Original Article

Evaluation of the Efficacy of Tranexamic Acid in Control of Bleeding in Total Knee Replacement: An Interventional Comparative Study

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Abstract

Introduction: Among the various strategies for in routine total knee replacement (TKR), tranexamic acid (TA) has always been a safer and affordable method. Surgeons have used it in intravenous, intraarticular or in a combined manner to reduce blood loss because it is easily available and has an easy dosing regimen. We aim to find out its efficacy and associated complication when used intravenously. **Materials and Methods:** This study was done in our institute among 27 cases who was operated for primary TKR. They were distributed into two groups based on the use of TA. Hemodynamic parameters such as blood loss, reduction in hemoglobin (Hb), and blood transfusion were assessed. Student's *t*-test and ANOVA were utilized for tests of significance. **Results:** Out of 27 patients, 17 (62.9%) were female and in the age group of 51–60 years. Most 22 (81.5%) had osteoarthritis. The difference in blood loss across various pathologies and comorbidities was statistically insignificant. Average blood loss was 266.2 ml ± 64 ml (Range = 150–406 ml) per TKR in the 1st group. In 2nd, it was 667.5 ± 111.5 ml (Range = 414–860 ml) ($P < 0.001$). Mean Hb loss was 0.78 ± 0.275 g/dl (Range = 0.1–1.2 g/dl) in Group A. It was statistically significant comparing to Group B where it was 1.86 ± 0.55 g/dl (Range = 1.5–3.7 g/dl). Tourniquet used though decreased blood loss, it was not statistically significant. **Conclusion:** TA used in intravenously is very effective in decreasing the loss of blood and transfusion requirements in patients of primary TKR.

Keywords: Arthroplasty, blood transfusion, knee, replacement, tranexamic acid

Introduction

With the increasing average life span of the population, the diseases of the geriatric age group are also on the rise. One of the common diseases is degenerative osteoarthritis of the knee joint. In advanced cases of arthritis surgical replacement of the joint called as total knee replacement (TKR) stands out as the treatment of choice. Just like total hip replacement, TKR has become one of the most successful surgeries in the world with more than 25,000 surgeries done in 2019.[1]

No surgery has zero complications and TKR as a major surgery of the lower limb has its own share of anesthetic and surgical complications. Among all the complications, intra- and postoperative bleeding has a major detrimental effect on the recovery of the patient. In an average surgery, the blood loss amounts up to 1500 ml.[2] Various methods of reducing blood loss include the usage of intravenous tranexamic acid (TA), epinephrine, Floseal(r), and auto transfusion.[3]

TA is derived from lysine. It binds to 5 lysine binding sites on plasminogen. Hence that it prevents the creation of plasmin and also dislodges plasminogen from the surface of fibrin. At higher concentrations, it also inhibits fibrinogenolysis.[4] The recommended IV dosage of TA is 10–20 mg/kg. Most of the times, a standardized 1 g dose is used. Continuous IV infusions have also been used with dose ranging from 2 to 10 mg/kg/h depending on the duration.[5]

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We aimed at analyzing the efficacy and safety of utilizing systemic intravenous TA as an agent for reducing bleeding and other subsequent complications in TKR.

Materials and Methods

Study design

This is an interventional comparative study done between two groups of patients conducted in a tertiary care institute.

Study setting

The study was carried out on patients who underwent TKR in our institute who gave consent and had no contraindications for the use of TA. The study was conducted from September 15, 2017, to September 31, 2019.

Sample size

A sample size of 27 patients were studied. Simple random sampling was done to divide patients into individual groups. All the surgery was done by a senior orthopedic surgeon as the chief and assisted by two of his residents.

Ethical approval

Before the commencement of the study Ethical Clearance was obtained from the Institutional Ethics Committee (IEC no:-255/July 26, 2017).

Informed consent

A written informed consent in both English/Odia was obtained from each patient.

All the procedures followed were in accordance with the ethical standards of our institutional ethical committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

All but patients with allergy to TA, any hypercoagulable disease, abnormal coagulation profile (deranged blood transfusion [BT], CT, prothrombin time [PT], activated partial thromboplastin time [aPTT], international normalized ratio, etc.), taking aspirin, renal insufficiency, prior history of DVT who gave consent and were deemed fit for TKR was counted in this research. The total study sample was 27. They were divided into two groups. In Group A, TA was administered while it was not in the other group. Fourteen cases in Group A and 13 cases in Group B were allotted. Other than the usual tests, specific hematological tests (such as BT, CT, PT, and aPTT) were done. Combined epidural with spinal anesthesia was administered to all cases. In all cases, tourniquet was used. Its pressure was predetermined as per the systolic blood pressure. All operations were completed through the medial parapatellar approach.

In Group A, 10 mg/kg body weight of TA was injected by slow i.v. 10 min before tourniquet deflation. The compressive dressing was given after placement of suction drain and then, tourniquet was released. Four h after the initial dose, 2nd shot of TA was injected as before (10 mg/kg) via the intravenous route. In Group B, TA was not used.

On postoperative day 1, blood loss and vital parameters were checked. BT was given as and so when required. As per the need of the patient diclofenac injection and fentanyl patch was used for analgesia. A close eye was kept on the occurrence of deep-vein thrombosis (DVT) and pulmonary embolism. One day after the surgery, the drain was removed and net loss of blood was quantified with a beaker.

On day 2, hemoglobin (Hb) and hematocrit (HCT) were checked. D dimer was also measured for screening thromboembolic events. On day 5, Doppler sonography of both legs was done to definitively look for DVT. Net loss of blood, Hb, and HCT was noted in all cases and assessments were made among groups.

Student *t*-test and ANOVA test were utilized for the evaluation of differences among the groups. $P < 0.05$ was set for statistical significance.

Results

In both groups, five patients were male and 9 (Group A) and 8 (Group B) were female. Within the first group, the mean age was 60.5 ± 7.48 years (Range 48–80 years) and in the second group, it was 56.38 ± 6.06 years (Range 45–65 years). Most of the patients 14 (51.8%) were in the age group 51–60 years.

Out of 27 patients, 22 patients had osteoarthritis of the knee and they had an average blood loss of 459.91 ml. Four patients had rheumatoid arthritis (RA) with an average blood loss of 486 ml. Only 1 patient had tubercular arthritis and had a blood loss of 195 ml. On applying the ANOVA test the $P = 0.492$ which is insignificant.

In Group A, there were 7 patients with hypertension, 1 patient with diabetes mellitus, 2 patients with both diabetes and hypertension, and 4 patients without any comorbid illness. In Group B, there were 5 patients with hypertension, 1 patient with diabetes, 2 patients with both diabetes and hypertension, and 5 patients without any comorbid illness.

Diabetic patients had a mean blood loss of 470 ml, hypertensive had 455.98 ml, patients with both diseases had 447.5 ml and patients without comorbid illness had 460.5 ml of loss of blood. When analyzed using ANOVA test *P* value came to be 0.999 which was not statistically significant.

In the 1st group, mean Hb was 12.02 g/dl (Range = 10–13.7 g/dl). In the 2nd group, the mean Hb was 12.01 g/dl, (Range = 10.6–13.8 g/dl. Average HCT in Group A and B were 36.14% and 36.98%, respectively. In Group A, it ranged from 30% to 41% and in Group B, it ranged from 33% to 42%. All the patients had a platelet count within the normal limits. Hematological parameters, such as BT, CT, PT, and aPTT, were normal in all cases.

In Group A, average blood loss was 266.2 ml ± 64 ml (Range = 150–406 ml) per case. In the other, it was 667.5 ± 111.5 ml (Range = 414–860 ml) per TKR. After applying the unpaired *t*-test, *P* value came out to be <0.05. Hence, this was a significant correlation. In Group A average

Hb loss was 0.78 ± 0.275 g/dl (Range = 0.1–1.2 g/dl) per case. In Group B, average Hb loss was 1.86 ± 0.55 g/dl (Range = 1.5–3.7 g/dl) ($P < 0.001$). This is also a significant correlation. In Group A, a total of 12 BT was given with a mean of 0.54% (189 ml) per case. In the 2nd group, 32 patients required BT and it was 1.6% (560 ml) per TKR. This difference was statistically significant.

We also analyzed the relationship between tourniquet pressure and duration with blood loss. The tourniquet pressure was set as per the blood pressure of the patient. During data analysis, the entire study population was divided into four groups based on the tourniquet pressure applied during surgery into groups 1, 2, 3, and 4 each with tourniquet pressure of 240, 250, 260, and 270 mm hg, respectively. Average blood loss in each group was 605.30, 405.22, 684, and 352.43 ml, respectively. After applying ANOVA, *P* value came out to be 0.324 which was statistically insignificant. Hence, this variance in blood loss amid the groups was purely by chance and not statistically significant. As per the tourniquet duration all patients were separated into four groups. Group A includes limbs with tourniquet time of 60–70 min, Group B with tourniquet time of 71–80 min, Group C with tourniquet time of 81–90 min, and Group D with tourniquet time of more than 90 min. Average blood loss in each group was 373.8, 395.92, 499.14, and 667 ml, respectively. *P* value was 0.060 after the application of ANOVA which was insignificant.

Regular screening for DVT was carried out on the 5th postoperative day. None of the cases had DVT. Hence, the drug does not increase the incidence of DVT.

Discussion

We studied a total of 27 patients with a slightly more females 17 (62.9%) than the males 10 (37.03%). Females are more prone to osteoarthritis. It has been supported by the systematic review done by Tschon *et al*. On his global analysis, he found out of 268956 patients nearly 61% (165,256) were female while only 39% (103,700) were male.[6] Our study comprised majority of patients 14 (51.8%) in the age group of 51–60 years. Although TKR in extremes of age is on a rise, still the age group of 70 years was found to benefit mostly by this surgery. This was concluded by Lee *et al*. in their systematic review.[7]

Majority of our patients had OA knee and had an average blood loss of 459.91 ml. It was little high in patients with RA. Although it has been seen that increases blood loss in seen in rheumatoid pathologies, it was not found to be significant ($P = 0.492$). Prasad *et al*. have similar results, i.e., patients with RA had an increased blood loss (235 ± 126 ml) comparing to OA knee (216 ± 104 ml). This was not having any significance.[8]

We compared the medical comorbidities of our patients such as diabetes, hypertension with the amount of blood loss. To our knowledge, no such study is available which did a direct disease to disease comparison with the blood loss. Diabetic patients had the highest (470 ml) mean blood loss among all. However, this when compared in ANOVA did not yield any significance ($P = 0.99$). Liu *et al*. have advocated the use of comorbid specific individual blood management strategies for TKR, but we did not find any relevance may be attributed to our small sample size.[9]

When TA was used the mean blood loss was 266.2 ± 64 ml per TKR. In the other group where TA was not used the mean was much high, i. e., 667.5 ± 111.5 ml. This difference was found to have extreme statistical significance ($P < 0.001$). Kakar *et al*. in their randomized trial found in patients without the use of TA the blood loss was 270 ± 88 ml, while in the other group where TA was used it was only 160 ± 87 ml. This had statistical significance.[2]

The mean Hb loss in Group A was 0.78 ± 0.275 g/dl per case. In Group B, the mean Hb loss was 1.86 ± 0.55 g/dl. This proved to be significant. Subsequent to smaller loss of Hb there was an equally less requirement of transfusion in postoperative period in patients, in whom TA was used. Sadigursky *et al*. studied 59 patients for the effectiveness of TA and found that its use is associated with a small reduction of postoperative Hb level.[10]

We only compared the use of intravenous TA with patients without using TA. In Group B, there was a higher requirement for BT (560 ml per TKR) while in Group A where TA was used it was only 189 ml per TKR. This has statistical significance. Many authors have used combined intravenous and intraarticular TA for reducing blood loss.[11-13] In all these studies, TA used has been associated with reduced postoperative transfusions.

We also analyzed the duration of tourniquet application and tourniquet pressure with that of the blood loss. However, it was found to be a mere chance association and did not have any significance. Xu *et al*. studied on the data from 6325 patients and compared the need for BT after dividing them into two groups based on tourniquet use. He found that with the use of tourniquet there is an increased transfusion rate (risk ratio = 1.888, 95% confidence interval 1.449–2.461, $P < 0.001$).[14]

The threat of DVT always exists in lower limb arthroplasty. Owing to the brittle soft-tissue envelope knee is more vulnerable to anti-coagulation than the hip. Benjamin and Warwick studied 884 TKR patients and 21 of them has a DVT.[15] None of the cases in our study population had any DVT or vascular accidents.

Conclusion

TA when use in intravenous route has a major positive impact on postoperative blood loss and the need for further transfusions. It reduces the mean Hb loss, the HCT loss also. It does not rise the incidence of DVT. Hence, due to its relatively safe nature, easy availability and affordability, and ease of dosing, it should be advocated in all routine TKR when no contraindication to its use exists.

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Conflicts of interest
There are no conflicts of interest.

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