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The Effect of Tranexamic Acid on Blood Loss and Hospital-Stay after Knee Replacement Surgery

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Abstract:

A widely used effective treatment for last stage osteoarthritis and other knee diseases to relieve pain and to have improved quality of life. While the benefit outweighs other methods there are also some risks involved including bloodloss thromboembolic events, infection and sometimes the need for additional surgical procedures. Tranexamic acid (TXA) is very effective in reducing hemorrhage after this major surgical operation.

Objectives: To analyze and determine the effect of Tranexamicd acid on blood loss and hospital stay after Knee replacement surgery

Methods & Materials: Total 104 TKA patients were enrolled in this study. The tranexamic acid group had of 52 patients who received an intravenous injection IVof tranexamic acid. The control group included 52 patients on those placebo injection was administered. The comparison factors were the amounts of drainage, postoperative hemoglobin, and transfusion between both groups.

Results: The results showed the lower mean amount of blood drainage in the teranexamic acid group than in the control group i.e(581.6±356mL) versus (887±376.5mL) and p value was found to be p=0.002There was observed to be reduced transfusion rate in the tranexamic acid group (42.3%) in comparison with the control group (63.5%). Postoperatively at 24 hours the levels of hemoglobin were observed to be higher in the tranexamic acid group than in the control group.

Conclusions: Decrease in the total blood loss and transfusion was found by the use of IV(intravenous) injection of tranexamic acid.

Key words:TKA, IV, Transexamic acid, Blood loss, Transfusion

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Introduction:

TKA (Total knee Arthroplasty) is known to be the one of the most widely used orthopedic surgeries opted for end stage osteoarthritis in relieving pain and restoring joint function, eitherdeteriorating or secondary to inflammatory arthritis, trauma, tumors, or infection around the knee joint[1-5]. There is also un avoidable risk of blood loss and requirement for blood transfusion involves in this surgery [6].With the transfusions there are also many risks involved in this such as infection, acute systemic reactions, and death[8]. It also lengthens rehabilitation time and hospital stay.[7] Therefore, blood loss control preoperative and postoperative are important considerable factor to achieve good results after TKA. Different methods including autologous blood transfusion, hypotensive anesthesia[9] use of fibrin tissue adhesive[10], drain clamping[11,12], and administration of tranexamic acid[13,14,15] are used to control blood loss. Tranexamic acid administration during TKA surgery is one of most studied method. Studies have reported tranexamic acid reduced blood loss and the amount of blood needed in transfusions[16,17]. The administration of tranexamic acid also reportedly reduces the decrease in hemoglobin levels postoperatively[18,19.] Previously in many studies the blood loss was measured as the loss during surgery plus the drainage volume. Since there may have been some hidden losses as a result of hemolysis and tissue extravasation, which was un able to be detected on drain output, the true effect of tranexamic acid on blood loss was not clear[20]. Total blood lossestimate can be more appropriately made by use of hemoglobin balance method[20,21]. The calculated blood loss based on hemoglobin drop and body volume takes into consideration both the hidden and evident blood losses. The objective of this study was to analyze the effect of tranexamic acid on total blood losses including hidden and evident losses via hemoglobin balance method[21].

Methods & Materials:

This study was condutced in Peoples University of medical health sciences Nawabshah Pakistan from January 2019 to January 2020

- **Inclusion and Exclusion Criteria**

  All patients with primary end-stage knee osteoarthritiswaiting for the surgery were eligible for the study. Patients with secondary osteoarthritis (e.g., rheumatoid arthritis, posttraumatic osteoarthritis, gouty arthritis), a cardiovascular problem (e.g., myocardial infarction, atrial fibrillation, angina, heart failure), simultaneous bilateral TKA, a history of thromboembolic disease, bleeding disorder, known allergy to tranexamic acid, and lifelong warfarin therapy for thromboembolism prophylaxis were excluded from this study. Total patient count was 104 enrolled in two different groups.

- **Methods of Tranexamic Acid and Outcome Assessment**

  In the first group that is tranexamic acid group Intra venus tranexamic acid (10 mg/kg) was administered 10 minutes prior tobandage deflation and again at 3 hours postoperatively[22,23]. Whereas in the second group i.e the control group placebo 5 mL 0.9% normal saline was administered at the similar timings of the tranexamic acid group. Preoperative data included factors like age at the time of the operation, gender, and preoperative hemoglobin level. There were no observed between groups regarding the preoperative data.Hemoglobin levels were measured two weeks preoperatively and six hours, 24 hours, 48 hours, and 5 days postoperatively. Total losses were calculated based on a hemoglobin balance method [24]. This method estimates the blood volume of a patient based on the postoperative hemoglobin drop. The lowest value of the postoperative hemoglobin level obtained until the 5th postoperative day was used to calculate the hemoglobin drop.

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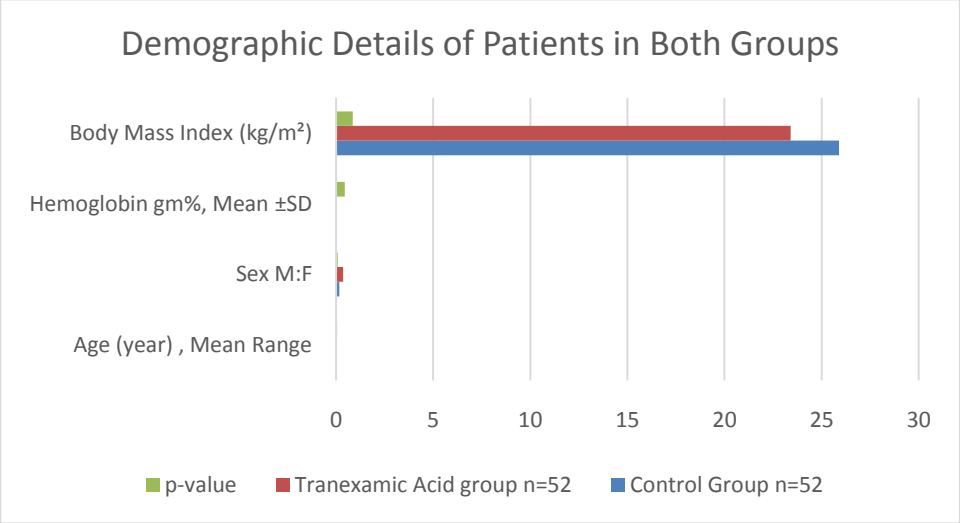

Table 1

Demographic Details of Patients in Both Groups

Variable	Control Group n=52	Tranexamic Acid group n=52	p-value
Age (year) , Mean Range	67 (51-82)	70(54-85)	0.053
Sex M:F	3:49	8:44	0.087
Hemoglobin gm%, Mean ±SD	12.4±1.3	12.2±1.5	0.442
Body Mass Index (kg/m²)	25.9	23.4	0.862

- **Surgical Technique**

All operations were performed or supervised by two surgeons using a midline skin incision and medial parapatellar arthrotomy. A posterior-stabilized type implant was used and the patella was not resurfaced in all cases. All patients received general or spinal anesthesia depending on the discretion of the anesthesiologist. A dose of 1 g cetrazole was given intravenously shortly before the operation. A tourniquet was applied around the upper thigh after elevation of the limb and exsanguination with an Esmarch bandage and inflated to a pressure of 280 mmHg before skin incision. An intramedullary alignment rod was used for femoral cutting and an extramedullary guide system was used for tibial cutting. Meticulous electric cauterization of the soft tissue bleeding points was performed throughout the surgery. The tourniquet was not released until skin closure and application of a compressive dressing. Intraoperative blood loss was negligible in all patients because the tourniquet was not deflated until wound closure. In each knee, one intra-articular drain was applied and connected to a high-vacuum drain bottle. The patients were asked to utilize an intermittent sequential pneumatic compression device for deep vein thrombosis (DVT) prophylaxis as soon as possible. The compressive dressing and Foley catheter were removed on the first day after surgery. The drains were emptied every day and the amount of drained blood was measured. The drains were removed only when this amount was less than 100 mL for 24 hours. On average, drains were kept for 3 days (range, 2 to 5 days). This has been our institution's policy, as we have observed that removal of drains at one preselected time may not work in all cases. Some cases have collection for longer periods and early removal in such cases may not only cause erroneous lower recordings of drained blood but also has a risk of hematoma formation. Both groups followed a standard postoperative

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rehabilitation protocol, including continuous passive motion of the knee and muscle strengthening exercises on the first day after surgery. All patients at discharge were given instructions regarding warning symptoms of infection and DVT and were asked to report immediately to the emergency department in case of development of such symptoms.

- **Data Evaluation**

The total volume of drained blood and the reduction in hemoglobin at 6 hours, 24 hours, 48 hours and 5 days after the surgical intervention were recorded. Blood transfusions were recorded as the number of units of packed erythrocytes. All patients were discharged from the hospital after two weeks of surgery. All quantitative data were expressed as mean±standard deviation. Statistical consequence of differences in the mean values of continuous variables such as age, preoperative hemoglobin, total volume of drained blood, and postoperative decrease in hemoglobin level were determined using Student t-test. Chi-square test was used for categorical data including the need for blood transfusion. A p-value less than 0.05 was considered as indication of statistical significance.

Results:

The mean level of postoperativehemoglobin was found to be lower in the tranexamic acid group (581.6±356mL) as compared to the in the control group (887±376.5mL) (p=0.002). the blood transfusion rate was also found to be reduced in Tranexamic group than the controlled (42.3% vs. 63.5%; p=0.017). same scenario was observed in the mean units of transfusion units having smaller p value equals to 0.008 and 0.77 units versus 1.27 units. After six hours of operation the hemoglobin level was found to be similar (p=0.801) in both groups, but after 24 hours, 48 hours and 5 days it was found to be greater in the tranexamic acid group than in the control group at statistically significant levels as shown in table 2

Table 2

Postoperative Hemoglobin, Total Drain Output, and Blood Transfusion

Variable	Control Group n=52	Tranexamic Acid group n=52	p-value
Total volume of drained blood mL	887±376.5	581.6±356	0.002
No. of patients receiving transfusion %	33(63.5)	22(42.3)	0.017
Mean units of transfusion unit	1.27	0.77	0.008
Hemoglobin g/dL postoperative			
6 hr	11±2.0	12.1±2.4	0.801
24 hr	10.3±1.8	10.8±1.4	0.042
28 hr	9.6±1.5	10.6±1.5	0.002
5 day	10.2±2.2	10.7±2.3	0.048
Hemoglobin drop	2.8±0.9	1.6±0.4	0
Total loss	1403	914	0.002

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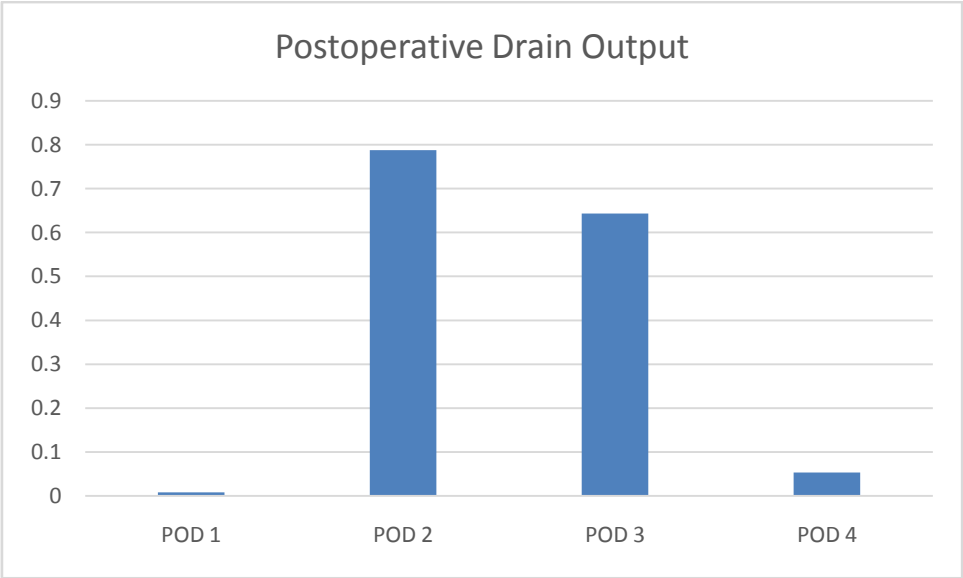
The drop in hemoglobin was calculated as the difference between the lowest postoperative hemoglobin level and the preoperative hemoglobin level. The control group was found to have the significant high drop level compared to the tranexamic acid group. The total amount of blood loss calculated using the hemoglobin balance method was significantly less in the tranexamic acid group than in the control group p value equaled .002.



The amount of evident blood loss on each postoperative day, as shown in table 3, measured based on the drain output and number of patients still using the drain. POD 1 (Postoperative day 1) losses were found to be significantly different in both groups, but on subsequent days there was not such significant difference found.

Table 3

Postoperative Drain Output

Variable	Control Group (n=52)	Tranexamic Acid Group (n=52)	p-value
POD 1	612.6±237.1(52)	368.1±248.0(52)	0.008
POD 2	1521.0±97.6(43)	147.6±69.3(45)	0.788
POD 3	134.0±59.0(29)	126.0±55.3(23)	0.643
POD 4	122.8±42.3(17)	97.0±27.6(9)	0.053
Values are presented as mean±standard deviation (number).			
POD: postoperative day.			
p-values are for unpaired two-tailed Student t-test.			

Discussion:

The very significant finding of the current study is that IV tranexamic acid reduces the perioperative blood loss, calculated total blood loss, hemoglobin drop, and need for transfusion. Moreover, this method did not cause an increase in the incidence of thromboembolic events.

On first day of postoperative day difference in drain output between two groups was found. This was mainly because of tranexamic acid has a half-life of 3 hours and it remains in the extravascular tissue up to 17 hours, after which it has no effect on postoperative bleeding. Therefore, postoperative bleeding after 1st postoperative day showed no significant difference between two groups. Despite this, the overall blood loss in the tranexamic acid group was less than that in the control group. This was because most bleeding after arthroplasty tends to occur during the first 24 hours.

We found that tranexamic acid was effective in decreasing not only the evident blood loss but also the total blood loss based on the calculation using the hemoglobin balance method. It is difficult to compare total losses in most studies, as there is no uniform criterion for measurement. Most studies have not calculated total losses. Few studies have used hematocrit drop while others have used hemoglobin drop. Some studies have taken 2nd postoperative day hemoglobin values31) while others have used 4th postoperative day values[21] for calculation. We believe that hemoglobin usually decreases for initial three to five days after surgery and then begins to rise. The lowest value measured during this period best shows the true loss. Therefore, instead of a fixed day value, we used the lowest hemoglobin value for our calculation. We saw a reduction in total blood loss in the tranexamic acid group compared to the control group. Despite the utilization of different methods for calculation, most authors have shown tranexamic acid decreases total blood loss [24,25].

Decrease in the in the need for transfusion in the tranexamic acid group was also observed , and this reduction was statistically significant in consensus with data in literature.. The rate of transfusions in our study was a little high in both groups probably because of the female predominance; females tend to have lower preoperative hemoglobin levels compared to those of males. Tranexamic acid creates a prothrombotic state by inhibiting fibrinolysis. However, it was observed that no adverse effects of tranexamic acid in terms of the development of symptomatic DVT and PE. The safety of tranexamic acid has been well established in literature. Recent reviews and meta-analyses have found no increased risk of thromboembolic events. They found that perioperative intravenous tranexamic acid administration was not associated with increased risk of complications.

Conclusion:

It can be concluded that a single injection of tranexamic could be effective (preoperative and postoperative) in total blood loss reduction and blood transfusion need for patients after total knee replacement surgery.

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