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Original Article

Effect of Tranexamic Acid on Transfusion and Blood Loss in Acetabular Fracture Surgery: A Randomized Clinical Trial

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Abstract

Background: Acetabular fracture surgery may be associated with complications such as blood loss during and after surgery, which can lead to increased morbidity and mortality. Tranexamic acid (TXA) reduces bleeding by reducing local fibrinolysis. This study aimed to evaluate the efficacy of TXA in reducing transfusion and blood loss in acetabular fracture surgery.

Methods: Overall 51 patients were randomly divided into two groups TXA and control. Preoperative and postoperative hemoglobin, intraoperative and postoperative bleeding volume, as well as deep vein thrombosis (DVT) symptoms, were recorded in both groups.

Results: Out of 51 patients, 41 (80.4%) were male, and 10 (19.6%) were female. Bleeding volume during surgery was 386.53±76.88 in the TXA group and 854.00±369.94 in the control group, indicating a significant difference (P<0.001). Also, 21 patients underwent packed cell transfusion, of whom19 were in the control group and two in the TXA group (P<0.001). The mean duration of surgery was 125.38±14.41 minutes in the TXA group and 156.40±16.74 minutes in the control group (P <0.001). Postoperative bleeding volume was reported as 105.76± 51.62 in the TXA group and 230.00± 47.87 in the control group (P<0.001). Furthermore, TXA did not increase the incidence of DVT.

Conclusion: Intravenous injection of TXA in acetabular fractures significantly reduced the need for blood transfusions, blood loss, and duration of surgery. Meanwhile, it did not increase the risk of DVT.

Keywords: Acetabular Fracture, Tranexamic acid, Transfusion.

Introduction

The prevalence of acetabular fractures is increasing among the elderly population. In the past, the treatment of acetabular fractures was absolute rest and traction, which in most cases, their non-surgical treatment had acceptable results. Unacceptable results in this type of treatment are associated with displaced weight-bearing fractures or intra-articular fractures. In the last 20 years, surgery has been regarded as a standard treatment for acetabular fractures with displacement of more than 2 mm or weight-bearing fractures [1].

Acetabular fractures, particularly associated type fractures caused by high energy trauma, cause severe blood loss [2]. Several studies showed that fractures of both columns are associated with significant bleeding [3]. Significant bleeding in transverse and anterior column fractures (T Type) has also been reported in several studies [4]. Open reduction and internal fixation (ORIF) of the fracture are associated with increased complications such as bleeding during and after surgery, which can lead to increased morbidity. Blood loss and transfusion of blood products are severe concerns for surgeons. Blood transfusions may cause complications such as infection, hemolytic reactions due to transfusions, increased mortality, and increased length of hospitalization. Tranexamic acid (TXA) reduces bleeding by reducing local fibrinolysis. It

saturates the lysine binding sites of plasminogen and inhibits plasminogen from binding to fibrin and inhibits the breakdown of clots [5]. Studies showed that TXA can be effective in reducing postoperative blood loss. The effectiveness of this drug in cardiovascular, spinal, and dental surgery has been confirmed [6]. Also, intravenous or local injection of TXA has been reported to reduce bleeding and the need for transfusions during and after surgery. Studies reported similar results in total knee and hip replacement surgery [7]. The field of orthopedics has rapidly expanded the use of TXA, with most evidence arising from the arthroplasty literature. By comparison, fracture surgery and TXA use have been relatively infrequent topics of investigation. Thus, research into TXA usage in specific orthopedic trauma surgical interventions is warranted. Notably, two recent randomized controlled trials found no benefit of routine TXA use in acetabular fracture surgery, and most studies investigated the effect of topical use of TXA. Intraoperative administration of systemic TXA would significantly reduce the risk of allogeneic blood transfusion and blood loss. Therefore, this study aimed to examine the use of TXA in patients undergoing ORIF of acetabular fractures.

Methods

This prospective clinical trial study included 51 patients who had undergone ORIF of acetabular fractures between 2019 and 2021. We conducted this study at Shohada Hospital of Tabriz, the major referral trauma center in northwestern Iran. However, due to the outbreak of the Covid-19 pandemic, the number of clients decreased drastically. Randomization sampling was done through Sealedenvelope.com. An estimated number of 55 participants was given to the server. The system created two groups (A and B) and randomly placed the patients in ten blocks (n=4 to 6 in each). Also, the order of people in each block was randomly determined by the system. A three-letter code for identification was determined for each person. In all stages of conducting data, sampling, and randomization, the data collector and the surgeon were blinded. However, the anesthesiology group was aware of the randomization for TXA drug injection. We identified 26 patients (Group A) in whom systemic injection TXA was used. This group was compared with 25 patients (Group B) who received 0.9% normal saline as a placebo (placebo was used to keep the surgeon blind during the surgery). Both control and intervention groups underwent surgery according to the standards of reference books, and there was no change in their treatment process. All patients were over 18 years old. Also, the exclusion criteria were allergy to TXA, receiving anticoagulants, a prior history of thromboembolic disease, congenital or acquired coagulopathy, renal or liver dysfunction, multiple trauma or other system involvement, or any other fracture requiring surgery, and patients with only fractures of the posterior wall or anterior wall of the acetabulum. We recorded demographic data (age, gender, body weight, height) and general health parameters (body mass index [BMI]). The preoperative hemoglobin (Hb) level was noted and a preoperative blood transfusion was performed to maintain Hb more than 10 g before surgery. After the patient was anesthetized and just before incisions, the intervention group received one dose of TXA (15 mg/kg/IV; maximum 1g), and the control group received the same dose of placebo (0.9% normal saline).

All surgeries were performed by the same surgeon. Intraoperative blood loss was measured by the collection of suction volume, the number of wet sponge gas, and blood loss in the surgery field. Surgery elongation was considered from the time of skin incision to the time of suturing the fascia. Postoperative hemoglobin and hematocrit levels were measured for two days consecutively. Drain output was recorded at 48h for estimated blood loss after surgery. All patients underwent deep vein thrombosis (DVT) prophylaxis. They received 4,000 units of subcutaneous enoxaparin daily during hospitalization. After discharge, they received 4,000 units of subcutaneous enoxaparin daily for two weeks and then 80 mg of aspirin twice daily orally for one month. The study groups were followed up after discharge for two weeks and evaluated for any evidence in favor of DVT, such as pain and asymmetric swelling of the leg. If DVT was suspected, the patient was referred to a radiologist for a Doppler ultrasound.

Data were analyzed using descriptive statistics (mean ± SD and percentage). The Mann-Whitney test was

used to compare the mean of two groups (quantitative), and the chi-square test was applied to qualitatively compare the two groups. Kolmogorov-Smirnov test was applied to test normal distribution. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 22. P-value<0.05 was considered statistically significant.

Result

In this study, out of 51 included patients (TXA group=26 vs. placebo group=25),41(80.4%)were male, and 10 (19.6%) were female. There was no significant difference in baseline characteristics (patient age, weight, height, BMI) between the two study groups (Table 1).

Table 1: Results of Demographic Data, Hb and HCT, Blood Loss volume in TXA and Control Groups

	TXA 26	Control 25	*P*-value
Age	40.42	39.52	0.96
Height	175	176	0.59
Weight	81.19	80.12	0.95
BMI	26.45	25.78	0.40
Hb before surgery	12.21	11.88	0.42
HCT before surgery	35.65	34.92	0.50
Blood loss in OR	386.53	854.00	<0.001
Operation time	125.38	156.40	<0.001
Hb after 24h of surgery	10.90	10.61	0.49
Hct after 24h of surgery	32.34	31.27	0.44
Hb after 48h of surgery	10.36	9.99	0.21
Hct after 48h of surgery	30.03	29.20	0.38
Blood loss after surgery	105.76	230.00	<0.001
EBL(Estimated Blood Loss)	492.30	1084.00	<0.001
DVT work-up in patients			0.7

Table 2 identifies the frequency of fracture typing. Fracture pattern distribution did not differ between the study groups (*P*=0.67). The average preoperative Hct and Hb counts in both groups (TXA Hct=35.65 vs. placeboHct=34.92, *P*=0.50; TXA Hb=12.21 vs. placeboHb=11.88, *P*=0.42) indicated no significant difference. Intraoperative estimated blood loss was significantly higher in the control group (854 mL vs. 386 mL) (*P*<0.001).

Table 2: Type of Fracture

		No TXA	With TXA	P-value
Type of Fracture	Transvers	1	2	0.67
	Bothcolumn	10	6	
	Postcolumn	1	4	
	Antcolumn	3	2	
	Ttypefrx	6	7	
	Posterior column with posterior wall	3	4	
	Anterior column with posterior hemitransverse	1	1	
Total		25	26	

In addition, 21 patients received a blood transfusion, of whom19 were in the control group and two were in the TXA group. Blood transfusion was significantly reduced in patients who received TXA (*P*<0.001). Among the patients who received a blood transfusion,12(57.1%) patients received one packed cell, and nine (42.9%) patients received two packed cells (*P*<0.001) (Table 3).

Table 3: Blood Transfusion in Operation Room.

		No TRX	TRX	p-value
Transfusion in OR	No	6	24	<0.001
	Yes	19	2	
Volume of Blood Transfuion	0.00	6	24	<0.001
	1.00	10	2	
	2.00	9	0	

Operative time in the control group was 156.4 min SD: 16.74 min, and 125.38 min SD14.41 min in the

TXA group (P <0.001). There was no significant difference in Hb (TXA: 10.9 vs placebo: 10.6, P=0.497) and hct (TXA: 31.27 vs placebo: 32.34, P=0.442) after 24h of surgery (Table 1). Postoperative blood loss (TXA: 105.76cc vs placebo: 230.0cc) was significantly reduced in patients who received TXA (P<0.001). Estimated blood loss (EBL) in TXA was 492.30 and in placebo was 1084.00 (P<0.001). After surgery and control of hemoglobin level, none of the patients underwent blood transfusion to correct hemoglobin level. There were no allergic reactions to TXA. All patients were treated with anticoagulants for DVT prophylaxis after surgery and followed up for two weeks. During this time, only one patient in each group had clinical symptoms of DVT. In a follow-up with Color-Doppler ultrasound, DVT was ruled out in both cases.

Discussion

One of the concerns of surgical treatment of acetabular fractures is significant bleeding during surgery which can cause anemia and lead to increased mortality and morbidity, prolonged recovery time, and the need for blood transfusions [6]. Some side effects of blood transfusion include hemolytic reactions, sepsis-associated with transfusions, and transmission of viral diseases [8-9]. Bleeding is a factor limiting the surgeon's ability to accelerate fracture stabilization, thereby increasing the duration of surgery and, as a result, alerting to the risk of prolonged anesthesia and its complications. Attempts to reduce bleeding during surgery can reduce the incidence of these complications. TXA prevents the formation of plasmin and its binding to fibrin by inhibiting plasminogen, thereby preventing the destruction of clot formation. This function reduces postoperative bleeding by performing effective homeostasis [5]. In our study, intravenous injection of TXA before surgery significantly reduced the volume of blood loss and the need for blood transfusions. In a meta-analysis of several surgeries, TXA (30-33%) reduced the need for transfusion [10]. Several studies in knee and hip arthroplasty also showed an intravenous injection of TXA significantly reduced the need for transfusion and blood loss [11-14]. In a meta-analysis by Lewis Katz et al., the efficacy of TXA in orthopedic fracture surgery was evaluated. The results showed a significant reduction in bleeding volume and the need for blood transfusion following TXA injection; also, the risk of DVT did not increase compared to the control group [15]. In a clinical trial conducted by William, the effect of TXA on blood transfusion in acetabular fractures was evaluated. There was no significant difference in transfusion rate, EBL, and DVT between the TXA and placebo groups. The author claimed that trauma surgeries, unlike elective surgery, are closely related to variables such as length of operation due to fracture complexity and variable levels of preoperative hemoglobin. Therefore, TXA which is useful in arthroplasty-related studies was not significantly effective in acetabular fracture surgery [16]; But our study indicated different results. In this study, all acetabular fractures, including posterior wall & anterior with complex fractures were evaluated together. Due to the type of fracture, the relatively low bleeding rate of these fractures, and the shorter time to obtain a reduction of this type of fracture than in other cases, this factor could lead to bias in the final results [16]. So, we excluded this type of fracture from our study. A clinical trial by Spitler reported no significant difference in reducing blood transfusion and intraoperative blood loss between TXA and control groups, while the estimated total blood loss was significantly reduced in the TXA group [17]. A retrospective study by Wadhwa showed similar results regarding the absence of significant differences between the two groups in reducing operative blood loss and the need for blood transfusions [18]. In the mentioned study, the distribution of participants into the groups was very different, there was no standard protocol for TXA injection, and the surgeon injected TXA only in patients at high risk of bleeding. In our study, the duration of surgery was significantly lower in the TXA group. This finding was in line with the results obtained in a recent study by Wadhwa[18]. On contrary, Lack and Spitler reported different results and did not observe a significant difference in this regard between the two groups [16-17]. Another retrospective study by Kashyap evaluated the effect of local injection of TXA on acetabular fractures. The results showed intraoperative and postoperative blood loss and blood transfusion were significantly lower in the TXA group, but there was no significant difference between the two groups in elongation of surgery [6]. Xie, J et al. evaluated the effect of TXA in geriatric hip fracture with hemiarthroplasty. The results showed

intraoperative bleeding, postoperative bleeding, duration of operation, and need for blood transfusion were significantly lower in the TXA group. This cohort study suggested TXA as a safe drug to reduce blood loss and the need for blood transfusion [19]. There was no significant difference in postoperative hemoglobin and hematocrit between the two groups in our study, which is inconsistent with the study by Clay et al. In our study, both the volume of bleeding and blood transfusion were significantly higher in the control group. In our study, only one participant from each group had DVT symptoms which were ruled out by a doppler sonography examination. There was no significant difference between the two groups, which is similar to the results of other studies [16-17]. Clinical evaluation was performed for the initial DVT screening due to the high cost of Doppler ultrasound. To achieve better results in this regard, we recommend that future studies consider using Doppler ultrasound for DVT screening. Unlike the effective results of TXA on reducing blood loss and transfusion in the Total Hip (THA) and Knee (TKA) which were recently reported, the results of the present study were different in the acetabular fractures. Due to the traumatic nature of this surgery and the patient's blood loss before surgery, as well as the complexity of the operation itself, the results of similar studies such as knee or hip replacement surgery could not be used directly in this procedure.

Conclusion

In this study, we found that TXA reduced blood loss and the need for blood transfusion in acetabular fracture surgery. However, due to the limited studies with different results (whether in the form of systemic or local injection of TXA), the effectiveness of this drug could not be concluded in acetabular surgery. Further studies with larger sample sizes and focusing only on complex acetabular fractures are needed to confirm these results.

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Authors' contributions

AS: Study design and study managing. AS: Intervention. MP: Intervention. AT: Manuscript preparation and submission. AT: Data Analysis. AT: Data Collection.

Conflict of interest

None.

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This study was sponsored by the Tabriz University of Medical Sciences.

Ethical consideration

Once ensuring the confidentiality of the information, patients were aware that all methods and measures used in hemorrhagic surgery are planned to save the life of the patient via maintaining the function of vital organs. The goal was to reduce the amount of blood loss during surgery and prevent complications related to blood loss, as well as the patient's need for blood transfusion. Informed written consent was obtained from all participants. The current study was approved by the ethics committee of the Tabriz University of Medical Sciences (NO: IR.TBZMED.REC.1398.946) and it was registered in the Iranian Registry of Clinical Trial (NO: IRCT20191208045664N1).

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