Intravenous administration of tranexamic acid to reduce blood loss during perioperative period in acetabular fracture surgery

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Abstract

Background: Literature have reported that topical use of TXA can reduce perioperative blood loss in acetabular fracture surgery. We aim to investigate the effect of intravenous administration of tranexamic acid (TXA) on perioperative blood loss during acetabular fracture surgery

Methods: From January 2016 to October 2019, 85 patients undergoing surgical treatment with intravenous TXA administration for acetabular fractures at our department were retrospectively analyzed. The patients were divided into three groups according to dosage of TXA: Single treatment group: patients receiving intravenous infusion of TXA (15 mg/kg) 20 min before surgery (n = 33), repeated treatment group: patients receiving intravenous infusion of TXA (15 mg/kg) 20 min before surgery and intravenous infusion of TXA (10 mg/kg) at 3 h (n = 26), and multiple treatment group: patients receiving intravenous infusion of TXA (15 mg/kg) 20 min before surgery and intravenous infusion of TXA (10 mg/kg) at 3 and 6 h (n = 26). Total blood loss, intraoperative blood loss, postoperative hemoglobin drop, surgery-related transfusion rate, postoperative thrombosis rate, and operation time were compared among these three groups

Results: Total blood loss, intraoperative blood loss, postoperative hemoglobin drop, and drainage volume in the single treatment group, repeated treatment group, and multiple treatment group were $932.7.0 \pm 181.8$ ml, 624.2 ± 138.7 ml, 32.2 ± 5.3 g/l, and 100.1 ± 30.1 ml; 843.4 ± 153.0 ml, 567.3 ± 144.1 ml, 27.6 ± 3.8 g/l, and 86.1 ± 42.2 ml; and 748.0 ± 145.2 ml, 521.1 ± 98.1 ml, 24.4 ± 4.4 g/l, and 64.8 ± 29.0 ml, respectively; the values were significantly different between groups ($P < 0.05$). The surgery-related blood transfusion rates in the single treatment, repeated treatment, and multiple treatment groups were 51.5% (17/33), 23.0% (6/26), 19.2% (5/26), respectively. There was no statistically significant difference in surgery-related blood transfusion rates between groups

Conclusions: Intravenous administration of TXA in acetabular fracture surgery can reduce total blood loss, intraoperative blood loss, and postoperative hemoglobin drop without increasing the risk of venous thrombosis. Multiple administrations before surgery, and at 3 h and 6 h during surgery are more effective than single and repeated administration

Background

In recent years, with the development of national transportation and construction, high-energy injuries have gradually increased, and acetabular fractures are often caused by high-energy violence [1]. The acetabulum has a complicated anatomical structure, surrounded by abundant venous plexus, and shows excessive bleeding during operation [2]. Thus, acetabulum surgeries often require a large amount of blood transfusion, causing great pressure to the clinical blood and increasing the risks associated with blood transfusion, such as infection and hemolysis [3].

Tranexamic acid (TXA) is a synthetic plasmin inhibitor that acts to stop fibrin by blocking the lysine-binding site of plasminogen molecules and acting against fibrinolysis. [3]. Several studies have reported that perioperative intravenous infusion of TXA can reduce total blood loss, intraoperative blood loss, and blood transfusion rate during joint replacement surgery, and that it does not increase the risk of venous thrombosis. Its safety has been recognized by clinical experts [4- 7]. Sandeep et al [8] have reported that topical use of TXA can reduce intraoperative and postoperative blood loss in acetabular fracture surgery. However, there have been no reports on the clinical application of TXA in the treatment of acetabular fractures. The purpose of this study was to determine whether intravenous administration of TXA can reduce total blood loss and intraoperative blood loss, whether it safe to use TXA multiple times, and whether it increases deep vein thrombosis.

Methods

Inclusion and exclusion criteria

Inclusion criteria: The inclusion criteria were as follows: 1. Preoperative HB, PLT, PT, and APTT were normal; 2. Preoperative imaging (X-ray and CT) suggested a diagnosis of acetabular fracture; and 3. Only one acetabular operation was performed, which was for a fracture.

Exclusion criteria: The exclusion criteria included the following: 1. Abnormal preoperative coagulation function and PT and APTT values; 2. Previous deep vein thrombosis (including history of intramuscular venous thrombosis), cerebral embolism, and cerebral infarction; 3. Clear TXA allergy and contraindications for TXA use; 4. High risk with regard to thrombosis, as in patients with atrial fibrillation, post-cardiac pacemakers, and stent implantations. 5. Severe liver and kidney dysfunction; and 6. Simultaneous acetabular fractures and other operations.

Clinical data

This study was retrospective in nature. From January 2016 to October 2019, 85 patients with acetabular fractures were enrolled in our study. They were divided into three groups according to different dosages of TXA. In the single treatment group, patients received intravenous infusion of TXA (15 mg/kg) 20 min before surgery ($n = 33$), in the repeated treatment group, patients received intravenous infusion of TXA (15 mg/kg) 20 min before surgery and intravenous infusion of TXA (10 mg/kg at 3 h ($n = 26$), and in multiple treatment group, patients received intravenous infusion of TXA (15 mg/kg) 20 min before surgery and intravenous infusion of TXA (10 mg/kg) at 3 and 6 h ($n = 26$); the basic data of the three patient groups, including the age, sex ratio, fracture type, and preoperative hemoglobin, are shown in Table 1. There was no significant difference in PLT, PT, and APTT between groups ($P > 0.05$). The study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University, and all selected patients signed informed consent forms.

Surgical methods and perioperative management

The surgical method used for the three groups was the same. The fracture types were divided into two categories according to the Letournel–Judet classification. Simple fractures (anterior wall, anterior column, posterior wall, posterior column, and transverse type) and complex fractures (posterior wall with posterior wall column, transverse type with posterior wall, double column, T-type, and anterior with posterior half-horizontal type). Simple and complex fractures in a single treatment group, repeated treatment group, multiple treatment group were found in 18 and 15, 14 and 12, and 13 and 13 cases, respectively. There were no significant differences in fracture types among groups ($\chi^2 = 0.133$, $P = 0.936$). All patients underwent general anesthesia, during which an anesthesiologist controlled their blood pressure to maintain it at 90/60 mmHg.

A drainage tube was routinely placed in the three groups of patients, and the drainage was recorded. The drainage tube was generally removed 24 h after surgery. No patient showed bleeding after surgery, and on the next day. According to the guidelines for the prevention of venous thromboembolism in major orthopedic surgery in China, low molecular heparin was combined with physical methods for anticoagulation. In cases where there was more drainage after surgery, the hemoglobin level progressively decreased; the hemoglobin level should be stabilized in such cases before anticoagulation. Ultrasound examination of both lower extremities was performed five days after surgery to confirm whether there was thrombosis. If there was swelling of the lower extremities accompanied by pain and to determine whether there is thrombosis, ultrasound examinations of both lower extremities were required to be performed. Pulmonary embolism was judged based on clinical manifestations.

The patient decided whether to sit up depending on the type of fracture and the degree of fixation stability during the operation. The lower extremities could perform quadriceps functional exercise and sputum pump exercise on the second day. Postoperative ultrasound could exclude thrombus formation and the extremities could be treated with lower extremity air pump.

Surgery-related blood transfusion rate: blood transfusion index: $Hb < 70$ g/L or $Hb \geq 70$ g/L, the patient develops dizziness, paleness, weakness, and other discomfort. During the operation, depending on the bleeding of the patient, it is up to the anesthesiologist and the clinician to decide whether blood transfusion is needed. Three categories of surgery-related blood transfusion rates were recorded. The blood transfusion rate in each category was calculated as number of patients requiring intraoperative blood transfusion + number of patients requiring postoperative transfusion / total number of patients.

Statistical analysis

Statistical analysis was performed using SPSS 23.0 (SPSS, USA) statistical software. The data are expressed as one-way analysis of variance for the normal distribution and Tukey method for comparison between groups. Categorical variables were analyzed via chi-square test or Fisher's exact test. $P < 0.05$ was considered statistically significant.

Results

Total and intraoperative blood loss

Total blood loss during the operation was calculated by Gross equation [9] in the three groups. Total blood loss in the single treatment group, repeated treatment group and the multiple treatment group was 932.7 ± 181.8 ml, 843.4 ± 153.0 ml, and 748.0 ± 145.2 ml, respectively. Intraoperative blood loss in these three groups was 624.2 ± 138.7 ml, 567.3 ± 144.1 ml, and 521.1 ± 98.1 ml, respectively. The values of total blood loss and intraoperative blood loss were lower in the repeated administration group and the multiple administration group than in the single administration group. Further, total blood loss and intraoperative blood loss values were lower in the multiple administration group than in the repeated administration group. The differences were statistically significant ($P < 0.05$) (see Figure 1).

Drainage and hemoglobin decline

The drainage rates in the single administration group, repeated administration group, and multiple administration group were 100.1 ± 30.1 ml, 86.1 ± 42.2 ml, and 64.2 ± 29.0 ml, respectively. The decline in hemoglobin level on the first day after operation was 32.2 ± 5.3 g/l, 27.6 ± 3.8 g/l, 24.4 ± 4.4 g/l in the three groups, respectively. The drainage rates and decline in hemoglobin level in the single treatment group were higher than those in the repeated treatment group and multiple treatment group; further, the values in the multiple dose group were higher than those in the repeated treatment group. There were statistically significant differences between groups ($P < 0.05$).

Preoperative blood transfusion rate and surgery-related transfusion rate

The damage mechanism is divided into high-energy damage (e.g., car accident and high-altitude fall injury) and low-energy damage (e.g., walking fall and falling at home) [10]. All patients in the three groups mainly showed high-energy injuries, and the damage mechanism was significantly different between groups ($P > 0.05$). Acetabular fractures were serious and resulted in a lot of bleeding. The preoperative blood transfusion rate was 75.7% (25/33) in the single treatment group and 69.2% (18/26) in the repeated treatment group. The preoperative blood transfusion rate in the multiple treatment group was 65.3% (17/26). There was no significant difference in the preoperative blood transfusion rate among the three groups ($P > 0.05$). The single treatment group showed a surgery-related blood transfusion rate of 51.5% (17/33), and the repeated treatment group showed a surgery-related blood transfusion rate of 23.0% (6/26). Further, the multiple treatment group showed a surgery-related blood transfusion rate of 19.2% (5/26). There was no significant difference in the transfusion rate among the three groups ($\chi^2 = 8.512$, $P = 0.014$).

incidence of thrombotic events

There were 6, 4, and 5 cases of intramuscular venous thrombosis in the single treatment group, repeated treatment group, and the multiple treatment group, respectively. There was no statistical difference among the three groups. No symptoms of deep venous thrombosis and pulmonary embolism were found in all three groups (Table 2).

Incision complications

Two patients in the single treatment group showed an incision redness and exudate, which healed after dressing change. One patient in the repeated treatment group had postoperative subcutaneous hematoma, which healed after drainage. No patient in the multiple treatment groups had incisions problem, and there was no statistical difference among the three groups in terms of incision complications.

Discussion

At present, a large number of studies report that TXA is safe and effective in hip and knee joint replacement, regardless of the mode of administration, intravenous, topical, or combination [11–14]. However, no study has reported on the intravenous infusion of TXA in the acetabulum in terms of its effect on blood loss during the perioperative period in these fractures. In this study, patients with acetabular fractures were treated with single, repeated, or multiple intravenous infusions. It was concluded that intravenous TXA administration can reduce total perioperative blood loss, intraoperative blood loss, and postoperative thrombotic events. There was a decrease in hemoglobin and a surgically relevant blood transfusion rate in all groups and the differences among the single treatment, repeated treatment, and multiple treatment groups were statistically significant. However, there was no statistically significant difference in the incidence of postoperative thrombotic events and incision complications among groups. Therefore, we conclude that intravenous infusion of TXA is safe and effective in reducing perioperative blood loss during acetabular fracture surgeries, and multiple doses of TXA are more effective than a single dose and repeated dose.

The effectiveness of intravenous use of TXA

TXA is a synthetic lysine analog that inhibits fibrinolytic activity by competitively inhibiting the binding of plasminogen to fibrin, thereby inhibiting fibrinolysis and reducing perioperative blood loss. Chen et al [11] conducted a meta-analysis using TXA in TKA and THA, and concluded that intravenous use of TXA can reduce perioperative blood loss, which is worthy of clinical recommendation. A multicenter retrospective study on simultaneous bilateral knee replacement surgery reported that intravenous use of TXA is safe and effective, and reduces perioperative blood loss without increasing complications [15]. Andersson et al [8] found that the half-life of aminocycline is approximately 3 h. Accordingly, in this study, we repeated the treatment, and the second and third intravenous infusions of TXA in the multiple treatment group were administered at intervals of 3 h, which can further reduce intraoperative and postoperative bleeding. It has been reported in the literature that the use of TXA in THA can reduce perioperative blood loss and hemoglobin loss in patients, and repeated application of TXA can further reduce perioperative blood loss and hemoglobin loss [16]. In the repeated treatment group and the multiple treatment group, TXA was administered again 3 h later and 3 h and 6 h later, respectively, and total blood loss, intraoperative blood loss, and postoperative hemoglobin drop were reduced. The conclusions reached are consistent with the abovementioned literature.

Safety of intravenous use of TXA

Although the literature reports that intravenous use of TXA can reduce perioperative blood loss during THA and TKA and reduce the clinical blood transfusion rate, whether TXA acts as an antifibrinolytic drug and whether TXA increases the incidence of thrombosis remain unknown and are important clinical questions that every clinician should consider. Husted et al [17] reported preoperative 10 mg/kg, followed by 1 mg/kg/h of continuous intravenous infusion of TXA for 10 h, and no increase in postoperative thrombosis-related events was observed. Another study reported [18] that intravenous infusion of aminocycline in total knee arthroplasty can reduce blood loss, but does not increase deep vein thrombosis and pulmonary embolism. Hines et al [19] reported that intravenous aminocycline can reduce the transfusion rate in total hip revision and does not increase the rate of deep vein thrombosis. In our study, patients in all three groups underwent double-limb arteriovenous color Doppler ultrasonography, and no deep vein thrombosis was observed in the three groups. There was no significant difference in the incidence of intramuscular venous thrombosis among the three groups. The conclusions are similar to those reported in the literature, suggesting that single and repeated intravenous TXA administration is safe and does not increase the incidence of thrombosis.

Advantages and disadvantages of this study

This study concluded that intravenous administration of TXA during acetabular fracture surgery can reduce the total amount of blood loss and intraoperative blood loss, and does not increase the incidence of thrombotic events. The conclusions reported in this study are more objective. First, the choice of patients undergoing acetabular fracture surgery who were included in the study had a strict case inclusion and exclusion criteria, which reduces the selection bias; Second, total perioperative blood loss was calculated by the Gross equation and the Nadler equation. The results were accurate and reliable. Third, the three groups of operations were completed by the same clinicians, which reduced the bias. However, there were some limitations of the current

study. First, the sample size of the three groups of patients was small, less than 30 cases, and larger samples randomized controlled study are required to draw a conclusion. Second, all postoperative venous thrombosis were evaluated with lower extremity venous ultrasound instead of lower extremity venography. Third, this study is retrospective in nature, the level of argument is not high. Thus, a large-sample prospective randomized study is required to be conducted in the future.

Conclusions

In summary, for patients with acetabular fractures, intravenous infusion of TXA can reduce total blood loss, intraoperative blood loss, and postoperative hemoglobin decline rate, and does not increase the risk of thrombosis. Compared with single intravenous infusion of TXA and repeated intravenous infusion of TXA, multiple administrations at 3 h and 6 h after surgery are highly recommended.

Abbreviations

TXA: tranexamic acid; HB: hemoglobin; PLT: platelet; PT: prothrombin time; APTT: activated partial thromboplastin time; CT: computed tomography scan

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University, and all selected patients signed informed consent forms.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to continuing research using this data, but are available from the corresponding author on reasonable request.

Conflict of interests

The authors declare that they have no conflict of interests.

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No funding was obtained for this study.

Authors' contributions

All authors made substantive intellectual contributions to this study to qualify as authors. ZW, ZW, HY and RZ contributed to study design, acquisition of data, analysis of data, and interpretation of results. GC and WS contributed to study coordination. XZ contributed to statistical analysis. ZW, ZW, HY and RZ contributed to manuscript preparation. All authors read and approved the final manuscript.

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Tables

Table 1 Preoperative patient data in the three groups

	Single treatment group	repeated treatment group	multiple treatment group	Test value	P value
age[year]	47.0±18.8	45.8±13.7	50.0±10.5	0.537	0.587
Preoperation HB	105.3±23.9	112.3±22.5	116.8±20.1	1.945	0.150
male/female(n)	22/11	18/8	20/6	0.770	0.680
Platelet[plt]	154.5±62.1	179.5±69.9	185.5±74.1	1.742	0.182
PT(S)	12.5±1.0	13.0±1.4	12.3±1.2	1.905	0.155
APTT(S)	29.9±6.3	29.2±5.8	29.1±4.0	0.183	0.833
preoperative blood transfusion rate[yes/no]	25/8	18/8	17/9	0.787	0.675
preoperative blood transfusion volume[ml]	581.8±439.7	646.1±467.5	607.6±471.5	0.144	0.866

Table 2: Comparison of surgery-related blood transfusion rate, incidence of thrombosis, drainage volume, and hemoglobin decline in Single treatment group, repeated treatment group, and multiple treatment group

Group	Number of cases	surgery-related transfusion case[%]	intramuscular venous thrombosis[%]	deep venous thrombosis[case]	pulmonary embolism[case]	Drainage [ml]	hemoglobin decline (g/dl)
Single treatment group	33	17[51.5]	6[18]	0	0	100.1±30.1	29.6±5.3
repeated treatment group	26	6[23.0]	4[15]	0	0	86.1± 42.2	26.8±3.1
multiple treatment group	26	5[19.2]	5[19]	0	0	64.8± 29.0	24.8±4.4
Test value	-	x ² =8.512	x ² =0.145	-	-	F=7.871	F=8.224
P value	-	P=0.014	P=0.930	-	-	P=0.001	P=0.001

Figures

Total and intraoperative blood loss

Figure 1

Total and intraoperative blood loss