Tranexamic Acid Reduces Blood Loss During Percutaneous Nephrolithotomy: A Prospective Randomized Controlled Study

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Purpose: Bleeding is a significant morbidity associated with percutaneous nephrolithotomy. This study was conducted to evaluate the safety and efficacy of the antifibrinolytic agent tranexamic acid in reducing blood loss in patients undergoing percutaneous nephrolithotomy.

Materials and Methods: A total of 200 patients undergoing percutaneous nephrolithotomy were randomized into 2 equal groups. Patients in the tranexamic acid group received 1 gm tranexamic acid at induction followed by 3 oral doses of 500 mg during 24 hours, while those in the control group did not receive tranexamic acid. The patient demographics and clinical data of the 2 groups were compared.

Results: Baseline patient demographics were similar in both groups. Mean hemoglobin decrease in the tranexamic acid group was significantly lower than that of the control group (1.39 vs 2.31 gm/dl, $p < 0.0001$). Mean operative time in the tranexamic acid group was significantly lower than that in the control group (48.3 vs 70.8 minutes, $p < 0.0001$). The stone clearance rate was similar in both groups (91% vs 82%, $p = 0.06$). The blood transfusion rate was lower in the tranexamic acid group (2% vs 11%, $p = 0.018$), as was the complication rate (33% vs 59%, $p < 0.0001$). Two patients with a solitary functioning kidney in the tranexamic acid group required ureteral stenting to relieve anuria due to clot obstruction.

Conclusions: The use of tranexamic acid in percutaneous nephrolithotomy is safe, and is associated with reduced blood loss and a lower complication rate.

Key Words: nephrostomy, percutaneous; nephrolithiasis; tranexamic acid; hemorrhage

Abbreviations and Acronyms

BMI = body mass index

PCNL = percutaneous nephrolithotomy

SWL = shock wave lithotripsy

TURP = transurethral prostate resection

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Study received institutional ethics committee approval.

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PERCUTANEOUS nephrolithotomy is the standard of care for the management of large upper urinary tract calculi.[1] PCNL has the advantages of higher stone clearance and cost-effectiveness when compared with other treatment alternatives such as SWL and flexible ureteroscopy. However, PCNL is associated with significant morbidity such as fever, urinary infection, septicemia and bleeding necessitating blood transfusion.[2] Of these complications bleeding is the most unpredictable and dreaded, and can lead to significant morbidity. Moreover blood transfusions have rare but potentially serious adverse effects including hemolytic reactions, acute lung injury, coagulopathic complications from massive transfusion, mistransfusion, nonimmune hemolysis and transfusion related infections.[3]

Tissue trauma during surgery releases tissue plasminogen activator which is a major enzyme responsible for the conversion of plasminogen to

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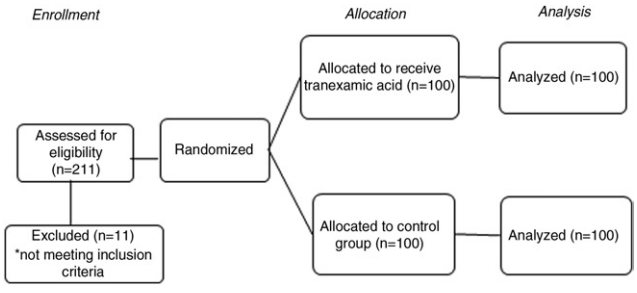
plasmin. Plasmin is the main enzyme involved in fibrinolysis. Urine and urothelium contain a high concentration of plasminogen activators that facilitate the lysis of clots. To reduce bleeding and the need for allogeneic blood transfusion, antifibrinolytic drugs such as tranexamic acid have been administered in association with a variety of surgical procedures.[4] Antifibrinolytic agents have been shown to reduce blood loss in patients with normal and exaggerated fibrinolytic responses to surgery, apparently without increasing the risk of postoperative complications.[5–8]

Tranexamic acid is a synthetic derivative of the amino acid lysine with strong affinity for 5 lysine binding sites of plasminogen. It acts as an antifibrinolytic which competitively inhibits the activation of plasminogen to plasmin, a molecule responsible for the degradation of fibrin. Fibrin is the basic framework for the formation of blood clot during hemostasis. A recent systematic review of randomized controlled trials with the use of antifibrinolytics in elective surgical patients showed that antifibrinolytics reduced the numbers needing transfusion by a third, reduced the volume needed per transfusion by 1 unit and halved the need for further surgery to control bleeding.[9] We evaluated the safety and efficacy of tranexamic acid in decreasing blood loss in PCNL, and assessed the various factors influencing blood loss.

MATERIALS AND METHODS

After institutional ethics committee approval this study was conducted from January 2011 to June 2012 at a tertiary care medical institute in North India. A total of 200 patients undergoing PCNL for renal stone disease were randomized into 2 equal groups (see figure). Written informed consent was obtained from each patient. Patients in the tranexamic acid group received 1 gm tranexamic acid at the start of the procedure followed by 3 oral doses of 500 mg at 8 hourly intervals, while those in the control group did not receive tranexamic acid. Randomization was computer generated, with allocation concealment by opaque sequentially numbered sealed envelopes. Patients with a serum creatinine greater than 1.5 mg/dl and specific contraindications to tranexamic acid, namely hypersensitivity to the drug, active intravascular clotting, acquired defective color vision and subarachnoid hemorrhage, were excluded from the study. Patient demographics and renal stone characteristics were noted preoperatively. All patients underwent ureteral catheterization followed by fluoroscopy guided puncture in the prone position, serial track dilatation up to 30Fr using fascial dilators and stone fragmentation using a pneumatic lithotripter. The use of nephrostomy tube and Double-J® stent were decided by the operating surgeon based on intraoperative parameters. The operating surgeon was blinded to the randomization and the treatment protocol was similar in both groups.



Hemoglobin and hematocrit estimated 24 hours before and 48 hours after the procedure as well as the number of units of blood transfused were used to determine the perioperative total blood loss. Intraoperative and postoperative factors analyzed included total blood loss, operative time, length of stay in hospital, duration of analgesia requirement, complications of PCNL and any adverse effects of tranexamic acid. All patients underwent abdominal radiography on postoperative day 2 to check for residual stone fragments. Success was defined as complete stone clearance or the presence of residual fragments smaller than 4 mm. Patients were followed clinically and with ultrasonography for a minimum of 1 month after removal of the ureteral catheter or Double-J stent.

The primary study end point was evaluation of the efficacy of tranexamic acid in reducing perioperative total blood loss in patients undergoing PCNL. Secondary objectives were to assess the influence of tranexamic acid in other complications associated with PCNL, and to study the factors influencing blood loss and the safety of tranexamic acid in PCNL. The sample size was calculated to test the hypothesis that tranexamic acid provided a fivefold reduction of the 12% blood transfusion rate in PCNL. To detect such a difference with 80% study power and a 2-sided 5% significance level, 200 patients (100 per group) were required.

Continuous data were given as mean ± SD or median and IQR as appropriate. Normality of quantitative data was checked by Kolmogorov-Smirnov tests of normality. The Mann-Whitney U test was used for statistical analysis of skewed continuous variables and ordered categorical variables. For normally distributed data the t test was applied. For more than 2 groups 1-way ANOVA was applied. Discrete categorical data are presented as number (%). For categorical data comparisons were made using the Pearson chi-square test and Fisher's exact test as appropriate. For time related variables (2-times) the paired t test or Wilcoxon signed rank test was applied. To estimate independent predictors for blood loss multivariate regression was applied. All statistical tests were 2-sided and performed at a significance level of $\alpha = 0.05$. All analyses were conducted using SPSS® for Windows (version 15.0).

RESULTS

Baseline patient demographics and clinical characteristics were similar in both groups (table 1). The mean estimated total blood loss in the tranexamic