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Research Article
Clinical Experiences with Tranexamic Acid for Open Reduction and Internal Fixation of Clavicle Fractures

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Abstract

Background and Objective: Open reduction and internal fixation of clavicle fractures is a common surgery and medications are considered to reduce intraoperative bleeding in this situation. This study aimed to observe the clinical effects of Tranexamic Acid (TXA) in open reduction and internal fixation of clavicle fractures. **Materials and Methods:** Forty-six patients who underwent open reduction and internal fixation of clavicle fractures were divided into two treatment groups. The observation group (n = 23) received an intravenous (IV) infusion of 0.8 mg TXA 0.5 hr before skin incision, an intraoperative topical injection of 1 mg TXA into the wound and a postoperative IV infusion of 0.8 mg TXA for 3 hrs. The control group (n = 23) did not receive any TXA treatment before, during, or after surgery. Patients in both groups were evaluated for the percentage decrease in red Blood Cell Count (RBC), Haemoglobin level (Hb) and Hematocrit (Hct) as well as the amount of total drainage within 72 hrs after surgery. All 46 patients were followed up and their complete data were collected. **Results:** Postoperatively, RBC, Hb and Hct levels in the observation group were similar to those in the control group, while the total postoperative drainage in the observation group was considerably lower than that in the control group. **Conclusion:** For open reduction and internal fixation of clavicle fractures, TXA was not significant in reducing total blood loss and haemoglobin drop but it had a significant reduction in mean postoperative total drainage and transfusion and did not increase the incidence of thrombosis and infection.

Key words: Clavicle fracture, clinical experience, open reduction, internal fixation, tranexamic acid, haemoglobin, hematocrit, intravenous

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The clavicles are the most common sites of fractures in the human body and clavicle fractures account for about 5-10% of all fractures[1]. Internal fixation of clavicle fractures achieved patients' satisfaction because of the relatively high rate of nonunion with conservative treatment[2]. In previous studies, internal fixation is an increasingly popular method for clavicle fractures treatment and various internal fixation techniques has progressed[2-6]. The clavicles are truncal bones, not extremity bones and hemostasis is not easily achieved with the use of tourniquets during the surgery for clavicle fractures. Therefore, hemostasis is the primary issue in open reduction and internal fixation of clavicle fractures and medications are generally considered to reduce intraoperative bleeding.

Antifibrinolytics can be applied to reduce blood loss in all kinds of surgeries[7]. Tranexamic acid (TXA) is a synthetic inhibitor of plasminogen activation derived from lysine and has been increasingly used in clinical application[7]. It has a high affinity to the lysine binding site of plasminogen, thereby blocking the lysine binding site and hence inhibiting the interactions between the fibrin containing the lysine residue and the plasminogen. As a result, the plasminogen loses the ability of binding to the fibrin and therefore has limited fibrinolytic activity[8,9].

Studies have shown that TXA can safely and reliably reduce wound bleeding in patients and may even reduce mortality without significant safety concerns[10-11]. However, the use of TXA should vary in various clinical settings and its safety remains to be explored[7]. One gram loading dose over 10 min followed by an infusion of 1 g over 8 hrs was suggested by a previous study[12]. In a study on total knee replacement, a single dose of IV TXA was recommended over topical TXA for safety reasons[13]. Another study showed that patient blood management and a single 20 mg kg^{-1} dose of TXA loaded with a continuous infusion of 20 mg kg^{-1} for the duration of the procedure was the best protocol to achieve minimal blood loss and that additional doses of TXA did not provide significant benefit[14].

Therefore, the usage and dosage of TXA should be considered according to the actual situation. TXA has been used clinically in other kinds of fractures, such as hip fractures[15-16], intertrochanteric fractures[17]. However, there are no reports on the use of TXA in open reduction and internal fixation of clavicle fractures. In this study, we reviewed preoperative and postoperative data of open reduction and internal fixation in patients with clavicle fractures at our hospital and observed the clinical outcomes of TXA in these patients.

MATERIALS AND METHODS

Study area: The present study was carried out at the Department of Orthopedics, the Affiliated Hospital of Shaoxing University from January, 2018-December, 2019.

Inclusion and exclusion criteria for patients selection: Fifty-eight patients who underwent open reduction and internal fixation of clavicle fractures at our hospital from January, 2018-December, 2019 were recruited. After screening according to the inclusion and exclusion criteria, 46 patients (20 males and 26 females) were finally selected (Fig. 1). Inclusion criteria: No history of infection in the affected limbs good patient compliance. Exclusion criteria and the number of excluded cases: Coagulation disorders (1 case); preoperative Hb level below 90 g L^{-1} (2 cases), cerebral haemorrhage (2 cases), thoracic bleeding (4 cases) recent history of venous thrombosis in the lower extremity (1 case) contraindications to TXA or low-molecular-weight heparin (2 cases).

All screened participants had unilateral clavicle fractures. They were further divided into the observation group (TXA treatment, n = 23, 9 males and 14 females) and the control group (n = 23, 11 males and 12 females) based on the preoperative and postoperative data. The present study was approved by the hospital ethics committee and oral informed consents were obtained from all patients.

The following information was recorded in detail for the included patients: (a) Age, gender and Body Mass Index (BMI), (b) RBC, Hb, Hct and preoperative blood transfusion and (c) Basic health status of the patient, typical co-morbidities including diabetes and hypertension.

TXA use and patient grouping: Red Blood Cell (RBC), Haemoglobin (Hb) and Hematocrit (Hct) levels (%) were recorded 72 hrs before surgery. Based on the literature review and our clinical experiences, patients in the observation group were given TXA at the following dosage: 0.8 g of TXA was added to 100 mL of 0.9% sodium chloride injection and administered by IV infusion at 0.5 hr before skin incision. After the completion of the surgery, 1.0 g of TXA was added to 20 mL of normal saline and injected locally into the wound before the skin was sutured. 3h after surgery, 0.8 g of TXA was added to 100 ml of 0.9% sodium chloride injection and

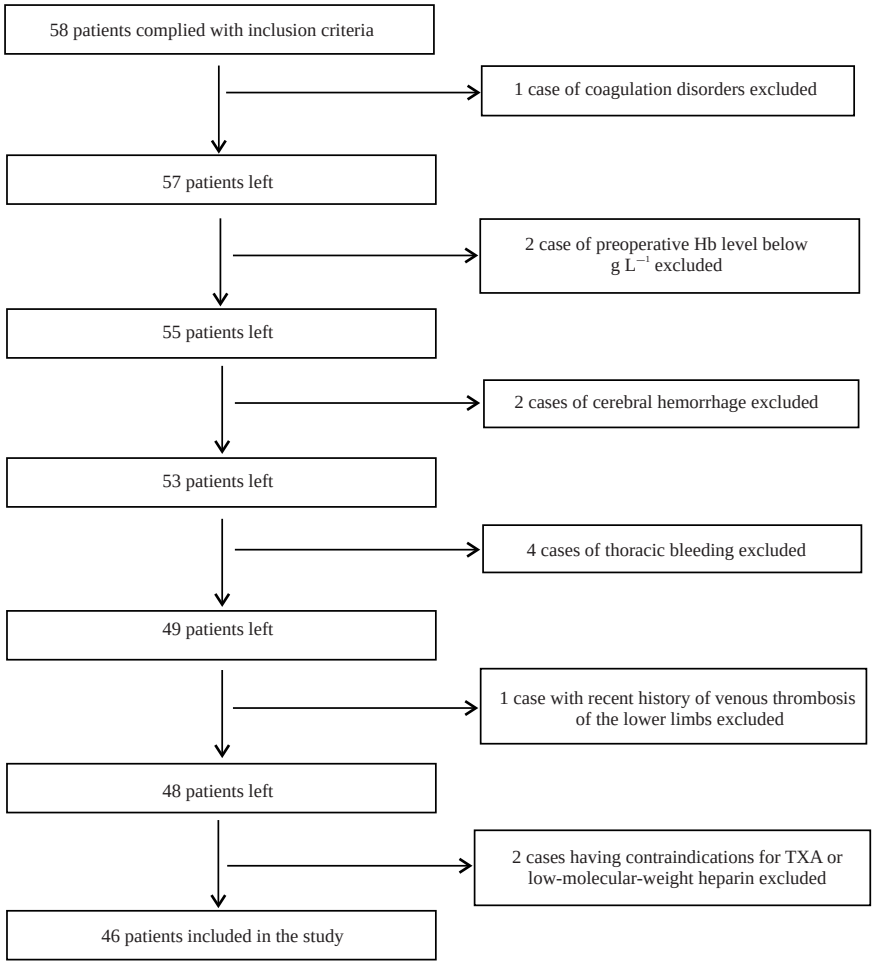

Fig. 1: Flow chart of the patients enrolled in the study

administered by IV infusion. The control group was not administered TXA preoperatively, intraoperatively, or postoperatively. all procedures in the observation and control groups were performed by equally qualified surgeons. All patients received combined intravenous-inhalational anaesthesia. The changes of RBC, Hb and Hct and the total drainage volume were evaluated on the two groups within 72 hrs after surgery. All patients received routine drainage with a drainage tube. The drains were clamped within 8 hrs postoperatively and were removed within 72 hrs postoperatively. All patients were followed up at the outpatient clinic.

Statistical analysis: The enumeration data were analyzed with the chi-square test (SPSS13.0 statistical software) and $p<0.05$ was considered to be statistically significant. Normal distribution and homogeneity of variance were assessed by the Kolmogorov-Smirnov test. Data presented as Mean±Standard deviation were assessed by ANCOVA (analysis of covariance) followed by a Student-Newman-Keuls *post hoc* test and $p<0.05$ were considered statistically significant.

RESULTS

Demographic and preoperative characteristics of the patients: Demographic and clinical characteristics of the 46 participants were observed and recorded in the postoperative period (Table 1). No significant differences were found between the two groups in terms of age, sex, BMI and preoperative blood transfusion. There were 1 diabetes and 1 hypertension patient in the observation group and 1 diabetes and 2 hypertension patient in the control group.

Outcome of blood loss: The preoperative RBC (4.33±0.53/4.29±0.48), Hb (131.57±17.50/129.13±13.61)

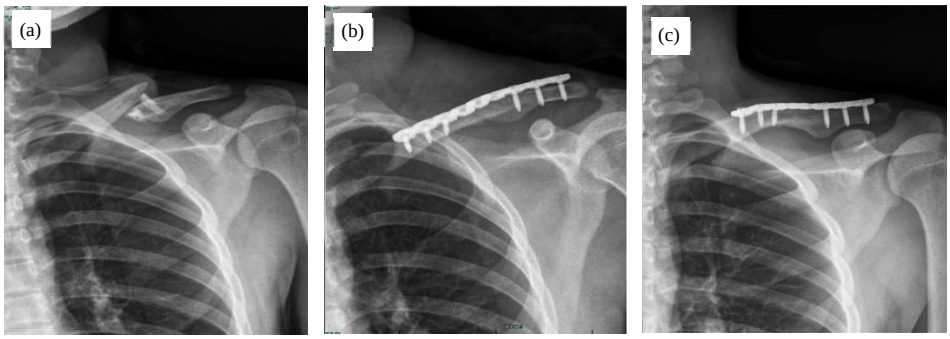

Fig. 2 (a-c): One patient's image of recovery, (a) Preoperative image of the clavicle fracture, (b) Image at 3 days postoperatively and (c) Image at 12 months postoperatively

Table 1: Demographic and clinical characteristics of the patients

Variables	Observation group	Control group	p-value
Average age (year)	50.57±14.27	57.26±12.19	0.094
Gender (male/female)	9/14	11/12	0.552
Average body mass index (kg m^{-2})	23.18±3.09	22.95±2.67	0.788
Average preoperative volume of blood Transfusion (U)	0	0	
Diabetes (n)	1	1	
Hypertension (n)	1	2	

Table 2: Comparison of the RBC, Hb and Hct levels after surgery

	Observation group		Control group			
Index	Preoperative	Postoperative	Preoperative	Postoperative	f-value	p-value
RBC (10^9)	4.33±0.53	4.15±0. 53	4.29±0.48	3.96±0.44	0.995	0.556
Hb (g L^{-1})	131.57±17.50	124.00±17.85	129.13±13.61	116.13±25.79	0.987	0.540
Hct (%)	39.38±4.71	37.67±4.79	38.87±4.03	35.81±3.86	1.797	0.194

Table 3: Comparison of postoperative drainage volume (Mean±SD, mL)

	Total drainage volume	p-value
Observation group	38.261±29.30	0.034
Control group	56.174±26.050	

Figure legends

and Hct% (39.38±4.71/38.87±4.03) data of the observation and control groups were used as the baseline to compare the postoperative RBC (4.15±0.53/3.96±0.44), Hb (124.00±17.85/116.13±25.79) and Hct (%) (37.67±4.79/35.81±3.86) data and found no statistically significant differences between these two groups for any of the three indicators (Table 2, $p>0.05$). The total postoperative drainage volume in the observation group (38.261±29.30 ml) was lower than that of the control group (56.174±26.050 mL, $p = 0.034$) (Table 3).

Postoperative complications: Only the patients with simple clavicle fractures but without serious complications were recruited. None of them had received a preoperative blood transfusion. No venous thrombosis, ischemic cerebral haemorrhage, hematoma and surgical site infection or other complications were found in either the observation or control group of patients. None of them required blood transfusion after surgery either.

Follow-up results: All 46 patients were followed up at the outpatient clinic with a high satisfaction rate and 100% follow-up rate. The follow-up period was 3-6 months, with an average of 5±1 months. No loosening or dislocation of the internal fixation occurred in all patients after surgery. There was no exudation, reddening, swelling or infection of the wounds during the follow-up period. During the follow-up phase, one patient's image showed a good recovery at one year postoperatively. The preoperative image of the clavicle fracture (Fig. 2a) showed quite a great trauma. After an operation, the bones were well connected (Fig. 2b). The image at 12 months postoperatively showed the patient recovered well with bone healing. (Fig. 2c).

DISCUSSION

Our study showed that the postoperative changes in RBC, Hb and Hct in the observation group were not significantly different from those in the control group, while the total

postoperative drainage in the observation group was considerably lower than that in the control group. Surgical drains have been used in surgery for several years to remove body fluids thereby preventing the accumulation of serous fluid and improving wound healing and help to reduce the risk of infection and seroma[18].

The half-life of IV TXA was about 3 hrs and topical TXA at hip fracture surgery and IV TXA at 3h after surgery were used in a randomized double-blind study to found that TXA reduced erythrocyte transfusion[16]. In our study, IV infusion of 0.8 mg TXA was used at 0.5 hr before skin incision, with a topical injection of 1 mg TXA into the wound during operation and an IV infusion of 0.8 mg TXA was used at 3h after surgery, considering our clinical previous experiences and published articles[12-14].

The hemostatic effect of TXA has been proven in surgeries for other bone fractures or bone replacements. TXA was found effective in reducing erythrocyte transfusion in hip fracture surgery[16]. Qi *et al.*[19], showed in a meta-analysis that IV TXA had great potential use in hip surgery on hip fractures as it could safely reduce blood loss and homologous transfusion. Total blood loss volume and transfusions were decreased under TXA administration and patient blood management in total hip replacements[14]. Zhu *et al.*[20], found that the use of TXA significantly reduced operative blood loss and total blood loss without dramatically increasing the blood transfusion rate, the need for postoperative drainage, or the risk of thromboembolism in intertrochanteric fracture surgery[20]. Intravenous administration of TXA reduced intraoperative and total blood loss significantly in intertrochanteric fracture surgery performed using PFNA, without increasing the rate of complications[17]. Although TXA is not effective in open reduction and internal fixation of clavicle fractures for TXA on reducing bleeding, TXA and drainage regimen should be recommended for reducing postoperative blood loss for open reduction and internal fixation of clavicle fractures[21].

In the study, no patients received a preoperative or postoperative blood transfusion. None of the patients was found to have postoperative complications. At the 6-month postoperative follow-up, none of the patients had loosening or dislocation of the internal fixation. The internal fixation was neither loosened nor dislocated in any patient during the follow-up time within 6 months after surgery. The patient satisfaction with TXA was higher.

Shortcomings of this study are: The sample size was small and the results may be biased. Future randomized controlled studies with larger sample sizes are needed. What's more, intravenous TXA and topical TXA were found to be feasible before and after surgery in this study, but the maximum allowable dose of TXA and the appropriate timing of TXA administration after surgery needs further validation. The applicable dose of TXA and the safety of TXA use remain to be investigated in further studies.

CONCLUSION

TXA is an appropriate and safe option for preventing bleeding during open reduction and internal fixation of clavicle fractures without increasing complications. TXA helps to improve patient satisfaction with open reduction and internal fixation in patients with clavicle fractures. Although the efficacy of TXA in reducing total blood loss and haemoglobin drop-in open reduction and internal fixation of clavicle fractures appears to be minimal, the TXA group had on average less postoperative drainage, significantly less fluid transfusion and no increased incidence of thrombosis and infection.

SIGNIFICANCE STATEMENT

This study discovers that the application of TXA is safe and suitable for preventing bleeding during open reduction and internal fixation of clavicle fractures without increasing the risks of complications. This study reports the application of TXA in open reduction and internal fixation of clavicle fractures for the first time. This study will help the researcher to uncover the critical role of TXA under different surgical situations. Thus, a new theory on the right dose of TXA application in different surgical situations may be arrived at.

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