

## Original Research Article

# Intraarticular versus intravenous tranexemic acid in reducing blood loss after primary total knee arthroplasty

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## ABSTRACT

**Background:** One of the substantial complications of total knee arthroplasty is major blood loss. Postoperative blood loss can range up to 2000 ml and 10-38% of patients may require blood transfusion. Among the sundry methods of preventing this prob, tranexamic acid, an anti-fibrinolytic, is one of the most effective options. It can be administered directly into the blood or injected locally. The purpose of this study was to compare the hemostatic effects of intraarticular versus intravenous administration of tranexamic acid in primary total knee arthroplasty.

**Methods:** A prospective comparative observational study was done from done September 2020 to February 2022 at Civil Service Hospital, Kathmandu. 64 patients randomized into two groups: an intraarticular tranexamic acid group (31 patients who received 3.0 grams of intraarticular tranexamic acid) and intravenous tranexamic acid group (31 patients who received 15 mg/kg intravenous tranexamic acid in two instances). The primary measure was the amount of hemoglobin loss. Secondary outcomes included comparison of hemoglobin level pre- and post- operatively at first and fifth day, drain volume at 48 hours and amount of blood transfusion. There were no significant differences in demographics or preoperative laboratory values between the groups.

**Results:** The baseline data, preoperative hemoglobin, and tourniquet time were similar in both groups. Hemoglobin at first and fifth operative day and drain volume at 48 hours were measured in both categories. There was no significant difference in perioperative blood loss, drain volume, rates of allogeneic blood transfusion between the two groups. No any thromboembolic complications occurred.

**Conclusions:** Intra-articular administration of tranexamic acid was found to be as effective and safe as intra-venous administration in reducing blood loss in primary total knee arthroplasty.

**Keywords:** Blood loss, Intraarticular, Intravenous, Total knee arthroplasty, Tranexamic acid

## INTRODUCTION

Total knee arthroplasty (TKA) is a routinely performed elective orthopaedic surgery.<sup>1</sup> Despite, substantial advances in surgical and anesthetic techniques, it is still associated with a notable perioperative blood loss, due to surgical trauma and fibrinolysis, necessitating transfusion in 10 to 38% cases.<sup>2-4</sup> Allogenic blood transfusion in this scenario may precipitate allergic reactions, increased risk of infection of the surgical incision, prosthetic joint infection, transmission of infectious diseases, immune

modulation/suppression, and increased hospitalization time, morbidity, mortality and costs.<sup>5,6</sup> Among the myriad strategies focused on minimizing this problem, tranexamic acid (TXA), a competitive blocker of lysine binding sites in plasmin and plasminogen activator molecules, reduces hemorrhage by preventing the cleavage of fibrin.<sup>7</sup> TXA can be administered topically, intravenously (IV), and orally.<sup>8</sup> It is still not clear which route of TXA administration is most optimal in TKA because studies report either no difference or support one form over another.<sup>9</sup>

So, with increasing number of TKA cases, with increased burden of transfusion requirements and variable results of previous studies, this study will help to see the efficacy and safety of intraarticular (TXA-IA) versus intravenous administration of TXA (TXA-IV) in reducing perioperative blood loss and allogeneic blood transfusion.

The primary outcome of our study was the comparison of hemostatic effects of these two methods. Secondary outcomes are comparison of hemoglobin level pre- and post-operatively at first and fifth day, drain volume at 48 hours and amount of blood transfusion.

**METHODS**

A prospective comparative study was done September 2020 to February 2022 at Civil Service Hospital, after obtaining ethical clearance from National Academy of Medical Sciences (NAMS). All patients undergoing primary TKA were included in the study. Exclusion criteria were allergy to tranexamic acid, major comorbidities (severe ischemic cardiomyopathy, hepatic diseases, renal diseases), coagulopathy, and history of thromboembolic events. Patients who refused to enroll or administer blood products were also excluded from the study. Informed and written consent was taken from all the patients. 31 patients in two groups after randomization using computer-generated randomization viz. TXA-IA and TXA-IV were studied based on route of application of tranexamic acid after primary total knee arthroplasty.

All patients underwent primary TKA by the same team, using the same technique and protocols. All operations were performed under nerve block, using a high thigh pneumatic tourniquet and a hybrid posterior cruciate retaining prosthesis was implanted through a standard midline skin incision and a medial parapatellar approach in all patients. Antibiotic prophylaxis, anticoagulation regime and immediate post-operative care and rehabilitation were the same for all patients. Intravenous

group was given 2 doses of tranexamic acid 15 mg/kg before deflation of tourniquet and next dose 15 mg/kg three hours after tourniquet release and topical group was given intra-articular 3 gm of tranexamic acid in 100 ml saline after the closure of wound and drain was released 3 hours after the application. Blood loss was determined by measuring total drain volume after 48 hours by the nursing team. Hemoglobin level (Hb) was measured on the first and fifth post-operative day.

Assuming, blood volume (BV) on the fifth day after surgery was the same as that before surgery, we calculated the loss of Hb using the formula.

$$Hb \text{ loss} = BV \times (Hb_i - Hb_e) \times 0.001 + Hb_t$$

Where Hb<sub>i</sub>- Hb (gm/l) concentration before surgery. Hb<sub>e</sub>- Hb (gm/l) concentration on the fifth day after surgery. Hb<sub>t</sub>- total amount of allogenic Hb transfused. BV- blood volume taken as 7% of total body weight of the patient.

Blood was transfused 1 U at a time to maintain a hemoglobin concentration >7 gm/dl, or at a higher hemoglobin concentration if continuing blood loss occurred or signs or symptoms of anemia developed.

Statistical analysis was performed with SPSS version 26. The results were presented as mean±SD. Categorical variables were described as frequency and percentage. Significance was assumed for p<0.05. Independent t-test and Chi square test were used wherever applicable.

**RESULTS**

A total of 31 patients undergoing primary total knee arthroplasty were studied in each group, viz. TXA-IA and TXA-IV. We analyzed the baseline difference between two groups. There were no significant statistical differences between means of age (p=0.833), BMI (p=0.19) and pre-operative Hb (p=0.19).

**Table 1: Demographic characteristics and comparison between TXA-IA and TXA-IV groups.**

Patient characteristics	TXA-IA	TXA-IV	P value
Age (years) (mean±SD)	65.32±6.53	64.97±6.65	0.833
BMI (kg/m <sup>2</sup> ) (mean±SD)	26.02±1.76	26.77±1.77	0.1
Pre-operative Hb (gm/dl) (mean±SD)	13.11±1.13	12.58±0.93	0.19
Fall in Hb (gm/dl) on first POD (mean±SD)	3.67±0.91	3.46±0.78	0.13
Fall in Hb (gm/dl) on fifth POD (mean±SD)	3.46±0.88	3.26±0.78	0.16
Drain volume at 48 hours (ml) (mean±SD)	368.71±84.52	384.52±78.22	0.44
Estimated blood loss (ml) (mean±SD)	1054±244.89	1020±223.40	0.57
Rates of ABT (%)	25.8	22.6	0.767

Similarly, there was no significant statistical differences between fall in Hb in first (p=0.13) and fifth post-operative days (p=0.16), drain volume at 48 hours (p=0.44), estimated blood loss (p=0.57) and rates of allogeneic blood

transfusion (p=0.767) between intra-articular and intravenous groups. Only 8 patients in group TXA-IA and 7 patients TXA-IV group required blood transfusion.

There was no incidence of thromboembolic complications in any patients.

## DISCUSSION

There are several methods of reduction of blood loss following primary TKA. Blood loss may amount up to 2000 ml and to abate this problem, various antifibrinolytic agents amongst all other techniques are popular, namely, TXA, aprotinin, and epsilon-amino caproic acid (EACA). TXA has very good safety profile than aprotinin and is more potent than EACA and causes less blood loss and rates of transfusion as well.<sup>10,11</sup>

However, there is still no unanimity between the multiple routes of TXA administration.<sup>12</sup> In theory, topical TXA, avoids local activation of fibrinolysis and promotes thrombus formation as well as lessens systemic absorption.<sup>13</sup> Further, true volume of blood lost during TKA surgery, is masked by hidden blood loss (tissue extravasation, hemolysis, residual blood), amounting as high as 50%, which is not controlled by TXA as latter affects only drain volume.<sup>14</sup>

Age enrolled in our study is like that of study by Patel et al.<sup>15</sup> Pre-operative hemoglobin between two groups were similar to the study by Gomez et al.<sup>16</sup> Similarly, doses of intra-articular and intra-venous TXA was similar to studies by Soni et al and Öztaş et al respectively.<sup>17,18</sup>

The principal findings from this study were that fall in hemoglobin, drain volume, blood loss and rates of transfusion did not significantly differ between intra-articular and intravenous modes of administration of tranexamic acid, following primary TKA. This is alike the findings of multiple studies, RCTs and meta-analyses done prior.<sup>9,19-27</sup>

In our study, we did not encounter any thromboembolic complications in any group as found by multiple studies, regardless of personal history and routes of administration.<sup>28,29</sup>

This study is first of its kind done in Nepal. Only one case-control study describing the usefulness of TXA in primary TKA has been done prior.<sup>30</sup> Hence, we expect this study to be a milestone for upcoming studies regarding the use of TXA and its various forms in various knee and hip surgeries.

Our study was limited by the fact that the sample size was lesser in the designated study time. This is because Nepal is a small country and the cases that require TKA are also less. We did not monitor plasminogen levels, D-dimer, fibrin degradation products and thromboelastography. This would have given us objective direct evidence of fibrinolysis and antifibrinolytic activity. Another factor to consider is the heterogeneity of the population studied in terms of the type of surgery performed that entailed the statistical analysis under-powered. Subgroup analysis for

homogenous entities could not be carried out due to the small sample size. Further, our study design was nonblinded and nonrandomized and can be regarded only as a prospective comparative trial, however first kind of it in this country. Multicenter randomized prospective comparative trials and RCTs are needed to further assess the relative efficacy and safety of TXA and dose-response studies

## CONCLUSION

Intra-articular administration of tranexamic acid was found to be as effective and safe as intra-venous administration in reducing blood loss in primary total knee arthroplasty.

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