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A randomized prospective study of efficacy of tranexamicacid on perioperative blood loss in thoracicspine fixation

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Background: Spine surgery is associated with significant blood loss, often requiring blood transfusion. The objective of this double blind study was to evaluate the efficacy of tranexamic acid (TXA) on perioperative blood loss in patients undergoing thoracic spine fixation.

Materials and Methods: Sixty adult patients were randomized into two groups of 30 each. Group I received a bolus of 15 mg/kg i.v. of TXA after induction followed by a maintenance infusion of 1 mg/kg/hr up to closure of skin and Group II received an equivalent volume of normal saline after induction followed by a maintenance infusion of saline up to closure of skin. Outcome measures included perioperative blood loss, amount of blood transfusion, postoperative haemoglobin and haematocrit levels.

Results: The mean perioperative blood loss was less in the TXA group compared to the placebo group (p value<0.001). The PRBCs transfusion was lower in the TXA group compared to the placebo group but there was no statistically significant difference between the two groups. The post-operative haemoglobin level was lower in the control group as compared to TXA group (p value <0.05).

Conclusion: TXA is effective in reducing peri-operative blood loss and blood transfusion.

Keywords: Thoracic spine; tranexamic acid; blood loss; haematocrit

Introduction

Thoracic spine surgeries are associated with significant blood loss, requiring transfusion due to extensive vascular supply, tissue dissection and significant bone bleeding during instrumentation and decortication.[1] Allogeneic blood transfusion has several risks like transmission of blood-borne infections, haemolytic and immune-mediated transfusion reactions.[2] Perioperative bleeding during spine surgery obscures the surgical field and enhances the risk of epidural haematoma, which may result in cord compression.

A variety of contemporary blood conservation techniques have been used to reduce exposure to allogeneic blood, including controlled hypotension, autologous blood transfusion, intraoperative blood salvage and administration of various parenteral medications. Despite current blood-conservation interventions, many patients still require blood transfusion with the associated risks and costs.[3,4,5] Antifibrinolytics have been demonstrated to reduce blood transfusion requirement during cardiac surgery, total knee and hip arthroplasty, and urological procedures.[6] suggesting that 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 tissue plasminogen activator, thereby retarding fibrinolysis and blood clot degradation. Spinal surgical procedures are routinely done at our institute hence a double-blind randomized

controlled study was undertaken to compare blood loss in two groups of patients, one group receiving TXA and the other group receiving normal saline infusion. All procedures were performed by a single surgeon.

Materials and Methods

After clearance from Hospital Ethical Committee and written informed consent 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 thoracic spine fixation surgery under general anesthesia. Patients with apreexisting renal or hepatic disorder, bleeding diathesis, history of malignancy or coronary artery disease, thromboembolic event 1 year prior to surgery, haemoglobin< 8gm/dL, and history of uncontrolled hypertension were excluded.

After pre-anesthetic evaluation, relevant investigations included haemoglobin, total count, differential count, liver and renal function tests, serum electrolytes, coagulation profile, random blood sugar, electrocardiogram, chest x-ray, and urine routine and microscopy. Patients who met inclusion criteria were randomly allotted into two groups of 30 each using sealed envelope technique. Group I received a bolus of 15mg/kg intravenous TXA shortly after induction of anaesthesia over 15 min, before skin incision followed by a maintenance infusion of 1mg/kg/hr of TXA up to closure of skin. Group II received an equivalent volume of normal saline after induction followed by a maintenance infusion of normal saline.

Since the number of levels fused is a factor influencing blood loss, a stratified randomization for the number of levels of vertebrae fused (1–2 levels, 3–5 levels, >5 levels) was used. A pharmacist who was not involved with care of the patient, prepared the placebo and treatment medicationsthat were identical in appearance. The research personnel, patients, anaesthesiologists and surgeons were blinded to the randomization.

All patients were premedicated with diazepam 5mg and ranitidine 150 mg orally on the night before the surgery. 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 5min, 10min, 15min, 20min, 30min, 45min, 60min, 75min, 90min, and 120min following induction of anaesthesia.

Patients were premedicated with glycopyrrolate 10µg/kg, ondansetron 0.15mg/kg, and midazolam 0.05mg/kg i.v. Induction of anaesthesia was with propofol 2mg/kg, fentanyl 2µg/kg, and vecuronium 0.1mg/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 anaesthesia was with nitrous oxide, oxygen, isoflurane, intermittent doses of fentanyl, vecuronium, and intermittent positive-pressure ventilation. Mild induced hypotension, i.e., mean arterial blood pressure (MAP) 20% below preoperative MAP or minimum MAP of 65mmHg was induced with the volatile anaesthetic until spinal manipulation or at any time requested by the surgeon. A forced-air warming blanket was used to maintain normothermia.

The incision time and blood loss were recorded. Intraoperative blood loss was measured by adding the volume of blood in the suction canisters and the weight of sponges. All fluids added to the surgical field intraoperatively were quantified and deducted from the measured blood loss. The number of units of packed red blood cell (PRBC) concentrates transfused to the patient was noted. Fluid therapy was managed by administration of crystalloid solution and colloid. Adequate replacement and maintenance of intravascular volume was guided by monitoring blood pressure, urine output (≥1ml/kg/h).

Patients were extubated at the end of surgery and observed in the post anesthesia care unit (PACU). Postoperative blood loss was measured from the

surgical drain for the first 24hrs. Postoperatively haemoglobin, packed cell volume (PCV) was repeated 12 hours after the surgery.

Statistical Analysis

Power analysis from similar study suggests that a sample size of 21 patients per group is required to get the power of the study 90% with $p<0.05$ significance. Quantitative data are presented as mean and standard deviation and qualitative data as frequency. Chi square test and t test was used for the analysis.

Results

Table 1: Demographic and baseline characteristics

	Group I	Group II	p value
Age (yr)	54.33 ±5.732	54.73 ±5.777	0.789
Gender (female/male)	52/21	48/26	0.408
Height (cm)	162.3 ± 12.5	165.2 ± 10.2	0.132
Weight (kg)	72.9 ± 17.2	73.9 ± 16.1	0.717
ASA status: I/II	13/17	16/14	0.166
No. of levels	2.7 ± 4.6	2.8 ± 4.3	0.910
Level groups: I/II/III	15/12/3	12/16/2	0.848

The demographic data (Table 1) of both groups were statistically comparable with respect to age, weight, height, gender, ASA status and number of levels fused.

Mean duration of surgery in Group I was 161.7±12.678min and in Group II was 171.3 ± 10.15min, which was statistically significant with a *p* value of 0.007.(Table 2) Mean intraoperative blood loss in Group I was 616.5 ± 204.756ml and in Group II was 828.2 ± 207.689ml, which was statistically significant with a *p* value of 0.001. (Table 2) Mean postoperative blood loss in Group I was 133.00 ± 45.117ml and in Group II was 269.80 ± 68.273ml, which was statistically significant with a *p* value of 0.001. (Table 2)

Table 2: Group characteristics

	Group I	Group II	P value
Duration of surgery (mins)	161.7 ± 12.678	171.3 ± 10.150	0.007*
Intraoperative blood loss (ml)	616.5 ± 204.756	828.2 ± 207.689	0.001*
Postoperative blood loss (ml)	133.00 ± 45.117	269.80 ± 68.273	0.001*
Preoperative Hb (g/dl)	14.0 ± 1.419	13.7 ± 1.677	0.48
Preoperative PCV (%)	41.86 ± 4.224	41.10 ± 5.013	0.52
Postoperative Hb (g/dl)	10.95 ± 2.092	9.25 ± 1.984	0.002*
Postoperative PCV (%)	33.01 ± 6.387	27.74 ± 5.872	0.002*

Hb: Haemoglobin, PCV: Packed cell volume

Mean preoperative haemoglobin in Group I was g/dL14.0 ± 1.419 and in Group II was13.7 ± 1.677g/dL. With the *p* value of 0.48 there was no statistical significance and the groups were comparable with respect to preoperative haemoglobin. (Table 2) Mean preoperative PCV in Group I was 41.86 ± 4.224 and in Group II was 41.10 ± 5.013; with the *p* value of 0.52 there was no statistical significance and the groups were comparable with respect to preoperative PCV. (Table 2) Mean postoperative haemoglobin in Group I was 10.95 ± 2.092g/dl and in Group II was 9.25 ± 1.984g/dl, which was statistically highly significant with a *p* value of 0.002. (Table 2) Mean postoperative PCV in Group I was 33.01 ± 6.387 and in Group II was 27.74 ± 5.872, which was statistically highly significant with a *p* value of 0.002.(Table 2)

Table 3: PRBCs transfused

No. of PRBCs	Group I	Group II	Total
1	6	8	14
2	4	6	10
3	2	4	6
Total	12	18	30

Table 3 shows the number of PRBCs transfused. In Group I, 12 patients received PRBCs, 6 patients received 1 PRBC each, 4 received 2 PRBCs each and 2 received 3 PRBCs each. In Group II, 18 patients received PRBCs, 8 received 1 PRBC each, 6 received 2 PRBCs and 4 received 3 PRBCs. There was no statistical difference between the two groups.

Discussion

Thoracic spine fixation surgery is associated with major blood loss, with requirement for blood transfusion.[1] Blood loss depends on the number of levels fused, duration of surgery, and physical status of the patient. Concerns regardingthe safety of transfused blood have led to the development ofa range of interventions to minimize blood loss during major surgeries. Both surgical and non surgical techniques have been used with varying success to reduce perioperative blood loss. The useof pharmacological therapies to reduce blood loss and blood transfusion during surgery is restricted to a few drugs, such as aprotinin, TXA, epsilon-amino-caproic acid, desmopressin, and recombinant factor VIIa. TXA has been used in orthopaedic procedures such as spine fixation, scoliosis correction, and hip and knee replacement procedures. TXA has been found to significantly reduce blood loss and blood transfusion requirements inpatients undergoing orthopaedic surgery, and does not appear to increase the risk of deep vein thrombosis.[6]

In the present study, 60 patients undergoing thoracic spine fusion surgery were randomly assigned to a TXA group I and a placebo group II of 30 each. Both groups were comparable in mean age, weight, height, ASA physical status, no. of levels fused, preoperative haemoglobin and haematocrit values. The technique of anaesthesia was standardized in both groups. Contributing factors such as coagulation profile and mean arterial blood pressure that could alter blood loss were monitored. Hypotensive anaesthesia was used in both groups i.e., mean arterial blood pressure (MAP) 20% below preoperative MAP or minimum MAP of 65mmHg was induced with the volatile anaesthetic until spinal manipulation or at any time requested by the surgeon.

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 *0.001*). Thereby, total blood loss (intraoperative plus postoperative) was consequently less in the TXA group. The mean duration of surgery was less in the TXA group compared to the control group (p value 0.007).

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 small sample size. These results were consistent with studies done by Wong *et al*[7] Elwatidy *et al*[8] and Wang *et al*.[9]

Wong *et al*[7] 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*[8] 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*[9] 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 haemoglobin and haematocrit values of patients in the TXA group compared to the control group (P <0.05). These results were consistent with studies done by Endres *et al*[10] and Elwatidy *et al*[8] in which the postoperative haemoglobin and haematocrit values were statistically significant in the TXA group compared to the control group.

A study done by Vel *et al*[11] 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 of using antifibrinolytics is 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. Studies have shown that the use of TXA in patients undergoing total knee arthroplasty did not experience an increased incidence of DVT.[12,13,14] 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 the dissolution of blood clots. A meta-analysis done by Li *et al*[15] to assess the effectiveness and safety of TXA showed that even a high dose of TXA (≥15mg/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 2.5mg/kg/BW to 100mg/kg/BW, and maintenance doses from 0.25mg/kg/BW/hr to 4mg/kg/BW/hr delivered over a period of 1–12hrs. In this study, patients received TXA as a loading dose of 15mg/kg over 15min before skin incision, followed by infusion of 1mg/kg/BW/hr up to closure of skin incision.With this dose, mean intraoperative blood loss and the amount of blood in the drains postoperatively were less in the TXA group compared to the placebo group.

A study done by Wong *et al*[7] using almost similar dose of TXA, 10 mg/kg i.v. of TXA after induction followed by a maintenance infusion of 1mg/kg/h, showed 30% reduction in perioperative blood loss.

Recently a systematic review and meta-analysis of perioperative intravenous TXA use in spinal surgery by Yang *et al*[16] 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. Thus, TXA is effective in reducing perioperative blood loss.

Conclusion

The perioperative blood loss and postoperative haemoglobin levels were significantly reduced in the TXA group and a reduction in blood transfusion was observed.

References

1. Shapiro F, Sethna N. Blood loss in pediatric spine surgery. Eur Spine J 2004; **13**: 6-17. https://doi.org/10.1007/s00586-004-0760-y PMid:15316883 PMCid:PMC3592180
2. Tasaki T, Ohto H. Nineteen years of experience with auto transfusion for elective surgery in children: More troublesome than we expected. Transfusion 2007; **47**: 1503-9. https://doi.org/10.1111/j.1537-2995.2007.01290.x PMid:17655595
3. Tai TW, Chang CW, Lai KA, Lin CJ, Yang CY. Effects of tourniquet use on blood loss and soft-

tissue damage in total knee arthroplasty: A randomized controlled trial. J Bone Joint Surg Am 2012;**94**:2209-15.
https://doi.org/10.2106/JBJS.K.00813
PMid:23318610

4. Cardone D, Klein AA. Perioperative blood conservation. Eur J Anaesthesiol 2009; **26**: 722-9.
https://doi.org/10.1097/EJA.0b013e32832c5280
PMid:19448549
5. Alshryda S, Sarda P, Sukeik M, Nargol A, Blenkinsopp J, Mason JM. Tranexamic acid in total knee replacement: A systematic review and meta-analysis. J Bone Joint Surg Br 2011; 93: 1577-85.
https://doi.org/10.1302/0301-620X.93B12.26989
PMid:22161917
6. Huang F, Wu D, Ma G, Yin Z, Wang Q. The use of tranexamic acid to reduce blood loss and transfusion in major orthopedic surgery: A meta-analysis. J Surg Res 2014; **186**: 318-27.
https://doi.org/10.1016/j.jss.2013.08.020
PMid:24075404
7. Wong J, El Beheiry H, Rampersaud YR, Lewis S, Ahn H. Blood loss in adult patients having spinal fusion surgery. AnesthAnalg 2008; **107**: 1479-86.
https://doi.org/10.1213/ane.0b013e3181831e44
PMid:18931202
8. Elwatidy S, Jamjoom Z, Elgamal E, et al. Efficacy and safety of prophylactic large dose of tranexamic acid in spine surgery: A prospective, randomized, double-blind, placebo-controlled study. Spine (Phila Pa 1976) 2008; **33**: 2577-80.
https://doi.org/10.1097/BRS.0b013e318188b9c5
PMid:19011538
9. Wang Q, Liu J, Fan R et al. Tranexamic acid reduces postoperative blood loss of degenerative lumbar instability with stenosis in posterior approach lumbar surgery: A randomized controlled trial. Eur Spine J 2013; **22**: 2035-8.
https://doi.org/10.1007/s00586-013-2836-z
PMid:23715891 PMCid:PMC3777047
10. Endres S, Heinz M, Wilke A. Efficacy of tranexamic acid in reducing blood loss in posterior lumbar spine surgery for degenerative spinal stenosis with instability: A retrospective case control study. BMC Surg 2011; **11**: 29.
https://doi.org/10.1186/1471-2482-11-29
PMid:22047046 PMCid:PMC3234174
11. Vel R, Udupi BP, Satya Prakash MV et al. Effect of low dose tranexamic acid on intra-operative blood loss in neurosurgical patients. Saudi J Anaesth 2015; **9**: 42-8.
https://doi.org/10.4103/1658-354X.146304
PMid:25558198 PMCid:PMC4279349
12. Poeran J, Rasul R, Suzuki S et al. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: Retrospective analysis of effectiveness and safety. BMJ 2014; **349**: 4829.
https://doi.org/10.1136/bmj.g4829
PMid:25116268 PMCid:PMC4130961
13. Gautam PL, Katyal S, Yamin M, Singh A. Effect of tranexamic acid on blood loss and transfusion requirement in total knee replacement in the Indian population: A case series. Indian J Anaesth 2011; **55**:590-3.
https://doi.org/10.4103/0019-5049.90614
PMid:22223903 PMCid:PMC3249866
14. Kakar PN, Gupta N, Govil P, Shah V. Efficacy and safety of tranexamic acid in control of bleeding following TKR: A randomized clinical trial. Indian J Anaesth 2009; **53**: 667-71.
PMid:20640094 PMCid:PMC2900076
15. Li ZJ, Fu X, Xing D, Zhang HF et al. Is tranexamic acid effective and safe in spinal surgery? A meta-analysis of randomized controlled trials. European Spine Journal 2013; **22**: 1950-7.
https://doi.org/10.1007/s00586-013-2774-9
PMid:23657623 PMCid:PMC3777050
16. Yang B, Li H, Wang D et al. Systematic review and meta-analysis of perioperative intravenous tranexamic acid use in spinal surgery. PLoS One 2013; **8**: 5543-6.
https://doi.org/10.1371/journal.pone.0055436