International Journal of Hospital Research 2022, 11(3)
http://ijhr.iums.ac.ir
Research Article

Investigation the effectiveness of Transamin on percutaneous nephrolithotomy surgery

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Abstract
Background and Objective: Percutaneous nephrolithotomy surgery (PCNL) is a common surgery method treatment of staghorn renal stones; however, it may be associated with multiple complications such as bleeding. In our clinical trial study, we investigated the effect of intravenous administration of transamin on reducing bleeding in patients undergoing PCNL surgery.
Methods: we started a clinical trial study. A total of 64patients with staghorn renal stone who was admitted to urological unit at Baqiyatallah Hospital for PCNL procedure from 2020 to 2021. Patients were randomly divided into two groups of cases (n=32) and controls (n=32).Patients in case group received intravenous injection of transamin (500 mg) during surgery and then up to 3 doses of 500 mg every 8 hours. After PCNL procedure, parameters such as Hb changes, Hb drop, surgery duration, and hospitalization duration were evaluated and compared between two groups.
Results: 36 patients (56.25%) were male and 28patients (43.75%) were female. There was no significant difference in the mean of age, weight, and the frequency of sex between two groups. No significant difference was observed in the mean of stone size between controls and cases (3.5 ± 0.78 cm vs.3.45 ± 0.87 cm; p=0.69).Patients in the case group revealed lower Hb drop compared to those in control group (0.82 ± 0.4g/dl vs. 2.51 ± 1.03g/dl; p<0.001).The mean of hospitalization time in control group was significantly higher than case group (3.25 ± 0.43 days vs. 3.03 ± 0.17 days; p=0.011).The mean of surgery time was higher in controls than cases (43.12 ± 3.96 min vs. 40.78 ± 3.38 min; p=0.014).
Conclusion: The intravenous injection of tranexamic acid not only decreases Hb drop, but also reduces the hospitalization and PCNL surgery times in patients with staghorn stones without serious side effects.
Keywords: Kidney stones, percutaneous nephrolithotomy, hemoglobin

Background and Objective

Kidney stones, also known as renal calculi, nephrolithiasis or urolithiasis, are defined as accumulations of hard minerals and small acidic salts inside the kidneys[1].The lifetime risk of developing kidney stones is about 1-15%, depending on age, sex, race and geographical area[2]. The prevalence of kidney stones in the United States is estimated at 10-15%. The incidence of urolithiasis reaches its peak in population aged over 40-60 years. Its incidence is more than 2-3 times higher in men than women[2]. Kidney stones form when too much minerals accumulate in urine and create crystals[3].Although kidney stones are heterogeneous, they can be divided into multiple groups. Calcium stones such as calcium oxalate stone and calcium phosphate are the most common type of kidney stones. Uric acid, struvite, and cystine are the other common types of kidney stones. They are usually asymptomatic at early stages, but they can develop symptoms such as severe lower back pain, lower abdominal pain, groin pain, painful urination, and hematuria when the stones accumulate around the kidney or inside the bladder. Nausea, vomiting, fever, and chills are the other kidney stone symptoms[2].

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Staghorn renal stones are large branching kidney stones that fill the renal pelvis and at least one renal calyx[4].They are mixed stones, composed of calcium carbonate apatite and struvite. Staghorn renal stones may be associated with serious complications such as azotemia, perinephric abscess, sepsis, hydropyonephrosis, and pyelonephritis[4]. Furthermore, they may destroy the kidney and cause the death of the patient. Given the morbidity and potential mortality of staghorn stones, early diagnosis and prompt treatment of the disease is mandatory. In the past, anatrophic nephrolithotomy was considered the standard treatment for these patients. However, rapid advances in endourological procedures and extracorporeal shock wave lithotripsy (ESWL) technology have led to changes in the treatment of staghorn stones. Currently, open surgery, percutaneous nephrolithotomy (PCNL), ESWL, and a combination of PCNL and ESWL are reasonable alternatives procedures for the treatment of staghorn stones[5].The choice of treatment depends on several factors such as the stone size and location, type of stones, and medical condition of patients (e.g. diabetes, pregnancy, solitary kidney, etc.), upper urinary tract anatomy, physical conditions, patient financial status and patient's preference[6].Surgeon experience, availability of facilities and equipment and ethical and legal issues are the other determining factors for treatment. PCNL is performed for large and complex stones that are not treated with other minimally invasive methods. This procedure seems to be the gold standard for staghorn stones[7-9]. Puppo *et al*., Puppo et al[10] showed that the success rate of PCNL for treatment of staghorn stones was 70%. Many attempts have been focused to enhance the efficacy and safety of current producers for efficient removal of stones with minimal complications. In this research, we applied transamin supplementation to improve the efficacy of PCNL for treatment of staghorn stones.

Transamin, also known as tranexamic acid, is an antifibrinolytic agent that acts by binding to plasminogen and promotes blood clotting[11]. Tranexamic acid has been applied in a wide range of surgeries such as sinus endoscopy, open heart surgery, knee replacement surgery, postpartum hemorrhage and prostate surgery to reduce blood transfusion. A single dose of 1g tranexamic acid is frequently sufficient to control bleeding without side effects[12]. Some studies reported that Tranexamic acid reduces bleeding during the removal of kidney stones[13,14]. Therefore, it appears the Transamin supplementation is useful for reducing of bleeding during PCNL procedure. Thus, this clinical trial study was designed to evaluate the effectiveness of Transamin on PCNL procedure in patients with staghorn stones.

Methods

This single blinded clinical trial study was conducted on 64 patients with staghorn renal stone who was admitted to urological unit at Baqiyatallah Hospital for PCNL procedure from 2020 to 2021. The current survey was approved by the institutional review board and ethical committee of Baqiyatallah University of Medical Sciences (IRCT20200526047576N1). Written informed consents were signed by all patients. Informed consent has been approved by the ethics committee of Baqiyatallah University. A checklist containing basic demographic and clinical data of all patients (e.g. age, sex, weight, and size of stones, blood pressures, history of kidney stones, underlying diseases, basic Hb contents, and Cr levels) was filled before the survey. The inclusion criteria were as follow: (i) age over 18 years, (ii) definitive diagnosis of staghorn renal stones, (iii) patients undergoing PCNL procedure, and (iv) signed informed

consent form. Patients who met the following criteria were excluded from the study: (i) a history of blood diseases such as thalassemia, etc., (ii) a history of using anticoagulants, and (iii) unwillingness to continue the study at any stage. The process of patients selection is summarized in figure 1.

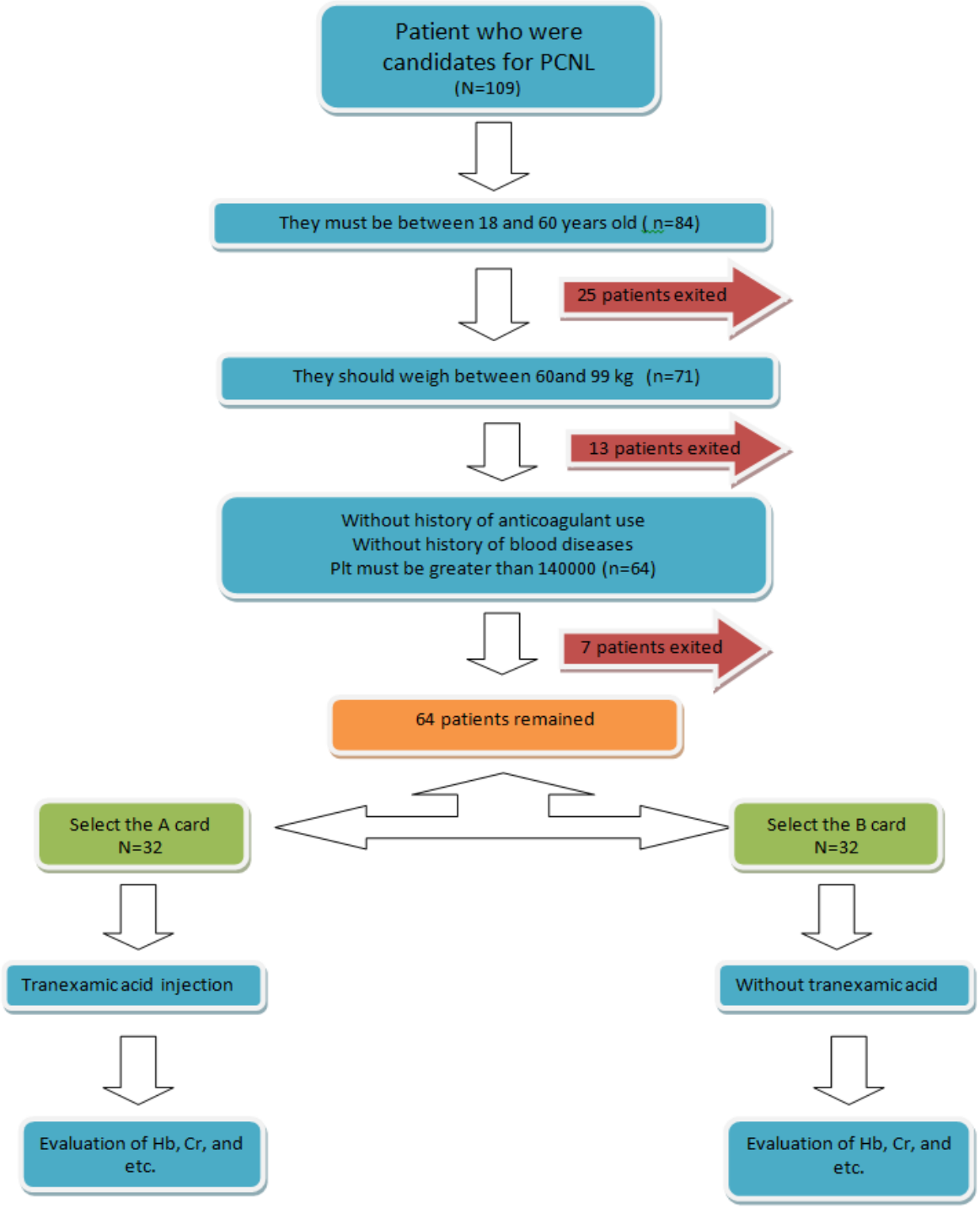

Figure 1. A diagram for the process of sample selection and study methods

Intervention and measurements

Based on similar previous studies comparing the amount of bleeding during surgeries using transamin using 95% confidence interval (CI = 95%) and significance less than 0.05, error 0.08 and 10% volume loss The sample was 32 people in the patient group and 32 people in the control group. After preliminary considerations and patients selection based

on inclusion (They must be between 18 and 60 years old and They should weigh between 60 and 99 kg) and exclusion (history of anticoagulant use, history of blood disease and Plt lower than 140000) criteria, they were randomly divided into two groups of cases (n=32) and controls (n=32).In the case group, patients received intravenous injection of transamin (500 mg)during surgery and then up to 3 doses of 500 mg every 8 hours. Patients in the control group didn't receive intravenous injection of transamin. After PCNL procedure patients in the both groups were checked. Then parameters such as Hb changes from admission time to discharge, Hb drop, surgery duration, and hospitalization duration were evaluated and compared between two groups.

Statistical analysis

All data were analyzed by SPSS software (version 19). Quantitative data were analyzed using descriptive test and presented as Mean ± SD. Crosstabs program and Chi-Square test were used to compare percentages or frequencies of data between groups. For qualitative variables, the frequency was calculated, and for quantitative variables, the mean and standard deviation were calculated in the case of normal distribution. In case of abnormal distribution, the median was compared. Comparison of mean parametric data between the two groups was compared by independent sample-t test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 64 patients with kidney stone were included in the study. 36 patients (56.25%) were male and 28patients (43.75%) were female. Comparison of the baseline demographic and clinical characteristics of the patients between two groups is shown in Table 1. There was no significant difference in the mean of age, weight, and the frequency of sex between two groups. 81.3% of patients in case group and 93.8% of controls had a history of kidney stones. No significant difference was observed in the mean of stone size between controls and cases (3.5 ± 0.78cm vs.3.45 ± 0.87 cm; p=0.69). 50% of patients in control and case groups didn't have a history of underlying diseases.

The mean of basic creatinine levels was significantly higher in cases than controls (1.12 ± 0.18mg/dL vs. 1.01 ± 0.19mg/dL; p=0.023).The mean of basic Hb was higher in controls than cases (14.51 ± 1.86g/dl vs. 13.42 ± 1.84g/dl; p=0.022).Patients in the case group revealed lower Hb drop compared to those in control group (0.82 ± 0.4g/dl vs. 2.51 ± 1.03g/dl; p<0.001). However, no significant difference was found in the mean of Hb on discharge and Hb change after two months between two groups (Table 2). The mean of hospitalization time in control group was significantly higher than case group (3.25 ± 0.43 days vs. 3.03 ± 0.17 days; p=0.011).Furthermore, the mean of surgery time was higher in controls than cases (43.12 ± 3.96 min vs. 40.78 ± 3.38 min; p=0.014). There was no significant difference in the mean of blood pressures, heart and respiratory rates between two groups (Table 3).

Table 1: The basic demographic and clinical characteristics of patients

	Control	Case	p-value
Age (year)	49.15 ± 7.23	53.46 ± 6.78	0.08
Gender			
Male	18 (56.25%)	18 (56.25%)	-
Female	14 (43.75%)	14 (43.75%)	
Weight (Kg)	78.62 ± 4.39	78.28 ± 5.04	0.84
History of kidney stone			

	Control	Case	p-value
Yes	30 (93.8%)	26 (81.3%)	0.13
No	2 (6.3%)	6 (18.8%)	
Stone size (cm)	3.5 ± 0.78	3.45 ± 0.87	0.69
Underlying diseases			
No	16 (50%)	16 (50%)	
DM	1 (3.1%)	4 (12.5%)	
HTN	9 (28.1%)	5 (15.6%)	0.37
DM + HTN	5 (15.6%)	7 (21.9%)	
Hyperthyroidism	1 (3.1%)	0	

Table 2: Comparison of the biochemical parameters between two groups

	Control	Case	p-value
Basic creatinine (mg/dL)	1.01 ±0.19	1.12 ± 0.18	0.023
Basic Hb (g/dl)	14.51 ± 1.86	13.42 ± 1.84	0.022
Hb drop (g/dl)	2.51 ± 1.03	0.82 ± 0.4	<0.001
Hb on discharge (g/dl)	11.97 ± 1.71	12.59 ± 1.84	0.16
Hb change after two months	0.9 ± 0.71	0.81 ± 0.48	0.82
Two month Hb			
No change	1 (3.1%)	1 (3.1%)	0.96
Increase	23 (71.9%)	22 (68.8%)	
Decrease	8 (25%)	9 (28.1%)	
INR	1.04 ± 0.08	1.02 ± 0.04	0.27
PTT	30.43 ± 3.78	30.21 ± 3.49	0.81
PT	13.42 ± 1.22	13.26 ± 0.74	0.53

Table 3: Comparison of the clinical parameters between two groups

	Control	Case	p-value
Hospitalization time (days)	3.25 ± 0.43	3.03 ± 0.17	0.011
Surgery duration (min)	43.12 ± 3.96	40.78 ± 3.38	0.014
Respiratory rate	15.84 ± 1.54	15.28 ± 1.22	0.11
Heart rate	74.71 ± 2.97	73.37 ± 3.73	0.11
SBP	125.31 ± 8.79	124.06 ± 10.27	0.6
DBP	89.68 ± 18.44	85.93 ± 17.47	0.4

Discussion

In this study, we evaluated the effectiveness of transamin on PCNL procedure in patients with staghorn stones. A total of 64 patients with kidney stones were included in the study and then divided into two groups of case and control. Patients in both groups were age and sex matched. Furthermore, there was no significant difference in the mean of stone size and other basic demographic data between two groups. Since treatment procedure depends on the multiple factors such as the stone size, location, and also patients' demographic and clinical data, we selected patients with similar conditions. Vincent *et al*., Vincent and Bernard[15] demonstrated that stone size, location and type are influencing factors affecting on treatment procedures. In another study, Blandy *et al*., Blandy and Singh[16] revealed that selection of appropriate method for treatment of staghorn stones depends on disease history of patients. In our study, patients in both groups had similar disease history. While 50% of patients in both groups didn't have a certain disease, the others had diabetes mellitus and/or hypertension. We found that Hb drop in patients receiving transamin was significantly lower than controls (0.82 ± 0.4 g/dl vs. 2.51 ± 1.03 g/dl). This data indicates that transamin significantly reduces Hb drop and bleeding

in patients undergoing PCNL procedure. To support this finding, there are some studies that reported positive effect of transamin administration in different surgeries. For example, Mohammadi *et al*., Mohammadi et al[13] found that administration of transamin reduced bleeding in patients undergoing PCNL procedure. In another study, Bansal *et al*., Bansal and Aditi Arora[17] showed that Hb drop in patients receiving transamin was significantly lower than those who didn't receive transamin (1.71 vs. 2.67, respectively). Kumar *et al*., (18) reported that Hb drop was significantly in controls than patients treated with transamin. These findings are consistent with the result of our study. Similarly, we found that Hb drop in patients treated with transamin was significantly lower than controls. Thus, these data indicate that transamin plays an important role in mitigating Hb drop or bleeding during PCNL procedure. Interestingly, we observed that the mean of PCNL surgery and hospitalization times were significantly lower in patients treated with transamin compared to controls. Similarly, Wang *et al*., Wang et al[19] reported that intravenous administration of transamin in patients undergoing PCNL procedure not only reduces bleeding, but also decreases the hospitalization time.

We didn't find a significant difference in the mean of blood pressures, as well as RR and HR between two groups. This finding emphasizes that intravenous injection of transamin is not associated with serious adverse effect in these patients. Furthermore, we didn't observe any side effects such as PTE, CVA, MI and ICU admission after treatment with tranexamic acid and PCNL surgery in both groups. Previous studies didn't report serious side effects caused by intravenous injection of transamin at standard dose. Hunt *et al*., Hunt[12] reported that intravenous administration of 1 g tranexamic acid isn't associated with serious adverse effects, but at higher concentration it may cause neurological damage. Therefore, these findings indicate that tranexamic acid is a safe drug for declining the bleeding and shortening the hospitalization and PCNL surgery times in patients with kidney stones.

Conclusion

In summary, findings of our study revealed that intravenous injection of tranexamic acid not only decreases Hb drop, but also reduces the hospitalization and PCNL surgery times in patients with staghorn stones without serious side effects. Therefore, intravenous injection of transamin at standard dose is efficient for treatment of staghorn stones in patients undergoing PCNL surgery.

Acknowledgments

None.

Conflict of interest:

None.

Competing interests

The authors declare no competing interests.

Authors' contributions

The authors are the same

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Please cite this article as:
Fateme Heidari, Shahin Abbaszadeh, Seyyed Mojtaba Mirzadeh. Investigation the effectiveness of Transamin on percutaneous nephrolithotomy surgery. Int J Hosp Res. 2022; 11 (3).