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Original Article

A randomized, non-crossover, parallel-group analysis of tranexamic acid in minimizing blood loss and transfusions in total knee arthroplasty

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ABSTRACT

Objectives: Total knee arthroplasty is associated with significant blood loss, necessitating blood transfusions. Due to the obvious risks and costs of allogeneic blood transfusions, techniques to minimize blood loss in surgery are needed. The objective of this study was to assess the efficacy of tranexamic acid treatment in reducing blood loss and blood transfusion requirements during total knee arthroplasty.

Materials and Methods: A prospective, randomized, double-blind, parallel-group, non-crossover trial was carried out in Prathima Hospital, Karimnagar. The trial involved 28 ASA I and II patients undergoing unilateral knee arthroplasty, 14 in each of the control and study groups. In the study group, a 10 mg/kg bolus of tranexamic acid was administered slowly IV 30 min before tourniquet deflation, followed by a 1 mg/kg/hr infusion for 12 h, compared to the standard medical treatment in the control group. Total blood loss during and after surgery was compared between the two classes. We also compared the hemoglobin drop after surgery, the number of people who needed blood transfusions, and the number of units needed between the two classes. Any complications were also reported.

Results: Total blood loss in the tranexamic acid group was 543.3 ± 184.85 versus 685.83 ± 176.74, a statistically significant difference ($P < 0.05$). Intraoperative blood loss was comparable, but post-operative blood loss was significantly lower in the tranexamic acid group (389.16 ± 174 ml vs. 514.36 ± 143.89 ml), indicating that it was statistically significant ($P < 0.05$). There were no complications reported from any of the groups.

Conclusion: Tranexamic acid is an effective strategy for minimizing overall blood loss and blood transfusions in patients undergoing total knee arthroplasty.

Keywords: Tranexamic acid, Total knee arthroplasty, Blood loss

INTRODUCTION

Total knee arthroplasty is associated with significant blood loss and, as a result, the need for blood transfusions.[1] The risks and costs of allogeneic blood transfusion necessitate blood loss reduction techniques in surgery.[2] Antifibrinolytics include tranexamic acid and E-aminocaproic acid (EACA) act by inhibition of plasminogen. Tranexamic acid is 6–10 times more potent *in vitro* than EACA. Management strategies include a wide variety of treatments such as improved surgical technique, topical hemostatic agents, improved anesthesia technique, conventional blood transfusion, and more modern techniques such as acute normovolemic hemodilution, cell salvage,

and antifibrinolytics agents.[3,4] Tranexamic acid has the ability to minimize blood loss during complete knee replacement. Tranexamic acid research is limited, especially in the Indian population. Furthermore, due to epidemiological factors, Western figures do not apply to the Indian population. As a result, it was proposed to conduct this study to evaluate the effectiveness of tranexamic acid treatment in reducing blood loss and blood transfusion requirements.

MATERIALS AND METHODS

This research was carried out at the Prathima Institute of Medical Science from May to October 2020. The approval of the Institutional Ethics Committee was obtained through infra IEC/PIMS/OCT/2020/august/21. This was a non-crossover, random, double-blind, parallel-group trial.

Estimates of sample size were made with alpha and beta set at 5% and 20%, respectively. A confidence interval of 95% and power of 80% were deemed adequate. From the previous studies, mean ± standard deviation in the tranexamic acid group is 440 ± 200 ml while in the control group, it is 660 ± 150. The sample size was estimated to be 22 total and 11 in each group.

The trial included 28 patients with ASA Grades 1 and 2. There were 14 in each of the control and research groups. Exclusion criteria included a history of tranexamic acid allergy, pre-operative hepatic or renal failure, serious cardiac or respiratory disorder, abnormally high prothrombin time or activated partial thromboplastin time, congenital or acquired coagulopathy, thromboembolic disease history, and any malignant disease.

The randomization was achieved with computer-generated random number table.

All patients received a subarachnoid block with 3 ml of 0.5% bupivacaine, as well as epidural anesthesia at the normal dose for T10 level. All participants were subjected to standard monitoring techniques.

A haemoglobin (Hb) level of less than 8 g/dl was considered a transfusion trigger in all patients except those with low tolerance to these levels due to related conditions such as myocardial ischemia, chronic obstructive pulmonary disease, cerebral arterial insufficiency, or patients with signs, symptoms, or both of hypoxia such as tachycardia, dyspnea, or syncope. For these patients, the transfusion trigger was set at <10 g/dl. During surgery and the post-operative period, measured blood losses were supplemented with a 3:1 ratio of ringer's lactate or a 1:1 ratio of tetra hydroxyl ethyl starch before Hb concentration drops below the transfusion trigger point. Patients were then given allogeneic packed red blood cells

Blood loss was measured during surgery by calculating the weight change of surgical swabs (through digital weighing scale) and the volume in the suction reservoir. The contents of the drain were measured and registered in the recovery room and post-operative ward. The number of units of blood transfused during the perioperative period and for the first 5 days after surgery was reported, and any complications were documented.

Patients were transferred to the post-anesthesia care unit following surgery. Post-operative pain was treated with 0.125% bupivacaine and a 4–6 ml/h fentanyl 2 g/ml epidural infusion.

Hb concentration and hematocrit were measured 24 h after surgery. After 24 h, the drains were removed. Pneumatic compression devices were used to prevent deep venous thrombosis (DVT) in all patients, and they were all clinically tested for DVT on a daily basis before discharge.

Statistical analysis

The open source calculator OpenEpi, Version 3, was used for statistical analysis. Two-sample independent *t*-test was used as the statistical test. The Shapiro–Wilk test was used to determine the normality of the study sample's distribution. $P < 0.05$ was deemed statistically significant.

RESULTS

As shown in [Table 1], demographic variables were comparable in both classes.

In total, 28 patients took part in the study, 14 in each group. [Table 1] shows that demographic variables such as age in years, male: female ratio, surgery time, tourniquet time, and prior surgical experience were identical in both classes, thus ruling out prejudice.

The amount of blood lost during surgery was comparable in both classes, with a non-significant *P* value. The impact would be secondary to that of the tourniquet. The post-operative blood loss was substantially different in both groups, with the tranexamic acid group having a mean blood loss of 389.16 ± 174 ml and the non-tranexamic acid group having a mean blood loss of 514.36 ± 143.89.

Because of all the substantial blood loss during the post-operative phase, the total blood loss (intraoperative + post-

Table 1: Demographic variables in both groups.

Demographic variables	Group A *n*=14	Group B *n*=14
Age in years	59.1±9.7	59.4±7.74
Male:female	8:22	7:23
Surgery time (minutes)	115.9±10.71	117.03±14.76
Tourniquet time (minutes)	119±12.29	118.36±15.37
Previous surgery	0	0

operative) was also significantly different. Although the drop in hematocrit was higher in the tranexamic acid group, it did not differ significantly, as shown in [Table 2].

As shown in [Table 3], the control group needed more blood transfusions. Even though the number of blood transfusions per patient was higher in the control group, the difference was statistically significant ($P < 0.05$).

DISCUSSION

Numerous studies have been conducted on hemorrhage, with many testing a wide range of therapeutic and pharmacologic maneuvers aimed at minimizing hemorrhage and the resulting complications when hemorrhage is not properly treated. We investigated a modern therapy aimed at reducing hemorrhage caused by surgical trauma in this report. We investigated the effect of a bolus dose of tranexamic acid just before tourniquet deflation followed by a 12 h infusion on blood loss and transfusion requirements in total knee arthroplasty.[5] The previous research has shown that variables such as cemented or uncemented arthroplasty, surgical technique, anesthesia type, and surgeon preferences can all affect blood loss.[6,7]

Table 2: Intraoperative blood loss in both groups.

Variable	Group A (tranexamic acid group)	Group B (control group)	*P* value
Intraoperative blood loss (in ml)	154.33±62.09	171.5±77.64	0.4311
Post-operative blood loss (in ml)	389.16±174	514.36±143.89	0.03467^
Total blood loss (in ml)	543.3±184.85	685.83±176.74	0.04701^
Pre-operative hemoglobin	12.20±1.79	12.22±1.33	0.2969
Post-operative hemoglobin	11.09±1.69	10.30±1.34	0.1822
Pre-operative hematocrit	35.80±5.51	35.50±5.91	0.8833
Post-operative hematocrit	32.30±4.20	30.31±3.87	0.1994

^Statistically significant, *two-sample independent *t*-test, results from OpenEpi, Version 3, and open-source calculator *t*-test mean

Table 3: Blood transfusion requirements in both groups.

Variable	Group A (tranexamic acid group)	Group B (control group)	*P* value
Number of patients requiring transfusion	3/14	5/14	0.0352
Total number of units transfused	6	15	0.053

We attempted to monitor these variables as much as possible when designing our research. We included only cemented arthroplasty procedures in our study. For post-operative analgesia, both patients were anesthetized with a sub-arachnoid block and an indwelling epidural catheter. All of the operations were carried out by a single surgical team.

The intraoperative blood loss in the tranexamic acid and control groups was comparable (154.3362.09 vs. 171.577.64), which was not statistically significant. This result was anticipated because antifibrinolytic agents have no direct effect on hemostasis and coagulation.

The post-operative blood loss in the tranexamic acid group was 389.16 ± 174 ml and 514.36 ± 143.89 ml in the control group, which was statistically significant ($P < 0.001$). And compared to the control group, the tranexamic acid group had a markedly decreased overall blood loss (543.3 ± 184.85 vs. 685.83 ± 176.74), which was statistically significant ($P < 0.05$).

According to the literature, blood transfusion is needed in approximately 39% of patients undergoing complete knee arthroplasty. As shown in [Table 3], 35% of patients in the control group required blood transfusions, while only 21% in the tranexamic acid group required blood transfusions.

In terms of dosage and duration of tranexamic acid treatment, researchers[8,9] discovered that 10 mg/kg/h followed by an infusion of 1 mg/kg/h was the bare minimum required to achieve the desired anti-hemorrhagic effect. Larger doses result in no potential blood loss savings, while smaller doses result in reduced hemostatic effectiveness.

Finally, tranexamic acid used in total knee arthroplasty was effective in decreasing blood loss and the need for transfusions. This treatment is risk free, with no thromboembolic complications, and it also allows for allogenic blood sparing.

CONCLUSION

We conclude that tranexamic acid, administered as an intravenous bolus dose of 10 mg/kg before tourniquet deflation, followed by 1 mg/kg/h for 12 h, can be safely advocated for use in total knee arthroplasty as an effective technique to minimize perioperative blood loss and hence the need for blood transfusions.

Limitations of the study

Since this is a single-center analysis, the findings may not be generalizable to a broader population with ethnic and racial diversity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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