

EVALUATION OF MULTIPLE DOSES OF TRANEXAMIC ACID ON BLOOD LOSS IN TOTAL KNEE ARTHROPLASTY

Victor Elias Titonelli¹ , Douglas Mello Pavão¹ ,
Pedro Purita Paes Leme¹ , Renan Teixeira Lobo¹ ,
Rodrigo Sattamini Pires e Albuquerque^{1,2} , Eduardo Branco de Sousa¹ 

ABSTRACT

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1 Instituto Nacional de Traumatologia e Ortopedia. Rio de Janeiro, RJ, Brasil.

2 Universidade Federal Fluminense. Niterói, RJ, Brasil.

Corresponding author:

Eduardo Branco de Sousa
eduardobranco.joelho@gmail.com
Instituto Nacional de Traumatologia e Ortopedia
Avenida Brasil, 500
20940-070, Rio de Janeiro, RJ, Brasil.

The aim of this study was to evaluate the efficacy of multiple doses of tranexamic acid (TXA) in blood loss in patients undergoing total knee arthroplasty (TKA). Seven patients of both genders over 50 years old undergoing TKA, who received 15 mg/kg intravenous (IV) TXA 30 minutes before the surgical incision and another 3 doses thereafter were included in this report. Blood loss analysis included blood loss at the drain, hemoglobin loss, and estimated blood loss. Statistical analysis was performed. There was a significant hemoglobin drop after 48 hours, compared to preoperative. Mean blood loss assessed by drain was 20.0 ± 25.17 mL after 24 h. Estimated blood loss was higher after 48 hours compared to 24 hours. No complications were reported in this sample, and no patient received transfusions. The use of TXA in multiple doses did not prevent the drop in postoperative hemoglobin levels and did not correlate with increased complications.

Keywords: Blood loss; Surgical; Arthroplasty; Replacement; Knee; Osteoarthritis; Knee; Tranexamic acid

INTRODUCTION

Total knee arthroplasty (TKA) is one of the treatment options in advanced osteoarthritis, presenting around 85% of good results, and low failure rates over time. Despite being an effective form of treatment, it may be related to several complications, such as infection, thrombosis, and hemorrhage¹.

TKA blood loss is a major concern due to its potential clinical complications^{2,3} often reaching the range of 900-2000 mL^{4,5}. Among the options for reducing intraoperative bleeding in TKA, TXA is considered a low-cost alternative and has been shown to be effective and safe, reducing the number of blood transfusions, the length of hospital stay and, therefore, decreasing surgical expenses⁶, besides showing no relation to the increase in thromboembolic event rates⁷.

Some studies have suggested that multiple TXA doses could be more effective than a single dose, although the optimal dosage has not yet been determined⁸⁻¹⁰. The goal of this study was to evaluate the efficacy of multiple intravenous doses of TXA blood loss reduction in patients undergoing cemented primary TKA.

METHODS

Seven patients of both genders over 50 years old undergoing cemented TKA, who received 15 mg/kg intravenous (IV) TXA 30 minutes before the surgical incision and another 3 doses thereafter, every 8h (total of 4 doses in 24h), were included in this report. Patients with major deformities, coagulopathies and inflammatory osteoarthritis were excluded. The study was approved by the Institutional Ethics Board (CAAE 66169717.0.0000.5273).

All the selected patients underwent the same standard surgical technique (transquadriceps approach and cemented unilateral primary TKA with posterior stabilization) with the implant ACS Knee System (Implantcast®, Hamburg, Germany). Surgical procedure was performed using a pneumatic tourniquet inflated 125mmHg above the systolic pressure and deflated

shortly after cementation. Then hemostasis was reviewed. A single 4.8-mm intra-articular Hemovac (Zimmer Biomet, Warsaw, IN, USA) drain with negative suction was used in all the patients and was maintained for 24 hours. Thromboembolic events were prevented in all the patients through a single daily subcutaneous dose of 40 mg of low molecular weight heparin; this treatment was initiated 12 to 24 hours after the end of the procedure and was maintained for 15 days.

The following parameters were considered for blood loss analysis: blood volume, blood loss at the drain, hemoglobin loss, and estimated blood loss. The blood volume of each patient was determined according to the Nadler formula¹¹. The drained blood loss volume was determined by the blood volume (mL) collected by negative suction through the Hemovac drain within 24 hours after the procedure.

Hemoglobin (Hb) loss after 24 hours was calculated using the formula:

$$\text{Lost Hb} = [\text{Hb at admission} - \text{Hb at discharge (24h)}] + \text{transfused Hb}$$

Where:

Lost Hb = total hemoglobin (g/dL) loss after the procedure

Hb at admission = Hb (g/dL) × estimated blood volume/100

Hb at discharge = Hb (g/dL) × estimated blood volume/100

Transfused Hb = total hemoglobin (g/dL) amount transfused through packed red blood cell transfusion. Each blood bag from the institution and state blood bank contains a mean hemoglobin concentration of 60 g/bag (0.6 g/dL).

Hemoglobin loss after 48 hours was calculated with the following formula:

$$\text{Lost Hb} = [\text{Hb at admission} - \text{Hb at discharge (48h)}] + \text{transfused Hb}$$

Estimated blood loss (mL) after 24 hours was calculated by the following formula:

$$\text{Blood loss} = \text{estimated blood volume} \times \text{lost Hb (24h)} / \text{Hb at admission}$$

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$$\text{Blood Loss} = \text{estimated blood volume} \times \text{lost Hb (48h)} / \text{Hb at admission}$$

Data from all the patients who received blood transfusions and the number of blood components bags used in each one of them was recorded. Complications, such as wound healing problems, deep venous thrombosis, and superficial or deep infection, were recorded if identified.

The results were presented with the corresponding standard deviation (SD) of the mean. A one-way ANOVA with Bonferroni post-hoc analysis was used for analysis of hemoglobin loss after 24h and 48h. Mean blood loss after 24 and 48 hours was compared by Student's t-test. A value of $p < 0.05$ was considered statistically significant in all the analyses.

RESULTS

Demographic data of the patients included is described in Table 1.

Table 1: Demographic profile of the patients included in the study (n = 7).

Variables	Mean ± SD
Age (years)	67.43 ± 6.65
Weight (kg)	83.29 ± 22.84
Height (m)	1.6 ± 0.13
BMI (kg/m ²)	32.8 ± 9.16
Estimated Blood Volume (L)	4.41 ± 0.91
Hb Pre (g/dL)	13.77 ± 0.77
Visible blood loss (mL)	20.0 ± 25.17
Tourniquet time (min)	108.7 ± 21.29
Hospitalization (days)	3.42 ± 0.78

SD: Standard deviation; n: Number of patients included in the sample; kg: Kilograms; m: Meters; Hb: Hemoglobin; g/dL: Grams per deciliter; min: Minutes; L: Liter.

There was a significant hemoglobin drop after 48 hours (10.49 ± 0.75 g/dL), but not after 24 hours (11.98 ± 1.82 g/dL), compared to preoperative (13.37 ± 0.77 g/dL) levels ($p = 0.013$ (Figure 1). Mean blood loss assessed by drain after 24 hours was 20.0 ± 25.17 mL.

Estimated blood loss was significantly higher after 48 hours compared to 24 hours (48h: 127.5 ± 32.16 mL vs. 24h: 57.69 ± 66.74 mL; $p = 0.02$) (Figure 2).

There were no complications reported by patients in this sample, and none received blood transfusions.

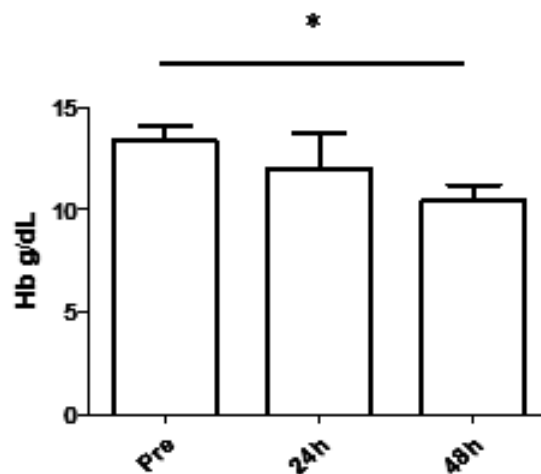


Figure 1: Hemoglobin loss at 24 and 48 hours. Hemoglobin loss was significant after 48 hours compared to preoperative levels ($p = 0.0013$).

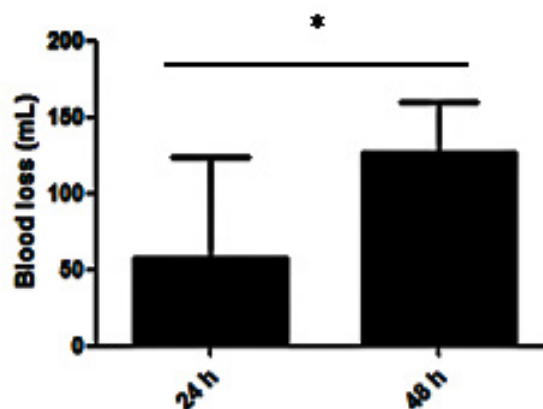


Figure 2: Estimated blood loss at 24 and 48 hours. Estimated blood loss was significant higher after 48 hours compared to 24 hours after surgery ($p = 0.02$).

DISCUSSION

Blood losses after TKA represent a major concern for the orthopedic surgeon, since it may lead to significant clinical complications as hemorrhage, infection, and thromboembolic events. Hence, TXA has emerged as a useful tool in the management of TKA bleeding. This study intended to evaluate the effect of multiple intravenous TXA doses in patients undergoing cemented primary TKA.

Regarding the postoperative hemoglobin drop at 24 and 48h, we observed that the use of tranexamic acid was not effective in preventing significant hemoglobin loss after 48 hours. Besides, estimated blood loss was also higher after 48 hours of surgery. On the other hand, there were no complications and none of the patients needed blood transfusion.

Zhang et al.¹⁰ observed an occult blood loss and mean hemoglobin drop in patients who received multiple dose group of TXA, totalizing 6g in 24h, which were significantly lower compared to the single and to the control group. Unlike our study, they did not use pneumatic tourniquet or joint aspiration drain.

Xie et al.⁸ found a significant reduction in blood loss measured by both occult loss and drop in hemoglobin levels receiving three doses of TXA compared to the group with two doses and even lower than the group receiving only one preoperative dose. Moreover, they also did not use an intraoperative pneumatic tourniquet, but all patients received 1 g topical TXA in the surgical site.

In a recent study, Lei et al.⁹ found a significant reduction in blood loss in 159 patients undergoing TKA receiving up to four doses of TXA, with a tendency

to decrease also with a fifth dose. The authors advocated the use of a five-dose TXA regimen with the possibility of a sixth dose if fibrinolysis continues. All surgeries were performed without tourniquet and without drain and all patients received 1 g topical TXA in the surgical site.

In the present study, all patients used tourniquet. We know that the use of the tourniquet may be correlated with greater postoperative bleeding compared to surgeries without its use, despite reducing intraoperative losses. This is due to the tissue aggression that causes locally and by the release of several inflammatory cytokines in ischemia-reperfusion syndrome^{12,13}.

We conclude that the use of TXA in multiple doses, used in TKA performed with pneumatic ischemia and revision of hemostasis before closure of the surgical wound, did not prevent the drop in postoperative hemoglobin levels. The use of multiple doses did not correlate with increased thromboembolic complications. Based on these findings we believe a prospective study comparing single and multiple TXA doses should be performed.

Conflicts of interest

The authors declare that they have no conflict of interest.

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