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Original Article

Effects of tranexamic acid on the postoperative hemorrhage and complications after arthrolysis for elbow stiffness

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Abstract: Objective: To explore the clinical efficacy of tranexamic acid (TA) on the postoperative hemorrhage and complications after arthrolysis for elbow stiffness. Methods: A total of 587 patients with elbow stiffness enrolled in this study were assigned into the case group (TA treatment, n = 291) and the control group (without TA treatment, n = 296). The included criteria were as follows: (1) patients were diagnosed with elbow stiffness by Kay classification; (2) patients diagnosed with heterotopic ossification of bone; (3) patients without skin sensibility aging from 45 to 81 years old; (4) patients without surgical contraindication. The excluded criteria were as below: (1) patients with muscle atrophy, nerve damage or poor postoperative recovery; (2) patients with severe primary diseases, mental disease, severe skin diseases or other complications affects elbow joint; (3) patients with a joint instability; (4) clinical trial subjects who didn't respond well to treatment or had other reasons. The ankylosis of the elbow joint was conducted in both groups. Blood loss, cases of blood transfusion, blood transfusion volume, hemoglobin (HB) concentration, hematocrit (HCT), fibrinogen (FIB), prothrombin time (PT), activated partial thromboplastin time (APTT), blood viscosity (BV) and postoperative complications were detected. Results: The intraoperative and postoperative blood loss and blood transfusion volume in the case group were significantly lower than that in the control group, and the blood loss and blood transfusion volume in two groups after surgery were higher than those during surgery. Twenty two hours after surgery, HB concentration and HCT were significantly increased in the case group as compared with the control group. FIB, PT and APTT during and after surgery in both groups revealed no significant difference, while the BV after surgery in the case group evidently decreased compared with that before surgery and that in the control group. The incidence of upset stomach, hematoma, ulnar nerve paralysis, cardiovascular events, and acute recurrent elbow stiffness and other implications obviously increased in the control group as compared with the case group. Conclusion: Our findings demonstrate that TA can reduce blood loss, blood transfusion volume, BV and incidence of hematoma after arthrolysis for elbow stiffness, indicating TA can be applied in the clinical treatment for the patients with elbow stiffness.

Keywords: Tranexamic acid, elbow joint, arthrolysis, postoperative hemorrhage, postoperative complication

Introduction

As a common and challenging problem faced by the upper extremity surgeons [1], elbow stiffness can be caused by several different etiologies, such as spasticity, osteoarthritis, burns, trauma, and septic arthritis, among which the commonest one is trauma to the elbow where intrinsic changes make causal conditions in motion [2]. In addition, elbow stiffness also happens for a variety of other reasons, including extra-articular or intra-articular fractures, thermal injury, prolonged immobilization, infection, osteoarthrosis, inflammatory arthritis and heterotopic bone formation. It is usually classified into intrinsic (influencing the synovial and also intra-articular structures), extrinsic (influencing the capsule as well as extra-articular soft tissues) and mixed forms [3]. Based on the previous evidence, about 5% of elbow injuries could lead to the occurrence of elbow stiffness [4]. One study once evaluated the effectiveness of computed tomography (CT) and conventional radiography for understanding the osseous causes of elbow stiffness, and the results showed that CT is more effective [5]. Recently, arthroscopic capsular release has been adapted as a safe but technically demanding technique [6]. Surgical treatment for the elbow stiffness like using a hinged external fix-

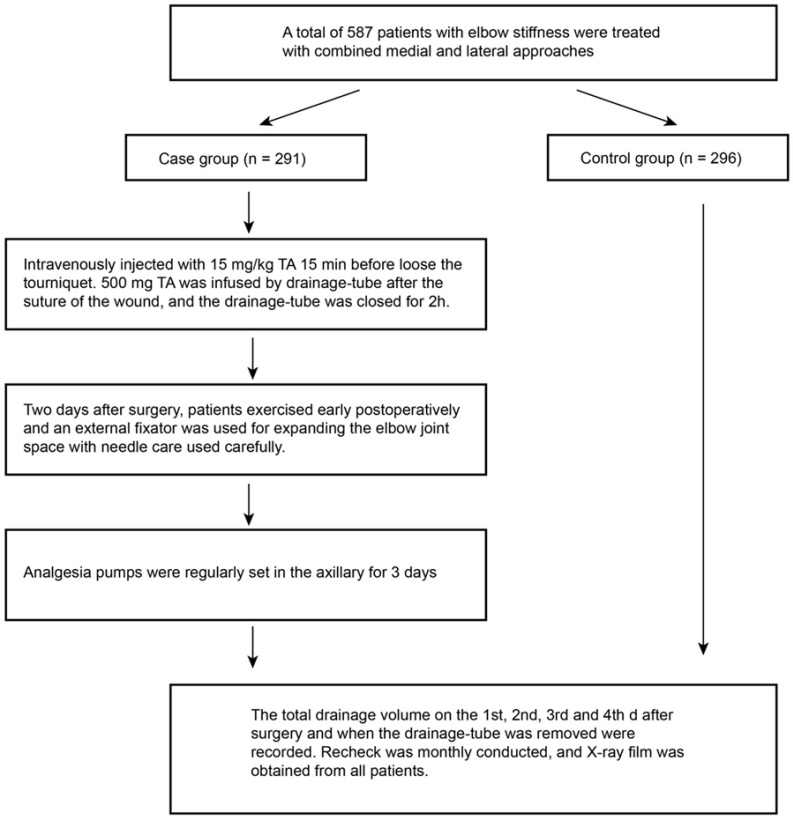

Figure 1. Flow chart of treatment methods.

ator along with open arthrolysis is also demonstrated as an effective procedure among children and adolescents [7]. Importantly, perioperative bleeding often occurs during elective joint replacement surgery which can result in delayed discharge, allogeneic blood transfusions, and slowed physical therapy progress, while tranexamic acid (TA) as a antifibrinolytics was performed in many surgical procedures to alleviate the bleeding [8].

TA, namely a kind of synthetic lysine derivative drugs, can bind to plasminogen and prevent the interaction between fibrin and plasminogen, eventually resulting in dissolution of the fibrin clots [9]. TA is also a synthetic antifibrinolytic drug that declines plasmin and fibrinolysis mediated platelet dysfunction, which can cause a decrease in 24 hour chest tube drainage and estimated blood loss after operation [10]. Different blood conservation methods have been developed to inhibit the need for allogeneic blood transfusion in patients undergoing total joint arthroplasty (TJA) [11]. And the administration of TA is identified as one of the most effective ones [12]. Open elbow arthrolysis was once performed in 30 adult patients, and its operative complications involved in 3 transient nerve palsies and 2 per-operative joint instabilities, 7 elbows were remobilized under anaesthesia, one month after the arthrolysis [13]. Thus, in this study, we aimed to clarify the clinical impacts of TA on the postoperative hemorrhage and complication after arthrolysis for elbow stiffness.

Materials and methods

Study subjects

Between 2012 December and 2015 January, a total of 587 patients with elbow stiffness for perspective study admitted in Jiangsu Taizhou People's Hospital recruited in this study were randomly assigned into case group (TA treatment, n = 291) and control group (without TA treatment, n = 296), among which 258 case were male and 329 cases were female aging from 52~78 years old with a mean age of 64.93 ± 3.92. The included criteria were as follows: (1) patients were diagnosed with elbow stiffness by Kay classification; (2) patients diagnosed with heterotopic ossification of bone and jointed by X-ray film or other imaging examination; (3) patients without skin sensibility aging from 45 to 81 years old; (4) patients without surgical contraindication. The excluded criteria were as below: (1) patients with muscle atrophy, nerve damage or poor postoperative recovery; (2) patients with severe primary diseases complicated with cerebrovascular, liver, kidney or hematopoietic system, mental disease, severe skin diseases or other complications affects elbow joint; (3) patients with a joint instability; (4) clinical trial subjects who didn't respond well to treatment or had other reasons. Our experiment was conducted in accordance with the Ethics Committee of Jiangsu Taizhou People's Hospital with confirmed consents obtained from all subjects.

Table 1. Baseline characteristics of patients between the case and control groups

Indexes	Case group	Control group	t/χ^2	*P* value
Gender (male/female)	125/166	133/163	0.233	0.629
Age (years old)	65.15 ± 3.52	65.30 ± 4.11	0.485	0.628
BMI	24.80 ± 2.71	25.16 ± 2.90	1.541	0.124
HB concentration (g/L)	122.99 ± 3.85	122.83 ± 7.73	0.309	0.758
HCT (%)	39.71 ± 3.76	39.78 ± 3.45	0.218	0.827
Platelet count ($\times 10^9$/L)	215.55 ± 29.02	216.74 ± 23.12	0.549	0.583
FIB (g/L)	3.77 ± 0.65	3.67 ± 0.76	1.668	0.096
PT (s)	11.39 ± 0.17	11.39 ± 0.18	0.078	0.938
APTT (s)	30.75 ± 3.09	30.78 ± 4.99	0.088	0.93

Note: BMI: body mass index; HB, hemoglobin; HCT, hematocrit; FIB, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time.

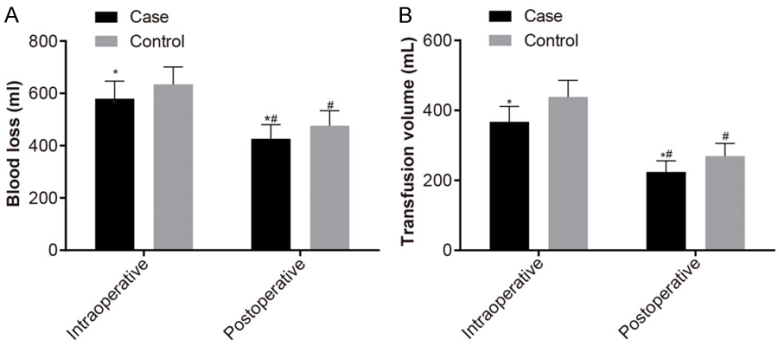

Figure 2. Comparisons of blood loss and blood transfusion volume in patients with TA between the case and control groups. A. Statistics of blood loss of the two groups; B. Statistics of blood transfusion volume of the two groups; *, $P < 0.05$ compared with the control group; #, $P < 0.05$ compared with the intraoperative ones of the same group; TA, tranexamic acid.

Treatment regimens

Internal combined with external arthrolysis for elbow stiffness was conducted for all patients in both groups. Patients in the case group were intravenously injected with 15 mg/kg TA 15 min before loose the tourniquet. After that, 500 mg TA was infused by drainage-tube after the suture of the wound, and the drainage-tube was closed, followed by opening 2 h later. Patients in the control group were treated as in the case group except for treatment of TA and infusion of 500 mg TA with drainage-tube. Then analgesia pumps were regularly set in the axillary for 3 d in two groups. In the second day after surgery, patients exercised early postoperatively, including the elbow flexion and extension and forearm rotation. After that, an external fixator was used for expanding the elbow joint space with needle care used carefully. The fixator was removed 6~8 weeks after surgery and the total drainage volume on the 1st, 2nd, 3rd and 4th d after surgery and when the drainage-tube was removed were recorded (the drainage-tube was removed when the remained drainage volume < 30 mL). Recheck was monthly conducted, and X-ray film was obtained from all patients (**Figure 1**).

Efficacy evaluation

The liquid weight infused by the negative pressure drainage ball was measured, and net weight of wound dressing was also calculated. The liquid weight plus net weight was regarded as blood loss volume after surgery, which was observed and calculated. All corresponded examination result, transfusion condition, transfusion volume and blood coagulation index value were recorded, as well as the ultrasound examination results.

Follow-up

In the first 3 months after surgery, the follow-up was conducted once a month. After that, follow-up was conducted once every three months. All the patients were all performed with the 6~10 months of follow-up with a median month of 8. The follow-up recorded several indexes, including postoperative blood loss, cases of blood transfusion, hemoglobin (HB) concentration, and hematocrit (HCT), and postoperative complications.

Statistical analysis

The SPSS 21.0 software (IBM Corp. Armonk, NY, USA) was adapted for data analysis. The measurement data obeyed normal distribution was presented as mean ± standard deviation and the t-test was used for the comparison. The count data were analyzed using the chi-square test. $P < 0.05$ means the statistical significant difference.

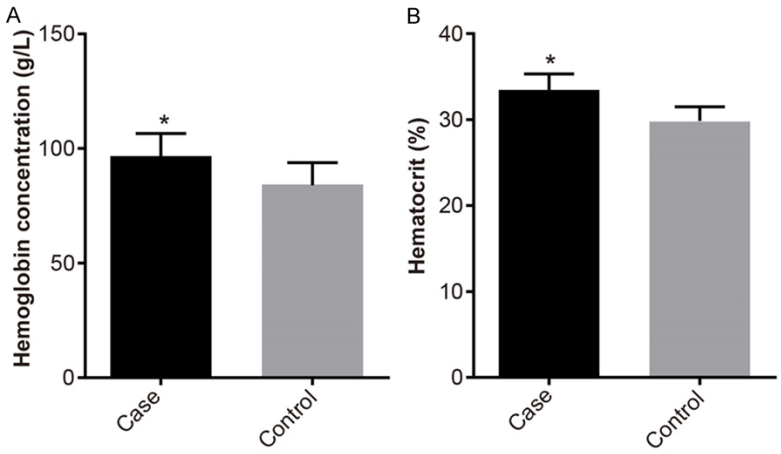

Figure 3. The comparisons of HB concentration and HCT in patients with TA between the case and control groups. A. Statistics of HB concentration of the two groups; B. Statistics of HCT of the two groups; *, $P < 0.05$ compared with the control group; TA, tranexamic acid; HB, hemoglobin; HCT, hematocrit.

Table 2. Comparisons of FIB, PT, APTT and BV in patients between the case and control groups

Items		Case group	Control group	t/χ^2	*P* value
BV (mPa.s)	During surgery	1.75 ± 0.41	1.79 ± 0.38	0.171	0.369
	After surgery	1.34 ± 0.25	1.58 ± 0.32	10.14	< 0.001
FIB (g/L)	During surgery	3.89 ± 0.11	3.91 ± 0.41	0.786	0.432
	After surgery	3.80 ± 0.25	3.82 ± 0.62	0.492	0.623
PT (s)	During surgery	13.89 ± 0.14	13.86 ± 0.35	1.502	0.134
	After surgery	13.05 ± 0.17	13.08 ± 0.20	1.008	0.314
APTT (s)	During surgery	37.44 ± 1.05	37.56 ± 2.54	0.722	0.471
	After surgery	36.60 ± 1.17	36.78 ± 1.40	1.753	0.08

Note: BV, blood viscosity; FIB, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time.

Table 3. The comparisons of complications after surgery in the case and control groups

Indexes	Case group	Control group	t/χ^2	*P* value
Upset stomach n (%)	21 (7.19)	26 (8.75)	0.44	0.507
Incidence of hematoma n (%)	7 (2.40)	18 (6.06)	4.862	0.028
Ulnar nerve paralysis n (%)	12 (4.11)	16 (5.39)	0.531	0.466
Cardiovascular events n (%)	47 (16.10)	41 (13.80)	0.609	0.435
Acute recurrent elbow stiffness n (%)	15 (5.14)	20 (6.73)	0.672	0.412

Results

Basic clinical characteristics in patients with elbow stiffness between the case and control groups were comparable

Patients in the two groups aged from 52~78 years old with a mean age of 64.93 ± 3.92 (258 males and 329 females). All patients showed no obvious anemia and normal coagulation function. There was no remarkable difference in the age distribution, mean age, body mass index (BMI), HB concentration, HCT, platelet count, FIB, PT and APTT in patients of the case and control groups (all $P > 0.05$) (**Table 1**).

TA affects both the intraoperative and postoperative blood loss and blood transfusion volume in patients with elbow stiffness between the case and control groups

The intraoperative and postoperative blood loss and blood transfusion volume in the case group were significantly lower than that in the control group, and the postoperative blood loss and transfusion volume in two groups were higher than those during surgery (all $P < 0.05$) (**Figure 2**).

Intraoperative and postoperative HB concentration and HCT in patients with elbow stiffness between the case and control groups may be influenced by AT

As the **Figure 3** demonstrates, 24 h after surgery, HB concentration and HCT were significantly increased in the case group as compared with the control group ($P < 0.05$).

TA affects FIB, PT, APTT and BV in patients with elbow stiffness between the case and control groups

There was no remarkable difference among the FIB, PT and APTT between the case and control groups ($P > 0.05$), showing as **Table 2**. And the FIB, PT and APTT during and after surgery in both groups revealed no significant difference

($P > 0.05$). However, the BV in the case group evidently decreased compared with that before surgery and that in the control group ($P < 0.05$).

TA lowers incidence of hematoma in patients with elbow stiffness after surgery in the case and control groups

Different degrees of upset stomach, hematoma, ulnar nerve paralysis, cardiovascular events, and acute recurrent elbow stiffness and other implications were observed both in the case and control groups after surgery. The incidence of hematoma obviously increased in the control group as compared with the case group ($P < 0.05$), while other complications demonstrated no remarkable difference in the case and control groups ($P > 0.05$) (**Table 3**).

Discussion

Elbow stiffness, as a common postoperative complication following joint trauma, can cause functional impairment in the upper limb and its dysfunction severity depends on the initial trauma and the surgical treatment adapted [14]. One study reveals that arthrolysis, the usage of a hinged external fixator and late internal fixation, can deal with problems related to stiff elbow after delayed capitellum fracture diagnosis [15]. Interestingly, TA significantly reduces blood loss as well as transfusion rates following total knee and total hip arthroplasty [16]. Thus, our study aims to elucidate the clinical role of TA in the postoperative hemorrhage and complication after arthrolysis for elbow stiffness, and the results demonstrate that TA can reduce blood loss, blood transfusion volume, BV and incidence of hematoma after arthrolysis for elbow stiffness, indicating TA can be applied in the clinical treatment for the patients with elbow stiffness.

Initially, our findings showed that the case group had declined blood loss, cases of blood transfusion, blood transfusion volume and incidence of hematoma as compared with the control group. TA, 4-aminoethyl cyclohexane carboxylic acid, a kind of synthetic derivative for the amino acid lysine [17], is a common synthetic antifibrinolytic substance adapted for bleeding control [18, 19]. Blood transfusion correlates with the additional cost, leading to great significance of its reduction in its use, and reduced postoperative blood loss is observed after TA, as reflected in decreases in the cases of blood transfusions [20]. Beside, typically in a study, administering TA is identified as a useful and safe method for inhibiting blood transfusion requirement postoperatively after the inter-trochanteric hip fractures [21]. More evidence shows that TA significantly decreases blood loss and transfusion rates after total hip and total knee arthroplasty [16], and reduces bleeding after certain surgical procedures to improve the quality of surgeon satisfaction, surgical field, bleeding volume and less surgery period during endoscopic sinus surgery with no remarkable side effect, as well as in children who undergoing craniosynostosis reconstruction surgery [22, 23]. Importantly, preoperative intravenous bolus administration of TA reduces blood loss significantly as compared with placebo during bimaxillary osteotomy [24]. Hematoma can limit postoperative rehabilitation and induce pain, and it is confirmed in a study that TA can reduce clinically apparent hematoma and hematoma volumes after total knee arthroplasty [25]. Interestingly, it is also demonstrated that hematoma expansion could be treated as a surrogate marker associating with poor outcome of the intracerebral hemorrhage trials [26]. All together, we have a standpoint to conclude that TA can suppress the postoperative hemorrhage after arthrolysis for elbow stiffness.

Importantly, the case group had elevated HB concentration and HCT but declined BV as compared to the control group. Low preoperative HB concentration is a well-known risk factor for adverse outcome, and postoperative HB concentration is the strongest predictor for the 30-day cardiovascular events [27]. HCT measurements are significant clinical diagnostic variables which help physicians diagnose as well as treat various ailments, medical conditions, and diseases [28]. And they are widely adapted to diagnose medical conditions and screen blood donors [29]. Hemoglobin and hematocrit levels were remarkably lower in the control group in anemic patients [30]. BV increased in diabetic patients and represented as a risk factor during the development process of insulin resistance and also type 2 diabetes [31]. It is also one of the most indispensable factors which can determine the blood flow [32]. Moreover, Intra-operative blood loss, pre and postoperative HB and HCT concentration,

and hospital stay time, are greater in the TA group, indicating that TA reduces volume of blood loss during the bimaxillary osteotomy [33]. In addition, TA can also reduce blood loss and allogenic blood transfusion requirements but improve postoperative HB for patients who undergoing bilateral staged total knee arthroplasty (TKA), suggesting that TA is an good option for patients who choose bilateral staged TKA to decline the risks related to the blood transfusion [34]. All studies above are in strict line with our findings, thus we can reach a conclusion that TA can elevate HB concentration and HCT but decline BV after arthrolysis for elbow stiffness in treatment of the elbow stiffness. Furthermore, the incidence of hematoma happened less commonly in the case group than that in the control group.

In conclusion, our findings demonstrate that TA reduces in the blood loss, blood transfusion volume, BV and incidence of hematoma after arthrolysis for elbow stiffness, suggesting that TA can be used with different injection ways for the treatment of the elbow stiffness. However, due to the limited data and restricted experimental environment, there are spaces remained to be improved. In the future studies, we will make all our efforts to better our study, so as to provide reliable method for patients who are suffering from elbow stiffness.

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Disclosure of conflict of interest

None.

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