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A PROSPECTIVE COMPARATIVE STUDY TO ASSESS THE EFFECT OF TRANEXAMIC ACID IN PATIENTS UNDERGOING CEPHALOMEDULLARY NAILING FOR HIP FRACTURES

Orthopaedics

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ABSTRACT

Background: The main objective of the present study was to assess the effect of TXA in patients undergoing cephalomedullary nailing fixation of hip fractures in comparison with patients not receiving TXA. **Methods:** This is a prospective comparative study done with eligible in-patients (n=71) with hip fractures, planned for cephalomedullary nailing in Department of Orthopaedics and Traumatology, Meenakshi Mission Hospital and Research Centre, Tertiary Health Care Centre, Madurai, Tamilnadu. All eligible patients were divided into two groups viz. Group T and Group S. For Group T (TXA Group), intravenous infusion of TXA at the dose level of 15 mg/kg was given at the time of inducing anaesthesia i.e., 15 minutes before skin incision in surgery. For Group S (Saline Group) intravenous infusion of normal saline at the dose level of 15 mg/kg was given at the time of inducing anaesthesia i.e., 15 minutes before skin incision in surgery. Group T and Group S were compared and evaluated for blood loss and requirement of whole blood transfusion. **Results:** Majority of the study subjects i.e., 80% had Intertrochanteric femur fracture and majority of the study subjects i.e., 68.60% underwent closed reduction and internal fixation with long Proximal Femoral Nail (PFN). Furthermore, our study findings delineated that study subjects who received TXA had 79.8 mL lesser peri- operative blood loss as compared to control subjects and this difference was statistically significant ($p = 0.002$) between the groups. In addition, number of study subjects who required blood transfusion was higher (44.44%) among Group S as compared to Group T (20.00%) and this difference was also statistically significant ($p<0.05$) between the groups. **Conclusion:** Tranexamic acid play a significant role in reducing postoperative blood loss and blood transfusion when used intravenously in patients undergoing cephalomedullary nailing fixation of hip fractures.

KEYWORDS

Tranexamic acid, Cephalomedullary nailing, Hip fractures, Blood loss, Blood transfusion

INTRODUCTION

There are approximately 300,000 patients annually hospitalized for hip fractures.[1] Intertrochanteric fractures represent one of the common types of hip fractures, and the 1-year mortality rate after intertrochanteric fractures is reported to be approximately 25%.[2] Dynamic hip screw with barrel plate and cephalomedullary nails are the usual methods of internal fixation in these fractures. The former method is associated with significant exposure and dissection for application of the plate.[3,4] Hip fractures are commonly associated with a relatively large amount of blood loss from the initial injury in addition to blood loss resulting from surgery. A range of between 20-60% of patients require blood transfusions after surgery, which may result in an increase in postoperative infections, increased length of hospital stay.[5]

Various pharmacological options like antifibrinolytics, fibrin glue, thrombin gelatin matrix and factor VIII concentrates are being used to reduce blood loss in orthopaedic surgeries.[6,7] Tranexamic acid (TXA) an antifibrinolytic agent that can help improve coagulation function by inhibiting the degradation of fibrin, has been confirmed to reduce blood loss and transfusion requirements in hip and knee arthroplasty.[8,9] TXA is now being increasingly used in various fracture surgeries.[10-12] Recently local infiltration of TXA has been proven to be more effective and less harmful in total knee arthroplasty.[13,14]

However, to the best of our literature knowledge there are scarce of studies on efficacy of TXA to reduce blood loss and transfusion requirements in cephalomedullary nailing fixation of hip fractures. With this scenario, the present study was carried out with the main objective to assess the effect of TXA in patients undergoing cephalomedullary nailing fixation of hip fractures in comparison with patients not receiving TXA.

METHODS

Study Setting And Participants

All eligible in-patients (n=71) with hip fractures, planned for cephalomedullary nailing in Department of Orthopaedics and Traumatology, Meenakshi Mission Hospital and Research Centre, Tertiary Health Care Centre, Madurai, Tamilnadu.

Study Design

This is a prospective comparative study done to assess the efficacy of tranexamic acid in reducing blood loss in patients with cephalomedullary nailing surgery in hip fractures. All eligible patients who are willing to be in compliances with the inclusion criteria were included in the study. The inclusion criteria are as follows; he/she i). should willing to provide consent, ii). Patients with acute intertrochanteric femur fracture, iii). Patients with basicervical neck of femur fracture. and iv). Patients over the age of 18 years.

All eligible patients were divided into two groups viz. Group T and Group S. For Group T (TXA Group), intravenous infusion of TXA at the dose level of 15 mg/kg was given at the time of inducing anaesthesia i.e., 15 minutes before skin incision in surgery. For Group S (Saline Group) intravenous infusion of normal saline at the dose level of 15 mg/kg was given at the time of inducing anaesthesia i.e., 15 minutes before skin incision in surgery.

METHODOLOGY

15 mg/kg of TXA (cyklokapron) diluted in 100 mL of normal saline was infused intravenously over 10 minutes about 15 minutes before skin incision.

Operative Procedure

All operations were performed by six experienced Orthopaedic surgeons. Prophylactic antibiotics were administered 30-60 min before operation. Either spinal or general anesthesia was administered, and the patients were positioned on the fracture traction table. Reduction was performed under C-arm fluoroscopy. Intramedullary nail or Proximal femoral nail was inserted using the minimally invasive technique. After closed reduction, an approximately 5 cm longitudinal skin incision was made proximal to the femoral greater trochanter. The tip of the greater trochanter was exposed by incision of the fascia and the gluteus medius. A guide wire was introduced into the femoral medullary canal from the lateral aspect of the greater trochanter, and the intramedullary nail or Proximal femoral nail was inserted through the guidewire. The blade was located in the lower half of the femoral head and neck in the anteroposterior view and centrally in the lateral view; the tip was inserted 5-10 mm into subchondral bone. The distal locking screw was inserted under an aiming device and was statically locked.

Postoperative Management

Antibiotic prophylaxis was administered routinely for 48 hours postoperatively. The volume of fluid transfusion was determined by the surgeon in charge according to the patient's blood pressure and amount of oral intake. Low-molecular-weight heparin was administered routinely every 24 hours postoperatively for 2 weeks to prevent thromboembolism. Active functional exercises were encouraged from postoperative day 1. The continuous passive motion was started in all patients on the second postoperative day. Partial weight-bearing with a walker was started within 1-week

postoperatively in stable fractures treated with satisfactory reduction and internal fixation; in those with unstable fractures, this was started 2–3 weeks postoperatively.

With the above information Group T and Group S were compared and evaluated for blood loss and requirement of whole blood transfusion.

Statistical Analysis

Data were edited manually, entered in MS-Excel (Office 365 Version) and analyzed using SPSS version 20. The continuous variables were expressed as Mean and Standard deviation. Categorical variables were expressed as frequency and percentage. Independent sample t-test was used to find the significance difference between groups. Univariate and Multivariable analysis, Chi-square test and Fisher's exact tests were used to find out association between the categorical variables. P<0.05 was considered as statistically significant.

RESULTS

The mean age of study subjects in Group T and Group S was found to be 56.30 and 51.20 respectively. However, age difference in Group T was not significantly (p = 0.547) different from the Group C (Table 1).

Table 1: Age Wise Distribution Of Study Subjects

Variables		Group T	Group S	P-Value
Age	18 - 30	3	9	0.547
		8.60%	25.00%	
	31 - 40	7	5	
		20.00%	13.90%	
	41 - 50	2	2	
		5.70%	5.60%	
	51 - 60	5	4	
		14.30%	11.10%	
	61 - 70	8	9	
		22.90%	25.00%	
	> 70	10	7	
		28.60%	19.40%	
	Mean	56.30	51.20	
	SD	18.80	21.50	

Males and females were equally distributed in both Group T and Group S, and hence gender difference in Group T was not significantly (p = 0.737) different from the Group C (Table 2).

Table 2: Gender Wise Distribution Of Study Subjects

Variables		Group T	Group S	P-Value
Gender	Male	22	24	0.737
		62.90%	66.70%	
	Female	13	12	
		37.10%	33.30%	

Majority of the study subjects i.e., 80% had Intertrochanteric femur fracture. However, there was no statistically significant difference (p = 0.908) in the surgical diagnosis between the groups was observed (Table 3).

Table 3: Distribution Of Study Subjects Based On Indication For Surgery

Variables		Group T	Group S	P-Value
Diagnosis	Basicervical Neck of Femur Fracture	3	3	0.908
		8.60%	8.30%	
	Intertrochanteric Femur Fracture	28	27	
		80.00%	75.00%	
	Subtrochanteric Femur Fracture	4	6	
		11.40%	16.70%	

Majority of the study subjects i.e., 68.60% underwent closed reduction and internal fixation with long Proximal Femoral Nail (PFN). However, difference in the proportion of surgical procedure done between the groups was not statistically significant (p = 0.908) and hence both the groups were comparable (Table 4).

Table 4: Distribution Of Study Subjects Based On Surgical Procedure Done

Variables		Group T	Group S	P-Value
Gender	Long PFN	24	32	0.105
		68.60%	88.90%	
	Short PFN	11	4	
		31.40%	11.10%	

Study subjects who received TXA had 79.8 mL lesser peri- operative blood loss as compared to control subjects. Moreover, this difference was found statistically significant (p = 0.002) between the groups (Table 5).

Table 5: Distribution Of Study Subjects Based On Blood Loss

Variables	Group T	Group S	Diff.	P-Value
Perioperative Blood Loss (mL)	507.40 ± 102.30	587.20 ± 103.80	79.80	0.002

Total number of study subjects who required blood transfusion was higher (44.44%) among Group S as compared to Group T (20.00%) and this difference was statistically significant (p<0.05) between the groups (Table 5).

Table 6: Distribution Of Study Subjects Based On Blood Transfusion Done

Variables		Group T	Group S	P-Value
No. of Patients with Blood Transfusion	Yes	7	16	<0.05
		20.00%	44.44%	
	No	28	20	
		80.00%	55.56%	

DISCUSSION

Tranexamic acid is a competitive inhibitor of plasminogen activation, and at much higher concentrations, a non-competitive inhibitor of plasmin. As a result of inhibition of the fibrinolysis it prevents the clots from being broken down thereby significantly reducing surgical haemorrhage. Fibrinolysis occurs at increased rate after surgical trauma especially in a major surgery like total knee arthroplasty. Fibrinolysis peaks at six hours after surgery and maintains at a high rate for up to 18 hours after surgery. Thus, tranexamic acid used in this period can significantly reduce the blood loss.[15] Moreover, to the best of our literature knowledge there are scarce of studies on efficacy of TXA to reduce blood loss and transfusion requirements in cephalomedullary nailing fixation of hip fractures. Hence in the current study we aimed to assess the effect of TXA in patients undergoing cephalomedullary nailing fixation of hip fractures in comparison with patients not receiving TXA.

In this study, we assessed the effect of local infiltration of tranexamic acid on various parameters related to blood loss like postoperative blood loss and requirement for blood transfusion during surgeries for fixation of cephalomedullary nailing of hip fractures. Our study results depicted that majority of the study subjects i.e., 80% had Intertrochanteric femur fracture and majority of the study subjects i.e., 68.60% underwent closed reduction and internal fixation with long Proximal Femoral Nail (PFN). Furthermore, our study findings delineated that study subjects who received TXA had 79.8 mL lesser peri- operative blood loss as compared to control subjects and this difference was statistically significant (p = 0.002) between the groups. In addition, number of study subjects who required blood transfusion was higher (44.44%) among Group S as compared to Group T (20.00%) and this difference was also statistically significant (p<0.05) between the groups. These findings were in concurrence with literature findings reported by various other research investigators.

Murphy and Scott reported that the potential benefit of decreasing blood loss and decreasing the number of transfusions following hip fracture surgery is overwhelming and will likely result in improved patient outcomes, shorter length of stay, and lower cost.[16] Oremus et al., and Ho et al., reported that TXA has been extensively used in joint replacement surgeries including total knee and total hip arthroplasty.[17,18] Various other research investigators demonstrated the clinical effect of intravenous TXA in reducing blood loss and need for blood transfusion in total knee arthroplasty.[17,19,20-22]

Furthermore, Drakos et al., conducted a randomized prospective trial with total of 200 intertrochanteric fractures treated with intramedullary nail. There results delineated that the patients in the trial group received 3g of tranexamic acid in the subfascial plane and around the fracture site resulted in 43% reduction in transfusion requirements (p<0.01).[23] These findings are in accordance with out study findings where in number of study subjects who required blood transfusion was higher (44.44%) among control as compared to TXA group (20.00%).

Although our study is prospective, it has certain limitations. Our study could not be double blinded and hence clinician bias could have been

introduced. The surgeries were not performed by a single surgeon, thereby leading to differential expertise amongst different surgeons.

CONCLUSION

In conclusion tranexamic acid play a significant role in reducing postoperative blood loss and blood transfusion when used intravenously in in patients undergoing cephalomedullary nailing fixation of hip fractures. However, there is necessity of a larger double blinded studies comparing various modalities of use of tranexamic acid in order to conclusively establish its role.

Declarations
Funding: Nil
Conflict of interest: None
Ethical approval: This study was approved by the Institutional Research and Ethics board of Meenakshi Mission Hospital and Research centre, Madurai, Tamilnadu.

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