RESEARCH ARTICLE

Which Route of Tranexamic Acid Administration is More Effective to Reduce Blood Loss Following Total Knee Arthroplasty?

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Received: 3 May 2015 *Accepted: 27 September 2015*

Abstract

Background: The most appropriate route of tranexamic acid administration is controversial. In the current study, we compared the efficacy of intravenous (IV) and topical intra-articular tranexamic acid in reducing blood loss and transfusion rate in patients who underwent primary total knee arthroplasty.

Methods: One hundred twenty 120 patients were scheduled to undergo primary total knee arthroplasty. Patients were randomly allocated to three equal groups: IV tranexamic acid (500 mg), topical tranexamic acid (3 g in 100 mL normal saline) and the control. In the topical group, half of the volume was used to irrigate the joint and the other half was injected intra-articularly. The volume of blood loss, hemoglobin (Hb) level at 24 hours postoperative, and rate of transfusion was compared between groups.

Results: The blood loss and Hb level were significantly greater and lower in the control group, respectively (P=0.031). Also, the rate of transfusion was significantly greater in the control group (P=0.013). However, IV and topical groups did not differ significantly in terms of measured variables. No patient experienced a thromboembolic event in our study.

Conclusion: Tranexamic acid is a useful antifibrinolytic drug to reduce postoperative blood loss, Hb drop, and rate of blood transfusion in patients undergoing total knee arthroplasty. The route of tranexamic acid administration did not affect the efficacy and safety.

Keywords: Blood loss, Blood transfusion, Hemoglobin, Total knee arthroplasty, Tranexamic acid, Route of administration

Introduction

Total knee arthroplasty (TKA) is a major advanced orthopedic surgery with satisfactory outcomes that are frequently performed worldwide. However, perioperative significant blood loss can be associated with high morbidity and mortality necessitating a blood transfusion. In previous studies, it has been reported that the amount of bleeding can range from 600-1970 mL and blood transfusion is necessary in 10% to 38% of patients after TKA (1-7). Allogenic blood transfusion bears its own documented complications such as hematogenic infections (viral infections) and immunological reactions such as graft-versus-host-disease. Additionally, allogenic blood transfusion carries a financial burden on patients and the health care system (8, 9).

Considering the effects of stable postoperative hemodynamics on fast recovery after the surgery, decreased perioperative morbidity and mortality, and complications of allogenic blood transfusion, reducing blood loss in patients who underwent TKA represents a challenging problem for surgeons (10). Several methods have been introduced to reduce bleeding following TKA such as autologous transfusion, hypotensive anesthesia, application of fibrin tissue adhesive, compression bandaging, cryotherapy, drain clamping, and use of antifibrinolytic agents (11-16).

Tranexamic acid is an antifibrinolytic agent that reversibly binds to the lysine blocking sites on plasminogen as a synthetic derivative, which results in the prevention of clot degradation (17, 18). In previous studies, intravenous or intra-articular administration of TXA successfully reduced

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Table 1. Baseline patient characteristics

Group		IV group (n=40)	Topical group (n=40)	Control group (n=40)	*P* value
Age (year)		68.4±10.4	67±11.9	63.9±9	0.079
Gender	Male	26	23	19	0.491
	Female	14	17	21	
ASA class	I	29	25	27	0.34
	II	11	15	13	
Body mass index (kg/m^2)		32.7 ± 5.5	31.3 ± 5.4	30.6 ± 4.1	0.163
Preoperative Hb (mg/dL)		13.1 ± 1.3	13.7 ± 1.1	13.5 ± 0.9	0.482
Hc (%)		39.2 ± 2.7	41.9 ± 8.5	42.7±3.5	0.262
PTT (s)		32.6 ± 2.1	31.2 ± 9.5	30.5 ± 5.6	0.233
INR		1.17 ± 0.07	0.98 ± 0.1	1.09 ± 0.07	0.64

Hb: hemoglobin; Hc: hematocrit; PTT: partial prothrombin time

blood loss and required allogenic blood transfusion in gynecological, dental, spinal, urological, hip, knee, cardiac and thoracic surgical procedures (15, 19-21). While there have been several reports regarding the satisfactory outcomes of using TXA in total knee arthroplasty (TKA), the optimal route of administration remains controversial (3, 16, 22-25). In the current study, we aimed to compare the efficacy of intravenous TXA and local administration of TXA in reducing blood loss in patients who underwent TKA.

Materials and Methods

Between June 2012 and August 2014, all patients with knee OA scheduled to undergo unilateral TKA with cemented implants were eligible to participate in the study. Before the study, the institutional ethical committee approved the study and patients signed informed consent forms. Patients with coagulation disorders, history of cardiovascular diseases, history of cerebrovascular disorders, history of thromboembolic problems, renal and hepatic diseases, pregnant women, anemia, abnormal thrombin and prothrombin time, and abnormal platelet counts were excluded.

Recruited patients were randomly assigned to one of the 3 groups: intravenous TXA, topical intra-articular administration of TXA, and the control. Preoperatively, the hematological parameters hemoglobin (Hb) and hematocrit (Hc) levels, partial thromboplastun time (PTT), and international normalized ratio (INR) were measured. All of the surgeries were performed by a single surgeon under general anesthesia. The joint was exposed through a midline skin incision and the parapatellar medial approach. A pneumatic tourniquet was inflated for all of the patients and was not released before skin closure.

In the IV group, patients received 500 mg of TXA in 100 cc saline at the end of the surgery (26). In the topical group, patients received an intra-articular dose of 3 g of TXA in 100 mL normal saline. Half of the solution was used to irrigate the joint before joint closure. The remaining half of the volume was administered in the joint after wound closure by a portovac drain (26). The patients in the control group did not receive TXA. After the operation, a single intra-articular drainage tube was placed and clamped for 2 hours. Then, the drainage tube was opened, and was removed at the end of the second postoperative day. Thromboprophylaxis was performed using low molecular-weight heparin (40 mg daily) which was administered subcutaneously for 2 weeks. Also, all of the patients received prophylactic antibiotic therapy. Postoperative Hb was measured 6, 24 and 48-hours after the operation. Blood transfusion was performed if the Hb level was less than 8 mg/dL. However, we considered the Hb level at 24 hours as the postoperative Hb level. Patients were examined daily until discharge. If a thromboembolic event was suspected Doppler ultrasound was performed. Rehabilitation was started after drainage tube removal. Before discharge, the patients were instructed about the symptoms of deep venous thrombosis formation and asked to return immediately if calf swelling, leg pain, and so on occurred.

The main outcomes of the current study were the volume of bleeding based on the amount of drainage, the level of Hb at 24 postoperative hours, the frequency of transfusion, and the number of packed red blood cells transfused. Also, all complications were recorded.

Statistics

SPSS statistical software (SPSS verison 16) was used for statistical analysis. One way ANOVA was utilized to compare the quantitative data between three groups. The qualitative data was compared using the Chi square test. $P<0.05$ was considered significant.

Results

There were no statistically significant differences between the three groups [Table 1]. The operation time averaged 87±12 min, 86±17 min and 83±13 min in the IV group, topical group and control group, respectively ($P=0.65$).

We found that the mean of postoperative blood loss based on the volume of collected blood in drains was significantly greater in the control group compared to the TXA groups ($P<0.05$), however, there was no significant difference between the two TXA groups ($P=0.31$) [Table 2]. Also, similar results were found in terms of postoperative Hb level. The Hb level was significantly lower in the control group, while it was the same in the two TXA groups ($P<0.05$) [Table 2].

Table 2. Comparing the volume of blood loss, postoperative Hb level and frequency and amount of blood transfusion

Group	IV group (n=40)	Topical group (n=40)	Control group (n=40)	*P* value
Blood loss (mL)	406±36	422±51	494±73	<0.001
Hb level at 24 postop. hour	11.3 ± 0.8	11.8 ± 1.6	10.1 ± 1.5	0.031
No. patients required BT	2	3	10	0.013
Total No. of transfused packed cell units	3 (0.075)	3 (0.075)	14 (0.35)	0.002

Hb: hemoglobin; Hc: hematocrit; PTT: partial prothrombin time; postop: postoperative; BT: blood transfusion

Blood transfusion was required for 2, 3, and 10 patients in the IV group, topical group and control group, respectively (*P*=0.013) [Table 2]. The number of transfused packed red blood cells were significantly greater in the control group (*P*=0.01) [Table 2]. In our study, there was no patient with thromboembolic events.

Discussion

The most important finding of the current study was that TXA can significantly reduce postoperative blood loss, hemoglobin drop, and the need for blood transfusion in patients who underwent TKA. However, we did not find any significant difference between IV or topical administration of TXA.

Intraoperative and postoperative blood loss is one of the most important challenges encountered in major surgeries. If it remains unmanaged or mismanaged, perioperative blood loss can be associated with several serious complications and finally resulting in death. Among the several methods introduced to control perioperative blood loss, TXA administration has attracted much attention.

It has been sufficiently shown that TXA administration is a useful tool to decrease postoperative blood loss in major orthopedic surgeries (15, 27-32). However, in spite of several studies performed, the most appropriate route of TXA administration remains controversial. It seems that in topical administration, the drug is directly applied to the bleeding vessels (1, 33). Furthermore, topical administration of TXA induces microvascular hemostasis via preventing dissolving the fibrin clot (3).

Our study confirms the outcomes of recent studies comparing the efficacy and safety of IV and topical TXA. In the current study, TXA administration was useful and safe for reducing the volume of postoperative blood loss, Hb drop, and frequency of blood transfusion. Also, we found no significant difference between two administration routes: intravenous or topical application. Soni et al. showed that intra-articular administration of TXA can equally be efficient as a three-dose IV regimen in reducing intraoperative blood loss during TKA (22). Also, in another recent study by Patel et al., Hb level drop was 3.06 in the IV group and 3.42 mg/dL in the topical group. They showed that two groups were statistically the same with regard to Hb drop, drain output, and rate of transfusion (23). Also, Gomez-Barrena et al. found similar results (16). In a recent meta-analysis, Wang et al. showed that topical TXA is similar to IV TXA in reducing blood loss and rate of transfusion without compromising patient safety (24).

In contrary, some studies have found that intra-articular administration of TXA leads to better results. Recently, Hamlin et al. showed that topical TXA diminished the rate of transfusion compared to IV TXA in patients who underwent primary TKA (0% versus 2.4%) (25). Also, Seo et al. found that topical TXA was more effective in terms of reducing blood loss and the frequency of blood transfusion in patients with TKA (3). In a systematic review and meta-analysis, Alshryda et al. showed that the indirect comparison of topical and IV TXA indicated that topical administration is a more appropriate route (15). To our knowledge, there is no study showing the best outcomes of IV TXA.

Although the antifibrinolytic characteristic of TXA caused some concerns about the increased rate of thromboembolic events in patients undergoing TXA, especially when administered intravenously, several studies like the current study have confirmed the safety of using this drug (15, 18, 34).

Like other studies, there were some limitations in our study. The sample size was limited and we did not compare the different regimens of TXA administration such as different doses of the drug. Also, in our study the level of TXA in circulation was not measured. The postoperative Hb level was compared only at 24 hours and it seems that a more detailed investigation can be helpful.

TXA is a useful antifibrinolytic drug to reduce postoperative blood loss, Hb drop, and rate of blood transfusion in patients undergoing TKA. However, in our study, topical or IV administration were equally efficient and more studies are required. Also, two routes of TXA administration are safe and did not increase the risk of thromboembolic events.

The authors did not receive any funding or grants in support of their research or preparation for this work. No funding source played a role in the study.

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