



Randomised Controlled Trial

## The topical application of tranexamic acid to control bleeding in inguinal hernia surgery candidate patients: A randomized controlled trial

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## ABSTRACT

**Background and objectives:** Inguinal hernia surgery is a common procedure, especially for the elderly, who usually use anticoagulants and antiplatelet drugs. In this study, we evaluated the effectiveness of tranexamic acid (TXA) on the complications of inguinal hernia repair in patients using antiplatelets.

**Patients and methods:** This study is a randomized controlled trial that was performed during the 2018–2019 years. Forty patients with inguinal hernia and antiplatelet use were enrolled randomly into the two groups. In the intervention group, the patients received two injectable form (500mg/5 mL) of TXA, totally 10 mL as a topical application at the surgical site, and then the patient's surgical site was seen every 8 h for 48 h, and the patient was examined daily for one week.

**Results:** The mean length of hospitalization, seroma, hematoma and infection in the two groups were not statistically significant ( $P > 0.05$ ). However, the duration of surgery in the TXA group was significantly shorter than in the control group (54.85 vs. 68.72 min) ( $P < 0.001$ ). The mean bleeding during surgery was significantly lower in the TXA group than in the control group ( $P < 0.001$ ).

**Conclusion:** The findings of present study indicate that topical TXA has a high ability to control bleeding. As a result, TXA is beneficial in terms of reducing bleeding and increasing the surgeon's satisfaction. Therefore, it is recommended that TXA be prescribed for patients requiring inguinal hernia surgery with a high risk of bleeding.

### 1. Introduction

Surgical procedures have a long history in human health. The majority of treatment procedures are performed on the human body using extensive surgeries, which can now be done with a low-invasive procedure in conjunction with better and brilliant results thanks to technological advancements [1].

Inguinal hernia is a common disease that consists of 75% of all types of hernia [2]. Because inguinal hernias are more common in men and

can result in dangerously adverse effects such as entrapment, ileus, ischemia, volvulus, and even death, surgery is the first choice for treating all types of hernias. There are two types of hernioplasty: open hernioplasty and laparoscopic hernioplasty [3]. Laparoscopic hernioplasty was first performed in 1990, and it is considered to be a less invasive surgery. The prevalence of inguinal hernia is two times in males than females and it contains 10% of the patient's surgical candidates [4].

Bleeding, hernia recurrence, [intestinal obstruction](#) and wound infection are some complications of inguinal hernia surgery. Also,

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postoperative complications such as wound seroma are a reason for postoperative wound infection, suppuration, and hernia recurrence [5].

Many patients who require inguinal hernia surgery due to a variety of co-morbidities and diseases may be prescribed antiplatelet medications [6]. Aspirin and clopidogrel are the most antiplatelet drugs that are used in patients with cardiovascular diseases [7]. Generally, it is recommended to discontinue antiplatelet drugs seven days before surgery to reduce the risk of major bleeding (because of their half-life elimination time) [8]. On the other hand, discontinuation of antiplatelet drugs in high-risk cardiovascular patients has been associated with some problems. In some studies, it has been suggested that aspirin continuation in elective hernia is safe and should be preferable, particularly in patients who need antiplatelet therapy, but the effect of taking aspirin and clopidogrel together has not been specifically studied. There is no consensus or guidelines regarding the adverse effects and safety associated with inguinal hernia surgery in patients with chronic use of antiplatelet drugs [9].

Several methods were used to minimize the risk of future inguinal hernia complications (especially bleeding). Anti-fibrinolytic agents are widely used in clinical practice to reduce some hernia complications. Aprotinin, Tranexamic acid (TXA) and aminocaproic acid are the three most used [10]. TXA is a synthetic anti-fibrinolytic agent that is a lysine amino acid derivative. This drug binds to lysine receptor sites on plasminogen and inhibits plasminogen formation. This prevents immediate annihilation of clots and massive bleeding [11,12].

Nausea, vomiting, headache, rhinosinusitis symptoms, back pain, abdominal pain, muscular cramps, anemia, and fatigue are some of its side effects. TXA is a cheap, cost-benefit, and useable drug in developing and developed countries [13].

TXA can decrease bleeding after CABG surgery, a 20 mL/kg (IV) or higher initial dose combined with a 15 mg/kg maintenance dose can reduce bleeding after surgery [14,15]. A study in 2014 to evaluate the efficacy of TXA results revealed a significant reduction in bleeding in traumatic patients or those who underwent surgical procedures. Intravenous TXA can control bleeding after surgery and reduce the need for blood transfusions, and topical TXA has the same effect [12]. Otherwise, in another study on the effectiveness of TXA in patients who underwent hip arthroplasty, results showed there was no difference in thrombosis occurrences in the placebo and TXA groups and, contrary to the other studies, a decrease in bleeding was not seen after the surgical procedure [15,16].

In most studies, the injectable or oral forms of TXA have been prescribed to reduce inguinal hernia surgery complications. According to the controversial results of studies and high limitations in clinical trials, we designed a randomized controlled trial to investigate the effects of topical TXA administration on hernia complications. The aim of this study was to assess the efficacy of TXA in reducing bleeding, duration of hospitalization, anaemia, seroma, hematoma, and other side effects secondary to the healing of inguinal hernia in patients using antiplatelet drugs (aspirin and clopidogrel).

## 2. Patients and methods

The present study is a randomized controlled trial research which has been conducted on patients who were referred to two teaching hospitals (Imam Khomeini and Razi) in Mazandaran Province, northern Iran. Forty referral patients with inguinal hernia and antiplatelet use were enrolled in a randomized, double-blind study. The group for which TXA has been prescribed and the group for which the drug has not been prescribed. In the recipient group, two injectable form (500mg/5 mL) of TXA, totally 10 mL was administered as topical usage on the surgical site and then, for a period of 48 h, the patient's surgical site was observed once every 8 h and the patient was examined daily for a week. In patients weighing less than 60 kg, the drug was administered locally 10 mL and in patients weighing more than 60 kg, 20 mL of TXA was used locally at the surgical site.

In order to examine the complications due to the prescription of TXA, a two week follow up stage after surgery is necessary. The inclusion criteria for enrolling in the study include patients who are candidates for an inguinal hernia and those using antiplatelet drugs (aspirin and clopidogrel). The exclusion criteria include, drug sensitivity, active intravascular coagulation, acquired color vision deficiency, subarachnoid hemorrhage, dissatisfaction with the continuation of the plan and lack of samples in the follow up stage (Fig. 1).

The information about each patient was kept confidential and the checklist had a code and was delivered to them if needed. This study was conducted based on the principles of the Declaration of Helsinki and did not impose any obligations on individuals. Patients entered the study after providing written consent, and they were assured that their information would not be disclosed if they were dissatisfied. The Declaration of Helsinki and ethical principles were observed in all aspects of this study. And the written consent was attached. Written informed consent was obtained from each individual to enter the study. The current study was reviewed and approved by the Research Ethical Committee (IR.MAZUMS.REC.1397.1439). The work has been reported in line with the STROCSS criteria [17]. This study is registered with the Research Registry, and the UIN is research registry 6906 ([https://www.researchregistry.com/browse-the-registry?\\_cf\\_chl\\_jschl\\_tk\\_\\_=pmd\\_edc6dd02fb90cab-baa74847e151589b3627527b5-1627884764-0-qNtZGzNAiKjcnBszQ-Zi#home/registrationdetails/60ce0630742d62001e22c1f2/](https://www.researchregistry.com/browse-the-registry?_cf_chl_jschl_tk__=pmd_edc6dd02fb90cab-baa74847e151589b3627527b5-1627884764-0-qNtZGzNAiKjcnBszQ-Zi#home/registrationdetails/60ce0630742d62001e22c1f2/))

## 3. Statistical analysis

In data analysis, first, the normality of the data was examined using a one-sample Kolmogorov-Smirnov test with Lilliefors's modified version. To confirm normality, appropriate parametric methods such as the Student t-test were used, and if this was not possible, the standard Mann-Whitney *U* test was used. The Chi-square test was used to analyze the data on a nominal scale and, in cases where more than 20% of the expected frequencies of the tables were less than 5 (Cochran), Fisher's exact test was used. Linear models were used to evaluate the results simultaneously. The software used in this study was SPSS v.20 and the significance levels of the tests were less than 0.05.

## 4. Results

In the current study, 80 patients entered the study (40 patients in the intervention group and 40 patients in the control group). 61 patients (76.2%) were male and 19 (23.8%) were female. The average age of patients was  $56.61 \pm 10.07$  years (32–75 years). Moreover, there was not any significant difference between the mean and standard deviation of age in both studied groups ( $p = 0.74$ ) (Table .1). There was not a significant difference in the frequency of the need for blood transfusions, seroma, hematoma and frequency of infection between the two studied groups ( $P > 0.05$ ) (Table .2). The duration of surgery in the TXA group was significantly shorter than in the control group ( $P < 0.001$ ) (Fig. 2A). However, the mean length of hospitalization in the two groups was not statistically significant ( $P > 0.05$ ) (Fig. 2B). The mean bleeding time during surgery was significantly lower in the TXA group than in the control group ( $P < 0.001$ ) (Fig. 3). The mean hemoglobin before the surgery was not a significant difference between the two studied groups, but after the surgery, the hemoglobin was significantly higher in the TXA than in the control group ( $P > 0.05$ ) (Fig. 4).

## 5. Discussion

Our data showed that topical TXA has a high ability to control bleeding potentially after inguinal hernia surgery. As a whole, the risk of bleeding is the most important problem for patients taking antiplatelet drugs. Continuation or discontinuation of antiplatelet drugs during the perioperative period is a challenge for surgeons [18]. Generally, it is

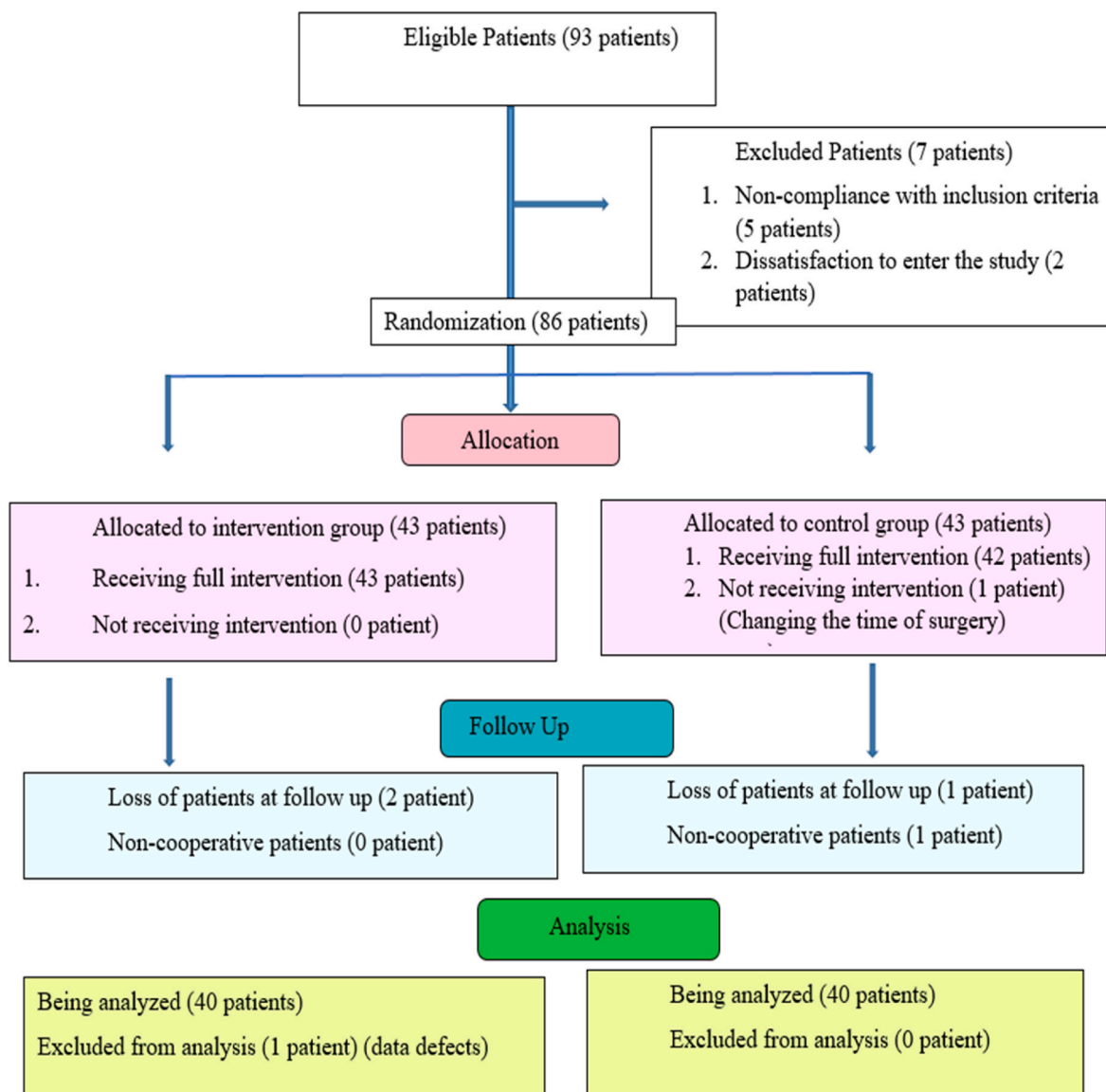


Fig. 1. Study flowchart (CONSORT format).

**Table 1**  
Mean age of studied groups.

Variable	Group	No	Mean ± SD	P-value
Age(years)	TXA	40	56.9 ± 8.38	0.74
	Control	40	56.32 ± 11.62	

TXA; Tranexamic acid.

**Table 2**  
The frequency of the need for blood transfusions, seroma, hematoma and frequency of infection.

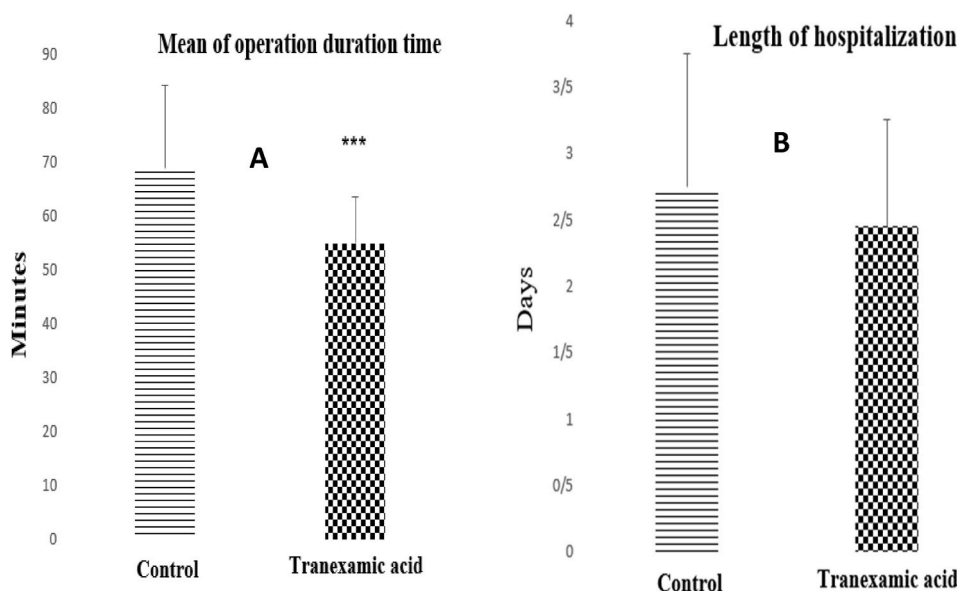
Variables		TXA	Control	Total	P-value
Blood transfusions	No. (%)	1 (2.5)	5(12.5)	6(7.5)	0.20
Infection	No. (%)	1(2.5)	2(5)	3(3.8)	0.99
Hematoma	No. (%)	1(2.5)	6 (15)	7(8.8)	0.10
Seroma	No. (%)	1(2.5)	3 (7.5)	4(0.5)	0.61

TXA; Tranexamic acid.

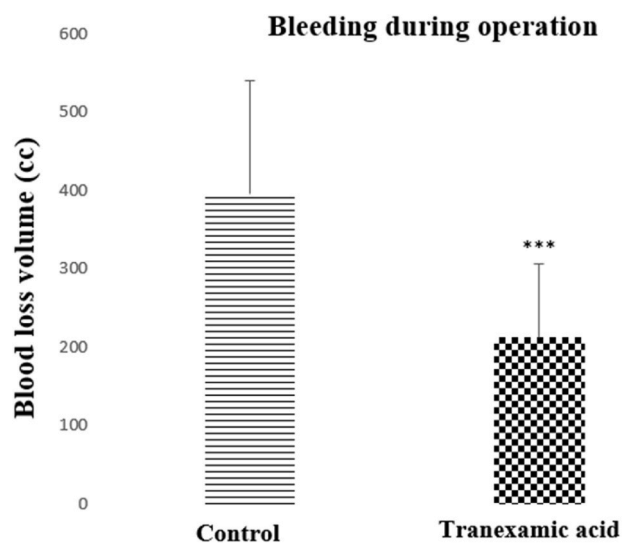
recommended to discontinue aspirin and clopidogrel seven days (average time) before surgery to reduce the risk of bleeding, but discontinuation of these drugs may be associated with various problems in high-risk cardiovascular patients (including thrombosis or ischemic events) [19].

It was demonstrated that the continuation of low-dose aspirin before laparoscopic inguinal hernia repair is safe [20]. Using aspirin alone in elective inguinal hernia surgery does not increase the incidence of bleeding or hematoma [21]. However, the effect of dual therapy (aspirin and clopidogrel together) is still unclear. So, we are investigating the effect of TXA on patients with inguinal hernia surgery who are receiving dual antiplatelet therapy. Based on the results of the present study, there was no statistically significant difference between the two studied groups in terms of hospitalization, need for blood transfusion frequency, seroma, infection and hematoma. However, the surgery duration was significantly shorter, and the mean bleeding during surgery was significantly lower in the group being treated with TXA compared to the control group.

TXA could significantly reduce bleeding in patients with traumatic bleeding or bleeding due to surgery. Intravenous injection of TXA could be quite helpful in reducing and controlling bleeding due to surgery and



**Fig. 2.** Operation duration time (A) and length of hospitalization (B). There was no significant difference between the mean lengths of stay of the two studied groups ( $P > 0.05$ ). But the operation duration in the recipient group was significantly less than in the control group (54.85 vs. 68.72 min) ( $P < 0.01$ ). Comparison of the control group with the intervention group: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ .



**Fig. 3.** The rate of bleeding. The mean bleeding during operation in the recipient group was significantly less than group control (212.5 vs. 395.5 cc) ( $P < 0.001$ ).

Comparison of the control group with the intervention group: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ .

reducing the need for blood transfusions [22].

A retrospective study has investigated the role of TXA after complete knee and pelvic arthroplasty in 2046 patients seeking complete knee and pelvic arthroplasty from 2007 to 2009. A treatment regimen with various anticoagulants was distributed to the patients in this study. The results indicated that the complications of bleeding and thrombosis were less prevalent among the groups taking TXA compared to the other groups [23].

It was demonstrated that TXA reduced blood loss in CABG patients with clopidogrel exposure within 48 h before surgery [24]. Our study also discovered that patients taking TXA were significantly less prone to bleeding during surgery and their post-surgery hemoglobin drop was much lower compared to the control group.

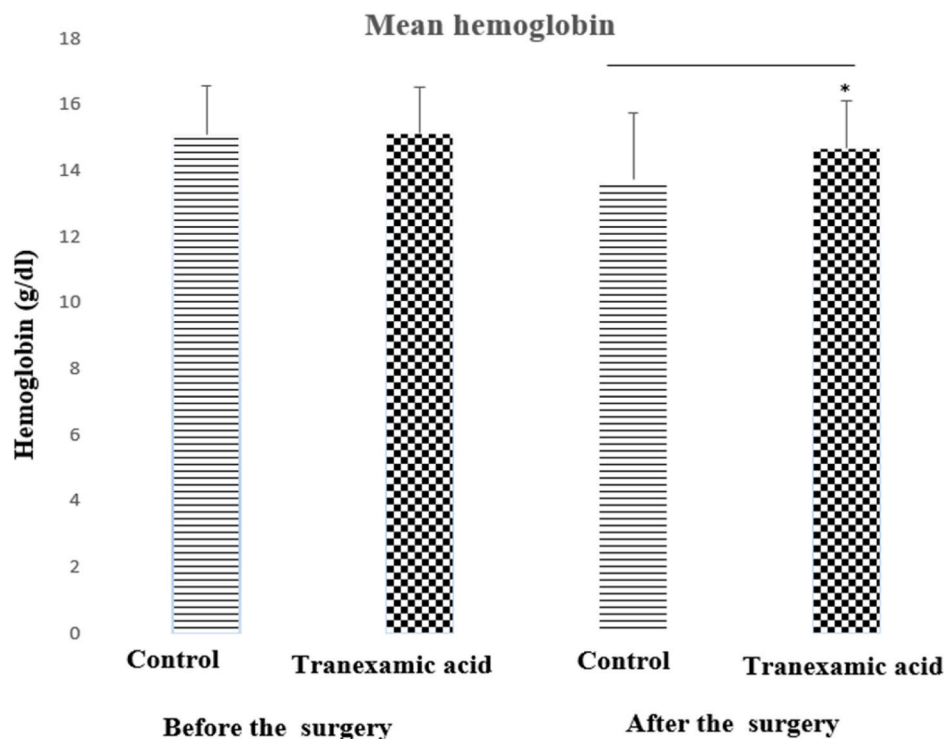
Moreover, according to the results of a review study on the role of

TXA in control of bleeding after surgical procedures, increasing the amount of TXA taken reduced the amount of bleeding significantly, according to the 104 studies in this regard that had been conducted up to that point. This study pointed out that the amount of bleeding and its decline due to the use of TXA vary after different types of surgeries. This study demonstrated that a dose of 1 g of TXA would be appropriate and sufficient for adults. The results of the study were consistent with ours [25].

The results of a case-control study conducted on the risk factors for hematoma following inguinal hernia surgery, revealed that taking warfarin and recurrent hernias were the most important hematoma risk factors following inguinal hernia surgery. The choice of anticoagulant is among the most crucial issues for patients with hernia recurrence. In our study, the control group that received no intervention had significantly higher incidences of hematoma compared to the normal amount associated with hernia surgeries, whereas the group that received TXA had a normal amount of hematoma, though this difference was not statistically significant. A study conducted on 60 patients suffering from chronic sinusitis and undergoing endoscopic surgery found that TXA reduces bleeding in sinus surgeries [26].

The prescription of TXA does not reduce the amount of mean arterial pressure (MAP) during surgery. The reason for reduced bleeding in patients taking TXA is that it is an anti-fibrinolytic drug inhibiting plasmin and plasminogen activity, which has no impact on platelet count or adhesion and coagulation parameters at therapeutic concentrations and no evidence of the risk of vascular occlusion. Reduced bleeding results in better vision in the surgical field, which reduces the number of errors made during the operation and, in turn, the amount of bleeding during the surgery [27,28].

In many studies, the injectable or oral effects of TXA have been examined, but the use of topical TXA is increasing. In primary total knee arthroplasty, intravenous and topical TXA have comparable efficacy [29]. TXA applied topically can reduce epistaxis in patients taking aspirin and clopidogrel [30]. In a cohort study, it was shown that topical use of TXA may prevent mild bleeding of an oral wound [31]. The therapeutic role of TXA's topical use has been confirmed in reducing post-surgery bleeding following a complete knee arthroplasty operation. Taking TXA reduces post-surgery bleeding by up to 20% and increases hemoglobin by 16% [32]. According to the results of the mentioned study and ours, one could conclude that topical TXA administration



**Fig. 4.** This means hemoglobin before and after the surgery. There was not a significant difference in the mean hemoglobin before the surgery between the two studied groups ( $P > 0.50$ ). But it was significantly more in the recipient group than in the control group after the surgery (14.69 vs. 13.73) ( $P > 0.05$ ). Comparison of the control group with the intervention group: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ .

significantly prevents bleeding. The topical use of TXA in patients undergoing surgery by screw fixation in lumbar vertebrae due to low back pain cuts the amount of blood lost in half. The results were consistent with the results of our study, although the types of patients studied differed [33].

## 6. Conclusion

The results of the present study demonstrated that topical TXA administration reduced the amount of bleeding during surgery significantly compared to the control group. Given that reduced bleeding in patients taking TXA is due to its antifibrinolytic and the fact that it inhibits plasmin and plasminogen activity, reduced bleeding due to TXA is helpful and increases the surgeon's satisfaction. On the other hand, TXA can reduce the adverse effects of surgery and its complications by decreasing hemoglobin drops and surgery duration in these patients. Therefore, it is recommended that topical administration of TXA could be helpful for all patients with a high risk of bleeding and requiring inguinal hernia surgery.

### Ethics approval and consent to participate

The protocol of the study was approved by the Ethics Committee of Mazandaran University of Medical Sciences (No: IR.MAZUMS.REC.1397.1439).

### Consent for publication

Not applicable.

### Provenance and peer review

Not commissioned, externally peer-reviewed.

### Availability of data and materials

The authors are responsible for data. Access to all relevant raw data will be free to any scientist.

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The study was funded by the Mazandaran University of Medical Sciences. The funder has no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

### Authors' contributions

MM GH, A A and S S designed the study, wrote the manuscript. M M analyzed and interpreted the data. J B, M N and S K were involved in writing, editing and preparing the final version of the manuscript. Z Z involved in interpretation and editing the manuscript. All the authors reviewed the paper and approved the final version of the manuscript.

### Trial registry number

researchregistry6906  
<https://www.researchregistry.com/register-now#home/registrationdetails/60ce0630742d62001e22c1f2/>.

### Guarantor

Seyed Muhammad Mehdi Ghaffari Hamedani.

### Declaration of competing interest

The authors have no conflicts of interest to declare.

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