Two Doses of Tranexamic Acid Reduce Blood Transfusion in Complex Spine Surgery

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A Prospective Randomized Study

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Study Design. Prospective, double-blinded, randomized controlled study.

Objective. To determine whether the use of 2 doses of tranexamic acid (TXA) can reduce perioperative blood loss and blood transfusions in low-risk adult patients undergoing complex laminectomy.

Summary of Background Data. Complex laminectomy (multilevel laminectomy or laminectomy and instrumentation) is a procedure with a medium risk of blood loss, which may require allogeneic blood transfusion. Previous studies of TXA showed its inconsistent effectiveness in reducing blood loss during spine surgery. The negative results may stem from ineffective use of a single dose of TXA during long and complex operations.

Methods. 80 adult (18–65 yr old) patients in Siriraj Hospital, Mahidol University, Thailand were enrolled and allocated into 2 groups (40 patients in each group) by computer-generated randomization. Patients with history of thromboembolic diseases were excluded. Anesthesiologists in charge and patients were blinded. Group I received 0.9% NaCl (NSS) or placebo and group II received 2 doses (15 mg/kg) of TXA. The first dose was administered before anesthesia induction and the second dose, after 3 hours. The assessed outcomes were the amount of perioperative blood loss and the incidence of blood transfusions.

Results. 78 patients were analyzed (1 patient in each group was excluded) with 39 patients randomized to each group. There were no differences in patient demographics and pre and postoperative hematocrit levels. The total blood loss in the control group (NSS) was higher [900 (160, 4150) mL] than in the TXA group [600 (200, 4750) mL]. Patients in the control group received more crystalloid, colloid, and packed red blood cell transfusions. Within 24 hours, we observed a 64.6% reduction of blood transfusions (43.5% vs.15.4%, $P = 0.006$). No serious thromboembolic complications occurred.

Conclusion. 2 effective doses (15 mg/kg) of TXA can reduce blood loss and transfusions in low-risk adults undergoing complex spine surgery.

Key words: antifibrinolytic drug, bleeding, blood loss, blood transfusion, laminectomy, randomized trial, risk factors, scoliosis, spine instrumentation, spine surgery, tranexamic acid, two doses.

Level of Evidence: 1
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Multilevel laminectomy or laminectomy with instrumentation (complex spine surgery) is a procedure with a medium risk of blood loss, requiring allogenic blood transfusion. Blood transfusions can increase the risks of infection, blood incompatibility, and allergic reactions. Many methods have been used to reduce allogenic blood transfusions, for example, autologous blood predonation, antifibrinolytic drugs, acute normovolemic hemodilution, red blood cell salvage, among others.[1,2]

Among the antifibrinolytic agents used, TXA (trans-4-aminomethyl-cyclohexane-1-carboxylic acid, TXA) is widely used for this purpose.[2,3] TXA is a lysine analogue and an antifibrinolytic agent that reversibly inhibits the activation of plasminogen to plasmin by binding to a specific lysine site of plasminogen, thereby delaying clot degradation.[4] Several studies have shown its effectiveness in cardiac surgery, liver transplantation, and joint arthroplasty.[5–8]

A review of the literature about the use of TXA in spinal surgery indicated that its effectiveness in reducing blood loss was inconsistent. Some studies showed a positive effect and some reported no effect of TXA on blood loss reduction. The negative results may stem from the ineffective use of a

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Assessed for eligibility (n=300)

Excluded (n=220)
Anemic (n=78)
>65 year (n=114)
Thromboembolic diseases (n=28)

Figure 1 : Consort diagram of the study. NSS indicates control group
that received 0.9% NaCl ; TXA, tranexamic acid.

Randomized (n=80)

Allocated to the NSS group (n=40)

Allocated to the TXA group (n=40)

Change to simple procedure (n=1)
Lost follow-up (n=0)

Change to simple procedure (n=1)
Lost follow-up (n=0)

Analyzed (n=39)

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TABLE 1. Patient Data

	Gr. I (NSS) n = 39	Gr. II (TXA) n = 39	P*
Age (yr)	53.1 ± 11.7	52.6 ± 12.8	0.869[†]
Male/female (n)	12/27	16/23	0.345[‡]
ASA I/II/III (n)	10/27/2	13/24/2	0.753[‡]
Weight (kg)	61.9 ± 11.3	63.3 ± 14.2	0.587[†]
Hemoglobin (g/dL)	13.5 ± 3.4	13.9 ± 1.4	0.161[†]
Hematocrit (%)	41.6 ± 2.9	42.1 ± 3.4	0.440[†]
Platelet count ($\times 10^3/mm^3$)	270 ± 64	275 ± 63	0.771[†]
Creatinine (mg/dL)	0.80 ± 0.17	0.86 ± 0.19	0.133[†]
Diagnosis (n, %)			
Spinal stenosis	15 (38.5%)	15 (38.5%)	0.742[‡]
Spondylolisthesis	16 (41.0%)	12 (30.8%)	
Bone metastasis/tumor	4 (10.3%)	5 (12.8%)	
Adolescent idiopathic scoliosis	2 (5.1%)	2 (5.1%)	
Others	2 (5.1%)	5 (12.8%)	

*Statistical analysis for comparison between groups: P < 0.05, statistical significance.
†Statistical analysis for comparison between groups: the unpaired t-test.
‡Statistical analysis for comparison between groups: χ^2 test or Fisher exact test.

TABLE 2. Intraoperative Data

	Gr. I (NSS) n = 39	Gr. II (TXA) n = 39	P
Operative time (min)	250 ± 86	227 ± 69	0.192*
Cases performed by			
<10 yr experience surgeon (n, %)	5 (12.8%)	4 (10.3%)	0.723[†]
≥10 yr experience surgeons (n, %)	34 (87.1%)	35 (89.7%)	
Estimated blood loss (EBL) (mL)	700 (150, 3500)	450 (80, 4000)	0.004[‡,§]
EBL>500 mL (n, %)	26 (66.7%)	15 (38.5%)	0.013[†,§]
EBL>1,000 mL (n, %)	11 (28.2%)	3 (7.7%)	0.018[†,§]
Fluid, crystalloid (mL)	3009 ± 1245	2330 ± 863	0.007[*,§]
Fluid, colloid (n, %)			
0	18 (46.1%)	26 (66.6%)	0.045[†,§]
500	13 (33.3%)	11 (28.2%)	
1000	8 (20.5%)	1 (2.5%)	
1500	0 (0.0%)	1 (2.5%)	
Patient receiving pack red cell (n, %)	13 (33.3%)	5 (12.8%)	0.032[†,§]
Hypotension (n, %)	24 (61.5%)	19 (48.7%)	0.255[†]
Vasopressor use (n, %)	22 (56.4%)	15 (38.4%)	0.112[†]
Oliguria (n, %)	10 (25.6%)	5 (12.8%)	0.151[†]

EBL presented as median (min, max) due to nonparametric distribution.

*Statistical analysis for comparison between groups: the unpaired t test.

[†]Statistical analysis for comparison between groups: χ^2 or Fisher exact test.

[‡]Statistical analysis for comparison between groups: Mann-Whitney U test.

[§]Statistical analysis for comparison between groups: $P < 0.05$, statistical significance.

TABLE 3. Intraoperative Procedures, Operative Time, and Estimated Blood Loss (EBL)

	Gr. I (NSS) n=39	Gr. II (TXA) n=39	P
Procedures			
(1) Multilevel laminectomy	1 (2.6%)	2 (5.1%)	0.684*
(2) Laminectomy with instrumentation[†]	20 (51.3%)	23 (59.0%)	
(3) Laminectomy with instrumentation with PLIF or TLIF or osteotomy[‡]	14 (35.9%)	8 (20.5%)	
(4) Posterior spinal fusion for scoliosis	2 (5.1%)	2 (5.1%)	
(5) Laminectomy and tumor removal	2 (5.1%)	4 (10.3%)	
Operative time (min)			
(1) Multilevel laminectomy	230	130 ± 7	N/A
(2) Laminectomy with instrumentation[†]	266 ± 103	228 ± 65	0.160[§]
(3) Laminectomy with instrumentation with PLIF or TLIF or osteotomy[‡]	227 ± 66	253 ± 49	0.341[§]
(4) Posterior spinal fusion for scoliosis	265 ± 63	308 ± 79	N/A
(5) Laminectomy and tumor removal	250 ± 98	170 ± 66	N/A
Estimated blood loss (mL)			
(1) Multilevel laminectomy	200	250 (200, 300)	N/A
(2) Laminectomy with instrumentation[†]	725 (250, 3500)	470 (80, 2400)	0.011[¶,‖]
(3) Laminectomy with instrumentation with PLIF or TLIF or osteotomy[‡]	700 (250, 3500)	350 (150, 1000)	0.082[‖]
(4) Posterior spinal fusion for scoliosis	950 (750, 1150)	2350 (700, 4000)	N/A
(5) Laminectomy and tumor removal	775 (150, 1400)	600 (200, 1000)	N/A

EBL presented as median (min, max) due to nonparametric distribution.

*Statistical analysis for comparison between groups: χ^2 or Fisher exact test.

[†]Instrumentation = pedicle screws, rods and posterolateral fusion.

[‡]PLIF = posterior lumbar interbody fusion, TLIF = transforaminal lumbar interbody fusion, osteotomy = pedicle subtraction osteotomy.

[§]Statistical analysis for comparison between groups: the unpaired t-test.

[¶]Statistical analysis for comparison between groups: $P < 0.05$, statistical significance.

[‖]Statistical analysis for comparison between groups: Mann-Whitney U test.

N/A indicates not applicable due to low number in each group.

TABLE 4. Risk Factors for Significant Bleeding (>500 mL) from Multiple Logistic Regression Analysis

Risk Factors	P	Odds Ratio	95% Confidence Interval
Surgical experiences <10 yr	0.315	2.24	0.46–10.82
Procedures 3, 4, 5	0.555	1.35	0.49–3.73
Operative time >180 min	0.006*	5.99	1.68–21.43
Received tranexamic acid	0.009*	0.25	0.09–0.70

*$P < 0.05$, statistical significance.

TABLE 5. Postoperative Data

	Gr. I (NSS) n = 39	Gr. II (TXA) n = 39	P
Hematocrit (%)	32.5 ± 3.5	33.7 ± 4.4	0.193*
Creatinine (mg/dL)	0.72 ± 0.20	0.79 ± 0.18	0.154*
Blood loss (mL)	257 ± 142	177 ± 136	0.014*,†
Patient receiving PRC in postoperative period (n,%)	8 (20.5%)	3 (7.6%)	0.104‡
Total blood loss (mL)	900 (160, 4150)	600 (200, 4750)	0.001†,§
Total fluid, crystalloid (mL)	4988 ± 1717	4213 ± 1200	0.024*,†
Total patient receiving PRC (n,%)	17 (43.5%)	6 (15.3%)	0.006†,‡
Length of hospital stay (d)	12.5 ± 8.6	11.1 ± 6.1	0.429*

EBL presented as median (min, max) due to nonparametric distribution.

*Statistical analysis for comparison between groups: the unpaired t-test.

†Statistical analysis for comparison between groups: $P < 0.05$, statistical significance.

‡Statistical analysis for comparison between groups: χ^2 or Fisher exact test.

§Statistical analysis for comparison between groups: Mann-Whitney U test.