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Original Research Article

Effectiveness of Tranexamic Acid in Minimizing Perioperative Blood Loss during Orthopedic Surgeries on the Lower Limb

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Conflict of interest: Nil

Abstract:

Background: The use of Tranexamic Acid (TXA) has been shown to significantly decrease blood loss in various surgical procedures and enhance survival rates in patients experiencing severe bleeding during orthopedic and trauma cases. The purpose of this study is to investigate the effects of tranexamic acid (TXA) on blood loss and hemodynamics in patients undergoing lower limb orthopedic surgeries.

Methods: Selected patients were randomly allocated to two groups In Group (T), consisting of 20 patients, tranexamic acid (TXA) was administered. After a test dose of 1 mL, each patient received TXA intravenously at a dose of 15 mg/kg (up to a maximum of 1,000 mg) before the surgical incision. An additional dose of TXA at 5 mg/kg was repeated intravenously 4 hours after the initial dose (referred to as the TXA group). In Group (C), also comprising 20 patients, normal saline (placebo) was administered at the same time points as the TXA group, i.e., before the skin incision and repeated 4 hours later (referred to as the placebo group).

Results: In the intraoperative period, the percentage of subjects requiring blood transfusion was remarkably lower in the tranexamic acid group, with only 10.0% needing transfusion, compared to 50.0% in the control group. This difference was found to be statistically significant ($p<0.05$). Thus, it can be concluded that tranexamic acid has the potential to reduce the need for blood transfusion by up to 40% in subjects.

Conclusion: The results of this study demonstrated that the use of Tranexamic acid (TXA) leads to a substantial reduction of approximately 40% in blood loss and the need for blood transfusion in patients undergoing trauma surgeries. Therefore, the routine administration of TXA could be advantageous for patients undergoing Orthopedic procedures, where significant blood loss is anticipated.

Keywords: Tranexamic acid, blood loss, lower limb orthopedic surgeries

Introduction

Fibrinolysis is a vital process responsible for breaking down and dissolving blood clots to restore normal vascular permeability. It occurs concurrently with hemostasis, the process of clot formation triggered by the interaction between platelets and fibrinogen, resulting in the production of thrombin. Thrombin facilitates the formation of a fibrin mesh, which is further reinforced by factor XIII and safeguarded against fibrinolysis by inhibitors such as plasminogen activator inhibitors (PAI-1), thrombin-mediated fibrinolysis activation inhibitors (TAFI),

and antiplasmin (alpha2-AP). These regulatory elements are predominantly located within the core of the clot, outnumbering the fibrinolytic components such as plasminogen activators (urokinase-type plasminogen activator [u-PA], tissue-type plasminogen activator [t-PA]), and the plasminogen substrate itself. However, in the vicinity of the fibrin mesh, the proportion of factors that promote fibrinolysis is higher. Consequently, they actively remodel the clot, maintaining vessel permeability, particularly in medium to small-caliber arteries. In individuals with impaired hemostasis, characterized by either bleeding or thrombosis, fibrinolysis may become excessively activated, leading to bleeding. [1, 2] Tranexamic acid (TXA) is a synthetic compound resembling lysine that acts as an inhibitor of fibrinolysis by impeding the interaction between plasminogen and fibrin. Extensive research has examined its prophylactic application in various surgical procedures, demonstrating its efficacy in reducing intraoperative bleeding. TXA is specifically recommended for surgeries where an anticipated blood loss exceeding 500 mL is expected. Moreover, TXA administration has been shown to decrease mortality rates in trauma patients with bleeding complications as well as in cases of postpartum hemorrhage. [3] There is also emerging evidence supporting the use of TXA in additional scenarios, including cardiovascular surgery, invasive procedures, or surgeries in patients with liver disease at risk of bleeding, and acute hemorrhagic conditions. [4, 5] However, further investigations are necessary to establish routine indications for its use in these contexts. The utilization of TXA in vascular and urologic surgery is currently being explored, with some published randomized evidence already demonstrating its favorable outcomes.[6, 7] The objective of this study was to assess the effectiveness and safety of administering tranexamic acid via injection, specifically 10 minutes before anesthesia induction, in reducing blood loss and the need for blood transfusion among patients undergoing lower limb orthopedic surgeries. These surgeries were performed without the use of a tourniquet and under spinal anesthesia.

Material and methods

This cross-sectional study was conducted in the Department of Anesthesiology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study.

Inclusion criteria

1. All the patients undergoing lower limb surgeries under local anesthesia.
2. Aged 18 – 50 years.
3. Males and Females
4. ASA I and II categories
5. Voluntarily willing to participate in the study.

Exclusion criteria

1. ASA-PS III, IV
2. Known allergy to tranexamic acid.
3. History /evidence of coagulopathy and bleeding disorder
4. Renal dysfunctions.
5. Use of antiplatelet agents.
6. Not willing to participate in the study.

The patients were subjected to pre-anesthesia examinations and recommended premedication with an oral dose of 5 mg diazepam and 150 mg ranitidine the night before surgery, followed by another dose on the morning of the surgery. In the operating theatre, intravenous access was established using an 18 G catheter, and all patients received a preload of 500 mL of normal saline before spinal anesthesia. The combined technique of spinal and epidural anesthesia was administered with strict aseptic measures, while the patient remained in a lateral position. The surgical procedure took place under the combined effect of epidural and spinal anesthesia. After the surgery, the patients received postoperative epidural infusion for pain

management. Randomization of the treatment allocation was performed using a computer program to ensure a randomized distribution.

In Group (T), consisting of n=20 patients, tranexamic acid (TXA) was administered. After a test dose of 1 mL, each patient received TXA intravenously at a dose of 15 mg/kg (up to a maximum of 1,000 mg) before the surgical incision. An additional dose of TXA at 5 mg/kg was repeated intravenously 4 hours after the initial dose (referred to as the TXA group).

In Group (C), also comprising n=20 patients, normal saline (placebo) was administered at the same time points as the TXA group, i.e., before the skin incision and repeated 4 hours later (referred to as the placebo group). The drug was prepared using loading ampoules of TXA with a concentration of 100 mg/mL. For the placebo group, normal saline was loaded into syringes, similar to the preparation of the study drug. The study drug (TXA) was administered intravenously at a dose of 15 mg/kg (maximum 1,000 mg) before the skin incision and 5 mg/kg 4 hours after the first dose. The controlled (placebo) group received normal saline using identical syringes before the skin incision and repeated 4 hours later.

Statistical analysis: The data was initially entered into Microsoft Excel 2010, and these spreadsheets were subsequently utilized for analysis. Statistical analysis was performed using SPSS version 20.0. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were calculated. The descriptive data were presented using various tables, graphs, and diagrams. Fisher's exact test was used to determine the p values.

Results

A total of n=40 cases were selected and studied for the duration of the study, and they were randomly allocated in two groups. The group (T) age ranged from 22 – 63 years and the mean age was 35.5 ± 4.5 years. Similarly, group (C) cases' age ranged from 21 – 61 years and the mean age was 33.45 ± 6.5 years. The majority of cases in both groups were found to be in the age group of 31 – 40 years with an overall 35% of cases followed by the age group 21 – 30 years with 27.5% of all cases details depicted in Table 1. The differences between the two groups based on age were analyzed and the p values were 0.258 hence not significant, therefore, the distribution of cases between the two groups was even.

Table 1: Distribution of cases included in the study.

Age group	*Group (T)*	*Group (C)*	*Total (%)*
21 – 30	6	5	11(27.5)
31 – 40	7	7	14 (35.0)
41 – 50	3	5	08 (20.0)
51 - 60	3	2	05 (12.5)
> 60	1	1	02 (5.0)
Total	20	20	40(100%)

In group (T) the total number of males was 16(80%) and females were n=4(20%) similarly, in group (C) the number of males was 17(85%) and females were n=3(15%). The p values were 0.871 and not significant. Therefore, the distribution of cases based on sex was even in both groups.

The weight range of patients in group (T) was 53.5 – 79.0 Kg and the mean weight was 59.5 ± 6.5 Kg. The weight range of patients included in group (C) was from 52.0 – 80 Kg and the mean weight was 58.3 ± 5.5 Kg. The differences between the groups were insignificant because the p-value was 0.542.

Table 2: Distribution of Hemoglobin levels among the cases of the study

Hb levels (gm/dl)	*Group (T)*	*Group (C)*	*Total (%)*
8.0 – 9.0	2	3	5 (25)
9.1 – 10.0	4	2	6 (30)
10.1 – 11.0	2	4	6 (30)
11.1 – 12.0	5	5	10 (50)
12.1 – 13.0	3	3	6 (30)
31.1 – 14.0	2	2	4 (20)
14.1 – 15.0	1	1	2 (10)
> 15.1	1	0	1 (5)

The estimation of hemoglobin levels in two groups of cases was recorded before the surgery as depicted in table 2. The mean hemoglobin levels in group (T) were 11.6 ± 0.54 gm/dl similarly the mean values of hemoglobin for group (C) was 12.5 ± 0.62 gm/dl. The differences between the two groups were not significant and the p-values were 0.472.

Table 3: Distribution of cases between the groups of the study

Diagnosis	*Group (T)*	*Group (C)*
Supracondylar fracture of the femur	12(60%)	11(55%)
Inter-trochanteric fracture of femur	4(20%)	2(10%)
Sub-trochanteric fracture of femur	3(15%)	6(30%)
The neck of the femur fracture	1(5%)	1(5%)
Total	20(100%)	20(100%)

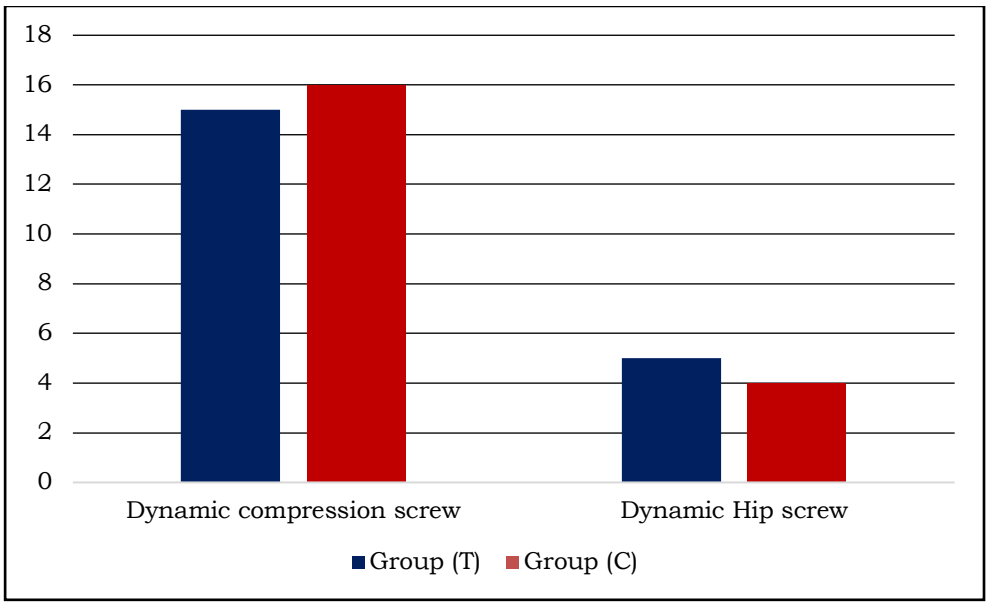

Figure 1: Showing the surgical procedures in both groups.

In this study, the majority of subjects underwent the insertion of a dynamic compression screw, and the slight disparity in the proportion of surgical procedures performed between the groups did not reach statistical significance (Figure 1). Therefore, both groups were considered comparable based on the type of procedure done.

Table 4: Comparison of intraoperative blood loss among the two groups.

Group	Group (T)	Group (C)
Mean blood loss (ml)	490	690
SD	80.5	125.5
Mean difference	200.0	
P value	0.0171	

Intraoperative blood loss was assessed by quantifying the number of pads (where 1 pad equaled 50 ml of blood loss) and the amount of gauze soaked (where 1 gauze equaled 5 ml of blood loss), in addition to considering the volume of the suction drain. The subjects who received tranexamic acid demonstrated a reduction of approximately 200 ml in intraoperative blood loss compared to the control group, and this disparity was found to be statistically significant ($p < 0.05$) depicted in Table 4.

In the intraoperative period, the percentage of subjects requiring blood transfusion was remarkably lower in the tranexamic acid group, with only 10.0% needing a transfusion, compared to 50.0% in the control group. This difference was found to be statistically significant ($p<0.05$). Thus, it can be concluded that tranexamic acid has the potential to reduce the need for blood transfusion by up to 40% in subjects.

Similarly, after 12 hours in the postoperative period, the percentage of subjects requiring blood transfusion was significantly lower in the tranexamic acid group, with only 5% needing a transfusion, compared to 30% in the control group. This difference was also statistically significant ($p<0.05$).

Discussion

Perioperative blood loss is a frequently encountered complication in major orthopedic surgery. Such substantial blood loss leads to alterations in the patient's hemodynamics during the perioperative period. To ensure stability in the patient's hemodynamics under these circumstances, blood transfusions become necessary. However, blood transfusions themselves present certain drawbacks, including the potential risk of infection transmission, the heightened likelihood of allergic reactions, and the possibility of circulatory overload resulting from the transfusion. To mitigate these disadvantages, it is crucial to minimize unnecessary blood transfusions. This can be achieved by actively reducing blood loss during surgical procedures. Elevated fibrinolytic activity is a contributing factor to perioperative blood loss. Therefore, the administration of an antifibrinolytic drug can potentially decrease blood loss during this period. Tranexamic acid is one of the most commonly utilized antifibrinolytic agents, alongside Epsilon Aminocaproic Acid and Aprotinin. Numerous studies have been conducted to investigate the effectiveness of tranexamic acid in reducing blood loss. Elwatidy et al. [8] conducted a study to assess the effectiveness and safety of administering prophylactic high doses of tranexamic acid during spine surgery. The findings of this study demonstrated that the prophylactic use of large doses of tranexamic acid offers a cost-effective and secure method for reducing blood loss both during and after spine operations. Moreover, it contributes to a reduction in transfusion-related complications.

In a similar vein, Sadehi et al., [9] conducted a study focusing on the impact of tranexamic acid on hip fracture surgery. Their conclusion highlighted that the group receiving tranexamic acid exhibited significantly lower perioperative blood loss. Another relevant study by Benoni G et al., [10] investigated the potential of tranexamic acid to inhibit fibrinolysis and reduce blood loss as well as the need for blood transfusions following knee arthroplasty. Employing a double-blinded design, their study revealed that the

tranexamic acid group experienced less blood loss compared to the placebo group. Yamasaki et al., [11] conducted a study to investigate the potential of tranexamic acid in reducing postoperative blood loss in cementless total hip arthroplasty. Their findings revealed that the most substantial reduction in blood loss occurred within the initial four hours of surgery in the group receiving tranexamic acid. Consequently, they concluded that administering tranexamic acid preoperatively to patients undergoing cementless total hip arthroplasty resulted in decreased postoperative blood loss, particularly within the first 24 hours and notably during the initial four hours following surgery.

Similarly, Lozano et al., [12] examined the effectiveness and safety of administering tranexamic acid during total knee arthroplasty (TKA). Their conclusion highlighted that the routine administration of tranexamic acid during TKA was associated with a significant 67% reduction in red blood cell transfusions. Furthermore, among those who required transfusions, the number of units administered was also reduced. Importantly, the administration of tranexamic acid did not lead to an increase in thromboembolic complications. Intraoperative blood loss: The mean blood loss in the Tranexamic acid group was 490 ml, while it was 690 ml in the control group. The mean difference between the two groups was 200ml, and the p-value was found to be less than 0.01. Subjects who received tranexamic acid had approximately 200ml less intraoperative blood loss compared to the control subjects, and this difference was statistically significant ($p<0.05$). Postoperative blood loss: In the Tranexamic acid group, the mean blood loss according to the suction drain was 62.5ml, 58.5ml, and 57.5ml at the 0th hour, 12th hour, and 24th hour postoperatively, respectively. In the control group, the corresponding values were 95.0ml, 105.0ml, and 103.2ml. Subjects who received tranexamic acid had approximately 80ml less postoperative blood loss according to the volume of the suction drain compared to the control subjects, and this difference was statistically significant. Blood transfusion requirement: In the intraoperative period, the percentage of subjects requiring blood transfusion was remarkably lower in the tranexamic acid group, with only 10.0% needing a transfusion, compared to 50.0% in the control group. This difference was found to be statistically significant ($p<0.05$). Thus, it can be concluded that tranexamic acid has the potential to reduce the need for blood transfusion by up to 40% in subjects.

Conclusion

The results of this study demonstrated that the use of Tranexamic acid (TXA) leads to a substantial reduction of approximately 40% in blood loss and the need for blood transfusion in patients undergoing trauma surgeries. Therefore, the routine administration of TXA could be advantageous for patients undergoing Orthopedic procedures, where significant blood loss is anticipated.

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