

The efficacy and safety of tranexamic acid in reducing perioperative blood loss in patients with multilevel thoracic spinal stenosis

A retrospective observational study

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Abstract

Study Design: A retrospective study.

Objective: To investigate the effectiveness and safety of intravenous tranexamic acid for reducing perioperative blood loss in patients with multilevel thoracic spinal stenosis (TSS).

Methods: This is a retrospective observational study of 42 patients with multilevel TSS admitted from December 2016 to October 2017 to the spine department of Honghui Hospital who underwent posterolateral bone graft fusion with posterior laminectomy and decompression fixation. The patients were divided into 2 groups. All the surgeries were completed by the same surgeon. Group A received an intravenous infusion of 15 mg/kg 15 min prior to surgery. Continuous infusion of tranexamic acid (TXA) at a dose of 1 mg/kg/h was provided throughout the operation until the skin was closed. Group B received no TXA as a blank control group. Group A comprised 10 males and 10 females with an average age of 53.41 ± 7.93 years; group B comprised 11 males and 11 females with an average age of 55.10 ± 8.43 years. The need for blood transfusion, volume of blood transfusion, blood coagulation function, extubation time, postoperative hospital stay and incidence of postoperative deep venous thrombosis (DVT) were recorded during and after the operation for the 2 groups.

Results: There was no significant difference between the 2 groups in general characteristics, such as age, sex and body mass index (BMI) ($P > .05$). There was no significant difference between the 2 groups in the levels are instrumented and the laminectomy levels in each group. The average postoperative blood loss, need for blood transfusion, time to postoperative extubation and length of postoperative hospital stay in group A were lower than those in group B, and there was a significant difference between the 2 groups ($P < .05$). The preoperative and postoperative coagulation, and postoperative DVT did not occur 48h after operation.

Conclusion: In the treatment of multilevel thoracic spinal canal stenosis using trabeculectomy with posterior laminectomy and posterolateral bone graft fusion, TXA can reduce the amount of blood transfused and the need for blood transfusion and can shorten the extubation time and the length of postoperative hospital stay without increasing the incidence of postoperative coagulation dysfunction or postoperative DVT.

Level of Evidence: 4

Abbreviations: BMI = body mass index, CSF = cerebrospinal fluid, CT = computed tomography, DVT = deep venous thrombosis, EACA = ϵ -aminocaproic acid, MRI = magnetic resonance imaging, PLT = blood platelet, TSS = thoracic spinal stenosis, TXA = tranexamic acid.

Keywords: blood loss, multilevel, thoracic spinal stenosis, tranexamic acid

1. Introduction

Thoracic spinal stenosis (TSS) refers to the hypertrophy and ossification of the thoracic vertebral canal ligament, disc

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herniation, vertebral osteophytes, spinal canal stenosis and other pathological changes.^[1,2] Compared with cervical or lumbar spinal stenosis, the prevalence of TSS is low, and conservative treatment is not effective; surgery is the only effective way to treat TSS.^[3] Surgical treatment for TSS is usually accompanied by substantial perioperative blood loss; according to the literature, blood loss volumes can reach 944 mL to 2112 mL.^[4,5] The use of antifibrinolytic drugs to reduce perioperative blood loss has drawn considerable attention in various fields of surgery. The use of antifibrinolytic drugs such as tranexamic acid (TXA) and ϵ -aminocaproic acid (EACA) has been shown to reduce blood loss in various types of surgery, including heart, trauma, hip and knee arthroplasty, gynecology and urinary. Tranexamic acid is a synthetic derivative of the amino acid lysine, an antifibrinolytic agent that prevents the binding of fibrin by binding to plasminogen and blocking the interaction of plasmin (fibrinogen) with fibrin clot lysis.^[6] Tranexamic acid has demonstrated efficacy in reducing blood loss and transfusion requirements in a

Table 1**Clinical information for the 2 groups of patients.**

Group number	Gender		Age	BMI	Surgical segments	Complications	
	Male	Female				HT*	DB**
A	20	10	53.41 ± 7.93	26.86 ± 3.58	4.18 ± 1.01	2	1
B	22	11	55.10 ± 8.43	26.70 ± 3.01	4.25 ± 1.12	3	0
p			0.51	0.87	0.84		

* HT = hypertension.

** DB = diabetes.

large number of randomized controlled trials of total knee arthroplasty and total hip arthroplasty.^[7–9] Recent studies of its use in spinal surgery and primary lumbar surgery^[10,11] have demonstrated the effectiveness of TXA for reducing perioperative blood loss in patients undergoing spinal surgery. In view of this, we will investigate the effect of intravenous TXA on the narrowing of the thoracic ducts of perioperative patients in terms of bleeding and other outcomes.^[12–14]

2. Information and methods

2.1. General information

Patients who underwent spinal treatment with column posterior laminectomy decompression nail fixation with lateral bone graft fusion at the Honghui Hospital, from December 2016 to October 2017 were selected (Table 1). Inclusion criteria: ① imaging data (X-ray, CT, MRI)-confirmed TSS involving more than 3 consecutive or discontinuous segments; ② patients with obvious symptoms for whom conservative treatment was ineffective and a clear surgical path was evident who agreed to be surgically treated; ③ patients without a coagulation or hemoglobin dysfunction before surgery. ④ patients with complete clinical data. Exclusion criteria: ① patients with TSS involving fewer than 3 segments; ② patients with mild symptoms or response to conservative treatment; ③ patients who refused surgery; ④ patients with preoperative coagulation disorders or hypoalbuminemia (male < 120 g/L, females < 110 g/L); ⑤ patients who were allergic to tranexamic acid or were taking drugs that interfere with coagulation (oral anticoagulants or antiplatelet drugs) ⑥ patient who with cerebrospinal fluid (CSF) leakage during or after surgery ⑦ surgery operation without costoversectomy or transpedicular disc removal.

2.2. Experimental methods

All the surgeries were completed by the same surgeon. Group A received an intravenous infusion of 15 mg/kg 15 min prior to surgery. Continuous infusion of TXA at a dose of 1 mg/kg/h was provided throughout the operation until the skin was closed. Group B received no TXA as a blank control group.

Procedures were in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Human Experimentation of Honghui Hospital, Xi'an Jiaotong University. All 42 patients and their relatives have been informed prior to the commencement of this study and corresponding informed consent has been signed as well.

2.3. Surgical operation

The surgical technique has been described in previous work. Briefly, the patients were placed in the prone position and general anesthesia was induced. Anatomical landmarks combined with

imaging or metal surface markers placed on the body surface were used to determine the surgical segment plane. A midline longitudinal skin incision was made. Electrocautery was performed to stop the bleeding. The erector spinae were cut away from the spinous processes and dissected subperiosteally along the lamina to expose the spinous process, lamina, and facet joints of the thoracic segment and the upper and lower segments of the thoracic plate. After adequate exposure, pedicle screws were placed successfully using C-arm fluoroscop. The medial articular process of the lamina and ossification of the whole ligament was resected to achieve laminectomy decompression with an ultrasound bone knife. A pre-bent longitudinal connecting rod was installed, the screws were tightened. After bilateral posterolateral bone graft, the wound was rinsed, a negative pressure drainage tube was placed, and the incision was closed in layers.

2.4. Blood transfusion indicators

In cases of intraoperative bleeding of more than 800 mL or postoperative hemoglobin concentration < 70 g/L and continued postoperative blood loss or anemia symptoms, patients were given 1 U red blood cells. The standard for infusing fresh frozen plasma (FFP, 200 mL each) was a baseline International normalized ratio (INR) > 1.5 or APTT > 1.5 × normal persistent bleeding. Platelet transfusion standards (1U each) were PLT < 100 × 10⁹/L with persistent bleeding.

2.5. Evaluation criteria

The main evaluation index was intraoperative blood loss and postoperative drainage collected in a drainage bag. The secondary outcome was the need for allogeneic blood transfusion, including red blood cells, FFP and platelets, during hospitalization as well as extubation time, postoperative hospital stay, coagulation and postoperative deep venous thrombosis (DVT). Intraoperative blood loss was estimated by measuring blood from gauze, gel sponges and the suction canister minus all the other irrigation fluid, including the irrigation volume of saline; the standard was 24 h drainage < 50 mL. The drainage from the drainage tube before the total drainage volume was calculated was recorded as the postoperative drainage volume. Prothrombin time (PT), partial prothrombin time (APTT), and D-dimer were measured preoperatively and on the first postoperative day. 48 h after surgery, a high-grade sonographer performed venous Doppler ultrasonography to assess the incidence of DVT.

2.6. Data analysis

Statistical methods SPSS 19.0 software was used to perform statistical analyses. Measurement data are expressed as the mean ± standard deviation ($\bar{x} \pm s$). The *t* test was used to compare the 2 groups, and the χ^2 test was used for count data. *P* < .05 was considered statistically significant.

Table 2
The number of instrumented levels.

Instrumented levels*	3	4	5	6	7	P
Group A (cases)	5	9	3	2	1	.702
Group B (cases)	6	7	7	1	1	

* Place 2 nails per vertebral body through the pedicle

3. Results

There was no significant difference between the two groups in general characteristics, such as age, sex and BMI ($P > .05$ Table 1). The levels are instrumented in group A and group B are 170 and 176, and the laminectomy levels in group A and group B are 64 and 69 respectively, and there is no significant differences in the levels are instrumented and the laminectomy levels in each group. ($P > .05$ Tables 2–4). patients in the tranexamic acid intravenous application group showed less bleeding during surgery, blood transfusion volumes, postoperative drainage and shorter drainage tube removal times and postoperative hospital stays (Table 5) compared with the control group ($P < .05$), suggesting that preoperative intravenous TXA can effectively control intraoperative bleeding. Although the PT, APTT, INR and D-dimer levels in group A were slightly higher than those in group B before and after the operation (Table 6), there was no significant difference between the 2 groups ($P > .05$). The incision healed well, and no incision infection or other complications occurred in either group. No deep venous thrombosis was found 48 h after surgery in the lower extremities, indicating that the intravenous administration of TXA was safe and feasible and did not increase the incidence of postoperative thrombosis.

4. Discussion

The documented use of TXA has been previously showing in multiple studies. but most of those studies did not have so much blood loss. Due to this point, we focus on whether it is still safe and useful in TSS who underwent posterolateral bone graft fusion with posterior laminectomy and decompression fixation.

Blood preservation strategies have been effectively used to reduce the need for surgical bleeding and allogeneic blood transfusions. These techniques include local anesthesia, antihypertensive anesthesia, intraoperative salvage of blood, intravenous injection, intramuscular injections, and oral medications. However, in spine surgery, the large wound area, prolonged operation time, and abundant supply of cancellous bone blood can cause operational blood loss to vary widely; depending on surgical and non-surgical factors, blood loss remains a primary concern in spine surgery. In a large number of high-blood-loss operations, allogeneic blood transfusion has become an effective means of supplementing blood volume; however, allogeneic blood transfusion carries additional risks, including hemolytic transfusion reactions, transfusion-related acute lung injury, infection transmission and immunoregulation effects. Due to the significant risks and complications associated with blood loss and allogeneic blood transfusions, it is crucial to find safe and effective ways to reduce blood loss during spinal surgery.^[15]

Table 3
The number of laminectomy levels.

Laminectomy level	2	3	4	5	6	P
Group A (cases)	6	8	3	2	1	.563
Group B (cases)	6	9	6	0	1	

Table 4
Surgery levels in 2 groups.

Group	Cases	TNOIL*	TNOLL**
A	20	170	64
B	22	176	69

* TNOIL = total number of instrumented levels;
** TNOLL = total number of laminectomy levels

Wang et al^[16] evaluated the efficacy of TXA for reducing perioperative blood loss and blood transfusions in adult patients with selective thoracolumbar posterior fusion in a randomized, prospective, double-blind, multicenter study. 175 adult patients were randomized to receive TXA intravenously, while the control group was given an equal volume of placebo (saline). Four patients were excluded from the study due to vertebral body rupture of the lamina, dural tear, or severe epidural hemorrhage, and the remaining 171 patients were included in the analysis. Compared with the placebo group, the TXA group showed a significant reduction in perioperative blood loss. Krohe et al^[17] also reduced perioperative blood loss in patients by using TXA locally. In our study, all the patients in the experimental and control groups received allogeneic transfusions. Tranexamic acid significantly reduced bleeding in the experimental group (intraoperative blood loss 1520.50 ± 419.66 mL vs 1994.75 ± 434.12 mL; postoperative drainage 352.14 ± 127.41 mL vs 438.00 ± 112.14 mL; $P < .05$). At the same time, the time of extubation and length of postoperative hospital stay of the TXA group were shorter than those of the control group (3.00 ± 1.27 d vs 3.85 ± 0.88 d; 4.23 ± 1.02 d vs 5.55 ± 1.28 d; $P < .05$), which indicated that the patients who received TXA recovered faster.

The safety of TXA is a valid concern, and potential adverse effects include postoperative epilepsy, renal damage and other disorders. A study by Murkin et al^[18] found that elderly adults with an average age of 69.9 years presented with epilepsy after receiving large doses of TXA during heart surgery. Martin^[19] and other studies of TXA use during heart surgery found that renal failure occurred in approximately 5.9% of patients in the TXA group. None of the patients in our study developed the above adverse reactions. In our study, the postoperative coagulation profiles, assessed with PT, APTT, INR, and D-dimer levels, were similar, indicating that TXA did not affect patients' early coagulation function. In the study by Puigdemívol^[20] et al, intracellular TXA reached peak plasma concentrations after approximately 1 hour, with an apparent elimination half-life of approximately 2 h. We believe that the high metabolism rate of TXA and the absence of postoperative complications are among the reasons TXA is gradually being applied in all fields of surgery. Tranexamic acid is relatively beneficial in patients with no significant comorbidities (severe ischemic heart disease, severe lung disease, chronic renal failure) when used intravenously. In our study, there were 2 and 3 patients with hypertension in the

Table 5
Comparison of the effectiveness of tranexamic acid vs control.

Category	A	B	P
Intraoperative bleeding	1520.50 ± 419.66	1994.75 ± 434.12	.01
Intraoperative blood transfusion	963.64 ± 341.63	1680.00 ± 442.01	.01
Postoperative drainage	352.14 ± 127.41	438.00 ± 112.14	.03
Drainage tube removal time	3.00 ± 1.27	3.85 ± 0.88	.02
Postoperative hospital stay	4.23 ± 1.02	5.55 ± 1.28	.01

Table 6
Comparison of the safety of tranexamic acid group vs control.

Category	A	B	P
D-dimer			
Preoperative	0.89±0.18	0.87±0.13	.74
48h after surgery	1.04±0.18	0.98±0.15	.29
INR			
Preoperative	1.04±0.17	1.03±0.20	.90
48h after surgery	1.05±0.17	1.04±0.15	.77
PT			
Preoperative	14.82±3.19	14.60±2.70	.30
48h after surgery	16.45±2.60	16.40±2.16	.16
APTT			
Preoperative	29.86±2.80	29.00±2.41	.81
48h after surgery	29.05±3.15	29.00±2.41	.94

INR=International normalized ratio; APTT=Activated partial thromboplastin time; PT=Partial thromboplastin time.

experimental group and the control group, respectively; one patient with type 2 diabetes in the experimental group; and no serious renal dysfunction in either group.

The primary concern with TXA is whether it promotes thrombus formation. A meta-analysis of the effects of TXA on transfusions, thromboembolic events and mortality in surgically treated patients showed that TXA was effective in reducing thromboembolic events such as myocardial infarction, stroke, deep venous thrombosis (DVT), and pulmonary embolism and that although its effects on mortality are still uncertain, it can clearly reduce the amount of blood loss in patients.^[21] Ross et al^[22] conducted a systematic review of the association between the frequency of thrombotic events and the use of TXA after spontaneous bleeding and found that the incidence of events such as DVT decreased with TXA treatment. We did not observe any thromboembolic events during the B-mode venous ultrasonography on the day before the patient was discharged.

Our study was performed in patients with lesions involving 3 or more segments. Because of thoracic spine exposure, decompression, and the placement of internal fixators, such operations often involve considerable blood loss. Clinical and intraoperative factors that affect blood loss include blood pressure control, intraoperative exposure time, timely anatomic hemostasis, individual coagulation etc. Although the intravenous administration of TXA effectively reduced perioperative blood loss in this study, a safe dose of TXA was used in patients with comorbid conditions due to limited sample size.

5. Limitations

Because other factors can increase the incidence of thrombotic events, studies with a more rigorous experimental design and larger sample sizes are still needed to determine the efficacy and safety of intravenous TXA for the treatment of patients with multilevel TSS.

6. Conclusion

Tranexamic acid achieves the goal of hemostasis via antifibrinolysis. In our preliminary study, patients with TSS undergoing posterior laminectomy, decompression and posterior lateral bone graft fusion were treated with an intravenous transfusion of TXA. They showed significantly reduced perioperative blood loss without an increased risk of postoperative coagulation dysfunction

and postoperative complications, such as the incidence of deep venous thrombosis.

Author contributions

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