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Original Article

The reduction in blood loss with an intravenous drip of tranexamic acid in decompression and fusion surgery for degenerative lumbar spinal stenosis: a randomized controlled trial

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Abstract: Background: The objective was to determine the effectiveness and safety of an intravenous drop of tranexamic acid (TXA) in reducing blood loss in the perioperative period of decompression and fusion surgery in degenerative lumbar spinal stenosis. Methods: Primary decompression and fusion surgery was performed on a total of 124 patients. TXA was given by intravenous drip to the TXA group (n = 62) at a dose of 15 mg/kg per 30 minutes, while the control group (n = 62) did not receive any hemostatic drug. The intraoperative blood loss, postoperative blood loss, the blood transfusion volume, and the number of blood transfusions were compared preoperatively, and at 24 hours and 48 hours postoperatively between the two groups. The complications of TXA were also recorded. Results: There were no significant changes noted in terms of coagulation function, and no complications associated with TXA were observed. In the TXA group, the postoperative blood loss was significantly lower than it was in the control group. Conclusions: An intravenous drip of TXA for patients undergoing decompression and fusion surgery could significantly reduce postoperative blood loss without increasing complications.

Keywords: Tranexamic acid, degenerative lumbar spinal stenosis, blood loss, randomized controlled trial

Introduction

Decompression fusion surgery is the most common surgical treatment for degenerative lumbar spinal stenosis. However, in most cases, it involves multilevel procedures, which carry a high risk of significant blood loss [1]. Excessive blood loss could result in anemia and coagulopathy or more serious complications. Thus, perioperative intervention has been adopted to reduce the risk of adverse effects, such as post-operative infection, blood-borne disease transmission, and greater mortality rates [2].

More recently, anti-fibrinolytics are usually used to enhance coagulation as a blood management strategy. Tranexamic acid (TXA) appears more effective than aprotinin and 6-aminocaproic acid (EACA) at reducing perioperative blood loss [3]. As reported before, the administration of perioperative TXA has shown a remarkable decrease of blood loss and need for transfusion in patients undergoing orthopedic surgery, particularly for hip and knee arthroplasty [4-6]. Also a number of studies demonstrated that TXA can efficiently reduce blood loss and transfusions in spinal correction surgery [7-9]. However, because of the different TXA dose regimens, different levels and numbers of fused segments, its role in posterior lumbar surgery for stenosis is not yet well established. Therefore, the objective of this study was to discuss the effectiveness and safety of an intravenous drip of tranexamic acid in reducing blood loss in the perioperative period of decompression and fusion surgery in degenerative lumbar spinal stenosis.

Materials and methods

Patients and design

From March 2016 to January 2018, all patients scheduled to have primary decompression and

fusion surgery for degenerative lumbar spinal stenosis were screened for recruitment into this study. The exclusion criteria included revisions, severe spinal deformity, spinal tumor, spinal tuberculosis, intervertebral space infection, rheumatoid arthritis, ankylosing spondylitis, congenital or acquired clotting disorders and hemophilia, preoperative anticoagulant or antiplatelet therapy within three months, and preoperative D-dimers not in the normal range. Patients with anemia (< 110 g/L for females, < 120 g/L for males), serious cardiac or cerebrovascular problems, preoperative hepatic or renal dysfunction, a previous history of deep venous thrombosis or pulmonary embolism, or contraindications for the use of TXA were excluded.

Consecutive adult patients (age > 18 years) (n = 124) were randomly assigned into two groups using a random number table. The process was conducted by researchers who were not involved in the evaluation of the results. The sequence numbers and groups were placed inside concealed envelopes, which were opened before the anesthetic induction. The study was approved by the medical experimental ethics committee of Chongqing Medical University. All patients provided written informed consent for the study and the surgery.

Demographic data collected before the operation included age, gender, height, and weight. The levels of hemoglobin (Hb), red blood cell (RBC), hematocrit (Hct), body mass index (BMI), D-dimer, fibrinogen (FIB), prothrombin time (PT) and activated partial thromboplastin time (APPT) were measured at 3 hours before each operation and 24 hours and 48 hours after each operation.

Surgery procedure

All the operations were performed in the same laminar flow operating room by an experienced surgical team. All the patients were under general anesthesia with blood pressure controlled within 90-110 mmHg/60-70 mmHg throughout the procedure. We carried out operations using the posterior midline approach. In the TXA group, the patients received an intravenous drip of TXA (15 mg/kg) after general anesthesia was induced. In the control group, the patients received an intravenous drip of the same volume of normal saline. In our study, most patients had severe lumbar spinal stenosis, and some also had lumbar instability. As a logical consequence, an interbody bone graft fusion, a posterolateral bone graft fusion, and internal fixation procedures were performed on all patients. The bone graft for fusion was a mixture of allogeneic bone and autologous bone obtained from the decompression procedure. A negative pressure drainage was placed, and a layer-to-layer suture was conducted to close the wound. The drainage was pulled out routinely after 48 hours. Anticoagulants were not used until the drainage was pulled out.

Evaluation

24 and 48 hour postoperative levels of RBC, Hct, Hb, D-dimer, FIB, PT and APTT, intra and postoperative blood loss were included in the postoperative data. Intra- and postoperative complications through hospitalization discharge were also collected. The patients were given a routine venous Doppler ultrasonography examination to screen for deep vein thrombosis (DVT) before they were discharged. The incidence of thromboembolic events (TE) was tracked for 1 month after surgery. Intra and postoperative blood loss for each patient, the number of patients requiring blood transfusions, and the intra and postoperative complications were measured by a staff member who was blinded to the patient groups.

Statistical strategies

All data analysis was performed using SPSS version 17.0 software. $P < 0.05$ was regarded as a significant difference. The continuous data were expressed by the mean ± standard deviation, using an unpaired *t* test. Count data were examined using a chi-square test. A value of $P < 0.05$ was considered statistically significant.

Results

124 patients who had undergone primary decompression and fusion surgery for degenerative lumbar spinal stenosis in our hospital were enrolled in the study from March 2016 to January 2018. They were randomized into the TXA and control groups (n = 62 per group). Among the patients, 29 were male and 33 were female with a mean age of 61 (ranging from 49-73 years old). There were no statistically significant differences between the two groups

Table 1. Common data of the patients

	TXA group (n = 62)	Control group (n = 62)	*P* value
Age (years)	60.6 ± 4.7	61.2 ± 4.3	0.490[a]
Gender (female/male)	36/26	30/32	0.368[b]
BMI	24.0 ± 3.0	23.9 ± 3.4	0.826[a]
Duration of disease (years)	4.9 ± 1.9	5.0 ± 1.6	0.680[a]

BMI = body mass index; [a]unpaired t test; [b]fisher's exact test.

Table 2. Preoperative hematologic data

	TXA group (n = 62)	Control group (n = 62)	*P* value
HB (g/L)	120.1 ± 12.2	119.6 ± 13.9	0.822[a]
RBC (10^9/L)	4.16 ± 0.40	4.29 ± 0.44	0.090[a]
HCT (%)	43.9 ± 4.5	43.8 ± 4.1	0.866[a]
PT (s)	12.2 ± 0.7	12.4 ± 0.8	0.097[a]
APTT (s)	26.1 ± 1.0	26.5 ± 1.0	0.037[a]
FIB (g/L)	3.19 ± 0.45	3.17 ± 0.47	0.787[a]
D-Dimer (mg/L)	0.34 ± 0.33	0.32 ± 0.29	0.700[a]

HB = hemoglobin, RBC = red blood cell; HCT = hematocrit; PT = prothrombin time; APTT = activated partial thromboplastin time; FIB = fibrinogen. [a]unpaired t test.

Table 3. Surgical characteristics and blood loss

	TXA group (n = 62)	Control group (n = 62)	*P* value
Operation time (min)	191.6 ± 26.6	195.4 ± 34.2	0.493[a]
Skin incision	11.6 ± 2.2	11.5 ± 2.3	0.785[a]
Intraoperative blood loss (ml)	311.4 ± 51.5	323.8 ± 62.0	0.228[a]
Postoperative 24 h blood loss (ml)	291.1 ± 66.2	361.2 ± 76.2	0.000[a]
Postoperative 48 h blood loss (ml)	329.8 ± 60.9	396.9 ± 71.9	0.000[a]
Intraoperative blood transfusion	0	0	1[a]

[a]unpaired t test.

regarding the preoperative data, age, sex, BMI, duration of disease, Hb, RBC, Hct, FIB, PT, APTT, and D-dimmer (P > 0.05) (**Tables 1**, **2**).

There were no significant differences in the operation time, incision size, or intraoperative blood loss between the control group and the TXA group (P > 0.05) (**Table 3**). The TXA group had significantly less postoperative blood loss during the first 24 h and 48 h as compared to the control group (P < 0.05) (**Table 3**).

The levels of Hb, RBC, and Hct content at 24 hours and 48 hours in the control group were significantly higher than the levels of the patients in the TXA group (P < 0.05) (**Tables 4**, **5**). The D-dimer content at 24 hours and 48 hours postoperatively was higher than the preoperative value in both the TXA and control groups, with the content in the TXA group being significantly lower than it was in the control group (P < 0.05) (**Tables 4**, **5**). In contrast, no statistically significant differences were observed between the two groups in terms of FIB, PT, and APPT during the first 24 h and 48 h (P > 0.05) (**Tables 4**, **5**).

No episodes of DVT or PE occurred in any of the cases. There were no other adverse events, such as allergies, atrial fibrillation, renal failure, and seizure. The intramuscular venous thrombosis frequencies were three and five in the TXA and control groups, but the differences were not statistically significant. (P > 0.05) (**Table 6**). The digestive response frequencies in the TXA group (n = 4) were significantly higher than the frequencies in the control group (P < 0.05) (**Table 6**).

Discussion

This study demonstrated that the use of TXA could significantly reduce blood loss in the perioperative period of decompression and fusion surgery for degenerative lumbar spinal stenosis. (P < 0.05). We observed that bleeding as well as reducing blood loss mainly happened in the first 24 hours. In addition, we did not find any apparent increase in the risk of postoperative complications, as reported in previous studies [10, 11], which suggests that a single low dose of TXA in posterior lumbar surgery is safe.

The etiology of perioperative bleeding during spine surgery is multifactorial due to the complex operating procedures (the interbody bone graft fusion, posterolateral bone graft fusion, and internal fixation) [12, 13]. The exposed bony surfaces are not amenable to standard

Table 4. Postoperative hematologic data at 24 hours

	TXA group (n = 62)	Control group (n = 62)	*P* value
HB (g/L)	104.5 ± 12.2	94.9 ± 10.4	0.000[a]
RBC (10^9/L)	3.86 ± 0.42	3.54 ± 0.43	0.000[a]
HCT (%)	36.9 ± 4.7	34.6 ± 4.5	0.007[a]
PT (s)	13.1 ± 1.1	13.4 ± 0.8	0.069[a]
APTT (s)	29.7 ± 1.6	30.4 ± 1.7	0.101[a]
FIB (g/L)	2.94 ± 0.39	2.90 ± 0.48	0.627[a]
D-Dimer (mg/L)	1.68 ± 0.44	1.87 ± 0.30	0.007[a]

HB = hemoglobin, RBC = red blood cell; HCT = hematocrit; PT = prothrombin time; APTT = activated partial thromboplastin time; FIB = fibrinogen. [a]unpaired t test.

Table 5. Postoperative hematologic data of 48 hours

	TXA group (n = 62)	Control group (n = 62)	*P* value
HB (g/L)	97.5 ± 12.1	88.4 ± 9.7	0.000[a]
RBC (10^9/L)	3.59 ± 0.39	3.29 ± 0.39	0.000[a]
HCT (%)	32.1 ± 4.4	29.7 ± 4.5	0.003[a]
PT (s)	12.3 ± 0.7	12.5 ± 0.7	0.062[a]
APTT (s)	30.8 ± 1.7	31.3 ± 1.9	0.107[a]
FIB (g/L)	3.02 ± 0.42	3.03 ± 0.47	0.888[a]
D-Dimer (mg/L)	1.79 ± 0.42	2.02 ± 0.25	0.000[a]

HB = hemoglobin; RBC = red blood cell; HCT = hematocrit; PT = prothrombin time; APTT = activated partial thromboplastin time; FIB = fibrinogen. [a]unpaired t test.

Table 6. Complications

	TXA group (n = 62)	Control group (n = 62)	*P* value
PE (n)	0	0	--
DVT (n)	1	0	1[a]
IVT (n)	7	11	0.445[a]
Allergies (n)	0	0	--
Renal failure (n)			
Atrial fibrillation (n)	0	0	--
Seizure (n)	0	0	--
Digestive response (n)	6	0	0.028[a]
Total (n)	14	11	0.655[a]

PE = pulmonary embolism; DVT = deep venous thrombosis; IVT = Intramuscular venous thrombosis. [a]fisher's exact test.

hemostatic maneuvers used during soft tissue surgery, and bleeding can continue after the wound is closed [14]. TXA is a type of synthetic amino acid analog which can block the lysine binding sites on plasminogen to inhibit the activation of plasminogen and interfere with fibrinolysis [15]. Wong and his colleagues [16] included patients undergoing the surgical treatment of degenerative lumbosacral disease in their study and reported a significant reduction in intraoperative blood loss relative to the patients receiving a placebo. Wang [17] reported a study of TXA use in patients undergoing pedicle screw fixation combined with PLIF who received a relatively low dose (15 mg/kg) of TXA. Postoperative blood loss in the TXA group was reduced by 13% compared with the control group, which is similar to our findings. We also found an almost 19% postoperative blood loss within about the first 24 hours, which was in accord with the earlier study. However, in these studies, the intraoperative blood loss in the TXA group was not statistically different from the control group. The amount of perioperative blood transfusion did not differ between the TXA and control groups. Elwatidy [18] reported a study of TXA used in various spine surgeries in which the intraoperative blood loss in the TXA groups was reduced by 49% and the postoperative blood loss in the TXA group by 55% compared to the control group, which saved 80% of the amount of blood transfusions in the TXA group. Probably because the two levels fused, and the average surgery was 3 hours long with no risk of major bleeding, so this was insufficient to confirm the effectiveness of the TXA administration [19]. In addition, we evaluated the effects of low dose of TXA through an intravenous drip in this study, so there was no continued medication after the operation.

TXA has been known to increase complications such as atrial fibrillation, renal failure, and seizure [11], especially for the patients who have significant comorbidities (i.e., severe ischemic heart disease, severe pulmonary disease, and chronic renal failure). The primary concern about administering TXA is the potential increased incidence of PTE. And theoretically, the use of TXA may potentially increase the risk of thrombosis. But several studies of orthopedic procedures have demonstrated no significant increase in rates of adverse events postoperatively, including thromboembolisms associated with TXA use [20, 21]. And Whiting [22] suggested that for the patients with severe systemic medical disease, TXA was not associated with an increase in symptomatic thromboem-

bolic events. Although intramuscular vein thrombosis and popliteal vein thrombosis were found in the TXA group, there was no statistical significance compared with the control group, and no pulmonary embolism occurred. Except for a digestive response, no other complications from TXA occurred in our study, such as seizures, allergies, atrial fibrillation, seizure, and renal failure. This may be related to the rapid rate of intravenous drop, so we recommend a drip rate of fewer than 50 drops per minute.

The present study has several limitations: (1) the number of cases was still not big enough; (2) the line of vertebral canal decompression range might affect the intra and postoperative blood loss; (3) the assumption that TXA could lower the need for blood transfusions was just systematically investigated.

Conclusion

In short, a preoperative-low dose of TXA can effectively reduce postoperative blood loss in posterior approach lumbar surgery, and without any significant side effects. Due to clinical heterogeneity, there is no consensus on the optimal dose of TXA, and further research will focus on this in spinal surgery procedures.

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Disclosure of conflict of interest

None.

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