



Effects of topical tranexamic acid during open reduction and internal fixation of acetabular fractures: A retrospective study



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ABSTRACT

Objective: The aim of this study was to assess the effect of topical tranexamic acid on blood loss and transfusion rates in acetabular fracture surgery.

Methods: The medical records of 61 patients who underwent open reduction and internal fixation for acetabular fracture between 2012 and 2015 were retrospectively reviewed. The patients were divided into two groups: Group I consisted of 31 patients (19 men and 12 women, mean age: 52 ± 19 years) who received intraoperatively a topical tranexamic acid solution of 3 g and Group 2 consisted of 30 control patients (17 men and 13 women, mean age: 48 ± 24 years) who received only 0.9% saline solution. The groups were compared based on their intraoperative blood loss, Postoperative drain output at 24 and 48 h, and postoperative hemoglobin levels, and transfusion rates.

Results: The mean intraoperative blood loss was 410 ± 100 ml in Group 1, compared to $570 \text{ ml} \pm 160$ ml of the control group ($p < 0.05$). The postoperative drain output after 24 h was 210 ± 70 ml in Group 1 compared to 330 ± 90 ml of the control group ($p < 0.05$). The drain output at 48 h was (50 ± 20 ml) in group 1 compared to 90 ± 40 ml of the control group ($p < 0.05$). The transfusion rate was significantly low group 1 (42%) than the control group (97%). Hemoglobin drop was again significantly less in tranexamic acid group (2.1 ± 1.1) than the control group (3.2 ± 1.3). The nadir postoperative hemoglobin was higher in the Group 1 (10.4 ± 1.5) than the control group (9.2 ± 1.3).

Conclusion: Topical administration of tranexamic acid reduces intraoperative and postoperative blood loss in acetabular fracture surgery, decreasing transfusion rates.

Level of Evidence: Level III, Therapeutic Study.

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Introduction

Open reduction and internal fixation of acetabular fractures is associated with increased perioperative and postoperative blood loss with substantial morbidity. The concern of reduced blood loss and the need for blood transfusions remains a major factor in the surgeon's mind. Tranexamic acid (TXA) reduces blood loss 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.^{1–3} The use of TXA has been shown to be effective in reducing postoperative blood loss in cardiac,^{4,5} dental⁶ and spinal surgeries.⁷ Both intravenous and topical TXA have been found to be effective in decreasing perioperative and postoperative total blood loss, and the need for blood transfusions in total hip and knee arthroplasties. And numerous studies have shown its efficacy and cost-effectiveness.⁸

There are only limited studies that have evaluated the efficacy of TXA on blood transfusion in patients undergoing open reduction and internal fixation of acetabular fractures⁹ although there has been recent addition of a fairly good volume of literature on the effect of TXA in trauma fracture surgeries.^{10,11} Therefore, we designed this study to evaluate the effects of this agent in acetabular fracture surgery. We preferred topical use of TXA as it targets blood loss locally and leads to less systemic absorption with less theoretical risk of thromboembolism.

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Patients and methods

This retrospective case–control study included 61 patients who had undergone open reduction and internal fixation of their acetabular fractures between the years 2012 and 2015 by the same surgeon (author). We identified 31 patients (Group 1) in whom topical TXA was used. This group was compared with a matched control group of 30 patients (Group 2) to whom 0.9% normal saline was given. All patients in Group 1 received a topical solution of 3 g of TXA in 100 ml of normal saline intraoperatively and the patients in Group 2 received only 0.9% normal saline.

All patients exhibited a normal coagulation profile. Patients with allergy to TXA, a prior history of thromboembolic disease, congenital or acquired coagulopathy and renal or liver dysfunction, in addition to patients with polytrauma or other system involvement or any other fracture that required surgery were excluded from the study. Patients taking antiplatelet drugs were asked to stop them at least 7 days before surgery. Demographic data (age, gender) and general health parameters (body mass index [BMI], American Society of Anesthesiologists [ASA] score) of the patients were recorded. Both groups were matched for age, gender, BMI, the preoperative hemoglobin (Hb) level and ASA score (Table 1).

The preoperative Hb level of each patient was noted and preoperative blood transfusion was performed to maintain Hb more than 10 g before surgery. Intraoperative blood loss was measured by collection of suction volume and change in the weight (wet vs. dry) of the sponges. Daily postoperative complete hemogram, Hb and hematocrit levels were measured for three days consecutively and then before discharge. Similarly, daily drain output was recorded and the drains were removed when the output had tapered to 10–20 ml per 8-h shift usually by 48–72 h. Any adverse events both related to the wound and to any medical complication were noted. All patients remained in the hospital for a minimum of 14 days till suture removal. The total blood loss was calculated from the formula described by Good et al.¹² and Nadler et al.¹³

Blood management

Patients were managed with a standard blood management program, which included a strict Hb transfusion trigger of 8 g/dL and the use of colloid volume expanders for postoperative hypotension, dizziness or lightheadedness prior to consideration of a transfusion.

Surgical procedure

All patients were given both spinal and epidural anesthesia. Epidural analgesia was given for three days postoperatively with 0.125% bupivacaine. The Kocher-Langenbeck, ilioinguinal or iliofemoral approach was employed depending on the type of fracture (Table 5). In both groups, prophylactic antibiotic (cefuroxime) was given intravenously before and after surgery. Major bleeders were identified and cauterized in a standard fashion. After fracture

exposure, the wound was bathed in 40 ml of 3 g/100 ml TXA solution and kept for 5 min. Again prior to starting the wound closure, the wound was bathed in 60 ml of the same solution and kept for 5 min. Then the solution was left within the wound. Two drains were used in each case; one in the deep space and the other on the superficial plane. The drain was clamped for one hour and then released. Venous thromboembolism prophylaxis was begun on the morning after the removal of the epidural catheter with a standard subcutaneous injection of enoxaparin 40 mg/daily till suture removal. For deep vein thrombosis (DVT), the patients were clinically assessed for calf swelling, tenderness and edema of the leg. When clinically indicated, duplex ultrasonography was performed. Oral warfarin was prescribed if DVT was confirmed. No patients were lost to follow-up and data collection was completed for all participants.

Outcome measures

Intraoperative blood loss, total blood loss, postoperative drain collection at 24 and 48 h, postoperative nadir Hb, Hb drop and transfusion rates were recorded.

Statistical analysis

The SPSS v.17.0 software was employed for data analysis using the Student t-test, analysis of variance and the chi-square test. A *p* value of less than 0.05 was considered statistically significant.

Results

The mean intraoperative blood loss in Group 1 was 410 ± 100 ml compared to 570 ± 160 ml and exhibited a statistically significant difference ($p < 0.05$). The postoperative drain collection after 24 h in Group 1 (210 ± 70 ml) was significantly lower than the 330 ± 90 ml in Group 2 ($p < 0.01$). The drain collection at 48 h in Group 1 (50 ± 20 ml) compared to that of Group 2 (90 ± 40 ml) was significantly lower ($p < 0.02$). The transfusion rates significantly dropped from 97% in Group 2 to 42% in Group 1 ($p < 0.01$). Twelve patients in the TXA group required postoperative blood transfusion compared to the 25 patients in the normal saline group. The hemoglobin drop was significantly less in the TXA group (2.1 ± 1.1) than in the normal saline group (3.2 ± 1.3) ($p < 0.05$) and the postoperative nadir hemoglobin was significantly higher in the TXA group (10.4 ± 1.5) compared to that in the normal saline group (9.2 ± 1.3) ($p < 0.05$). The total blood loss, as measured by the formula of Good et al.,¹² was 988 ± 370 ml in the TXA group compared to the 1356 ± 410 ml in the control group. This difference was also statistically significant ($p < 0.05$).

Table 2 lists the primary outcomes in each group. Table 3 lists the acetabulum fracture type in each group. The complications in each group are shown in Table 4. No patient in either group had pulmonary thromboembolism while one patient in the normal saline group had DVT which was managed with oral warfarin. The

Table 1
Baseline clinical and demographic data of the study and control groups.

	TXA (Group 1, n = 31)	Normal saline (Group 2, n = 30)	<i>p</i>
Gender (M/F)	19/12	17/13	0.28
Age	52 ± 19	48 ± 24	0.45
BMI	32 ± 9	31 ± 8	0.36
Preoperative Hb (g/dL)	11.8 ± 1.5	12.1 ± 1.8	0.42
ASA score (1/2/)	18/13	20/10	0.32

BMI: body mass index, Hb: hemoglobin, ASA: American Society of Anesthesiologists.

Table 2
Primary outcomes of the study and control groups.

	TXA (Group 1, n = 31)	Normal saline (Group 2, n = 30)	p
Intraoperative blood loss (ml)	410 ± 100	570 ± 160	<0.05
Hb level at discharge (g/dL)	11.9 ± 1.4	10.4 ± 1.2	<0.01
Postoperative nadir Hb (g/dL)	10.4 ± 1.5	9.2 ± 1.3	<0.05
Hemoglobin drop (g/dL)	2.1 ± 1.1	3.2 ± 1.3	<0.05
Total blood loss (ml)	988 ± 370	1356 ± 410	<0.05
Blood transfusion rate (%)	42	97	<0.01
Postoperative drain collection at 24 h (ml)	210 ± 70	330 ± 90	<0.01
Postoperative drain collection at 48 h (ml)	50 ± 20	90 ± 40	<0.02
Time between injury and surgery (days)	5.7 ± 6.1	6.3 ± 6.7	>0.05
Intraoperative duration (min)	206 ± 42	215 ± 55	>0.05

Hb: hemoglobin.

Table 3
Distribution of fractures in each group based on the type.

Type of acetabulum fracture	TXA (Group 1, n = 31)	Normal saline (Group 2, n = 30)
Posterior wall	7	8
Posterior column	5	4
Posterior column and posterior wall	2	1
Anterior column	2	1
Transverse	4	5
Transverse with posterior wall	1	2
Anterior column posterior hemitransverse	3	3
T-type	1	1
Bicolumnar	6	5

Table 4
Distribution of complications by the groups.

	TXA (Group 1, n = 31)	Normal saline (Group 2, n = 30)
Superficial infection	6	7
Deep infection	0	2
Deep vein thrombosis	0	1
Pulmonary thromboembolism	0	0
Sciatic nerve palsy	1	2

superficial infection in each group required extended course of antibiotics as per culture sensitivity, and two patients having deep infection in the normal saline group had resolution of the infection after surgical debridement.

Discussion

Open reduction and internal fixation of acetabular fractures is associated with considerable blood loss. This predisposes to postoperative anemia that can lead to increased mortality and morbidity rates^{14,15} and delayed rehabilitation.¹⁶ Blood transfusion is not without hazards and can cause several well-recognized risks and complications including transfusion-related acute lung injury, hemolytic transfusion reactions, transfusion-associated sepsis¹⁷ and transmission of infectious agents.^{18,19} Avoidance of allogenic

Table 5
Distribution of the type of incision/approach by the groups.

Type of incision/Approach	TXA (Group 1, n = 31)	Normal saline (Group 2, n = 30)
Kocher-Langenbeck	20	18
Ilioinguinal	9	11
Iliofemoral	2	1

blood transfusions has economic benefits with reduced morbidity and shorter hospital stays.^{20–22} This study found that topical TXA significantly reduces intraoperative and total blood loss with less hemoglobin drop and decreased transfusion rates.

Tranexamic acid is an analog of the amino acid lysine.²³ Surgery and venous stasis increase the release of tissue plasminogen activator and activate the fibrinolytic system. Tissue plasminogen activator is a major enzyme responsible for the conversion of plasminogen into active plasmin. This is because generation of the tissue plasminogen activator (activating the fibrinolytic pathway) ensues in wounds.^{24,25} Since TXA works by reducing the breakdown of fibrin once formed, it is not procoagulant per se, but rather supportive of the coagulation already in progress. This makes it potentially well suited for use in reducing postoperative bleeding, where surgical hemostasis has been achieved and fibrinolytic activity needs to be suppressed to help maintain hemostasis without promoting venous thrombus formation.

In a meta-analysis of several surgeries, TXA has been shown to reduce the risk of receiving transfusions by 30–33%.²⁶ It has been used successfully in orthopedic surgery via an intravenous route, with several studies showing significant reductions in bleeding and the risk of transfusion after total hip and knee arthroplasty.^{8,27–30} However, concerns remain over the risk of thromboembolic complications after systemic administration.^{23,31} The potential advantages of topical application of TXA are direct targeting of the site of bleeding and prevention of systemic side effects. Topical administration of TXA leads to higher concentration of drug reaching the target site with minimal side effects, whereas only a small portion of intravenously administered drug reaches the target surgical site with more albeit theoretical risks of systemic side effects. Topical application leads to 70% lower systemic absorption, and may therefore be a safer alternative.³² However, systemic administration also seem to be more effective as TXA is directly loaded into the vascular system and can penetrate the large joints relatively quickly.³³ Moreover, in total knee arthroplasty, intravenous application of TXA may decrease external blood loss only, i.e. measured intraoperatively or in the drain and has minimal effect on ongoing postoperative blood loss that likely contributes to hematoma formation.³⁴ Recent literature has cited the advantage of topical TXA in decreasing intraoperative and postoperative bleeding, but these studies have been limited to hip and knee arthroplasties.^{27–32,35–37} We preferred a topical dose of 3 g per 100 ml as this dose has been found to be effective in reducing the bleeding in hip and knee arthroplasty²³ and a recent randomized control trial by Wong et al³² found that the dose of 3 g per 100 ml was more effective in reducing blood transfusion rates.

A systematic review of intraarticular application of TXA by Panteli et al found a mean reduction of 268 ml in drain collection, mean reduction of –0.94 g/dL in hemoglobin drop, lower risk of

transfusion with a relative ratio of 0.47 and no increase in venous thromboembolism.³⁶ In a recent randomized control trial by Wong et al, topical TXA was effective in reducing blood loss in total knee arthroplasty by 20–25%, hemoglobin drop was 16–17% less and the blood transfusion rates fell from 14.3% to 0%.³² In a further study by König et al, topical TXA was effective in reducing blood loss by 20–25%, hemoglobin drop was 20–27% less and the blood transfusion rates fell from 15% to 1% in total hip arthroplasty and from 10% to 0% in total knee arthroplasty.³⁵ This is similar to the results from our study as the total blood loss was less by 27% and the hemoglobin drop was less by 18%. However, the transfusion rates fell from 98% to 42% in our study. Our baseline transfusion rates are higher than those from the above studies, as these studies were on total hip and knee arthroplasties. A similar baseline transfusion rate of 94% has been reported by Seo et al.³⁸ And in a meta-analysis by Tan et al,³⁹ there was 29% rate of blood transfusion with TXA compared to 55% with placebo. This discrepancy in transfusion rates between our study and others may be due to differences in clinical threshold or due to the acetabular fracture in our group.

In our study, we kept the wound bathed in topical TXA solution for 5 min and also the suction drain was inflated after 60 min of wound closure. This is different from the study of König et al³⁵ as we think that any collection in the deep or superficial space can lead to postoperative discharge or infection that could be more detrimental.

There has been a concern that the lack of a clear benefit may be related with the fact that the exposed fracture surfaces are one of the primary sources of intraoperative bleeding during the acetabular fracture reconstruction. However, the reduction and fixation of the fracture usually lead to the control and thus containment of the intraoperative and postoperative bleeding. Tranexamic acid also decreases the blood loss from the soft tissue and other structures incised during surgery, leading to decreased intraoperative and postoperative blood loss. The effect of TXA on hemostasis is the reason for using it in spinal surgeries although its effect is less potent and inconsistent compared to those in total hip and knee replacements.^{40–43}

Since the study group in our series consisted of trauma patients instead of elective arthroplasty cases; these patients had an increased propensity of DVT due to preoperative and postoperative immobilization. Hence preoperative routine duplex ultrasound is performed to rule out DVT before initiating TXA therapy (both intravenous and topical), and postoperative duplex ultrasound to find the incidence of DVT with TXA therapy can be considered as a necessary modality in future.

Although we have not performed a cost analysis, it is worth mentioning that the study drug is affordable. The dramatic reduction in intraoperative and postoperative bleeding and the decrease in transfusion rates would definitely reduce the economic burden. This is especially the case in developing countries where the facility of autologous blood transfusion and cell salvage is virtually nonexistent and the blood bank has real constraints in catering to the demand of whole blood to all specialties in the hospital.

Our study is the first to report the decrease in intraoperative, postoperative and total blood loss, less Hb drop and decreased transfusion rates in acetabular fracture surgery with the use of TXA. The performance of the surgeries by a single surgeon eliminates the inter-surgeon variability. The results are promising and suggest that topical application of TXA may be a way to significantly reduce blood loss and the risk of exposure to allogeneic blood in open reduction and internal fixation of acetabular fractures. The small sample size, though statistically significant, and its retrospective nature may be considered as the limitations of our study. Further prospective randomized studies including large sample sizes will further contribute to the existing knowledge.

Conflicts of interest

The authors declare that they have no conflict of interest.

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