

To Analyze the Role of Intravenous Tranexamic Acid in Hip Fracture surgeries in Orthopedic Trauma

Abstract

Introduction: Hip fractures in orthopedic trauma cases are increasing. Majority of such patients undergoing surgery require blood transfusion of one or more units. Intravenous (I. V.) Tranexamic acid (TXA) may decrease loss of blood, decrease need of blood transfusion, and improve postoperative hemoglobin (Hb) along with lesser adverse effects. Risk of thromboembolic phenomena remains a concern. A study was done to analyze the role of I. V. TXA in hip fracture surgeries in trauma cases. **Materials and Methods:** Sixty patients were included in the study; in two groups (37 males and 23 females), Group A in which two doses of I. V. TXA 15 mg/kg were given and Group B in which two doses of I. V. placebo were given. **Results:** Total number of randomized hip arthroplasty cases was 22 (11 in Group A and 11 in Group B) whereas randomized osteosynthesis cases were 38 (19 in Group A and 19 in Group B). Mean preoperative Hb value in Group A was 10.8 gm% and in Group B was 10.7 gm% ($P > 0.005$). Mean postoperative Hb value in Group A was Hb 9.8 gm% and in Group B 9.5 gm% (difference of 3.061%). Mean duration of surgery in Group A was 64.2 min and in Group B was 66.3 min. Mean total blood loss (intraoperative and postoperative) in Group A was 384.6 ml and in Group B was 448.7 ml (14.29% less in Group A). A total of 14 patients in Group A (17 red blood cells [RBCs] units) and 17 patients (21 RBC units) in Group B required RBC transfusion. No major vascular event, severe bacterial infections, symptomatic deep vein thrombosis, pulmonary embolism, limb ischemia, acute coronary syndrome, or immediate postoperative mortality was noted in either group. **Conclusion:** I. V. TXA has the potential to decrease risk of blood transfusion, decrease total blood loss, and to maintain a higher postoperative Hb value with no significant adverse reactions. As the number of cases of hip fractures continues to increase along with increase in age, so the use of TXA in such cases may improve clinical outcomes, lessen number of inpatient days and hence decrease overall cost.

Keywords: Hip fractures, intravenous tranexamic acid, thromboembolism, total blood loss

Introduction

Hip trauma in orthopedic patients leads to a considerable amount of morbidity and mortality. Majority of these require blood transfusions preoperative, intraoperative, or postoperatively. Resulting anemia due to hip trauma is a predisposing factor to delayed recovery from illness, prolonged immobilizations, and increased long-term mortality. As majority of patients of hip trauma are of elderly age group; given their age and diminished cardiopulmonary reserves, they are more susceptible to cardiopulmonary decompensation in the event of blood loss. Blood transfusions in itself can cause bacterial infections, disease transmissions, and adverse reactions.

There are many options in orthopedic surgeries to decrease the loss of blood

such as thrombin gelatin matrix, factor eight concentrates, and antifibrinolytics. Tranexamic acid (TXA), a lysine analog can be used as an antifibrinolytic agent.^[1] Various studies have been conducted till date describing the use of TXA by intravenous (I. V.) method,^[2] along with some studies mentioning local infiltration of TXA by intramuscular and subfascial routes before wound closure.^[3,4] I. V. TXA has been used in hip arthroplasty, knee arthroplasty, and spine surgery. Local infiltration of TXA has been proved to be much effective and less harmful to total knee arthroplasty, though role in fracture surgery is still not much elaborately studied. Virani *et al.*^[5] described local infiltration of TXA in the vastus lateralis muscle in peritrochanteric hip fractures in the elderly population treated with dynamic hip screw and observed no significant role

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How to cite this article: Sahni G, Sood M, Girdhar D, Sahni P, Jain AK, Kumar S. To analyze the role of intravenous tranexamic acid in hip fracture surgeries in orthopedic trauma. *Int J App Basic Med Res* 2021;11:139-42.

**Girish Sahni,
Monika Sood¹,
Deepak Girdhar,
Priya Sahni,
Ayush Kumar Jain,
Sanjeev Kumar**

*Department Of Orthopaedics,
¹Department Of Microbiology,
Government Medical College
and Hospital, Patiala, Punjab,
India*

Submitted: 07-Oct-2020

Revised: 15-Dec-2020

Accepted: 05-Jan-2021

Published: 19-Jul-2021

Address for correspondence:

*Dr. Sanjeev Kumar,
6c, Ambey Apartment, Near
Sai Market, Patiala - 147 001,
Punjab, India.
E-mail: virgosanjeevarora@
gmail.com*

Access this article online

Website:
www.ijabmr.org

DOI:
10.4103/ijabmr.IJABMR_638_20

Quick Response Code:



while Drakos *et al.*^[6] found 43% reduction in transfusion requirement ($P < 0.01$) with local infiltration of TXA in 200 intertrochanteric fractures treated with intramedullary nail.

There remains a concern that TXA may promote a hypercoagulable state. Zufferey *et al.*^[7] studied the safety of TXA on venous and arterial outcomes and observed an increased risk of vascular events in the TXA group as compared to placebo (statistically insignificant, $P = 0.10$). Analysis study was done by us to compare the additional beneficial effect of I. V. TXA with placebo in surgeries around the hip in a total of 60 patients to determine total blood loss, in reducing overall blood transfusion, risk of thromboembolic events and bacterial infections, etc.

Materials and Methods

Ethical committee approval was taken and patients were randomized with envelop method in two groups Group A where two doses of I. V transfusion of TXA 15 mg/kg were given and Group B where two doses of I. V. placebo were given. Definitive management of the patient as planned for surgery was done in both groups.

Inclusion criteria were patients with hip trauma undergoing surgery, age group of 50–75 years, and hip surgery within 5 days of injury. Exclusion criteria were multiple fractures, pregnant or breastfeeding patients, any contraindication to TXA such as previous seizures, previous arterial, or venous thrombosis patients on anticoagulant therapy that could not be stopped.

Surgical technique varied according to the type of fracture. A predetermined hemoglobin (Hb) level was fixed in both Group A and B as a trigger point for transfusion of blood as 9 g/dl postoperatively and in those cases where hypotension could not be corrected despite adequate volume replacement during surgery. Preoperative Hb, values of Hb at the day of surgery, and values at postoperative day 7 were noted. A total number of blood transfusions, intraoperative and postoperative blood loss, postoperative bacterial infections including superficial and deep wound infections, septic arthritis, and any other major infection were noted up to 6 weeks following surgery. Any major incidence of postoperative bleeding was noted. Length of stay in hospital, any thromboembolic events, and long-term mortality up to 6 months, if any, were noted. Type of anesthesia was spinal or epidural in all cases. Patient characteristics and surgical characteristics were similar in two groups; stratification was done as per type of surgery (arthroplasty or osteosynthesis with dynamic hip screw/proximal femoral nailing). The efficacy endpoint was the proportion of patients receiving at least 1 unit of allogeneic red blood cells (RBCs) as per transfusion protocol. Standard protocol for postoperative analgesics, antibiotics, and venous thromboprophylaxis was followed. Drain was removed on the 2nd post operative day. Primary and secondary efficacy outcomes and primary safety outcomes were noted.

Results

Total number (n) of cases in test Group A (TXA) and in control Group B (placebo) were 30 each. There was a total of 37 males and 23 females in both groups. Age of patients varied from 52 to 74 with a mean of 65 in Group A and 67.2 in Group B ($p > 0.05$). Total number of randomized hip arthroplasty cases was 22 (11 in Group A and 11 in Group B), whereas randomized osteosynthesis cases were 38 (19 in Group A and 19 in Group B). Patients' demographics are given in Table 1.

Mean preoperative Hb value in Group A was 10.8 gm% and mean postoperative value was 9.8 gm%. Mean preoperative Hb value in Group B was 10.7 gm%. Mean postoperative Hb value in Group B 9.5 gm% (difference of reduction in preoperative and postoperative Hb values in intervention and placebo group, $P < 0.05$). Mean duration of surgery in Group A was 64.2 min and in Group B was 66.3 min. Mean total blood loss (intraoperative and postoperative) in Group A was 384.6 ml and in Group B was 448.7 ml (14.29% less in Group A than Group B, $P < 0.05$). A total of 14 patients in Group A (17 RBCs units) and 17 patients (21 RBC units) in Group B required RBC transfusion. This difference was not statistically significant, yet lesser blood transfusions were required in the intervention group. No major vascular event, severe bacterial infections, symptomatic deep vein thrombosis, pulmonary embolism, limb ischemia, acute coronary syndrome, or immediate postoperative mortality was noted in either group.

There was clinical and statistically significant difference of reduction of mean preoperative and postoperative Hb values in the intervention group as compared to the placebo group ($P < 0.05$) [Table 2]. Mean total blood loss (intraoperative and postoperative) and mean number of

Table 1: Patients' demographics

Variables	Group A (TXA) n=30	Group A (placebo) n=30
Mean age (years)	65	67.2
Gender (female/males)	11/19	12/18
Mean duration of surgery (min)	64.2	66.3
Mean total blood loss (ml)	384.6	448.7
Osteosynthesis/arthroplasty	11/19	11/19
Number of RBC transfusions	17	21

TXA: Tranexamic acid, RBC: Red blood cell

Table 2: Pre- and post-operative hemoglobin values in both groups

	Group A (TXA), mean Hb value (g %)	Group B (placebo), mean Hb value (g %)
Preoperative	10.8	10.7
Postoperative	9.8	9.5

TXA: Tranexamic acid, Hb: Hemoglobin

allogenic (RBC) transfusions were also less in intervention Group A as compared to control Group B. There was no postoperative major vascular event or incidence of any thromboembolic phenomena. There was no incidence of immediate mortality.

Discussion

Nearly all orthopedic patients suffering from hip trauma (majority being elderly) and undergoing subsequent surgery require one or more units of blood transfusions. There are consistent reported results of the beneficial role of I. V. TXA in elective hip arthroplasty.^[2,8] TXA is both a competitive inhibitor and noncompetitive inhibitor (at higher concentrations) of plasmin and prevents the blood clot from being broken.^[5] TXA rapidly diffuses into the joint fluid and synovial membrane. Following I. V. injection; it can attain similar concentrations in joint fluid and serum. TXA used within 18 h of major surgery (peak at six hours) can significantly reduce blood loss.^[9] TXA has been used in total knee arthroplasty and spine surgery also.^[10-14] Even local administration of TXA in knee arthroplasty has been described and is considered by some studies to have efficacy and lesser adverse features as compared to I. V. mode.^[3,4]

A meta-analysis by Gausden *et al.*^[1] identified 1333 patients from 12 studies. They observed that TXA significantly reduces the risk of blood transfusions and lessens blood loss in orthopedic trauma surgery. They observed that the effect of TXA in reducing blood loss was strongest in the first 24 h compared to total blood loss (half-life of TXA is 3 h). No significant difference was found by them between the effect of topical TXA and I. V. TXA in terms of reducing the risk of blood transfusion. Their findings were consistent with those of Shin *et al.*^[15] and Chen *et al.*^[16] who also reported no significant difference between topical TXA and I. V. TXA in arthroplasty patients. We have compared the use of I. V. TXA in hip trauma surgery cases (involving both arthroplasty and osteosynthesis) and observed lesser packed RBC transfusions in the intervention group as compared to placebo.

Hip fractures population involves majority of elderly people who are likely to undergo cardiovascular decompensation even with minor blood loss.^[17] Preoperative Hb value, age, and type of surgery were risk factors for erythrocyte transfusion independent of treatment group as observed in a logistic regression analysis by Zufferey *et al.*^[7] Yet the relative odds reduction after adjustment for these covariates was 70% ($P = 0.03$) in favor of TXA and even the rate of postoperative bacterial infection at 6 weeks was 25% in the TXA group compared to 38% in the placebo group ($H 0.58$; $P = 0.12$).

There are concerns regarding the hypothetical increase of thromboembolic complications such as venous thromboembolism (VTE), deep-vein thrombosis, and

pulmonary embolism after systemic administration of TXA in major surgeries in orthopedic practice. A meta-analysis study of randomized controlled trials by Massimo Franchini *et al.*^[18] evaluated I. V. use of TXA in major orthopedic surgeries. They observed that overall incidence of VTE was 86 in 4174 (2.1%) patients with I. V. infusion of TXA and 55 in 2779 (2.0%) in the control group. Out of 86 cases in intervention groups, 6 (7.0%) had pulmonary embolism while 5 out of 55 (9.1%) in the control group had pulmonary embolism. Remaining cases of VTE in both groups had deep venous thrombosis. We did not encounter any major thromboembolic complications with I. V. infusion of TXA and no significant difference was observed in the study group and control group as for risk of thromboembolic complication. Haj-Younes *et al.*^[19] observed no significant difference in the rate of cerebrovascular accidents or wound complications. Our findings were consistent with them.

In our study, mean total blood loss in Group A (cases with I. V. TXA) was 14.29% less than that of Group B (placebo). Even number of packed RBC units transfused was less in Group A; 17 as compared to 21 in Group B. Mean postoperative Hb value was also higher in Group A; the difference of reduction in mean preoperative and mean postoperative Hb values in both groups $P < 0.05$. Thus, there is lesser risk of adverse reactions and inadvertent disease transmission with the use of TXA.

Conclusion

I. V. TXA may decrease risk of blood transfusion, decrease total blood loss and maintain a higher postoperative Hb value with no significant adverse reactions. The time to surgery, method of hip fracture fixation, threshold for RBC transfusion, the optimum dose of I. V. TXA, and time of infusion of TXA may vary from region to region. As the number of cases of hip fractures continues to increase along with increase in age, so the use of TXA in such cases may improve clinical outcome, lessen number of inpatient days and hence decrease overall cost.

Limitation of the study

The sample size is small because of single-center trial. A larger study involving multicenter trials may be conducted.

Acknowledgment

The authors are thankful to the department of orthopedics, department of anesthesia, and whole supporting staff, without whose help this study would not have been possible.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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