ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 12 | December - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFECT OF TRANEXEMIC ACID IN REDUCING BLOOD LOSS IN ELDERLY PATIENTS UNDERGOING HIP SURGERIES

Anesthesiology

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ABSTRACT

All major Orthopaedic surgeries are associated with high intraoperative and post-operative blood loss, especially hip fractures, which may result in whole blood transfusions in majority of patients. Allogenic blood transfusions increase the risk of adverse events, such as blood borne infections, immune reactions, volume overload, electrolyte disturbances and finally adding to the cost of health care. A variety of methods are used in orthopaedic surgery to reduce blood loss, including the application of tourniquets, autologous blood transfusion, controlled hypotension, intraoperative blood salvage, navigation, and minimally invasive surgery. However, these methods cannot be effectively implemented in elderly patients posted for hip surgeries. So we conducted this study to determine the efficacy of tranexamic acid in reducing the blood loss in patients undergoing total replacement surgeries. We included 70 elderly patients in two groups, tranexamic acid group received 15mg/kg iv, 15min before skin incision whereas control group received normal saline. Demographic data were comparable between the groups. we found that blood loss was less in tranexamic acid group without any incidence of deep vein thrombosis in the 6weeks follow up period.

KEYWORDS

tranexamic, knee replacement, blood loss

INTRODUCTION

All major Orthopaedic surgeries are associated with high intraoperative and post-operative blood loss, especially hip fractures, which may result in need for whole blood transfusions in majority of patients. There is a high incidence of blood transfusion in elderly patients (1,2)following hip surgeries. Allogenic blood transfusions increase the risk of adverse events, such as blood borne infections, immune reactions, volume overload, electrolyte disturbances and finally adding to the cost of health care (3,6). A variety of methods are used in orthopaedic surgery to reduce blood loss, including the application of tourniquets, autologous blood transfusion, controlled hypotension, intraoperative blood salvage, navigation, and minimally invasive surgery. However, these methods cannot be effectively implemented in elderly patients posted for hip surgeries.

Fibrinolytic system will be activated transiently after any surgery and use of tourniquet can also induce local fibrinolysis in the operated limb. This increased fibrinolytic activity increases blood loss during the first few postoperative hours. This justifies the use of antifibrinolytic agents in the perioperative period. Tranexamic acid, which is an antifibrinolytic agent is useful in decreasing blood loss in general trauma patients as well as patients undergoing elective orthopaedic surgery (6,10). Tranexamic acid being an analogue of lysine(6,9,10), binds to the lysine binding site of plasminogen and blocks the binding of plasminogen to the fibrin surface. Thus plasminogen activation is prevented and fibrinolysis is delayed. Currently, there is sufficient literature evidence concerning the efficacy of natural (aprotinin) or synthetic (tranexamic acid) antifibrinolytic agents in reducing blood loss and transfusion requirements in liver transplant, thoracic surgery, gynaecological, orthopaedic and urological procedure to reduce blood loss.

Deep vein thrombosis is considered as a very common postoperative complication after major orthopedic surgery especially in elderly and obese patients. Use of tranexamic acid also increases the risk of thrombotic events (6,10). The purpose of this study is to know whether tranexamic acid reduces the perioperative blood loss and blood transfusion requirements, along with increase in incidence of postoperative deep vein thrombosis in hip surgeries in elderly patients(2).

AIM

To analyse the efficacy of tranexamic acid in reducing blood loss in elderly patients undergoing hip surgeries.

OBJECTIVES

Our primary objective was to assess the effect of tranexamic acid in elderly patients undergoing surgeries for hip fractures in terms of intraoperative blood loss, haemoglobin level, and the need for blood transfusion between the tranexamic acid group and the control group. Our secondary objective was to assess the incidence of deep vein thrombosis due to the use of tranexamic acid.

Inclusion Criteria

70 elderly Patients aged between 50-80years of age, belonging to ASA PS 1,2, admitted in our institute with intracapsular / extracapsular hip fractures ,Acute intertrochanteric femur fracture, Basicervical neck of femur fracture were included in the study.

Exclusion Criteria

Patient who had documented allergy to Tranexamic acid, History of DVT or pulmonary embolus and patients not giving consent were excluded from the study.

Study Design

After obtaining institutional ethics committee approval, written informed consent were taken from the patients. Seventy patients were included in the study. They were randomly assigned to two groups based on computer randomisation. Anesthesiologist who assessed the intraoperative parameters was blinded to the study. patients were randomly allocated into two groups : Group S (study group) who received 15mg/kg of intravenous infusion of tranexamic acid in 100 ml normal saline and Group C (control group) ,who received 100ml of normal saline infusion at the time of induction of anaesthesia, 15 minutes before skin. Patients in both the groups was evaluated for Intraoperative blood loss (in ml), Haemoglobin (Hb) levels (in gm/dL) and Packed cell volume(PCV) levels (in %): in the Postoperative day 1 and day 2 , number of units of packed red blood cells transfused and incidence of Deep vein thrombosis in the post-operative period.

After shifting to operation theatre, non invasive blood pressure (NIBP), electrocardiogram (ECG) and saturation probe (SpO2) were connected. All patients received combined spinal epidural, with 2mlof 0.5% hyperbaric levobupivacaine in L4-5 space using 25G quinckie's needle. Epidural catheter also secured at the same space and epidural infusion with 0.5% bupivacaine was started 90 minutes after spinal anesthesia.at Intraoperative blood loss was evaluated by measuring

the blood collected in suction apparatus which had graduated markings on it and the number of blood soaked gauzes. A completely soaked blood gauze was amounted to 50ml blood loss. Same method was followed for calculating blood loss in drapes at surgical site. The requirement for allogeneic PRBC in each group was recorded. The American Academy of Orthopaedic surgeons recommends postoperative blood transfusion in hip fracture patients when Hb is <10 g/dL, even if symptoms are not present. So in our study, blood transfusion was administered if Hb was <10 g/dL even if there were signs of excess blood loss such as tachycardia, tachypnea, or hemodynamic instability. Measured blood loss was replaced with crystalloids in a 3:1 ratio till blood loss reached half that of allowable blood loss and thereafter with colloid in 1:1 ratio until trigger for blood transfusion is reached. Once the trigger point was reached, they recieved blood.

Blood samples were sent for repeat haemoglobin and haematocrit levels for all the patients in the postoperative day1,2. Any signs of early deep vein thrombosis like limb swelling and reduced distal arterial pulses were also noted. Doppler ultrasonography was done for the patients who showed any early signs and treated accordingly.

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.

All the patients were asked to come after one month of surgery for follow up, to look for any signs and symptoms of deep vein thrombosis. The primary safety outcome was the occurrence of thrombotic events within 6 weeks after operation; these included lower limb DVT, pulmonary embolism, myocardial infarction, acute coronary syndrome, cerebral infarction, and extremity ischemic necrosis. All patients underwent Doppler ultrasonography of both lower limbs before operation as well as at discharge. Patients who did not visit the hospital for follow-up were contacted over the telephone to obtain information on lower limb swelling or other complications.

Table-1: Age Distribution Of The Study Population (n=70)

parameter	Group S	Group C	
50-60yrs	17	16	
60-70yrs	10	14	P value-0.557
70-80yrs	8	5	

Table 2: Gender Distribution Of The Study Population:

parameter	Group S	Group C	
Male	22	24	P value -0.737
Female	13	11	

The demographic parameters were comparable between the groups.(table-1,2)

Table 3: Intraoperative Blood Loss In The Study Population

Parameter	Group S (Mean ± SD)	Group C (Mean ± SD)	P value
Intraoperative Blood loss	508.6 ± 102.4	597 ± 106.9	0.002

Table 4: Number Of Patients Received Blood Transfusion In The Study Population:

Parameter	Group S	Group C	p value
No. of patients received PRBC	7	16	0.002
No. of patients who didn't receive PRBC	28	19	

Table 5: Haemoglobin Levels In The Postoperative Day 1 & 2 In The Study Population

Parameter	Preop Hb (Mean ± SD)	POD-1 Hb (Mean ± SD)	POD -2 Hb (Mean ± SD)
Group S	10.2 ± 2.2	9.0 ± 1.2	9.7 ± 1.6
Group C	11.2 ± 2.1	8.1 ± 1.6	9.4 ± 1.9
p value	0.252	0.010 (SIG)	0.390

Table 6: Haematocrit Levels In The Postoperative Day 1 & 2 In The Study Population :

Parameter	Preop PCV (Mean ± SD)	POD-1 PCV (Mean ± SD)	POD -2 PCV (Mean ± SD)
Group S	32.1 ± 6.9	27.3 ± 5.7	30.9 ± 5.8
Group C	35.2 ± 6.5	24.6 ± 6.5	29.6 ± 5.3
p value	0.452	0.015 (SIG)	0.306

DISCUSSION

Orthopedic surgical procedures are associated with significant bleeding, that can cause significant haemodynamic instability. The amount of blood loss may vary widely between different surgical procedures and depends on surgical as well as patient factors. Multimodal approach to reduce the blood loss has been widely practised like using regional nerve blocks, providing hypotensive anesthesia and use of antifibrinolytic drugs. Tranexamic acid has proven to be efficacious in elective Orthopaedic surgeries, but still the optimal dosing and timing of tranexamic acid administration is debated. Also, there is not much literature available to study the efficacy of tranexamic acid in elderly patients with hip fractures. Surgeons usually avoid using hemostatic drugs in surgeries for hip fractures, because it is a minimally invasive procedure with mild to moderate blood loss. However, the surgery is associated with massive hidden blood loss that is followed by acute anemia and haemodynamic alterations, especially in elderly patients, and these patients often need allogenic blood transfusion postoperatively. But blood transfusion itself causes certain disadvantages like risk of transmission of infections, increased chance of allergic reactions, circulatory overload due to transfusion, transfusion related acute inflammatory response and immunomodulation. Therefore, it is necessary to identify methods that can reduce blood loss in these patients. Increased fibrinolytic activity is one of the reason for blood loss perioperatively. So the use of an antifibrinolytic drug may cause reduction in perioperative blood loss. One of the most widely used antifibrinolytic is Tranexamic acid. Other antifibrinolytic agents are Epsilon Amino Caproic Acid and Aprotinin.

Pharmacological therapies to reduce blood loss has been used in cardiac surgery, liver transplantation, and urogynaecological procedures as well. Currently, there is sufficient literature evidence concerning the efficacy of natural (aprotinin) or synthetic (tranexamic acid) antifibrinolytic agents in reducing blood loss and transfusion requirements in orthopaedic surgery. Amongst all fibrinolytics, tranexamic acid has been shown to be effective than aprotinin and epsilon amino caproic acid, for effectively reducing blood loss, with less incidence of allergic reactions, and with less cost of treatment. Tranexamic acid is one of the most widely used and is on the World Health Organisation list of Essential medicines. We investigated 70 patients undergoing hip surgery and Patients were randomized into two groups- group tranexamic acid (group T) and group control (group S). Patients in group T were administered tranexamic acid preoperatively and patients in control group received normal saline. Demographic data were comparable between the groups. There are various methods of measuring blood loss like visual estimation, direct measurement of moistened surgical gauzes and observing the fluid level of suction reservoirs (gravimetric), colorimetric method, measurement of haematocrit in the intraoperative drains and postoperative evaluation of haematoma by ultrasonography. Estimation of blood loss using a gravimetric method is accurate and applicable in the clinical setting and also it is a simple and objective tool to evaluate intraoperative blood loss, compared to others.

In this study gravimetric method was followed by observing the fluid level in the suction reservoirs and measuring the number of soaked gauges. In Tranexamic acid group, mean perioperative blood loss was 508.6 ± 102.4 ml and that for control group was 597.3 ± 106.9 ml. Mean difference was 88.7 ml with p value 0.002. Hence, patients who received tranexamic acid had around 88ml of lesser perioperative blood loss than the control group and this difference was statistically significant ($p<0.05$).

In our study, the transfusion trigger was set to 10gm % considering older population (high risk) and as per AO guidelines. This was comparable to that of study done by P. J. Zufferey et al (13) with Hb trigger of 9 gm %, and 0.28-0.30 level of haematocrit. Out of the 23 patients who crossed the blood transfusion trigger in our study, 7 patients belong to the group treated with tranexamic acid (7/35).The remaining 16 belonged to control group (16/36). Total number of patients who received blood transfusion was higher 44.44% among

control group as compared to 20% in those treated with tranexamic acid. This difference was statistically significant. The preoperative Hb in the study and control group was comparable. The mean preoperative Hb was 10.2 ± 2.2 gm% & 9.0 ± 1.2 gm% in tranexamic acid and control group respectively. Hb in the postoperative period day 1 was 9.0 ± 1.2 gm% and 8.1 ± 1.6 gm% in tranexamic acid and control group respectively. There was significant difference in the fall in mean Hb between the two groups on postoperative day 1 (mean difference in the fall in Hb was 1.9 gm/dl). On postoperative day 2, haemoglobin levels were comparable between the groups (mean difference in the fall in Hb was 0.3 gm/dl) and statistically insignificant.

The preoperative PCV in the study and control group was comparable. The mean preoperative PCV was 32.1 ± 6.9 % & 35.2 ± 6.5 % in tranexamic acid and control group respectively. PCV in the postoperative period day 1 was 27.3 ± 5.7 % and 24.6 ± 6.5 % in tranexamic acid and control group respectively. PCV in post operative day 2 was 30.9 ±5.8% and 29.6 ± 5.3% in tranexamic acid and control group respectively. There was significant difference in the fall in mean PCV between the two groups on postoperative day 1 (mean difference in the fall in PCV was 5.3 %) and the fall in PCV in the postoperative day 2 (mean difference in the fall in PCV was 4.6 %) was not statistically significant. Even with the evident benefits from the administration of tranexamic acid in hip surgeries, there are concerns about the incidence of thrombotic events after the use of tranexamic acid. Zuffereyet al(13) have reported that using Tranexamic acid in hip fracture surgery increased the risk of vascular events compared with placebo. However, many recent studies(9,10,18) have demonstrated that administration of Tranexamic acid in orthopaedic surgeries does not increase the risk of deep vein thrombosis. In our study, none of the patients treated with tranexamic acid were found to have any adverse thrombotic events, which included deep vein thrombosis, pulmonary embolism, myocardial infarction, acute coronary syndrome, cerebral infarction and extremity ischemic necrosis even after 6 weeks of surgery.

CONCLUSION

We concluded that tranexamic acid is effective in reducing the perioperative blood loss in patients with surgeries for hip fractures with no significant thromboembolic adverse events.

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