Original Article

Effect of Tranexamic Acid on Blood Loss and Transfusion Requirements in Lumbar Spine Fixation

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Abstract

Background: Lumbar spine surgery in adults is associated with significant blood loss, often requiring allogeneic blood transfusion. The objective of this study was to evaluate the efficacy of tranexamic acid (TXA) in reducing perioperative blood loss and transfusion requirements in patients undergoing lumbar spine fixation. **Materials and Methods:** Sixty adult patients were randomized to receive either a bolus of 10 mg/kg IV of TXA after induction followed by a maintenance infusion of 1 mg/kg/hr of TXA up to closure of skin, or an equivalent volume of normal saline. Outcome measures included perioperative blood loss, amount of blood transfusion, as well as postoperative hemoglobin and hematocrit levels. **Results:** The mean intra-operative blood loss and the amount of blood in the drains post-operatively was less in the tranexamic acid group compared to the placebo group (P =0.0001). The blood transfusions received in both the groups was not statistically significant (P = 0.362).However, clinically there was reduction of transfusion requirement in the tranexamic acid group. The drop in post-operative hemoglobin levels was statistically significant in the control group as compared to tranexamic acid group (P = 0.002). The mean duration of surgery was less in tranexamic acid group compared to the control group (P = 0.008). **Conclusion:** Thus, tranexamic acid is effective in reducing peri-operative blood loss and transfusion requirements .Furthermore, TXA administration was not associated with any significant complications including DVT.

Key words: Blood loss, blood transfusion, hematocrit, lumbar spine surgery, tranexamic acid

Introduction

Posterior lumbar spine fixation surgery in adults is often associated with significant blood loss, requiring transfusion due to extensive soft tissue dissection and significant bone bleeding during instrumentation and decortication.[1] Allogeneic blood transfusion has several inherent risks, including the transmission of blood-borne pathogens, and haemolytic and immune-mediated transfusion reactions such as graft versus host disease. Homologous blood, when available, decreases but does not eliminate the risks associated with transfusion[2] due to immunomodulator effects. In addition, the costs associated with transfusions are significant.[3] Perioperative bleeding during spine surgery enhances the risk of epidural hematoma, which may potentially result in cord compression, causing permanent neurological deficit.

A variety of contemporary blood conservation techniques have been used to reduce exposure to allogeneic blood, including controlled hypotension, regional anesthesia, autologous blood transfusion, use of tourniquet,[4] intraoperative blood salvage, and administration of various parenteral medications.[5]

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Antifibrinolytics have been demonstrated to reduce blood transfusion requirement during cardiac surgery, total knee and hip arthroplasty, and urological procedures,[6] suggesting that tranexamic acid (TXA) may have a similar effect in spine surgery. However, there are only a few studies evaluating the role of TXA in spine surgery. TXA, a synthetic antifibrinolytic agent, competitively blocks the lysine-binding sites of plasminogen, plasmin, and the tissue plasminogen activator, thereby retarding fibrinolysis and blood clot degradation.

Lumbar spine fixation and stabilization is routinely done at our institute using pedicle screws and rods. A double-blind randomized controlled study was undertaken to compare blood

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loss in two groups of patients, one group (TXA) receiving TXA infusion and the other group (Placebo) receiving normal saline infusion. All the surgeries were performed by a single team of spine surgeons.

Aims and objectives

To evaluate the efficacy of TXA on blood loss and the need for blood transfusion in lumbar spine stabilization

Group I: Received normal saline (Placebo)

Group II: Received TXA (TXA).

Materials and Methods

After the approval of the Hospital Ethical Committee and written informed consent were obtained, the study was conducted on 60 patients with American Society of Anesthesiologists (ASA) physical status I and II, of either sex, 30–60 years of age, who were posted for elective lumbar spine fixation surgery under general anesthesia. Patients with a preexisting renal or hepatic disorder, bleeding diathesis, history of malignancy or coronary artery disease, thromboembolic event 1 year prior to surgery, hemoglobin less than 8 gm/dL, and history of uncontrolled hypertension were excluded from the study.

Patients were randomly allocated into two groups by computer-generated randomized tables. Group I received placebo (100 mL of 0.9% normal saline only) and Group II received TXA (10 mg/kg of body weight mixed in 100 mL normal saline) shortly after induction of anesthesia over 15 min before skin incision, followed by infusion of 1 mg/kg of body weight per hour up to closure of skin incision. After Pre-anesthetic evaluation, relevant investigations included hemoglobin estimation, total count, differential count, liver function tests, renal function tests, serum electrolytes, coagulation profile, random blood sugar, electrocardiogram (ECG), chest x-ray, and urine routine and microscopy.

All patients were premedicated with tab. alprazolam 0.25 mg and tab. pantoprazole 40 mg orally at 10 PM on the night before the surgery Patients, surgeons, anesthesiologists, nurses, and the investigator collecting the data were blinded as to which solution was being administered. Intraoperative monitoring included ECG, noninvasive blood pressure (NIBP), pulse oximetry, capnography, temperature, and urine output. Baseline vitals were recorded. The heart rate and NIBP were recorded preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 60 min, 75 min, 90 min, and 120 min following induction of anesthesia.

Patients were premedicated with inj. glycopyrrolate 10 mcg/kg, inj. ondansetron 0.15 mg/kg, and inj. midazolam 0.05 mg/kg intravenously (IV). Induction of anesthesia was with inj. propofol 2 mg/kg, inj. fentanyl 2 mcg/kg, and inj. atracurium 0.5 mg/kg. After intubation the patient was positioned prone, ensuring that the abdomen was free and there was no undue compression to the vessels or hindrance to respiration. Maintenance of anesthesia was with nitrous oxide, oxygen, isoflurane, intermittent doses of fentanyl, atracurium infusion, and intermittent positive-pressure ventilation.

Shortly after induction of anesthesia, patients received either TXA or placebo as a loading dose of 10 mg/kg over 15 min before skin incision, followed by infusion of 1 mg/kg body weight per hour up to closure of skin incision. The incision time and blood loss were recorded.

Total blood loss was calculated as the sum of blood in swabs, blood in suction bottles, and blood in surgical drain. The number of units of packed red blood cell (PRBC) concentrates transfused to the patient was noted. Patients were extubated at the end of surgery and observed in the postanesthesia care unit (PACU). Postoperatively hemoglobin, packed cell volume (PCV), prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT) were repeated 12 h after the surgery.

Data analysis

The age, duration of surgery, total perioperative blood loss, pre- and postoperative hemoglobin, postoperative INR, and pre- and postoperative PCV among the two groups were analyzed for frequencies, percentages, mean, standard deviation (SD), and minimum and maximum values. The independent *t*-test was applied to assess the mean difference and significance (at 0.05 level) between the two groups. The data were analyzed by means of Statistical Package for the Social Sciences Version 12.0. The results were presented as mean ± SD. The independent Student's *t*-test was used to compare the two groups, and differences were considered significant if the *P* value was <0.05.

Results

Tables 1 and 2 show the demographic data. Both groups were statistically comparable with respect to age and weight. Mean duration of surgery in Group I was 171.03 ± 20.5 min and in Group II was 162.73 ± 25.8 min, which was statistically highly significant with a *P* value of 0.008 [Table 3]. Mean intraoperative blood loss in Group I was 830.23 ± 208.86 mL and in Group II was 618.53 ± 205.95 mL, which was statistically highly significant with a *P* value of 0.0001 [Table 3]. Mean postoperative blood loss in Group I was 269.8 ± 68.27 mL and in Group II was 133 ± 45.11 mL, which was statistically

Table 1: Age

Group	*N*	Mean	Std. deviation	*P*
I	30	54.33	5.732	0.789
II	30	54.73	5.777	

Table 2: Weight

Group	*N*	Mean	Std. deviation	*P*
I	30	70.17	11.22	0.747
II	30	69.33	8.5	

highly significant with a *P* value of 0.0001 [Table 3]. Mean total blood loss in Group I was 1100.3 ± 249.3 mL and in Group II was 750.3 ± 238.96 mL, which was statistically highly significant with a *P* value of 0.0001 [Table 3]. Mean preoperative hemoglobin in Group I was 13.72 ± 1.67 g/dL and in Group II was 14 ± 1.41 g/dL; with the *P* value of 0.48 there was no statistical significance and the groups were comparable with respect to preoperative hemoglobin [Table 3]. Mean preoperative PCV in Group I was 41.1 ± 5.01 and in Group II was 41.86 ± 4.22; with the *P* value of 0.52 there was no statistical significance and the groups were comparable with respect to preoperative PCV [Table 3]. Mean postoperative hemoglobin in Group I was 9.25 ± 1.98 g/dL and in Group II was 10.95 ± 2.09 g/dL, which was statistically highly significant with a *P* value of 0.002 [Table 3]. Mean postoperative PCV in Group I was 27.74 ± 5.87 and in Group II was 33.01 ± 6.38, which was statistically highly significant with a *P* value of 0.002 [Table 3].

Table 4 shows the number of PRBCs transfused. In Group I, 15 patients did not receive any PRBCs, 3 patients received 1 PRBC each, 6 patients received 2 PRBCs each, 3 patients received 3 PRBCs each, and 3 patients received 4 PRBCs each. In Group II, 25 patients did not receive any PRBCs, 4 patients received 2 PRBCs each, and 1 patient received 3 PRBCs. This difference between the groups is clinically significant.

Discussion

Surgical procedures are inevitably associated with bleeding. Adult lumbar spine fixation surgery can be associated with major blood loss, with requirement for blood transfusion. Blood loss depends on the number of levels fused, duration of surgery, and physical status of the patient. Concerns regarding the safety of transfused blood have led to the development of a range of interventions to minimize blood loss during major surgeries. Hence, a comprehensive blood conservation strategy gains paramount importance to ensure decreased complications in the perioperative period and the overall success of the operative treatment.

Both surgical and nonsurgical techniques have been used with varying success to reduce perioperative blood loss. The use of pharmacological therapies to reduce blood loss and blood transfusion during surgery is restricted to a few drugs, such as aprotinin, TXA, epsilon-amino-carporic acid, desmopressin, and recombinant factor VII a.

With the exception of aprotinin, the side-effect profiles of these agents have not been shown to cause any substantial morbidity or to increase the rate of thromboembolic events.

TXA has been used in orthopedic surgeries such as spine fixation surgeries, scoliosis surgeries, and hip and knee replacement surgeries. TXA has been found to significantly reduce blood loss and blood transfusion requirements in patients undergoing orthopedic surgery, and does not appear to increase the risk of deep vein thrombosis (DVT).[7]

In the present study, 60 patients undergoing lumbar spine fixation surgery were randomly assigned to a placebo group and a TXA group. Both groups were comparable in mean age, body weight, ASA physical status, preoperative hemoglobin and hematocrit values, and type of surgical procedure. The technique of anesthesia was standardized in both the groups. Contributing factors such as coagulation profile and mean arterial blood pressure that could alter blood loss were monitored. Hypotensive anesthesia was not used in both groups.

In this study we found that both the mean intraoperative blood loss and the amount of blood in the drains postoperatively were less in the TXA group compared to the placebo group (*P* = 0.0001). Thereby, total blood loss (intraoperative plus postoperative) was consequently less in the TXA group (32% reduction in total blood loss with *P* = 0.0001).

The blood transfusions received in both groups were not statistically significant (*P* value = 0.362). However, clinically there was reduction in requirement of blood transfusion in Group II (TXA group), the discrepancy being most likely due to the

Table 3: Group statistics

	Group	*N*	Mean	Std. deviation	Std. error mean
Duration of surgery	I	30	171.03	10.250	1.871
	II	30	162.73	12.916	2.358
Intraop. blood loss	I	30	830.23	208.869	38.134
	II	30	618.53	205.954	37.602
Postop. blood loss	I	30	269.80	68.273	12.465
	II	30	133.00	45.117	8.237
Total blood loss	I	30	1100.03	249.328	45.521
	II	30	750.33	238.965	43.629
Preop. Hb	I	30	13.72	1.677	0.306
	II	30	14.00	1.419	0.259
Preop. PCV	I	30	41.10	5.013	0.915
	II	30	41.86	4.224	0.771
Preop. INR	I	30	1.04	0.079	0.014
	II	30	0.99	0.041	0.008
Postop. Hb	I	30	9.25	1.984	0.362
	II	30	10.95	2.092	0.382
Postop. PCV	I	30	27.74	5.872	1.072
	II	30	33.01	6.387	1.166
Postop. INR	I	30	1.15	0.398	0.073
	II	30	1.06	0.368	0.067

Hb: Hemoglobin, PCV: Packed cell volume, INR: International normalized ratio

Table 4: PRBCs

No. of PRBCs	Group I	Group II	Total
1	3	0	3
2	6	4	10
3	3	1	4
4	3	0	3
Total	15	5	20

PRBC: Packed red blood cell

small sample size. The number of units of PRBCs received in the TXA group and in the control group was 5 and 15, respectively [Figure 1]. These results were consistent with studies done by Wong *et al*.,[8] Elwatidy *et al*.,[9] and Wang *et al*.[10]

Wong *et al*.[8] reported that total estimated and calculated perioperative blood loss was approximately 25% and 30% lower in patients given TXA versus placebo (P =0.017), respectively, in adult patients undergoing spinal fusion surgery.

Elwatidy *et al*.[9] reported that patients who received TXA showed 49% reduction of blood loss ($P < 0.007$) compared to the control group in spine surgeries.

Wang *et al*.[10] reported that postoperative blood loss was significantly lower in the TXA group than in the control group (13.0%) in posterior-approach lumbar surgery for degenerative lumbar instability with stenosis.

There was also significant difference in the postoperative hemoglobin and hematocrit values of patients in the TXA group compared to the control group ($P = 0.002$). These results were consistent with studies done by Endres *et al*.[11] and Elwatidy *et al*.,[9] in which the postoperative hemoglobin and hematocrit values were statistically significant in the TXA group compared to the control group.

The mean duration of surgery was less in the TXA group compared to the control group ($P = 0.008$).

A study done by Vel *et al*.[12] in neurosurgical patients receiving TXA has shown that the mean heart rate in the TXA group was significantly lower compared with the saline group. Mean arterial pressure and fibrinogen levels were higher in the TXA group. The mean total blood loss in the TXA group was less than in the saline group. Blood transfusion requirements were comparable in the two groups.

The major concern surrounding the use of TXA and other antifibrinolytics is the potential for an increased risk of thrombotic events. No patient in our study experienced a complication from the use of TXA, although no investigations beyond a physical examination and history-taking were conducted. Patients were observed for a period of 72 h for evidence of any thromboembolism. The studies examining the use of TXA in patients undergoing

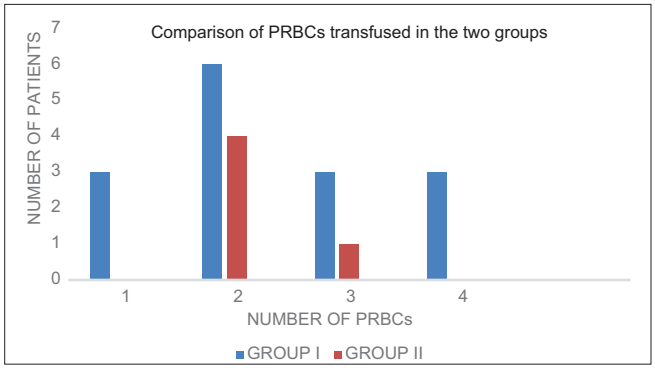

Figure 1: Comparison of PRBCs transfused in the two groups

total knee arthroplasty also did not experience an increased incidence of DVT.[13-15] Reports of thromboembolic events attributed to TXA are uncommon, occur in the nonoperative setting, and are primarily anecdotal in nature. A common misconception is that these drugs are procoagulants and that they will increase blood clotting. These drugs do not alter blood clotting, but instead slow dissolution of blood clots. A meta-analysis done by Li *et al*.[16] to assess the effectiveness and safety of TXA showed that even a high dose of TXA (≥15 mg/kg) does not increase the risk of postoperative DVT. The beneficial effects are believed to be probably due to inhibition of local fibrinolytic activity in the surgical field. None of our patients experienced any allergic reactions to TXA.

Dose regimens of TXA vary widely in the literature: Loading doses from 2.5 mg/kg of body weight to 100 mg/kg of body weight, and maintenance doses from 0.25 mg/kg of body weight per hour to 4 mg/kg of body weight per hour delivered over a period of 1–12 h. In this study, patients received TXA as a loading dose of 10 mg/kg over 15 min before skin incision, followed by infusion of 1 mg/kg per hour of body weight up to closure of skin incision.

With this dose, adequate haemostasis was achieved (32% reduction in blood loss). A study done by Wong *et al*.[8] using a similar dose of TXA, 10 mg/kg IV of TXA after induction followed by a maintenance infusion of 1 mg/kg/h, showed 30% reduction in perioperative blood loss.

Verma *et al*.[17] did a randomized, double-blind comparison of TXA, epsilon-aminocaproic acid, and placebo used intraoperatively in patients with adolescent idiopathic scoliosis. They found that TXA is more effective at reducing postoperative drainage and total blood loss than epsilon-aminocaproic acid.

Recently a systematic review and meta-analysis of perioperative IV TXA use in spinal surgery by Yang *et al*.,[18] showed that when patients were treated with TXA, perioperative blood loss was reduced. Furthermore, the number of patients who required allogeneic blood transfusions was lower by 35%. This persistent positive effect of TXA was dose- and administration timing-independent.

A comparative study done by Khurana *et al*.[19] showed that perioperative blood loss is less with TXA than with aprotinin. However, the difference between the two groups was not statistically significant. The drug reduces postoperative blood loss and transfusion requirements, with potential cost and tolerability advantages over aprotinin. Concerns have been raised about the safety of aprotinin after an association with increased renal dysfunction, myocardial infarction, encephalopathy, stroke, and mortality was shown in retrospective observational studies.

Recently, a meta-analysis done by Zhang *et al*.[20] showed that the use of TXA in patients undergoing spinal surgery appears to be effective in reducing the amount of blood loss,

the volume of blood transfusion, the transfusion rate, and the postoperative APTT.

Thus, TXA is effective in reducing perioperative blood loss. Furthermore, TXA administration was not linked with any significant increase in complication rates, including DVT.

Conclusion

We conclude that perioperative blood loss is significantly reduced in patients undergoing lumbar spine fixation surgery who receive TXA. Hence, TXA may help in reducing not only transfusion-related complications but also operative expenses.

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Conflicts of interest

There are no conflicts of interest.

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