The Effects of Tranexamic Acid on Bleeding Control During and after Percutaneous Nephrolithotomy (PCNL): A Randomized Clinical Trial

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Purpose: Tranexamic acid is a fibrinolysis suppressor that is used for a variety of bleeding control procedures such as hematuria, surgery bleeding, and trauma caused bleeding. The advantages of using tranexamic acid are bleeding control and less need for blood transfusion.

Materials and Methods: This double blind clinical trial was conducted on 108 patients in Imam Khomeni Hospital, Urmia, Iran 2013-14. The control and intervention groups consisted of 54 randomly selected participants each. The intervention group received 1gr of intravenous tranexamic acid with initiation of surgery and 500mg orally each 8hrs afterwards up to three days. The control group received placebo capsules containing starch of the same form.

Results: The mean term of hospitalization in the intervention group was significantly shorter than that of the control group ($P < 0.001$). The difference between the two groups in terms of preoperative hemoglobin was not significant. However, the decrease in postoperative hemoglobin, intraoperative hemoglobin count in washing liquid, and hemoglobin count in the intervention group were significantly different from those of the control group ($P < 0.001$).

Conclusion: The findings showed that tranexamic acid decreased bleeding during PCNL and the need for blood transfusion. It also decreased the hospitalization time.

Keywords: tranexamic acid; bleeding; percutaneous nephrolithotomy; Iran

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is one of the minimally invasive and efficient methods to treat kidney stones. This treatment is the first-line treatment for large or complex renal pelvis stones and lower calyx stones. It is recommended for large, rigid and infectious, and obstructive upper ureteral stones when extracorporeal shock wave lithotripsy is not effective[1]. Studies have shown that the success rate of this method is more than 90%; whoever, bleeding is one of the serious and prevalent side-effects that lowers hemoglobin level down to 2.1-3.3g/dl. Although most of the bleeding cases are treatable, about 0.8% of cases have severe bleedings that need kidney arthrography[2,3]. In general, intraoperative and postoperative bleeding happens in 5.7%-23% of patients under PCNL[4]. In general, there are different methods to control intraoperative bleeding including anti-fibrinolytic materials like tranexamic acid (TXA) that suppresses plasminogen – plasmin conversion - and controls bleeding[5]. The TXA is a suppressor of fibrinolysis and it is used to treat specific types of bleeding such as hematuria, postoperative bleeding, and trauma bleeding. It helps the patients by controlling blood loss and attenuating the need for blood transfusion[6-8]. Taking into account the high prevalence of kidney stones in Iran and that there is a paucity of studies on the effects of TXA on bleeding during and after PCNL, the present study is an attempt to examine the effects of TXA on bleeding during and after PCNL.

MATERIALS AND METHODS

Study design and participants

Totally, 108 patients in Imam Khomeini Hospital in Urmia– Iran took part in this double blind clinical trial study in 2013-2014. Inclusion criteria were having kidney or upper ureteral stone (stones bigger than 2cm at pelvic or upper calices and bigger than 1.5cm of lower calices), failed ESWL, and candidate of PCNL. In addition, patients with a history of DVT, PTE, and Cr>1.5, drug allergy, cerebral arteries damage or SAH, color blindness, using OCP pills, using coagulation factors, surgery and heart valve transplantation were excluded (**Figure 1**). The intervention and control groups each included 54 individuals who were randomly allocated. The intervention group received TXA (1gr intravenously at the beginning and 5mg orally every 8hrs for

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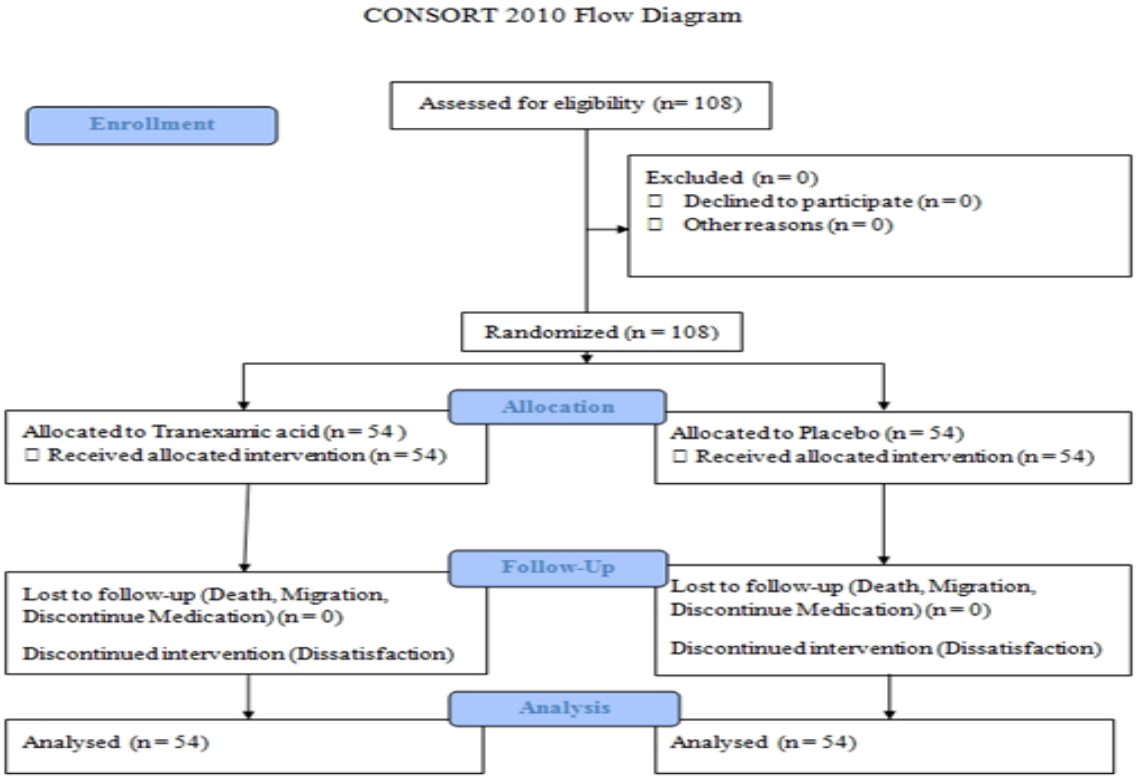

Figure 1. CONSORT flow diagram

3days) and the control group received normal saline and placebo capsules (starch) of the same form and dose. The surgeon and patients were blind to the allocation of participants and the patients signed an informed letter of consent.

A 5F ureteral catheter was affixed to the patients in lithotomic position and then PCNL surgery was performed in the prone position. All the operations were performed by one surgeon. To determine the effects of medication on intraoperative bleeding, intraoperative mean hemoglobin count in the return washing liquid (the washing liquid samples were collected in one container routinely and then 10cc of the sample was sent to a lab). Based on the total volume of the washing liquid, the volume of lost blood during the operation was calculated. For the two groups, Hb and Hct were measured 24hrs before and 48hrs after the operation to determine the effectiveness of the medicine in controlling postop-

Table 1. Comparisons of the parameters between the two groups of patients during and after percutaneous nephrolithotomy (PCNL)

Variable		Intervention N (%)	Control N (%)	*P*-value
Age (Mean ± SD)		39.5 ± 14.01 (26.2-48.7)	42.4 ± 11.21 (34.1-50.3)	.12
Sex	Male	28 (51.9)	30 (55.6)	.70
	Female	26 (48.1)	24 (44.4)	
ESWL	No	31 (57.4)	30 (55.6)	.974
	1	10 (18.5)	10 (18.5)	
	>1	13 (25.9)	14 (24.1)	
Location	Middle calyx	10 (18.5)	13 (21.4)	.492
	Upper calyx	6 (11.1)	8 (14.8)	
	Ureter	1 (1.9)	3 (5.6)	
	Lower calyx	37 (68.5)	30 (55.6)	
	Pelvis	-	-	
Kidney parenchyma	Normal	43 (79.6)	46 (85.2)	.44
	Decreased	11 (20.4)	8 (14.8)	
Transfusion	Yes	1 (1.9)	6 (11.1)	.05
	No	53 (98.1)	48 (88.9)	
Size of stone (Mean ± SD)		36.16 ± 13.71 (28.4-45.2)	35.81 ± 13.16 (27.9-44.6)	.89
The number of tracts taken (Mean ± SD)		1.22 ± 0.46 (1.08-1.36)	1.27 ± 0.45 (1.04-1.32)	.52
Time of operation (Hour) (Mean ± SD)		2.07 ± 0.51 (1.65-2.54)	2.16 ± 0.49 (1.57-2.43)	.37
Time of hospitalization (Day) (Mean ± SD)		2.88 ± 0.63 (1.95-3.24)	3.46 ± 0.81 (2.74-3.87	< 0.001
Hemoglobin Before surgery (Mean ± SD)		13.36 ± 2.08 (11.20-14.12)	12.99 ± 1.52 (11.35-14.12)	.30
Hemoglobin After surgery (Mean ± SD)		12.37 ± 1.58 (10.84-14.01)	10.72 ± 1.47 (9.47-11.03)	< 0.001
Liquid hemoglobin (Mean ± SD)		18.38 ± 7.73 (13.52-23.45)	28.22 ± 8.5 (22.34-36.54)	< 0.001
Decreased hemoglobin after surgery (Mean ± SD)		0.98 ± 0.98 (2.27 ± 0.89)		< 0.001

erative bleeding. Moreover, the number of blood units were logged and compared between the patients[9,10].
The factors under study were demographical variables, number of accesses, total blood loss, operation term, hospitalization time, period of using analgesics, and analgesic dose. Pharmaceutical side-effects in the two groups were recorded. In the case of thrombotic side-effects, the medicine would not be administered anymore and the specific treatment for the side-effect or other side-effects would be implemented.

Ethical considerations

This study was approved by the ethics committee of Urmia University of Medical Sciences (IR.UMSU.REC.1392.162) and ID of trial registry (RCT20180625040232N4).

Statistical analysis

Frequency and percentage of each one of the variables were determined in the two groups and independent qualitative and quantitative variables were analyzed using Chi square test and t-test. Data analyses were performed in Stata 14 ($P < 0.05$).

RESULTS

The effect of TXA on controlling bleeding during and after PCNL operation was examined in an intervention and a control group each with 54 members (**Figure 1**). The mean age of the participants in the intervention and control groups was 39.5 and 42.4 years respectively. The number of men in the intervention and control group was 28 (51.9%) and 30 (55.6%) respectively. Totally, 13 (24.1%) in the intervention group and 14 (25.9%) in the control group had a history of ESWL and there was no significant difference between the two groups in this regard ($P = 0.97$). The highest frequency of stones in the two groups was at the lower and mid kidney and there was no significant difference between the two groups in terms of normal and attenuated renal parenchyma ($P = 0.44$). The mean size of stones, obtained tract, and time duration of operation are listed in Table 1. Thrombotic side-effects were not reported in any of the patients in the intervention group and only 38 patients (70.4%) reported nausea.
The mean time of hospitalization in the intervention group was significantly shorter than that of the control group ($P < 0.001$). There was no significant difference between the two groups in terms of preoperative hemoglobin count. However, postoperative hemoglobin, liquid hemoglobin, and decrease in hemoglobin count in the intervention group had a significant decrease compared to the control group ($P < 0.001$) (**Table 1**). The side-effects of TXA including thrombotic side-effects (severe pain in the chest, groin, and splint, sudden headache, vision disorders, speech problem, and weakness of limbs) and non-thrombotic side-effects (dizziness, weakness, blood pressure decrease, nausea, diarrhea, and vomiting) were examined. As the results showed, none of the former side-effects were reported in the intervention. As to non-thrombotic side-effects in the intervention group, 38 patients (70.4%) reported nausea and 16 patients (29.6%) reported vomiting.

DISCUSSION

The highest frequency of stone in both groups was at the lower and mid kidney and there was no significant difference between the two groups in terms of normal and attenuated kidney parenchyma. Siddiq et al. reported that the highest frequency of stone was at the lower and pelvic areas, while there was no significant difference between the intervention and control groups. Their findings are consistent with the present findings[11].
Hospitalization time and the need for blood injection were significantly lower in the intervention group compared to the control group. In addition, preoperative hemoglobin levels in the two groups were not significantly different. On the other hand, postoperative hemoglobin, liquid hemoglobin, and hemoglobin count decline in the intervention group was significantly lower than that of the control group. Mohammadi et al. reported that the mean level of postoperative hemoglobin in TXA group was significantly higher than that in the control group (normal saline)[12]. Yao et al. studied patients with polycystic and showed that bleeding term and the volume of injected blood in TXA patients was significantly lower than those in the control group[13]. Mihai et al. showed that the need for blood injection in the intervention group was less than that in the control group and that the use of TXA in PCNL was safe, economic, and acceptable[14].
Siddiq et al. reported that hemoglobin and hematocrit levels in intervention and control groups were not significantly different and the mean level of changes in hemoglobin level in the placebo group after the operation was higher than that of the intervention group. They also showed that the need for blood injection in TXA group was significantly less than the placebo group[11].
Using TXA in PCNL operation attenuates bleeding and hemoglobin loss. Studies have shown that a decrease in intraoperative bleeding decreases the operation time duration, mortality rate, and side-effects in patients[15,16]. Yao et al. reported that creatinine serum level and eGFR in TXA group were at desirable levels[13].
The results showed that there was no thrombotic side-effect in the intervention group and non-thrombotic side-effects were observed in 38 patients (70.4%) as nausea and 16 patients (29.6%) as vomiting. Rashid et al. reported that the side-effects in the intervention group were bleeding (4%), PCS rapture (4%), and UTI and fever (16%); and in group B were bleeding (8%), PCS rapture (8%), and UTI and fever (20%). These differences were not significant[17]. As the results showed, postoperative fever is one of the most common side-effects of PCNL (32.7%) and the sepsis rate ranges from 0.97% to 4.7% (18).

CONCLUSIONS

The results showed that using TXA in PCNL surgery attenuated bleeding, the need for blood transfusion, and hospitalization time.

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CONFLICT ON INTEREST

The authors declare that there is no conflict of interest.

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