vascular injury. Perforation of the collecting system with subsequent urine extravastion [7]. Blood loss depends largely on renal availability. The best approach enters a posterior calyx at the fornix, reducing renal parenchyma travelled and major vascular damage [8]. Mild bleeding may be treated with water, hypothermia avoidance, nephrostomy tube clamping, diuretics, and hemostatic medications. Moderate bleeding requires blood transfusion and careful treatment. Super selective renal angiography is recommended for hemodynamic instability. Upper caliceal puncture, single kidney, staghorn stone, numerous punctures, and unskilled surgeon increase bleeding risk. If embolization fails, urgent open exploration with nephrectomy is required [9]. Post-discharge bleeding may occur. Postoperative pseudoaneurysm or arteriovenous fistula haemorrhage typically begins 8 days after PNL, however patients might present months later. Embolise these patients [8]. Bleeding is the most unexpected and potentially fatal of these problems. Hemolytic responses, acute lung damage, coagulopathic problems from heavy transfusion, mistransfusion, nonimmune hemolysis, and transfusion-related infections are uncommon but significant side effects of blood transfusions [10]. To prevent bleeding, antifibrinolytic agents such as tranexamic acid have been administered intravenously in various surgical procedures. Tranexamic acid is available in intravenous and oral formulations. Intravenous TXA has a reported half-life of two hours when studied in healthy volunteers [11]. Bioavailability of oral and intravenous TXA was reported to be 33%–34%. Elimination of the intravenous form of TXA is exponential with approximately 90% cumulative excretion of the drug in urine in a time span of 24 hours. Renal clearance is the major mechanism of excretion. This correlates to an increased incidence of complications of TXA with renal dysfunction. A dose reduction in both oral and intravenous formulations should be made depending on serum creatinine measurements [12, 13].

The Aim of This Study: To evaluate the efficacy and safety of the antifibrinolytic agent tranexamic acid in reducing postoperative hemoglobin and hematocrit drop, operative time, postoperative complication, and hospitalization in patients undergoing percutaneous nephrolithotomy.

Method

Randomized controlled clinical trial concluded from January 2020 to July 2022 in a Al-Hilla Teaching hospital, with 40 patients included in this study. All patients undergoing PCNL under ultrasound guidance for renal stone disease and the patients was randomized into 2 groups. Group A was 20 Patients (13 males and 7 female), with mean age of (45.05 ±12.23) years old who received tranexamic acid (1gm slow intravenous infusion diluted in 100 cc normal saline over 10 minutes) on call to surgery and then (0.5 gm infusion every 8 hours for the first 24 hours postoperatively). While Group B was 20 patients (9 males and 11 female) with the mean age of (42.15 ±10.64) years didn't received tranexamic acid. All patients underwent preoperative workup and anesthetics assessments.

Exclusion Criteria

1. Pediatric age group.
2. Patients with renal stone who need for redo PCNL.
3. Patients with renal anomaly such as pelvic kidney, horse show kidney.
4. Patients with single kidney.

5. Patients need more than single access in to the target stone.
6. Patients with Contraindications for TXA: subarachnoid hemorrhage, anticoagulant usage, abnormal liver function test, unstable cardiovascular disease, acute or chronic renal failure or any hematological disease and Patients with known hypersensitivity to the TXA.

History of bleeding tendency (bleeding after trivial trauma or tooth extraction). Drugs history which include antiplatelet, anticoagulants and non-steroidal anti-inflammatory drugs that was discontinued before planned surgery as follows: aspirin, 1 week; warfarin, 1 week; clopidogrel, 5 days, and non-steroidal anti-inflammatory drugs 3 to 5 days. History of previous intervention for renal stone such as (ESWL, flexible URS, previous PCNL, and or open pyloolithotomy). History of diabetes mellitus and hypertension.

Physical Examination

For any signs or symptoms of active or untreated UTI, blood pressure measurement, abdominal examination by inspection and palpation to exclude skin infection, previous scar, or any skeletal abnormality.

Investigations

Laboratory test which include: Complete blood count, Virology screen, blood urea, serum creatinine, coagulation profile (prothrombin time, partial prothrombin time, international normalize ratio), serum electrolyte, Urinalysis. Imaging which include: KUB, Abdominal ultrasonography, Native abdominal CT scan. Blood preparation (ABO and cross match). Anesthetics assessment for fitness of patients for general anesthesia by obtaining chest x-ray, Echocardiography (ECHO), Electrocardiography (ECG). Patients should be informing to be kept nil per month for 8 hours previous to the surgery for solid and 6 hours for the liquid. The patient should schedule an appointment for the surgery if neither the procedure nor the anesthesia were contraindicated.

Fellow up visit

After 10-14 days for all patients: History: Ask the patients about any history of sever flank pain, hematuria. Physical Examination: for any sign of active infections, abdominal examination for leak or tenderness. Investigation: Urinalysis, Radiological assessment inform of abdominal US if there is hydronephrosis or residual stone. Then we prepare the patient for DJ stent removal. Statistical analysis: Data were collected and entered into Excel 2010 and SPSS 23. Quantitative data were reported as mean, range, and standard deviation, whereas qualitative data were expressed as number and percentage (SD). The independent sample t-test compared the means of any two groups, while the chi-square test or Yates correction test assessed the association between any two categorical variables. $p < 0.05$ defined significance.

Results

General characteristics of the group A and group B are shown in table 1. There was no significant difference in mean age between groups, 45.05 ±12.23 years versus 42.15 ±10.64 years, respectively ($p = 0.429$). There was also no significant variation in the proportions of males and females between groups, 13 (65.0 %) and 7 (35.0 %) versus 9 (45.0 %) and 11 (55.0 %), respectively ($p = 0.204$). There was in addition no significant difference in the frequency of previous ESWL, diabetes mellitus and hypertension between study groups ($p > 0.05$).

Table 1: General characteristics of the study group and control group

Characteristic	Group A n = 20	Group B n = 20	P
Age (years)			
Mean ±SD	45.05 ±12.23	42.15 ±10.64	0.429 I
Range	24 -73	20 -58	NS
Gender			
Male	13 (65.0 %)	9 (45.0 %)	0.204 C
Female	7 (35.0 %)	11 (55.0 %)	NS
Previous ESWL			
Yes	3 (15.0 %)	4 (20.0 %)	1.000 Y
No	17 (85.0 %)	16 (80.0 %)	NS
Hypertension			
Yes	4 (20.0 %)	3 (15.0 %)	1.000 Y
No	16 (80.0 %)	17 (85.0 %)	NS
Diabetes mellitus			
Yes	3 (15.0 %)	2 (10.0 %)	1.000 Y
No	17 (85.0 %)	18 (90.0 %)	NS

n: number of cases; SD: standard deviation; I: independent samples t-test; C: chi-square test; Y: Yates correction; NS: not significant; ESWL: extracorporeal shock wave lithotripsy

Stone characteristics of the group A and group B are shown in table 2. There was no significant difference in mean size of stones, type of stones and side of kidney involved between groups ($p > 0.05$).

Table 2: Stone characteristics

Characteristic	Group A n = 20	Group B n = 20	P
Stone size			
Mean ±SD	35.13 ±10.44	35.90 ±8.79	0.801 I
Range	25 -55	20 -55	NS
Stone type			
Staghorn	3 (15.0 %)	4 (20.0 %)	0.677 C
Non-staghorn	17 (85.0 %)	16 (80.0 %)	NS
Side			
Right	8 (40.0 %)	7 (35.0 %)	0.744 C
Left	12 (60.0 %)	13 (65.0 %)	NS

n: number of cases; SD: standard deviation; I: independent samples t-test; C: chi-square test; Y: Yates correction; NS: not significant

At baseline, there was no significant difference in mean hemoglobin level between groups, 13.58 ± 1.23 g/dl versus 13.24 ± 1.56 g/dl, respectively ($p = 0.456$). After operation, there was no significant reduction in hemoglobin level in group A, but the reduction in case of group B was significant and in comparison the level of Hb after operation in group B was significantly lower than that of group A, 11.82 ± 1.44 g/dl versus 12.97 ± 1.21 g/dl, respectively ($p = 0.010$), as shown in figure 1. At baseline, there was no significant difference in mean PCV between group A and group B, 41.38 ± 3.79 versus 39.39 ± 4.33 %, respectively ($p = 0.120$). After operation, there was no significant reduction in PCV level in group A, but the reduction in case of group B was significant and in comparison the PCV level after operation in group B was significantly lower than that of group A, 34.86 ± 3.73 % versus 39.11 ± 3.95 %, respectively ($p = 0.010$), as

shown in figure 2.

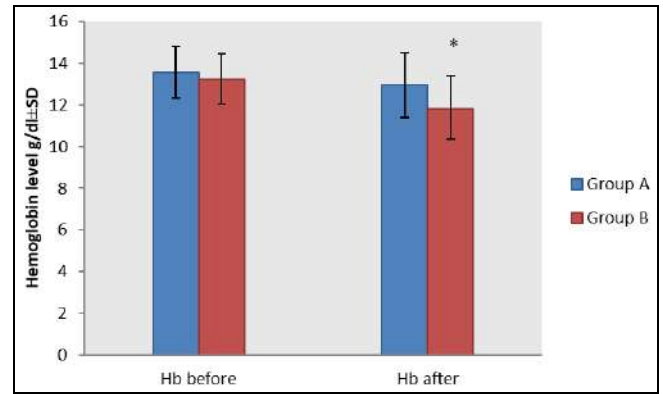


Fig 1: Comparison of hemoglobin levels between group A and group B before and after operation

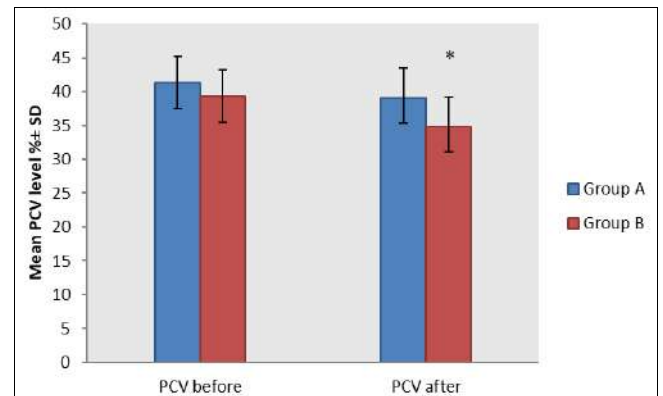


Fig 2: Comparison of PCV levels between group A and group B before and after operation

The operative time in group A was significantly less than that in group B, 63.25 ± 10.79 minutes versus 73.50 ± 16.31 minutes, respectively ($p = 0.024$), as shown in figure 3. In addition, the hospitalization time in group A was significantly less than that in group B, 54.00 ± 10.66 hours versus 60.60 ± 11.74 hours, respectively ($p = 0.021$), as shown in figure 4.

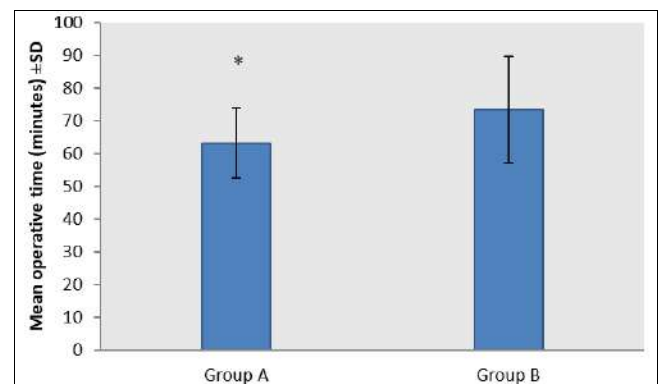


Fig 3: Comparison of mean operative time between group A and group B

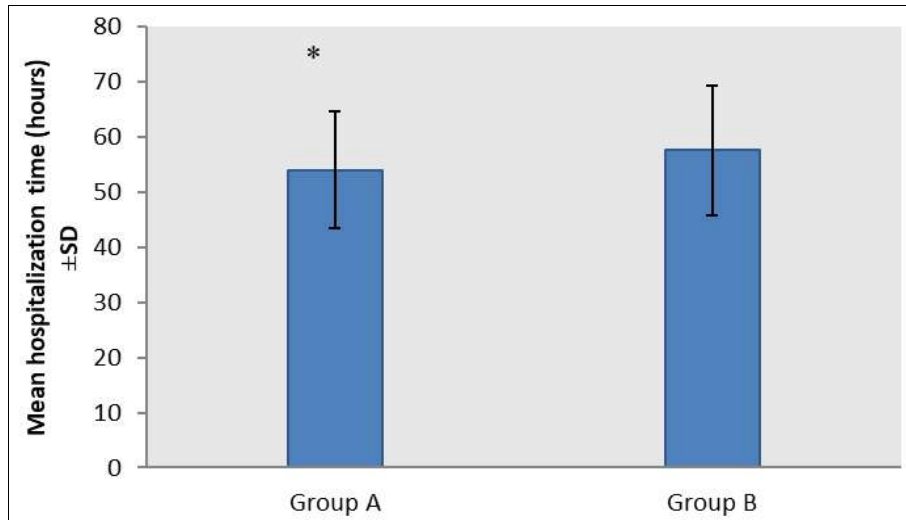


Fig 4: Comparison of mean hospitalization time between group A and group B

There was no significant difference in rate of fever between groups, 6 (30.0 %) versus 6 (30.0 %), respectively ($p = 1.000$), as shown in figure 5. Severe hematuria was significantly more frequent in group B as it was reported in 4 (20.0 %) of cases; whereas, in group A it was reported in a single case (5%) and the difference was significant ($p = 0.047$), as shown in figure 6. Need for blood transfusion was reported in 4 (20.0 %) cases of group B and in a single case (5 %) in group A and the difference was statistically significant ($p = 0.047$), as shown in figure 7.

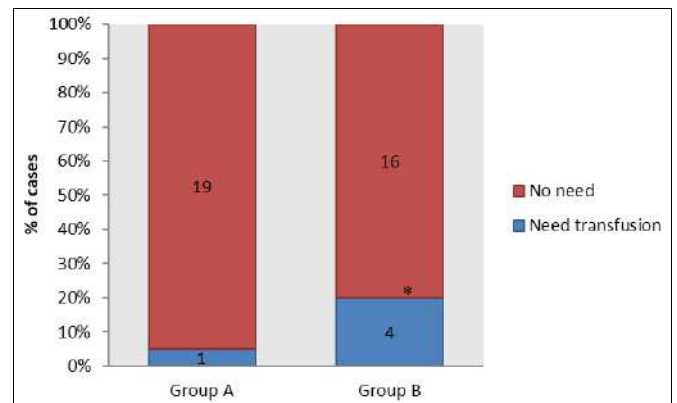


Fig 7: Comparison of rate of need for blood transfusion after operation between group A and Group B

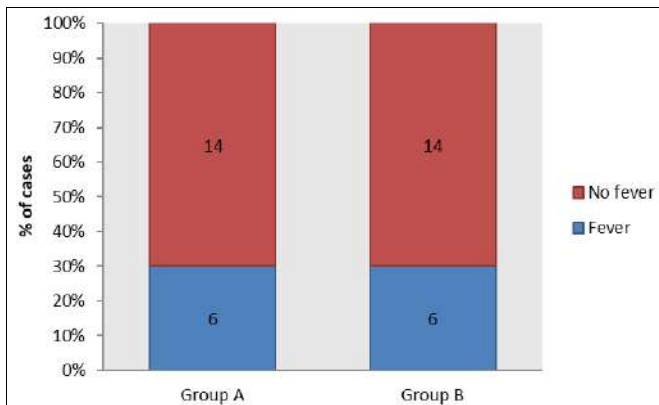


Fig 5: Comparison of rate of fever after operation between group A and Group B

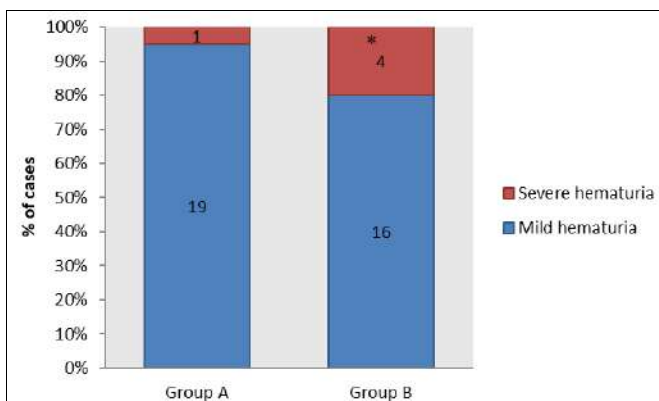


Fig 6: Comparison of rate of hematuria after operation between group A and Group B

Discussion

For large mass renal calculi, PCNL is typical. SWL and flexible ureteroscopy have lower stone removal and cost than this surgery. Stone clearance requires good renal collecting system access [14]. Intrarenal procedures including dilatation, nephroscopy, and intrarenal lithotripsy may traumatise segmental and interlobal vessels, causing substantial bleeding. 5.7% to 17.5% of PCNL patients need blood transfusions. Intractable PCNL bleeding requires angioembolization in around 1% of patients [15]. To reduce excessive bleeding non-surgically and cheaply, several changes have been studied [15]. Many studies have demonstrated TXA to be safe and effective in orthopedic, cardiac, cranial, hepatic, ear, nose, and throat, and gynecological procedures [16]. It also greatly reduced intraoperative bleeding [17]. In our investigation, patient general features and stone properties were not statistically different. Rashid *et al.* 2018 [18] also found this. Both groups had similar demographics and clinical features (p -value = 0.858). Rashid also found no significant variation in stone properties across groups with $p = 0.559$. In our investigation, group A had a significantly lower postoperative haemoglobin decline than group B, 12.97 ± 1.21 g/dl vs 11.82 ± 1.44 ($p = 0.010$). Group A had a much lower postoperative hematocrit decline than group B (39.11 ± 3.95 vs. 34.86 ± 3.73) ($p = 0.001$). TXA stabilises the clot, prevents bleeding, and lowers Hb and PCV by blocking the

conversion of plasminogen to plasmin, which is needed for fibrinolysis. According to Wang *et al.* 2020^[19], TXA may significantly minimise Hb decline, which is why it drastically lowers blood transfusions after PCNL patients. Group A had a significantly shorter operational duration than group B, 63.25 ±10.79 minutes' vs 73.50±16.31 minutes (p = 0.024). Tranexamic acid improves vision and shortens the operation. Surgeon expertise reduces operational time. PCNL operation length depends on calculus location, density, size, renal anatomy, lithotripsy efficacy, and intraoperative complications Rashid *et al.* (2018) found that the mean operational time was also considerably decreased in the tranexamic acid group (48.40 ± 17.95 vs 62.40 ± 15.487 minutes, P = 0.0005)^[18]. We also identified a significant reduction in hospitalisation duration in group A against group B, 54.00 ±10.66 hours versus 60.60 ±11.74 hours, respectively (p = 0.021), due to decreased postoperative hematuria, which accelerated the removal of nephrostomy and foley catheters and discharge of patients. Iskakov *et al.* 2016^[20] found that postoperative PCNL patients stayed in the hospital until external drainage was removed and post-surgery problems were resolved. PCNL patients get 32.7% postoperative fever. Sepsis is 0.97%–4.7%^[21] we found no significant difference in postoperative fever between group A and B (6 (30.0%) versus 6 (30.0%), respectively (p = 1.000), while in Kumar^[15] study fever developed in 14 (14%) patients in the tranexamic acid group and 15 (15%) in the control group, Kumar attributed this to the most had infected stones, preoperative bacteriuria, prolonged operative time, or greater volume of irrigate fluid used. In our study, all patients developed postoperative mild hematuria, but severe hematuria was significantly more common in group B, where it was reported in 4 (20%) of cases, compared to a single case (5%) in group A (p = 0.047). These patients were managed conservatively with close monitoring, fluid resuscitation, blood transfusion, and bladder wash, which lengthened their hospital stay. One patient in group B needed angioembolization for severe hematuria and recurring clot retention. According to Kumar *et al.*^[15], 2 individuals in the tranexamic acid group and 11 in the control group experienced moderate to severe hematuria. These individuals exhibited transitory blood pressure drops, repeated clot retention, and haemoglobin drops requiring blood transfusions. The need for blood transfusion was recorded in 4 (20.0%) instances of group B and in a single case (5%) of group A, and the difference was statistically significant (p = 0.047) because TXA decreased the decline in Hb, operative time, and transfusion rate in group A. PCNL requires 10% blood transfusions, according to a research^[21]. This shows that TXA reduces PCNL blood transfusions. Wang *et al.* 2020^[19] found that the control group received 4.4-fold more blood transfusions than the TXA group. TXA reduces transfusion rates from 11.5% to 2.7%. Our investigation showed that tranexamic acid caused higher nausea in group A than group B. These findings were comparable to Kumar *et al.* 2012^[15] who observed that nausea was greater in tranexamic acid group with significant P value =0.061. We did not detect any pharmacological adverse effects such allergic reactions, impaired vision, chest discomfort, abrupt shortness of breath, redness, or swelling in the arms and legs, or thromboembolic complications. Kumar *et al.* 2012 discovered our prospective randomised research and the preceding studies had no pulmonary embolism, symptomatic deep vein thrombosis, or myocardial infarction^[15].

Conclusion

In PCNL, TXA found to reduce the drop in hemoglobin and

hematocrit and then diminish the requirement for blood transfusions with a minimal side effects of drug and also lowering the operative time and hospital stay.

Conflict of Interest

Not available

Financial Support

Not available

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