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ORIGINAL RESEARCH ARTICLE

TRANEXAMIC ACID IN REDUCING BLOOD LOSS IN PROXIMAL FEMUR FRACTURE SURGERY: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Blood transfusion during orthopedic surgery is associated with different types of complications. The goal of this research was to observe if tranexamic acid could help in reducing perioperative blood loss after proximal femur fracture surgery.

Methods: At Shree Birendra Hospital, a total of 60 patients with proximal femur fractures participated in this one-year observational study. The study group (n=30) received 1g intravenous tranexamic acid at induction of anesthesia, whereas the control group (n=30) received intravenous normal saline. Using a proximal femoral nailing device, all patients underwent closed reduction and internal fixation. Preoperative and postoperative hematological parameters, as well as intraoperative blood loss were measured. Patients were followed up till the third day for the need of blood transfusion. Statistics Program for Social Sciences version 20.0 was used to analyze the data.

Results: The study's preoperative hemoglobin and hematocrit were 10.5±1.43gm/dl versus 10.9±1.2gm/dl and 31.5±4.19% versus 32.7±3.6%, respectively, compared to the control group. In the study versus control group, the values were 10.1±1.0gm versus 9.9±0.8gm (p=0.01) and 30.3±3% versus 29.7±2.4% (p=0.03) on day one and 10±0.69gm versus 9.68±0.51gm (p=0.049) and 30±2.07% versus 29.04±1.53% (p=0.049) on day three. Total blood loss in the study group was 156.79±43.46ml compared to 392.63±92.32ml in the control group (p=0.00), with both apparent and hidden blood loss being lower in the study group.

Conclusions: In patients undergoing minimally invasive surgery of proximal femoral fractures using proximal femoral nailing system, intravenous administration of a single dose of 1g tranexamic acid at the time of induction of anesthesia lowers blood loss by a significant amount.

INTRODUCTION

Proximal femur fractures in adults are generally referred to as fractures of the hip which include intertrochanteric fracture, sub-trochanteric fracture, and neck of femur fracture. These fractures mostly require surgical fixation, whereas isolated fractures of lesser trochanter or greater trochanter are uncommon and rarely require surgical fixation.[1]

Peritrochanteric fracture causes an excessive amount of blood loss which can lead to hypovolemic shock and possibly death. The rate of blood transfusion used to compensate for blood loss during the perioperative period has been reported between 20% and 60%.[2–5] Allogeneic blood transfusion, on the other hand, has various drawbacks, including an increased risk of bacterial infection, a longer hospital stay, and a higher cost.[6]

Researchers have proposed numerous anti-fibrinolytics to limit blood loss during orthopedic surgery.[7,8] Tranexamic acid, a synthetic derivative of the amino acid lysine, is one of these anti-fibrinolytics. It inhibits plasminogen in a competitive manner to plasmin activation, hence inhibiting fibrin breakdown.[9]

In joint arthroplasty, intravenous tranexamic acid has been shown to minimize blood loss and transfusion rates without increasing thrombotic events. This drug's capacity to significantly minimize blood loss has been established in a variety of surgical procedures, including knee and hip arthroplasty, which can result in a significant amount of blood loss.[10]

To our knowledge, no study of this kind has been conducted in Nepal. As a result, the purpose of this study was to see how effective intravenous tranexamic acid was at preventing perioperative blood loss during proximal femur fracture surgery.

METHODS

From March 2019 to March 2020, an observational study was conducted in the Department of Orthopedics at Shree Birendra Hospital. The research included 60 individuals who had proximal femur fractures, 30 of whom were randomly assigned to the study group and 30 to the control group using computer-generated numbers.

Because the intramedullary nail is a load-sharing device and the femur is a weight-bearing bone, they all underwent close reduction and internal fixation with the proximal femoral nailing system as an operative treatment.

Patients who wished to give consent, those of both the sexes and aged more than 18 years with intertrochanteric and sub-trochanteric fracture cases were included in the study.

Patients using anticoagulants during admission, having thromboembolic events and coronary artery or cerebrovascular disease in the previous 12 months were all excluded from the study. Patients having a history of hepatic and renal impairment, as well as those who were allergic to tranexamic acid or who refused to give consent, were also excluded.

Before starting the study, informed written consent was obtained from the participants. The Institutional Review Committee of the Nepalese Army Institute of Health Science gave their approval to this observational study. During the experiment, patients were treated with care and patient confidentiality was maintained.

Patients in the experimental group received one gram of intravenous tranexamic acid at the time of anesthesia induction, while patients in the control group received normal saline (Placebo).

The Gross equation and Nadler's formula were used to calculate the estimated blood loss:

- Women's blood volume = height(m)^3 x 0.356 + weight(kg) x 0.033 + 0.183
- Men's blood volume = height(m)^3 x 0.356 + weight(kg) x 0.032 + 0.604
- Blood volume x (Hct_{preop} – Hct_{postop}) = estimated total blood loss

The following methods were used to determine intra-operative blood loss:

- Counting partial/complete blood-soaked gauze pieces (3/5ml) by weighing them.
- Weighing partial/ complete blood-soaked mops or pads counts (30/50ml).
- Deducting the volume of saline used for irrigation from the volume of blood collected in the suction container.

Blood extravasates into tissues, remains in joint cavities, and lost by hemolysis, all of which contribute to hidden blood loss.

The following are the formulas for calculating concealed blood loss:

- (Surgical blood loss + drainage) x (Hct_{preop} + Hct_{postop})/2 = visible blood loss
- Total blood loss - apparent blood loss + transfused blood = hidden blood loss

Preoperative hematological parameters as well as intraoperative blood loss were measured and blood transfusion in the postoperative period was considered if Hemoglobin (Hb) ≤ 8gm/dl.[11]

The statistical analysis was conducted using Statistics Program for Social Sciences (SPSS) version 20.0. Tables, graphs, and diagrams were used to represent descriptive data. The significant mean difference of variables between the study group and the control group was tested using an independent t-test for parametric data. A p-value less than 0.05 was considered significant.

RESULTS

To determine the role of perioperative tranexamic acid administration in minimizing postoperative blood loss in proximal femur fracture surgery, a thorough review of the various literature was done and compared to this study.

The patients in the research population ranged in age from 53 to 87 years old. The majority of the patients in the study with proximal femur fracture were between the ages of 65 and 70, with 34% (n=10) in the study group and 30% (n=9) in the control group. Cases under the age of 60 had the fewest proximal femur fractures, with three patients (10%) each in the study and control group (Table 1). The research and control groups' mean ages were 68.40±7.19 and 68.07±7.6years, respectively (Table 1). With a total of 40 males in the research group, the sex distribution of patients revealed a male predominance. The male to female ratio of proximal femur fracture patients was 2:1. They were divided into two groups: research (18 males and 12 females) and control (22 males and 8 females) (Table 1).

Table 1: Patient's demographics

Parameters	Study group	Control group
Total sample	30 (50%)	30 (50%)
Age (Years)		
<60	3 (5%)	3 (5%)
60-64	6 (10%)	7 (11.67%)
65-69	10 (16.67%)	9 (15%)
70-75	7 (11.67%)	6 (10%)
>75	4 (6.67%)	5 (8.33%)
Mean age (Years)	68.40±7.195	68.07±7.6
Sex		
Male	18 (30%)	22 (36.67%)
Female	12 (20%)	8 (13.33%)

Intertrochanteric fractures were found in 44 patients (73%) and sub-trochanteric fractures were found in 16 patients (27%) of the total patients (Figure 1). The study group included seven individuals with sub-trochanteric fractures, while the control group included nine patients with the same disease. Similarly, the study group included 23 patients with intertrochanteric fractures, while the control group included 21 individuals with the same characteristics (Figure 1).

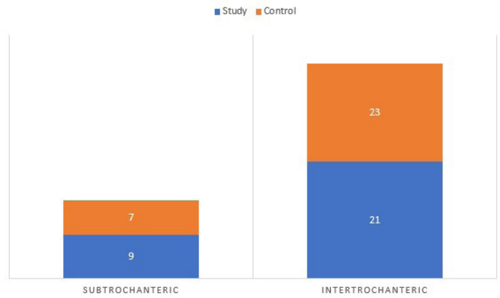

Figure 1: Patient's allotment according to diagnosis

Fall from height was the most commonest mode of injury (67%) followed by farm animal injury (28%). The least common mode of injury was a road traffic accident (5%) (Figure 2).

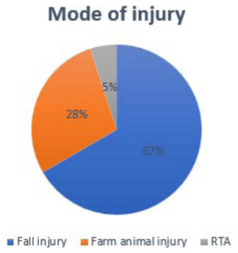

Figure 2: Mode of Injury

Patients in the study group had a mean preoperative hemoglobin of 10.5±1.43gm/dl, compared to 10.9±1.2gm/dl in the control group (p-value 0.2). The study group's mean preoperative hematocrit was 31.5± 4.19%, compared to 32.7±3.6% in the control group (p-value 0.19) (Table 2).

The study group's mean hemoglobin was 10.1±1gm/dl, compared to 9.9±0.8gm/dl in the control group (p-value 0.01) on first postoperative day. Also, the study group's mean hematocrit was 30.3±3%, compared to 29.7±2.4% in the control group (p-value 0.03) (Table 3).

On the third postoperative day, the study group's mean hemoglobin was 10±0.69gm/dl, compared to 9.68±0.51gm/dl in the control group (p-value 0.049). Also, the study group's mean hematocrit was 30±2.07%, compared to 29.04±1.53% in the control group (p-value 0.049) (Table 3). The study group's mean total blood loss was 156.79±43.46ml, compared to 392.63±92.32ml in the control group (p-value 0.00). The study group's mean visible blood loss was 91.5±26.75ml, compared to 221.66±56.022ml in the control group (p-value 0.00). Patients in the study group had a mean concealed blood loss of 65.79± 19.07ml compared to 170.96±43.72ml in the control group (p-value 0.00) (Table 3).

Table 2: Mean hemoglobin and mean hematocrit level in preoperative period (n=60

Parameters	Study group (Mean ± SD)	Control group (Mean ± SD)	p-value
Mean hemoglobin (mg/dl)	10.5 ±1.43	10.9 ±1.2	0.2
Mean hematocrit (%)	31.5 ±4.19	32.7 ±3.6	0.19

Table 3: Mean hemoglobin, mean hematocrit, mean total blood loss, mean visible blood loss, and mean hidden blood loss on day one and postoperative day three

Parameters	Study group (Mean ± SD)	Control group (Mean ± SD)	p-value
Mean hemoglobin (gm/dl) (POD1)	10.1 ±1	9.9 ±0.8	0.01
Mean hematocrit (%) (POD1)	30.3 ±3	29.7 ±2.4	0.03
Mean total blood loss (ml) (POD1)	156.79 ±43.46	392.63 ±92.32	0.000
Mean visible blood loss(ml) (POD1)	91.5 ±26.75	221.66 ±56.02	0.000
Mean hidden blood loss (ml) (POD1)	65.79 ±19.07	170.96 ±43.72	0.000
Mean hemoglobin (gm/dl) (POD3)	10 ±0.69	9.68 ±0.51	0.049
Mean hematocrit (%) (POD3)	30 ±2.07	29.04 ±1.53	0.049

Abbreviations: - POD1: Postoperative day one; POD3: Postoperative day three

DISCUSSION

Blood loss during major orthopedic surgery is a common complication. To maintain the hemodynamics of the patient, blood transfusions are required. However, unnecessary blood transfusion is better avoided because of disadvantages like the risk of transmission of infection, allergic reaction, circulatory overload, transfusion-related acute inflammatory response, and immunomodulation. One strategy for reducing blood transfusions during the perioperative phase is to minimize blood loss during the surgical operations. The present study demonstrates that intravenous tranexamic acid treatment decreases perioperative blood loss.

The study and control groups were comparable in terms of age, gender, fracture type, side distribution, and anthropometric characteristics, indicating that randomization was successful. Patients in our study ranged in age from 53 to 87 years. Patients in the study group had an average age of 68.40±7.19 years, while the control group had an average age of 68.07±7.6 years (Table 1). The majority of patients (19 patients; 32 %) were between the ages of 65 and 70 years. The least number of patients (6 patients; 10%) were under the age of 60 (Table 1). Our findings were consistent with those of Lei et al., who found that the mean age of patients in the study group was 77.80±9.75 years, while the mean age of patients in the control group was 79.18±6.50 years.[12] The findings of this

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study are likewise comparable to those of Xin-die et al., who found that the mean age of patients in the study group was 75.1±8.27 years and that of patients in the control group was 77.82±6.42 years.[13] Similarly, Yasir et al. found that the average age of patients in the study group was 69±10 years, whereas the average age of patients in the control group was 70±9.4 years.[14] This age group resemblance may be explained by the increased prevalence of proximal femur fractures in the elderly due to osteoporosis, senile muscle insufficiency, and associated comorbidities.

Males account for the majority of proximal femur fractures in our study (Table 1), with a male to female ratio of 2:1. (40 males, 20 females). This is in contrast to research conducted in western countries, which indicate that females are more likely to sustain proximal femur fractures. Tomak et al. found that the male to female ratio was 1:1.4. (17 males, 25 females).[15] Male predominance in our study could be explained by men's involvement in outdoor activities.

The most prevalent cause of injury (67%) was a fall while walking, followed by farm animal injuries (28%), and road traffic accidents (5%). (Figure 2). This corresponds to a research conducted in Dharan by Karn NK.[16] The most common cause of injury in their study (77%) was falls, followed by road traffic accidents (17%). Similarly, Tomak et al. found that the most common mode of injury (92%) was fall, followed by road traffic collision (8%). The significant percentage of patients who experience injuries from simple falls may be explained by the different degrees of osteoporosis present in these elderly patients.

Preoperative hemoglobin levels in the study group were 10.5±1.43gm/dl, compared to 10.9±1.2gm/dl in the control group ($p > 0.05$). Patients in the study group had a mean preoperative hematocrit of 31.5±4.19%, compared to 32.7±3.6% in the control group ($p > 0.05$) (Table 2). On postoperative day one, the mean hemoglobin level in the study group was 10.1±1gm/dl, compared to 9.9±0.8gm/dl in the control group ($p< 0.05$) (Table 3). This demonstrates that the study group experienced much less hemoglobin loss on day one than the control group. On postoperative day one, the mean hematocrit of patients in the study group was 30.3±3%, compared to 29.7±2.4% in the control group ($p <0.05$) (Table 3). This demonstrates that the study group's hematocrit decreased much less than the control group's on day one.

On day three, the mean hemoglobin level in the study group was 10±0.69gm/dl, compared to 9.68±0.51gm/dl in the control group ($p <0.05$) (Table 3). This also demonstrates that the study group's hemoglobin drop on day three was much less than that of the control group. On day three, the mean hematocrit of patients in the experimental group was 30±2.07%, compared to 29.04±1.53% in the control group ($p< 0.05$) (Table 3). This demonstrates that the decrease in hematocrit on day three was likewise much less in the study group than in the control group.

The mean total blood loss was 156.79±43.46ml in the study group, compared to 392.63±92.32ml in the control group (Table 3). Patients receiving tranexamic acid experienced a 236ml reduction in mean total blood loss compared to those receiving normal saline (placebo), a result that was statistically significant ($p <0.05$). There was a statistically significant difference in mean apparent blood loss and mean covert blood loss between the study group and the control group. The mean visible blood loss in the study group was 91.5±26.75ml, compared to 221.66±56.02ml in the control group (Table 3). Patients who received tranexamic acid had a 130ml lower mean visible blood loss than those who got normal saline (placebo), which was statistically significant ($p <0.05$).

Our findings are comparable to those of Baruah et al.[17] Preoperative hemoglobin levels in the study group were 10.03±1.36 gm/dl, compared to 10.02±1.56 gm/dl in the control group (p-value 0.97). Preoperatively, patients in the study group had a mean hematocrit of 33.32±2.21% compared to 33.18±2.16% in the control group (p-value 0.80). However, on day three, the mean hemoglobin level in the study group was 9.65±1.38gm/dl, compared to 8.92±1.30gm/dl in the control group (p-value 0.039), which is statistically significant. On day three, the mean hematocrit of patients in the study group was 32.29±2.41% against 30.58±1.49% in the control group (p-value 0.002, likewise statistically significant). Mean blood loss was 408.97±106.35 ml in patients who received tranexamic acid preoperatively, compared to 676.67±87.88ml in patients who received a placebo (p-value 0.001). The outcomes of this study indicate that the tranexamic acid group experienced statistically significantly less blood loss than the placebo group.

In comparison to a study conducted by Jinlai lei et al., who conducted a single-center RCT to determine the role of tranexamic acid in lowering concealed blood loss after proximal femoral nail antirotation (PFNA) - treated intertrochanteric fracture. Although there was no statistically significant difference in preoperative hemoglobin and hematocrit levels between the study group and the control group, the study group experienced statistically significantly less blood loss than the control group. The mean total blood loss was 279.35±209.11ml in patients administered tranexamic acid, compared to 417.89±289.56ml in patients given a placebo. The mean concealed blood loss in the study group was 210.09±202.14ml, compared to 359.35±290.12ml in the control group (p-value 0.049).

Additionally, our study is equivalent to that of Chen F, Jiang Z, Li M, and Zhu X. (2019). Preoperative mean hemoglobin levels were 11.68±1.34gm/dl in the study group and 11.73±1.35gm/dl in the control group in their study (p-value 0.81). On postoperative day one, the mean hemoglobin level was 10.9±0.53gm/dl in the study group, compared to 10.3±0.67gm/dl in the control group (p-value 0.004). The mean total blood loss was 411±108.8ml in the study group, compared to 616.5±106.3ml in the control group (p-value 0.001).

In our investigation, neither the study group nor the control group required blood transfusions. This may be due to the fact that all patients undergoing surgery with the Proximal Femoral Nailing System undergo minimally invasive surgery. However, as compared to the control group, there was a statistically significant drop in hemoglobin, hematocrit, and blood loss in the study group.

The research was carried out at Shree Birendra Hospital on a diverse sample of Nepalese army personnel and their families. It has generated gross idea regarding the use of tranexamic acid as a substitute for blood transfusions in orthopedic surgery to reduce postoperative blood loss. However, the study did not cover the problems associated with the use of tranexamic acid to avoid blood loss. The primary outcome was computed using a number of clinical characteristics that potentially could introduce bias. Additionally, the long-term effect on thrombosis incidence was not determined.

CONCLUSION

One gram of intravenous tranexamic acid administered prior to surgery significantly lowers blood loss in patients undergoing surgery for proximal femoral fractures utilizing the proximal femoral nailing technique. A randomized controlled trial with a high sample size and a longer follow-up period is recommended to get a more certain conclusion about the drug's long-term negative effects.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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