

Research Article

The Role of Tranexamic Acid (TXA) In Spine Surgery for Patients with Comorbidities in Basra/Iraq

Ali B. Al-Mahfoodh¹, Darren F. Lui², Thamer A. Hamdan²

¹Basrah Teaching Hospital, Iraq/ Basrah

²St. Georges Hospital, London

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Abstract:

Background: Blood loss occurs frequently and remains a challenge in spinal surgery. As significant intra and postoperative hemorrhage negatively affects patient outcomes by increasing coagulopathy, postoperative hematoma, and anemia. The need for allogenic blood transfusions can lead to potential transfusion reactions and infections, in addition to increasing long-term mortality rates. Although there are many randomized control trials and meta-analysis investigating the role of tranexamic acid (TXA), we could not find any study that investigated the role of TXA in patients with medical comorbidities. Therefore, tackling the role of TXA in patients with single or multiple comorbidities is of valuable outcome to our locality as most of the patients have indeed associated comorbidities.

Objectives: to investigate the role of tranexamic acid in decreasing perioperative blood loss in patients with multiple comorbidities as compared to otherwise healthy individuals.

Patients and methods: A single center randomized control trial. We included patients that were about to undergo simple decompressive surgeries for lumbar canal stenosis and fixation with decompression for spondylolisthesis. Patients were randomly categorized into cases (who received TXA) and controls who received NS. Patients then were subcategorized according to comorbidities and types of surgeries. Intraoperative blood loss was calculated using the suction drain and the gauze while the post operative bleeding was calculated using the drain output.

Results: There was 441.84 ml (49.6 %) decrease in intraoperative bleeding for patients who received TXA as compared to controls regardless the type of surgery and regardless the presence or absence of comorbidities. Hypertensive patients had 52.7 % reduction in intraoperative bleeding when received TXA, Diabetic patients showed 44.4 % reduction in bleeding, Obese patients showed 51.1% reduction and patients with multiple comorbidities showed 51% reduction in intraoperative bleeding while healthy individuals showed 38.9% reduction in intraoperative bleeding.

Conclusion: TXA was even more effective in decreasing intraoperative bleeding in patients with multiple comorbidities as compared to healthy individuals.

Introduction:

Massive blood loss occurs frequently and remains a challenge in spinal surgery.^[1] As significant intra and postoperative hemorrhage negatively affects patient outcomes by increasing coagulopathy, postoperative hematoma, and anemia. ^[2] The need for allogenic blood transfusions can lead to potential transfusion reactions and infections, in addition to increasing long-term mortality rates. ^[2] There is an economic disadvantage associated with iatrogenic major blood loss relating to the direct costs of the blood products and intraoperative blood salvage technology and indirect costs of prolonged patient hospitalization and complication management. ^[3]

Increasing numbers of meta-analyses of RCTs in recent years are contributing to our body of knowledge regarding the hemostatic benefits of TXA in spinal surgery. Wong *et al.* administered TXA intravenously with an initial bolus dosage of 10 mg/kg and 1 mg/kg per hour of maintenance

infusion until skin closure for 147 patients who underwent elective posterior instrumented spinal fusion.^[4] Estimated blood loss from the procedure was reduced by as much as 30% in patients who were given IV administration of TXA as measured by higher postoperative hemoglobin levels and decreased need for red blood cell saver use. Yang *et al.* conducted a meta-analysis of 9 studies comprising of 581 patients and demonstrated that patients receiving TXA perioperatively had a reduction of blood loss along with a statistically significant decrease in the need for blood transfusion.^[5] Raksakietisak *et al.* showed a statistically significant decrease in blood loss in patients receiving TXA following a complex laminectomy procedure. Patients who received two doses of TXA at 15 mg/kg compared to those who received placebo demonstrated decreased blood loss and decreased use of IV crystalloid fluids including packed red blood cells.^[6]

In Iraq the Most Commonly performed Spinal Surgeries are for degenerative lumbar spine disorders and most of the patients are middle to old age having associated comorbidities like Diabetes, Hypertension as well as Obesity Which may be associated with other mal habits like Smoking and alcohol consumption. Unfortunately, not much was written about the specific effect of comorbidities on perioperative bleeding in spine surgeries. Once again, these procedures are often Complicated by intraoperative and postoperative bleeding which may disturb the work, lead to confusion, failure to achieve the goal and negatively affects patient's outcome. (Hamdan personal communication)

Therefore, it was worthy to study the Effect of Tranexamic Acid in decreasing intraoperative and postoperative bleeding in spine surgeries especially for stenosis and spondylolisthesis for patients with comorbidities taking into Consideration the safety profile of TXA in those patients.

Methodology:

Study Design

A Single Center experimental randomized control Trial.

Study duration

The time of the study was 3 years (January 2021- January 2024)

Target Population

Adult patients Undergoing Surgeries For 1-Spinal Stenosis (single or 2 levels laminectomy) 2-Spodylolisthesis (2 levels fixation with laminectomy)

Inclusion criteria

- 1-Patients Undergoing Surgeries for Spinal Stenosis and Spondylolisthesis.
- 2-Preoperative Adults Admitted to spine wards With or without preexisting comorbidities: hypertension, Diabetes Mellitus and obesity.
- 3-Patients who are aged >18 years
- 4-Patients who are Able to Give Informed Consent.

Exclusion Criteria

- 1-Patients on anticoagulants.
- 2- Patients with Bleeding Tendencies.
- 3- Patients with hemoglobinopathies.
- 4- Patients with renal impairment.
- 5-Patients with previous known Allergic reaction to Tranexamic Acid and/or having a contraindication for TXA (previous thromboembolic disease or having active thromboembolic disease or previous seizures).
- 6-Patients with history of vascular occlusive disease (eg. Myocardial infarction, peripheral vascular disease).
- 7-Patients Under 18 years Old.
- 8-Patients Unable to Give Informed Consent.
- 9-Patients undergoing revision spine surgeries
- 10-Patients went through intraoperative complications such as dural-tear and/or unusually prolonged operative time

Study procedure

-The research Clinical team liaised to identify potential patients.
-Patients recruitment was done within 24 hours of their admission.

-Identified eligible patients (see inclusion /exclusion criteria) were given an internal Study Number, the participant Number, i.e 001, 002,003 for the first, second and third patient that has been identified.

-The Front sheet of the case report form (CRF) contained the participant number, details to Identify the patient (hospital number, name and the age).

-Participant number was recorded on each page of the case report form.

-Patients age in years and gender was recorded on the case report form.

-Details about the patient's comorbidities and chronic Drug use as well as number of medications. The First set of observations was recorded on the case report form.

-Baseline investigations were done for each patient (CBC, renal Function test, RBS HbA1C and viral markers).

-Patients were divided into 2 groups randomly (1-placebo group (controls) 2-IV TXA group (Cases)) in a one-by-one bases (odd numbers being controls and even numbers being cases).

-Patients were also divided into groups according to the comorbidities into:

1- Hypertension group 2-Diabetes group 3- Obese group (BMI >30) 4- Multiple comorbidity group (having 2 or more of the previous comorbidities).

-Controls received receive 100 ml I.V N/S 20 minutes preoperatively

-Cases received 10 mg/kg I.V TXA in 100 ml N/S 20 minutes preoperatively

-Tranexamic Acid that was used during this Trial Will be of a Single Pharmaceutical Company (Pfizer).

-Blood loss During the Operation was Calculated Using the 1-suction container After subtraction the amount of Fluid used for irrigation 2-weight of the gauze used for swapping the Field and subtracting the equivalent weight of the Dry Gauze then conversion of the weight in to volume depending on the fact that the density of the blood is 1.0565 g/ml

The operative time for single level decompression was 45 minutes +/- 10 minutes. For 2 levels decompression was 60 minutes +/- 10 minutes and for fixation was 90 minutes +/- 15 minutes. And any procedure that took longer than this time resulted in exclusion from the study.

- Post operative bleeding was recorded using the Drain output, immediately post operatively, at day 0 and day 1 post operatively

-Any Adverse Effects of TXA were to be recorded in the CRF (Symptomatic deep veinous thrombosis, Symptomatic Pulmonary embolism, symptomatic myocardial infarction, cerebro-vascular Accident) but non actually happened.

Data Analysis

Statistical analysis was performed with SPSS (statistical package for social sciences) version 22 and R Studio (© 2009-2020 Studio, Inc.).

Demographic distribution:

Table 1: Demographic Distribution

		Number	Percentage
Sex	Males	43	23.4%
	Females	141	76.6%
	Total	184	100%
Age	20-40 years	8	4.3%
	41-60 years	119	64.7%
	61 years and above	57	31%
	Total	184	100%
Surgery	Single level decompression	75	40.8%
	Two levels decompression	65	35.3%
	Two levels Fixation with decompression	44	23.9%
	Total	184	100%
Comorbidity	Hypertension	15	8.2%
	Diabetes	4	2.2%
	BMI above 30	29	15.8%
	Multiple comorbidities	92	50%
	Otherwise healthy	44	23.9%
	Total	184	100%
Type	Case	92	50%
	Control	92	50%
	Total	184	100%

The total sample size was 184 patients, 43 males (23.4%) and 141 females (76.6%). 8 patients (4.3%) were of 20-40 years of age and 119 patients (64.7%) were between 41-60 years of age while 57 patients 31% were of 61 years of age and above. 75 patients (40.8%) underwent single level decompression, 65 patients (35.3%) underwent two levels decompression and 44 patients (23.9%) underwent Two level Fixation with decompression. 15 patients (8.2%) were hypertensive, 4 patients (2.2%) were diabetic, 29 patients (15.8%) were of BMI above 30, 92 patients (50%) had multiple comorbidities, and 44 patients (23.9%) were otherwise healthy. 92 patients (50%) were cases that received (TXA) and 92 patients (50 %) were controls.

The effect of comorbidities on intraoperative bleeding:

Table 2: The Effect of comorbidities on intraoperative bleeding (p value <0.005)

Comorbidity	Average bleeding in ml	Number
Hypertension	528.43	3
Diabetes	382.2	2
BMI 30 and above	480.11	13
Multiple Comorbidities	456.63	48
Otherwise healthy	389.98	26

Table 2 shows that having comorbidities are associated with increased intraoperative bleeding among controls. Patients with hypertension have shown intraoperative bleeding to be 528 ml (1.3 times that of the healthy individuals), Obese patients with BMI 30 and above showed 480.11 ml (1.2 times more bleeding than healthy ones), patients with multiple comorbidities also showed 456.63 (1.2 times more bleeding) while diabetic patients bleeding to be 382.2ml (0.2 that of healthy individuals).

The overall effect of (TXA) on intra operative bleeding:

Table 3: The Overall effect of (TXA) on intraoperative bleeding in ml (p value <0.005)

No. of cases	No. of controls	Average Bleeding in Cases in ml	Average bleeding in Controls in ml	Difference
92	92	441.84	222.33	219.51 (49.6%)

Table 3 shows that controls had 441.84 ml bleeding while cases had 222.33 ml bleeding (49.6 % reduction in bleeding) regardless the type of surgery and regardless the presence or absence of comorbidities.

The effect of TXA on different types of comorbidities:

Table 4: The effect of TXA on Different types of comorbidities. (p value: < 0.005)

Comorbidity	No. of Cases	No. of Controls	Average Bleeding in cases in ml	Average bleeding in Controls in ml	Difference in ml
Hypertension	12	3	218.2	528.43	310.23
Diabetes	2	2	212.5	382.2	169.7
BMI 30 and above	16	13	234.5	480.11	245.61
Multiple comorbidities	44	48	223.55	456.63	233.05
Other-wise healthy	18	26	212.34	389.98	72.67

The effect of TXA on different surgeries:

Table 5: comparison of the effect of TXA on different types of surgeries. (p value < 0.005)

Surgery	No. of cases	No. of Controls	Average Bleeding in Cases in ml	Average Bleeding in controls in ml	Difference in ml
Single level decompression	34	41	189.42	364.60	175.18
2 levels decompression	35	30	225.38	511.14	285.76
Fixation+ decompression	23	21	266.36	493.62	118.8

Table 5 shows that there was 175.18 ml (48%) decrease in intraoperative bleeding when patients underwent single level decompression received TXA and 285.76 ml (55.9%) decrease in intraoperative bleeding for patients who underwent two

levels decompression, while there was 118.8 ml (24%) decrease in intraoperative bleeding for patients who underwent fixation with decompression.

The effect of TXA on Single level decompression:

Table 6: intraoperative bleeding for single level decompression in ml (p value < 0.005)

Comorbidity	No. of Cases	No. of Controls	Average Bleeding in cases in ml	Average bleeding in Controls in ml	Difference in ml
Hypertension	6	1	182.91	591.00	408.1
Diabetes	1	1	252.00	332.00	80
BMI 30 and above	3	7	147.73	400.92	253.2
Multiple comorbidities	17	21	192.64	374.23	211.59
Other-wise healthy	7	11	195.12	305.49	42

The effect of TXA on two levels decompression:

Table 7: intraoperative bleeding for 2 levels decompression (p value < 0.005)

Comorbidity	No. of Cases	No. of Controls	Average Bleeding in cases in ml	Average bleeding in Controls in ml	Difference in ml
Hypertension	3	1	239.33	441.50	202.17
Diabetes	1	1	173.00	432.40	259
BMI 30 and above	12	4	246.54	641.25	394.7
Multiple comorbidities	14	17	208.56	538.85	330.29
Other-wise healthy	5	7	223.78	390.70	69.55

Table 7 shows that the intraoperative bleeding has 202.17 ml (45.7%) decrease among hypertension group who received TXA. For diabetic patients 259 ml (59.9%) decrease in bleeding, obese patient showed 394.7 ml (61.5%) decrease, while patients with multiple comorbidities showed 330.29 ml (61.3%) decrease and the otherwise healthy group showed 69.55 ml (42.7%) decrease in intraoperative bleeding.

The effect of (TXA) on two levels fixation with decompression

Table 8: intraoperative bleeding for 2 levels fixation with decompression (p value < 0.005)

Comorbidity	No. of Cases	No. of Controls	Average Bleeding in cases in ml	Average bleeding in Controls in ml	Difference in ml
Hypertension	3	1	267.63	552.80	285.17
Diabetes	0	0	0	0	0
BMI 30 and above	4	2	351.40	435.00	83.6
Multiple comorbidities	13	10	280.12	489.89	209.77
Other-wise healthy	6	8	221.73	505.55	283.82

Table 8 shows that hypertension group showed 285.17 ml (51.5%) decrease in bleeding while obese patients showed 83.6 ml (19%) decrease in bleeding. The Multiple comorbidity group showed 209.77 ml (42%) decrease in bleeding and otherwise healthy patients showed 283.82 ml (56%) decrease in bleeding.

The effect of tranexamic acid on post-operative bleeding

Table 9: The effect of TXA on postoperative bleeding (p value < 0.005)

No. of cases	No. of controls	Average bleeding in Cases in ml	Average bleeding in Control in ml	Difference in ml
92	92	84.54	86.35	1.81

This table shows that the difference in post-operative bleeding between cases and controls was 2ml, which is only 2.3% reduction the drain output regardless the presence or absence of comorbidities.

Postoperative bleeding in different comorbidities

Table 10: Postoperative bleeding in different comorbidities

Comorbidity	Average bleeding in ml	Number
Hypertension	84.66	15
Diabetes	107.5	4
BMI 30 and above	92.24	29
Multiple Comorbidities	85.38	92
Otherwise healthy	79.38	44

This table shows that hypertensive patients have average post-operative bleeding of 84.66 ml, diabetic patients had average of 107.5 ml, obese patients had 92.24 ml, patients with multiple comorbidities had 85.38 ml and otherwise healthy patients had 79.38 ml post-operative bleeding

Discussion:

Tranexamic acid has been used for long period to decrease intra and post-operative bleeding; not only in orthopedic surgery but in many other surgical fields. There are many studies on the effect of TXA in spine surgery. Some researches experimented the effect of the systemic TXA, others used topical and local while some researchers used a combination of different methods of administration of TXA.

The overall study provided insights about the role of systemic tranexamic acid in different types of spine surgeries, it also provided important clues about how different comorbidities responded to tranexamic acid in details. And there was obvious correlation between the comorbidities and increased perioperative bleeding.

184 patients were included in this study and the demographic distribution of the study population actually reflects demographic distribution of degenerative spine diseases in our locality. It is well known that degenerative spine disease are more common in females than in males, Chantal et al (7) found

in their study (Prevalence of spine degeneration diagnosis by type, age, gender, and obesity using Medicare data) that Female to Male Ratio was 1.3. Interestingly, in our study females contributed to 76.6% of the sample, while males were only 23.4%. mirroring a Female to Male Ratio of 3.2 which was obviously much higher than what Chantal et al⁽⁷⁾ found in their study in USA. The majority of patients that were included in our study were of 41-60 years of age, while Chantal et al⁽⁷⁾ found that prevalence of spine degeneration was the highest in 75-84 years group. This supports that demographic distribution varies in different geographical regions which could be attributed to genetic or environmental factors.

Half of the patients that were included in our study were case and the other half were controls, there was overall 49.6 % decrease in intraoperative bleeding which was a promising result. 75% of the included population had either single or multiple comorbidities and 25% were otherwise normal, patients with hypertension have benefited the most from TXA with total reduction in intraoperative bleeding was 52.7% regardless the type of procedure. Obese patients and multiply comorbid patients showed 51.1% and 51% reduction in bleeding respectively. Diabetic patients showed 44.4% reduction in bleeding while otherwise healthy patients showed 38.9% reduction in bleeding, these results indicate that tranexamic acid is even more effective in patients with multiple comorbidities than in healthy individuals and that was the opposite of what we have expected; as by common sense healthy individuals are expected to benefit more than patients with multiple medical comorbidities. Anyhow we could not find an explanation to this finding.

Patients who underwent single level decompression had 48% reduction in bleeding regardless the comorbidities of the patients. Patients who underwent two levels decompression had 55.9% reduction in bleeding while patients who underwent fixation with decompression had 24% decrease in intraoperative bleeding. These results were consistent with (Elwatidy et al)⁽⁸⁾ in their study about the prophylactic use of TXA spinal decompressive surgery. However, they were inconsistent with the results of (Elmose et al)⁽⁹⁾ who didn't find any statistical significance in the intraoperative blood loss when they used tranexamic acid for simple decompressive surgeries for degenerative lumbar spine disorders.

Larson et al⁽¹⁰⁾ found that perioperative use of TXA is associated with significant decrease in the postoperative drain output which was inconsistent with our results as post operative bleeding was only decreased by 2.3%, which was not significant enough and this is explained by the short half-life when administered intravenously which is 2 Hours, which means that by the time the patient is discharged back to the ward, the effect of tranexamic acid had decreased.

Medical comorbidities have shown to increase the post operative bleeding along with the intraoperative bleeding, healthy individuals have a shown an average of postoperative bleeding as calculated by drain output to be 79.38 ml while Hypertensive patients showed an average of 84.66 ml, Obese patients had 92.24 ml, patients with multiple comorbidities had 85.38 ml and finally diabetic patients have shown post-

operative bleeding to be 107.5 ml it was the highest reading among all other comorbidities but it's worth mentioning that that total number of diabetic patients that were included in this study were 4 out of a total 184 patients.

There was 0% complication rate or side effects that could be attributed to TXA which was consistent with the results of Xue et al⁽¹¹⁾ who also found that tranexamic has a safe profile and did not cause any side-effects or complications like DVT and pulmonary embolism in their study to test the efficacy and safety of tranexamic acid in reducing perioperative blood loss in patients with multilevel spinal stenosis.

3.12 Conclusion

1-Low dose Tranexamic acid had proven its efficacy in decreasing intraoperative bleeding for simple lumbar decompressive procedures and posterolateral fusion surgeries.

2-Patients with multiple comorbidities have benefited more than the otherwise healthy individuals from the use of TXA

3-The was no significant statistical difference in post-operative bleeding between cases and controls.

4-the safety profile was high for the low dose TXA even with the background of multiple or single comorbidities.

References

1. Tse E Y, Cheung W Y, Ng K F et al. Reducing perioperative blood loss and allogeneic blood transfusion in patients undergoing major spine surgery. *J Bone Joint Surg Am.* 2011;93(13):1268–1277.
2. Zollo R A, Eaton M P, Karcz M et al. Blood transfusion in the perioperative period. *Best Pract Res Clin Anaesthesiol.* 2012;26(4):475–484.
3. Hofmann A, Ozawa S, Farrugia A et al. Economic considerations on transfusion medicine and patient blood management. *Best Pract Res Clin Anaesthesiol.* 2013;27(1):59–68.
4. Wong J, El Beheiry H, Rampersaud YR et al. Tranexamic acid reduces perioperative blood loss in adult patients having spinal fusion surgery. *Anesth Analg.* 2008 Nov; 107(5):1479-86
5. 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(2):e55436.
6. Raksakietisak M, Sathitkarnmanee B, Srisaen P et al. Two Doses of Tranexamic Acid Reduce Blood Transfusion in Complex Spine Surgery: A Prospective Randomized Study. *Spine (Phila Pa 1976).* 2015 Dec; 40(24):E1257-63.
7. Chantal.S., Lau, E.C., Campbell, I.C. et al. Prevalence of spine degeneration diagnosis by type, age, gender, and obesity using Medicare data. *Sci Rep* 2021 11, 5389
8. Elwatidy S, Jamjoom Z, Elgamel 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 Nov 15;33(24):2577-80.
9. Elmose S, Andersen MØ, Andresen EB, et al. Double-blind, randomized controlled trial of tranexamic acid in minor lumbar spine surgery: no effect

- on operative time, intraoperative blood loss, or complications. *J Neurosurg Spine*. 2019 Apr 12:1-7.
10. Larson E, Evans T, Long J, et al. Does Prophylactic Administration of TXA Reduce Mean Operative Time and Postoperative Blood Loss in Posterior Approach Lumbar Spinal Fusion Surgery Performed for Degenerative Spinal Disease? *Clin Spine Surg*. 2019 Aug;32(7):E353-E358.
11. Xue P, Yang J, Xu X, et al. The efficacy and safety of tranexamic acid in reducing perioperative blood loss in patients with multilevel thoracic spinal stenosis: A retrospective observational study. *Medicine (Baltimore)*. 2018 Dec;97(50):e13643

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