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Comparison of Two Different Prophylactic Tranexamic Acid Doses Impact on Patients Undergoing Orthopaedic Surgeries

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ABSTRACT

Background: A considerable blood loss risk is linked with major orthopaedic surgeries. Transfusions of red blood cells avoid these problems, although they carry a risk of their own. Tranexamic acid prevents plasmin from dissolving and breaking down fibrin clots. This research aims to evaluate the efficacy of intravenous infusion of prophylactic dosages of tranexamic acid (10 mg/kg) vs 20 mg/kg) one hour before orthopaedic surgery to compare two different prophylactic tranexamic acid doses' impact on patients undergoing orthopaedic surgeries.

Methods: The study was a parallel group interventional randomised control experiment. Sixty ASA 1 and ASA 2 patients formed 2 groups; Group A received an injection of tranexamic acid 10 mg/kg in 100 ml NS, while Group B received 20 mg/kg in 100 ml NS one hour before surgery. Postoperative drain collection was seen in the sixth, twelve, and twenty-four hours. Differences in Hb before and after surgery were observed.

Results: Age, sex, body weight, length of operation, and amount of intravenous fluid transfusion did not differ statistically significantly across the groups. Both groups had a statistically significant difference in Hb between pre- and post-op. Group A's mean difference in Hb levels revealed noticeably lower values. Group A required a lot more blood transfusions than the other group.

Conclusion: Higher doses of tranexamic acid (20 mg/kg bolus) used prophylactically are inexpensive, safe, and effective ways to lower intraoperative blood loss and, thus, the need for postoperative blood transfusions.

Key-words: Bleeding, Blood loss, Orthopaedic surgery, Postoperative blood transfusions, Prophylactic Tranexamic Acid

INTRODUCTION

Significant blood loss [1], acute anemia [2], perioperative noxious cardiovascular complications [3], blood transfusion requirements [4,5] and mortality [6] are linked to major orthopaedic surgeries such as total hip replacement, internal fixation of femur fracture, spine instrumentation, hip fractures including fracture neck of femur, intertrochanteric and subtrochanteric fractures of femur and fractures of the acetabulum, dynamic hip screw fixation, intramedullary nailing, hemiarthroplasty, and fixation of the acetabulum. Transfusions of red blood cells can avoid these consequences, but they still carry a risk of infection [7,8], and as well as an increased chance of an immunological response and related costs [9]. Numerous variables influence patient outcomes in

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orthopaedic surgery regarding bleeding. Surgical factors include things like widespread venous bleeding, large surgical incisions, bone haemorrhage, and hidden sources of bleeding [10], in addition to patient variables such as coagulopathies [11], anticoagulant and antiplatelet medications, and other illnesses [12]. Surgeons benefit from effective hemostasis during surgery because it stops diffuse bleeding from venules and capillaries, which otherwise obstructs the surgical field, prolongs the process, and raises the risk of infection [13,14].

Major elective orthopaedic operations like joint replacements carry a high risk of significant blood loss and increased transfusion requirements if preventive measures are not taken. Apart from the conventional blood management strategies like tourniquet use when needed and preoperative optimisation, intraoperative techniques like cauterization and cell saver, topical and pharmaceutical hemostats, and biosurgical procedures can offer some great ways to reduce the need for transfusions and achieve hemostasis [15-17]. Serious postoperative problems are also more likely in cases of high intraoperative blood loss [18]. Thus, patient outcomes are optimal when bleeding and clotting are balanced during surgery to provide appropriate tissue perfusion without excessive blood loss [19].

According to several high-quality randomised control studies [20], tranexamic acid can help surgeons conduct knee and hip arthroplasty surgeries with less blood loss and less need for transfusions. The administration methods employed in the studies, such as a single intravenous bolus dose, several boluses, prolonged infusions, intraarticular injections, and various dosing schedules, vary widely [21]. In total knee arthroplasty, one intraoperative dosage is sufficient to minimise the requirement for transfusions and postoperative bleeding.

Aprotinin is one example of an antifibrinolytic. In orthopaedic surgery, it has been repeatedly seen that tranexamic acid and epsilon aminocaproic acid minimise bleeding. Postoperative bleeding is thought to be primarily caused by hyperfibrinolysis. Bovine lung-derived apitinin inhibits serine protease during the last step of fibrinolysis; nevertheless, it also causes spongiform encephalitis, allergies, thrombosis, and nephrotoxicity. Comparing aminocaproic acid to tranexamic acid, aminocaproic acid is more costly, less effective, and has less evidence from studies [22].

An artificial lysine analogue antifibrinolytic is tranexamic acid. It prevents plasminogen from being competitively activated into plasmin. Tranexamic acid prevents plasmin from dissolving and breaking down fibrin clots at greater doses by noncompetitively blocking plasmin. Tranexamic acid inhibits fibrinolysis by reversible binding and competitive inhibition of the lysine moieties on plasminogen, plasmin, and tissue plasminogen activator (tPA). In cases of trauma and postpartum haemorrhage, tranexamic acid reduces bleeding during surgery and mortality due to bleeding [23]. Tranexamic acid lowers the need for blood transfusions and has been shown to minimise blood loss in major orthopaedic surgery by one-third. Despite several studies demonstrating Tranexamic's effectiveness in lowering blood loss, there is still disagreement on the recommended dosage. and the schedule for administering tranexamic acid.

The risk of intravascular thrombosis was assessed with tranexamic acid injection intra-particularly and a placebo. While fewer blood transfusions were required, the trials did not demonstrate a reduction in blood loss. Only one RCT—conducted by Seo et al., 28—showed that the requirement for transfusions was decreased by intraarticular (20%) as opposed to intravenous (34%) or placebo (94%). Since the data supporting intraarticular tranexamic acid in total hip replacement is not as robust as for knee arthroplasty, more studies are necessary [24].

MATERIALS AND METHODS

Research Design- This study included sixty individuals scheduled for orthopedic procedures. Data was collected using a pre-structured proforma, with patients fully informed about the study's purpose and providing written informed consent. A thorough pre-anesthesia evaluation was conducted for each participant, documenting demographics, baseline vitals, and laboratory results. Participants were randomly assigned to two groups via a computer-generated random number allocation mechanism. Patients were instructed to avoid oral medications for eight hours, semi-solids for four hours, and clear liquids for two hours before the procedure. An 18-gauge intravenous access was established under local anesthesia and aseptic conditions. Oral anticoagulants were discontinued five days before surgery, while antiplatelets and NSAIDs were

stopped seven days prior. Antihypertensive medications were continued until the morning of the procedure, but insulin and oral hypoglycemic medications were halted on the morning of the operation. The pre-anesthetic medication regimen included 150 mg of oral ranitidine the night before surgery. To ensure blinding, study medications were prepared by an anesthesiologist involved in the trial, using identical 100 ml 0.9% normal saline volumes. The administering anesthesiologist was unaware of the study's medication details. The study medication was administered one hour before surgery. Upon arrival at the surgical table, patients were positioned supine, and baseline vitals were recorded. Monitoring included five-lead electrocardiography (ECG), saturation probe, and non-invasive blood pressure (NIBP). Intravenous fluids were administered according to departmental guidelines.

Inclusion Criteria

- All patients scheduled for various orthopaedic surgeries belonging to physical status ASA class 1 & 2
- All patients aged between 20 and 80 are not coming under exclusion criteria.

Exclusion Criteria

- Those allergic to Tranexamic acid.
- Haemoglobin <8 gm%, pregnant women and breastfeeding women.
- Patients with h/o severe Ischemic heart disease (IHD).
- Patients with h/o pulmonary embolism, epilepsy, deep vein thrombosis.
- Patients who are known to be allergic to propofol, food allergy
- Patients on drug or alcohol abuse
- Patients with severe liver and renal insufficiency.
- Patients who refused physical status ASA Class 3 or more.
- Body mass index >35.

Statistical analysis- The study used SPSS 25 for effective analysis. MS Excel was used to create graphs and other calculations. The continuous data like ASA status and other parameters were expressed as mean±standard deviation while the discrete data were expressed as frequency and its respective percentage. The statistical analysis was done between the two groups. The study used ANOVA as the statistical tool for comparing the variables. The level of significance was $p<0.05$.

Ethical Approval- The study was approved by the Ethical Committee of Sri Sridevi Institute of Medical Sciences and Research Hospital Tumakuru, Karnataka.

RESULTS

Two patients did not fit the inclusion criteria out of the 65 patients with various orthopaedic operations. Before randomization, three patients who had been rejected to participate were removed. The age, sex, weight, and pre-induction opioid usage of the groups were all the same. Vitals at baseline were similar. Similar general anaesthesia anaesthetic methods were administered to both groups. The groups' surgical specifics were similar in terms of the kinds of operations performed, the induction-incision time, the length of the surgery, the starting pump pressures, and the flows.Pre- and post-operative haemoglobin levels, intraoperative blood loss, suction drain collection, number of mop-needed, and total blood loss were all measured.

Using the Shapiro-Wilk test, all demographic information and baseline vitals were examined for distribution and determined to be regularly distributed. Suppose a single parameter recorded data set is abnormally distributed. In that case, one might create a graph to illustrate it and reference it in the text, as all demographic data and baseline vitals were examined for distribution using the Shapiro-Wilk test and found to be normally distributed. p-values less than 0.05 were regarded as statistically significant.

Table 1 shows the comparative values for the two groups, which are shown as mean, standard deviation, and median age. The unit is in year. The data were non-parametric and were compared using Mann Whitney U test ($p<0.05$), N=number of patients, SD=standard deviation, SE standard error mean, CI=confidence interval. Inference: Age was comparable between the two groups. The mean age for Group A was 52.7±14.97 and Group B was 55.77±17.22 years. The comparative values for the two groups are shown as percentages. The data was compared with the Chi-square test (p-0.796). Inference: The distribution of gender was comparable between the two groups. In group A there were 15 males (50%) and 15 females (50%). In Group B there were 17 males (56.6%) and 13 females (43.3%).

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Table 1: Comparison of age and gender distribution between two groups

Age Distribution						
	N	**SD**	**SE Mean**	**Mean**	**95% CI of Mean**	**p-value**
Group A	30	14.97	2.734	52.7	46.4 to57.6	0.2036
Group B	30	17.22	.144	55.77	49.3 to62.20	
Gender Distribution						
	Male	Female	Total	Chi-square	p-value	
Group A	15 (50%)	15 (50%)	30	0	0.7961	
Group B	17(56.6%)	13(43.33%)	30			
Total	28	32	60			

The mean age was 37.02±8.32 years in group A (Magnesium sulphate) and 34.89±10.50 years in group B (Fentanyl). The groups were comparable with p=0.065. The male gender distribution was 56.1% in Group A (Magnesium sulphate) and 43.9% in Group B (Fentanyl). The female gender distribution was 53.7% in Group A (Magnesium sulphate) and 46.3% in Group B (Fentanyl), with a p-value of 0.824. Fig. 1 shows the age distribution and sex distribution.

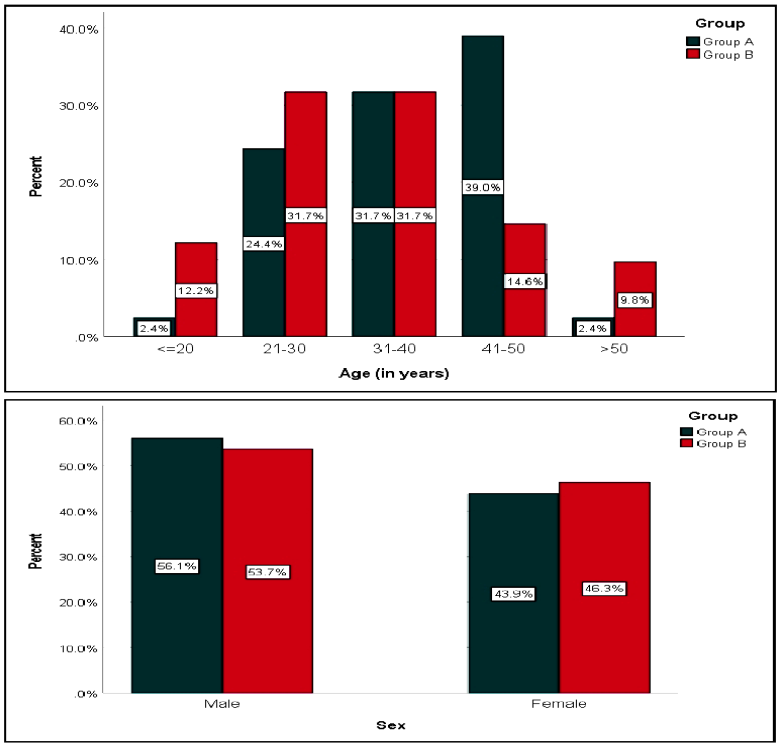

Fig. 1: Age and Sex Distribution of the patients in this study

Table 2 shows the comparative values for the two groups as the standard error of the mean and standard deviation of weight. The unit is in Kg. The data were parametric, and the comparison was made using an unpaired T-test (p<0.05), N= number of patients, SD= standard deviation, SE= standard error mean CI= confidence interval. Inference: Weight was comparable between the two groups. The mean weight for Group A was 67.1±13.43, and Group B was 67.13±11.17 (p=0.9912).

Table 2: The Comparison of Weight Distribution Between Two Groups

	N	**SD**	**SE Mean**	**Mean**	**95% CI of Mean**	**p-value**
Group A	30	13.43	2.452	67.1	62.08 to 72.12	0.9912
Group B	30	11.17	2.040	67.13	62.96 to 71.30	

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Fig. 2 shows that the mean weight in group A (Magnesium sulphate) was 65.37±8.837 Kg, which was similar to group B (fentanyl), which had a mean weight of 68.17±11.27 kg.

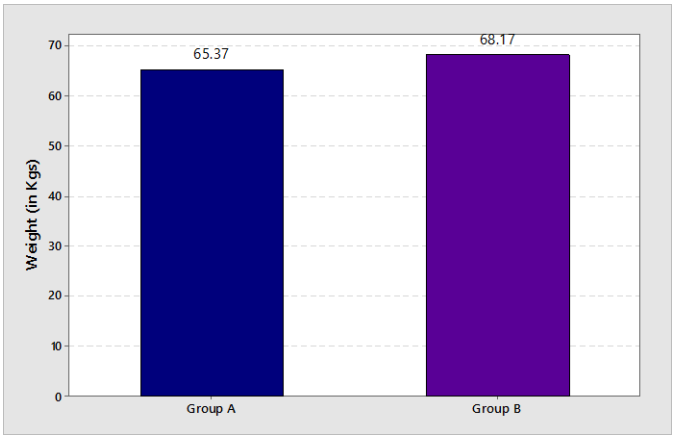


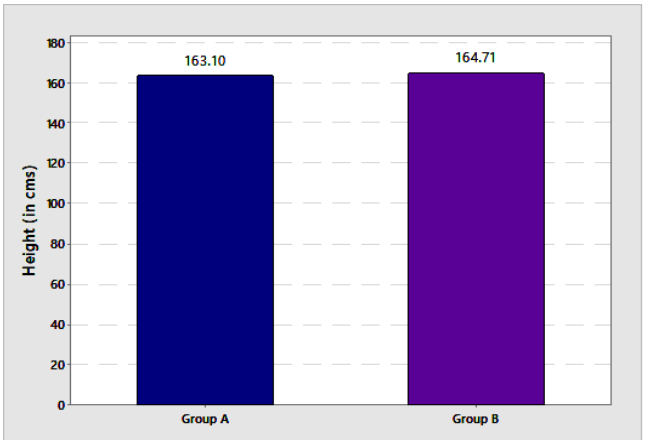
Fig. 2: Comparison of Mean Weight of Patients between Groups

The comparative values for the two groups are shown as percentages. The data was compared with Fischer's exact test (P=0.2949). Inference: The ASA-PS distribution was comparable between the two groups. In Group A there were 15 ASA 1(50%) and 15 ASA 2 (50%) patients. In Group B there were 10 ASA 1 (33.33%) and 20 ASA 2(66.67%) patients. The comparative values for two groups are shown as standard error of mean and, standard deviation, median of duration of surgery. The unit is in minute. The data were non- parametric and the comparison was done by Mann Whitney U (P<0.05), N= number of patients, SD= standard deviation, SE= standard error mean, CI= confidence interval. The duration of surgery was comparable between two groups. The Mean duration of surgery for Group A was 161±28.17 minutes. The mean duration of surgery for Group B was 152.7±29.24 minutes (Table 3).

Table 3: Comparison of ASA-PS Distribution and Duration of Surgery (Minutes) Between Two Groups

	ASA-PS 1	ASA-PS 2	N	p-value	
Group	15(50%)	15(50%)	30	0.2949	
Group	10(33.33%)	20(66.67%)	30		
Total	25	35	60		
	SD	SE Mean	Mean	95% CI of	p-value
Group	28.17	5.144	161.7	151.1 to 172.2	0.3006
Group	29.24	5.338	152.7	141.7 to 162.6	

Fig. 3 shows that the Mean height in group A (Magnesium sulphate) was 163.10±8.230 cm, which was similar to group B (fentanyl)'s mean height of 164.71±8.7 cm, respectively.



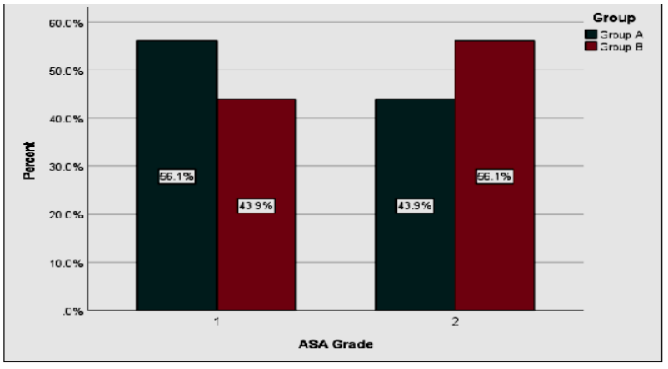


Fig. 3: Comparison of Mean Height of Patients Between Groups and ASA Status of both groups

DISCUSSION

We conducted a study to compare the efficacy of two different prophylactic doses of tranexamic acid in different orthopaedic surgeries [25]. We found that prophylactic tranexamic acid administration reduced the incidence of intraoperative blood loss and that higher doses of tranexamic acid were more effective than lower doses in lowering the risk of both intraoperative and postoperative blood loss. The group that got a greater dose of tranexamic acid saw a lower incidence of blood transfusion requirements and, consequently, a lower risk of complications related to blood transfusion. An artificial counterpart of lysine is tranexamic acid. This powerful antifibrinolytic drug inhibits plasminogen as well as plasmin.

It competes by inhibiting plasmin, tissue plasminogen activator, and plasmin with lysine, preventing fibrinolysis. It lessens tissue plasminogen activator's capacity to bind fibrin [19,20]. This prevents plasminogen from being activated into plasmin, aiding in reducing inflammation and platelet aggregation [20,21].

A previous study by Ramakrishnan A and colleagues found that group B, which received a bolus dose of 50 mg/kg of tranexamic acid followed by an infusion of the drug at a rate of 15 mg/kg/hr, experienced a significant reduction in blood loss and a decreased need for postoperative transfusion. Randomised controlled research by McCormack *et al.* [25] and colleagues revealed that the group receiving medication infusion after bolus dosage had considerably less intraoperative blood loss and less need for blood transfusion [21,26]. The study showed reduced blood loss in the second and third groups. Still, it was more pronounced in the group receiving continuous infusion, and there was also a statistically significant decrease in the difference between preoperative and postoperative haemoglobin levels [22,24]. On the other hand, a single dosage of 30 mg/kg of tranexamic acid given on the day of surgery was shown to be just as safe as a continuous infusion of 2 mg/kg/hr for a single day in research done by Ker *et al.* [27], Seo *et al.* [28] colleagues on 164 patients having unilateral THR. Our research supported the earlier results of a substantial reduction in intraoperative blood loss and a drop in blood transfusion in the group with a larger tranexamic acid dosage.

Our research supported the earlier results of a considerable reduction in intraoperative blood loss and a drop in blood transfusion in both groups receiving a larger tranexamic acid dosage. However, the differences between the groups were not statistically significant. While there is a difference in pre-op and post-op Hb readings, with group A showing a greater change, the difference in Hb is not statistically significant, according to our study, which also looked at blood loss differences. This might result from a lower tranexamic acid dose and a short sample size. Additionally, group B required less postoperative blood transfusions than group A.

CONCLUSIONS

In comparison to a lower dose of tranexamic acid, the prophylactic use of a higher dose (20 mg/kg bolus dose) is a safe, effective, and economical intervention to decrease intraoperative blood loss and, consequently, the requirement for postoperative blood transfusion in various orthopaedic surgeries. Thus, tranexamic acid somewhat reduces the risks associated with blood transfusions and the need for surgery in these individuals. Although we only followed up on the cases for the first 24 hours, no incidence of thromboembolic consequences was noted in our investigation. Additional research is necessary to determine the potential risks of the ideal tranexamic acid dosage.

CONTRIBUTION OF AUTHORS

Research concept- Ashith Acharya
Research design- Om Shiva ST, Ashith Acharya
Supervision- Om Shiva ST, Ashith Acharya
Materials- Nithin KM, Sunil Kumar Krishnappa
Data collection- Om Shiva ST
Data analysis and Interpretation- Om Shiva ST
Literature search- Ashith Acharya
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Article editing- Nithin KM
Final approval- Gururaj Tantry S, Nithin KM, Ashith Acharya

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