

## The Comparison of Systemic and Local Tranexamic Acid Application Use in Reducing Bleeding in Spinal Surgery

### Abstract

**Background:** The application of Tranexamic Acid (TA) is one of the methods to control and reduce bleeding in spinal surgery. The aim is to compare systemic (TA) with local (TA) administration for reduction of blood loss during spinal surgery in order to promote health economics.

**Method:** The research schema was cross-sectional and retrospective in the community of patients undergoing spinal surgery in the Baqiyatallah Hospital. The inclusion criteria were elective spinal surgeries of three levels or more. The exclusion criteria were bleeding disorder. The required analyses are performed using SPSS software. Moreover, the significance level of the statistical test is 0.05. The intravenous dose is selected to be 10mg/kg. The maintenance is also 1mg/kg/h. The topical dosage is one gram in 300ml at the beginning and 500mg in 50ml at the end. The amount of calculated bleeding is the volume of blood in the drain.

**Results:** In this research, 22 patients (%44.9 of 49 patients) received TA intravenously and 27 patients (%55.1 of 49 patients) received local TA. There was no remarkable relationship between the amount of bleeding in different groups with the surgery type ( $p: 0.48$ ), surgery level number ( $p: 0.48$ ), and the amount of total bleeding ( $p: 0.14$ ). The local TA group's intra-operative and post-operative bleeding amounts were  $563.89 \pm 367.48$ ml and  $116.30 \pm 71.37$ ml, respectively. These intra-operative and post-operative bleeding amounts were  $496.64 \pm 296.84$ ml and  $75.84 \pm 120$ ml for the case of the intravenous (TA) group.

**Conclusion:** The results do not confirm the effectiveness of the local administration compared with the intravenous administration. However, the average amount of bleeding in the local application of tranexamic acid is similar to the systemic one.

**Keywords:** Intravenous Administration, Topical Administration, Tranexamic acid, Spinal Fusion, Bleeding

Received: 1 month before printing; Accepted: 20 days before printing

Hamid Hesari Kia, MD<sup>1</sup>; Alireza Rahimnia, MD<sup>2</sup>; Gholamreza Farzanegan, MD<sup>3</sup>; Musa Reza Anbarloui, MD<sup>4</sup>;  
Amin Hamidzadeh Khayavi, MD<sup>1</sup>

<sup>1</sup>Assistant Professor of Orthopaedics,

<sup>2</sup>Professor and Head of Orthopaedic Department,

<sup>3</sup>Associate Professor and Head of Neurosurgery Department,

<sup>4</sup>Assistant Professor, Department of Neurosurgery,

<sup>1,2,3,4</sup>Baqiyatallah University of Medical Sciences, Tehran, Iran.

**Corresponding author:**  
A Hamidzadeh Khiavi  
**Email Address:**  
drahkh2000@gmail.com

### Introduction

Nowadays, the number of spinal surgeries is increasing, and consequently, the bleeding amount is highly influential on postoperative outcomes. Blood loss is one of the most common complications of major spinal surgeries and necessitates blood transfusions <sup>(1)</sup>. More bleeding demands greater blood transfusions and intensifies the impacts on organs, body fluid, the immune system, and the infection rate. One method to control bleeding in elective surgeries is using anti-fibrinolytic agents, one of the most effective drugs known as tranexamic acid <sup>(2)</sup>. Recent research on the application of tranexamic acid on patients with hemorrhagic trauma demonstrated the benefits of mortality without a marked increase in the risk of thromboembolic events. It is speculated that this survival benefit may be attributed to an anti-inflammatory effect rather than an anti-fibrinolytic effect <sup>(3)</sup>.

Several works are also conducted on the effectiveness of tranexamic acid on the spine. In a research conducted by Viswanadha Arun-Kumar (2021), it is revealed that the intravenous and local tranexamic acids effectively reduce intraoperative blood loss similarly in instrumental spine surgeries. This is the first detailed study

on the safety and efficacy of local tranexamic infiltration in spinal surgeries. It is shown that this method is an effective and safe way of reducing intraoperative blood loss<sup>(4)</sup>.

Zhencheng Xiong demonstrated that tranexamic intravenous administration significantly decreases the blood loss and blood transfusion compared to the local one during the spinal deformity surgeries in his paper entitled "Comparison of total tranexamic acid in spinal deformity surgery" (2020). According to the collected PT and APTT analyses, intravenous and topical tranexamic applications may have different effects on the coagulation pathways. Higher qualities of RCTs are needed to discover the optimal dose, method, and timing in the future in order to recommend the widespread use of tranexamic surgery in spinal surgery<sup>(5)</sup>. Ketan Yerneni (2019) concluded that topical TXA optimally decreases postoperative blood loss and the length of hospital stay in patients undergoing spinal surgery. However, more randomized controlled trials will be required to determine the optimal therapeutic doses needed for bleeding management and pharmacodynamics of TXA in spinal surgery<sup>(6)</sup>. Apparently, conducting research on the effects of bleeding control using safe and inexpensive methods will profoundly influence the operation quality and patients' lives after their surgeries due to the growing number of spine surgeries and the effects of bleeding control on the outcomes. The fact is that the successful application of local tranexamic acid in reducing postoperative bleeding and the need for blood transfusions has paved the way to study this drug in the field of spine surgery<sup>(10)</sup>. Therefore, defining an application protocol of intravenous and local tranexamic in patients with spine surgeries is vital to decrease postoperative bleeding to reduce complications, treatments, and hospitalization costs and, consequently, to promote health economics. The objective of this paper is to realize whether the local tranexamic can be as effective as the intravenous type in controlling postoperative bleeding in patients of the intravenous type.

Moreover, the differences between patients' postoperative bleeding rates in each of the topical and injection methods will be investigated.

## Methods

The current study is a retrospective cross-sectional research. The study population consists of patients who underwent spinal surgeries for six months in Baqiyatallah Hospital. Two groups of 20 people are randomly selected from patients who are chosen for elective spine surgeries. Among those, patients with at least three levels of spinal operations are included in the study. However, patients with known bleeding disorders, Doras during surgeries, and long surgery times (more than three hours) are excluded from this work. The dosage of the injection is as follows:

For the first group:

Intravenous tranexamic is administered at a loading dose of 10mg/kg and subsequently 1mg/kg/h<sup>(8)</sup>.

For the second group:

To prepare the required solution, one gram of tranexamic acid is diluted in a 300ml sterile normal saline solution.

Tranexamic-impregnated gases are used to pack the operating environment during the application.

The fluid is poured into the wound after completing the approach. After a pause for 5 minutes, the following steps (laminectomy and instrumentation) are taken.

The surgical wound is washed using 500mg diluted Tranexamic Acid in 50ml of normal saline for 2-5 minutes before closure.

The following efforts are taken to calculate the amount of bleeding:

For intra-operational bleeding: The bloody Gauzes are weighted, and their dry weights are subtracted. Then, the blood volume in the suction container (after deducting the volume of used fluids) is added to acquire the bleeding during the operation.

For postoperative bleeding: The drain is eliminated after 6 hours, and the amount of blood inside the drain is recorded. Obviously,

**Table 1. Gender frequency in local and intravenous administration groups**

Valid percentage	percentage	frequency	gender	Administration type
54.5	54.5	12	male	intravenous
45.5	45.5	10	female	
100	100	22	total	
25.9	25.9	7	male	local
74.1	74.1	20	female	
100	100	27	total	

**Table 2. Distribution of operation type in local and intravenous administration groups**

percentage	Total	Local	intravenous		
85.71429	42	24	18	instrumentation	Operation type
14.28571	7	3	4	laminectomy	
	49	27	22		total

**Table 3. Frequency of surgical level in local and intravenous administration groups**

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Valid percentage	percentage	frequency	Operation type	Administration type
45.5	45.5	10	3	Intravenous
31.8	31.8	7	4	
9.1	9.1	2	5	
13.6	13.6	3	6	
100	100	22	Total	
51.9	51.9	14	3	Local
44.4	44.4	12	4	
3.7	3.7	1	6	
100	100	27	Total	

**Table 4. Relationship between bleeding volume in local and intravenous administration groups**

Table 4. Relationship between bleeding volume in local and intravenous administration groups					
Total Bleeding	Postoperative Bleeding	Intra-operative Bleeding			Administration type
22	22	22		Number	Intravenous
616.6364	120	496.6364	Mean	Normal variables	
311.45282	75.84445	269.84035	Standard deviation		
27	27	27		Number	Local
680.1852	116.2963	563.8889	Mean	Normal variables	
394.8305	71.36839	376.47586	Standard deviation		

if the drain box is exchanged, its values are added to the registered number to obtain postoperative bleeding<sup>(7)</sup>.

The data collection tool is a questionnaire.

## Results

Data analysis is performed using the well-known statistical software SPSS (version 24). Mean and standard deviations are considered for quantitative variables. In addition, frequency and its percentage are considered for quantitative variables. The statistical tests and their significance level are 0.05.

The total number of patients participating in this project is 49. Among this population, 22 patients (44.9%) are allocated to the intravenous group and 27 patients (55.1%) to the local group. Regarding gender, 19 males and 30 females took part in this research.

Age-based analysis by injection type (first and second groups): There is no significant difference (Spearman correlation coefficient due to the lack of normal distribution).

The relationships between gender, age, and bleeding types (during and after the operation and their total amount): The only significant relationship is between sex and postoperative bleeding (p-value = 0.047).

The total number of patients with diabetes in this study is 9. Five patients with diabetes are classified in the intravenous administration group and four patients in the topical administration group. Forty patients (81.6% of the total patient population) had no history of diabetes, while nine patients (18.4% of total) had diabetes.

According to the achieved values, a significant relationship is realized between local and intravenous groups with and without diabetes and the amount of bleeding (p-value = 0.04).

According to the achieved values, no significant relationship is found between local and intravenous groups with and without hypertension and bleeding rate (p-value = 0.9). Most patients in this group had spinal instrumentation surgeries. According to the obtained values, there are no significant relationships between local and intravenous groups with the surgery type and the bleeding amount (p-value = 0.48).

According to the acquired values, no significant relationships are realized among local and intravenous groups with the extent of surgery and the bleeding amount during and after surgery and also the total value (p-value = 0.48, 0.79, and 0.48, respectively).

By comparing the obtained values, no significant relationships are detected between local and intravenous bleeding and the amount of bleeding during and after the operation (p-value = 0.14).

**\*\*The relationship between surgery duration and bleeding rate:** The time of surgery is correlated to intraoperative bleeding and the total amount of bleeding.

The correlation test is performed based on the distribution type. Evidently, a significant relationship is found between the surgery time, intraoperative bleeding, and total bleeding in the intravenous group. However, no significant relationship is detected between the surgery time and postoperative bleeding in the local type.

## Conclusion

Using the tranexamic method can lead to significant cost savings by lowering blood transfusions, transfusion-related complications, and length of hospital stay. Although, there are little data about the functional outcomes of patients receiving tranexamic and patients not receiving it. Future research will push the borders of knowledge on the effectiveness of tranexamic acid in total joint replacement and complex spinal replacement surgeries and continue to shed light on the length of hospital stay and the consequent reduction in health care costs<sup>(9)</sup>. There are no significant relationships between local and intravenous bleeding during intraoperative, postoperative bleeding, and total bleeding based on the comparison of our research's obtained values (p-value = 0.014). This indicates that local administration is as effective as intravenous administration. TA is used at the beginning of the procedure in spinal surgeries to reduce surgical bleedings during the surgeries and the following 24 hours. This is recommended for patients with haemoglobin amounts less than 12gr/dl due

to the possible side effects. Future studies are required to deduce the advantages and disadvantages of TA application in spinal surgeries<sup>(10)</sup>. This study confirms our findings while recommending further research.

Tranexamic does not significantly reduce the need for blood transfusions. However, it substantially decreases the preoperational blood loss risk in adults undergoing major spinal surgery<sup>(11)</sup>.

Weera Sudprasert evaluated local tranexamic acid in patients with thoracolumbar spinal trauma in a study for postoperative bleeding in a total of 57 patients (2019). This research is different since the solution containing one gram of tranexamic acid is applied to the surgical site after closing the spinal fascia through a drainage tube, and consequently, the drainage is clamped for 2 hours. They revealed that applying one gram of local administration in cases of the spinal cord and lumbar spinal trauma minimizes the postoperative bleeding effectively as determined by the total drain volume<sup>(12)</sup>. This study merely examined the local type. However, it confirms our findings. In our research, the volume of postoperative bleeding is  $116.30 \pm 71.37$  ml, which is much less than the mentioned work. This is probably because of choosing trauma patients.

According to the results, there is no significant relationship between the type and amount of bleeding in the local and intravenous groups. Moreover, there is no meaningful relationship between the local and intravenous groups with the surgery type (device and laminectomy) and the amount of bleeding ( $p$ -value = 0.48). This indicates the effectiveness of tranexamic topical administration in reducing blood loss in surgeries.

This finding is consistent with the results of the research by Kumar (2021). His work demonstrates that intravenous and local tranexamic methods are equally influential in reducing intraoperative blood loss in instrumental spine surgeries.

Intravenous TXA is an effective bleeding agent in spinal surgeries. The topical application of TXA in surgeries demonstrates similar haemostatic efficacy and potentially improves safety compared to intravenous TXA. For

spinal surgeries, the local use of TXA is rare but promising. The findings of this study open up the field on further research as the efficacy of local TXA is to be studied in complex spine procedures where the blood loss is expected to be even more<sup>(13)</sup>. Despite representing the effectiveness of intravenous TXA, lack of research on topical administration, and its hopefulness in this work, the need for more research is still announced. Despite showing the effects of intravenous TXA, the lack of research on topical administration, and its promising nature in this study, they still announce the need for more research evident in our quest. Although, local TA is indicated to be as effective as intravenous administration in our study.

Tranexamic intravenous administration has no remarkable effect on reducing blood loss and blood transfusion rate compared to the local group during spinal deformity surgeries. Based on the collected analysis, intravenous and local tranexamic applications may affect the coagulation pathway differently. Higher quality RCTs are required to discover the optimal dosage, method, and time schedule to recommend tranexamic widely used in spinal surgery in the future<sup>(5)</sup>. It could be deduced from the collected data from six RTC studies that local tranexamic method is as effective as the intravenous one, which is consistent with our findings.

Zakk Walterscheid (2017) showed that tranexamic acid is widely accepted to reduce blood loss and transfusion rate in spinal surgery<sup>(9)</sup>. Both IV and topical administration show a reduction in EBL and decreased transfusion rates. It is shown in more recent studies that oral TXA has similar effects on IV and topical dosing. IV TXA is the predominant route of administration in spine surgery. This is likely due to its increased ability to provide therapeutic levels over such a large wound surface area. The increased risks of Thromboemboli events from TXA treatment are not shown to be clinically important when pharmacological and/or mechanical VTE prophylactic measures are taken after total joint surgery. However, certain common exclusion criteria eliminate a subset of high-risk patients in which TXA use in total joint arthroplasty is not thoroughly studied.

Similarly, the recorded articles in the literature on TXA in spine surgeries are not sufficient to make a definitive claim about the risks of DVT and PE. TXA application can lead to substantial cost-savings associated with decreased transfusions, transfusion-related complications, and length of hospital stay. Although, there is a paucity of data to study the functional outcomes of administering TXA. Future investigations will build up the knowledge on the efficiency of the TXA in total joint arthroplasty and complex spinal surgeries. These efforts will continue to shed light on the potential to reduce the length of stay and, consequently, decrease healthcare costs<sup>(9)</sup>. Although, this study confirms both intravenous and intravenous administrations and suggests an oral option. It also discusses side-effects and lack of adequate background in functional outcomes and generally concludes that medication should be prescribed. And again, like other studies, more research is called for.

Xue et al. realized that intravenous TXA is an effective bleeding agent in spinal surgeries. The use of local TXA in surgeries has similar homeostatic efficiency and improves safety compared with the intravenous TXA. Articles on local TXA in spinal surgeries are rare but promising. Thus, further clinical research has been considered a clinical option in cases with expected significant blood loss at the surgical location<sup>(13)</sup>. Although this study confirms our findings and evaluates several studies, it faces a lack in the literature for topical administration, similar to the problem in this research. The bleeding rates in the topical administration group for intraoperative, postoperative, and total bleeding are reported as  $363.89 \pm 367.48\text{ml}$ ,  $116.30 \pm 71.37\text{ml}$ , and  $680.19 \pm 394.83\text{ml}$ , respectively. In addition, these values are reported for the intravenous administration group as  $496.64 \pm 296.84\text{ml}$ ,  $120 \pm 75.84\text{ml}$ , and  $616.64 \pm 311.45\text{ml}$ , respectively. The results do not confirm the hypothesis that topical administration is more effective than intravenous administration. However, it is deduced that the average bleeding rate in topical application of tranexamic acid is

similar to the injectable type. Although, the side effects of topical administration are fewer.

Our achieved results are similar to the findings of Jianjiang Li (2020) regarding the effects of topical and intravenous administration. The results for the combined, IV, local, and control groups are  $635.49 \pm 143.60\text{ml}$ ,  $892.62 \pm 166.85\text{ml}$ ,  $901.11 \pm 186.25\text{ml}$ , and  $1225.11 \pm 186.25\text{ml}$ , respectively<sup>(4)</sup>. This research calculates the total bleeding amount for different groups during and after the surgery. However, the total bleeding is not measured separately. The total rate of local and intravenous haemorrhage in this study is higher than the rate of our study. This is probably because of doing research on patients older than 60 years old who underwent a 2-level lumbar fusion. Although, their rate of local application is one gram more (2g locally used). In comparison of the volume of bleeding in the local and intravenous groups based on the duration of surgery considering the type of distribution, correlation tests were performed. In the intravenous injection group, a significant relationship was found between the duration of surgery and intra-operative bleeding as well as total bleeding. However, in the local group, no significant relationship was found between the duration of surgery and postoperative bleeding. We did not find any study that specifically examined this relationship, and it only generally stated that they would have more bleeding during long surgeries.

### Funding

Baqiyatallah University of Medical Sciences.

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