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Does Topical Tranexamic Acid Make Bilaterally Total Knee Arthroplasty Safer and Effect Early Functional Outcomes?

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Abstract. The aim of this study was to show the effects of intra-articular topical tranexamic acid administration on the postoperative bleeding and early postoperative functional outcomes in the simultaneous bilateral total knee arthroplasty. To determine its effectiveness in reducing the need for blood transfusion, the number of the complications and morbidity rate. *Material and Method*. 40 patients who underwent simultaneous bilateral total knee arthroplasty between January 2015 and September 2018 were included in the study. The patients were divided into two groups: patients receiving tranexamic acid (group 1) or patients not receiving (group 2). Tranexamic acid was prepared as 1 g in 100cc sf and administered intra-articular through the hemovac drain following the closure of the surgical wound. Retrospectively, the amount of bleeding from the hemovac drain, blood transfusion needs, postoperative complication rates recorded. Early postoperative functional outcomes including range of motion (ROM) of the knee and the cadence were evaluated. *Results*. There was no statistical difference between the two groups in terms of demographics and preoperative hemoglobin, platelet counts. In Group 1, the mean amount of hematoma from the hemovac drain was 592.5 cc on the 1st day; 291.25 cc on 2nd day and total blood loss was 881.25 cc, whereas, in Group 2, it was 1360 on the 1st day, 412.50 on the 2nd day and 1770 cc in total, respectively. An average of 1.5 (0-4) units of blood transfusions was performed in Group 1 and 4 (2-5) units in Group 2. There were no differences between two groups in terms of ROM and cadence. Complications such as infection or pulmonary embolism were not defined in the two groups. *Discussion*. Intra-articular usage of tranexamic acid makes bilateral simultaneous knee arthroplasty safer reducing bleeding. But It has no impact on early postoperative functional outcomes. It does not increase the risk of complications as well.
Key words: *knee arthroplasty, tranexamic acid, blood loss, functional outcomes.*

Introduction

The reliability of simultaneous bilateral total knee arthroplasty (TKA) surgery has been still controversial in the literature. The advantages of simultaneous bilateral TKA include that patients experience anesthesia and surgical stress only once and duration of rehabilitation is reduced (1). Some studies suggest no difference in complication rates between unilateral and bilateral TKA in terms of morbidity and mortality (2-4) while some of the studies reported completely the opposite findings. The meta-analysis by Restrepo et al. reported that cardiac and pulmonary complications were higher in bilateral simultaneous TKA than unilateral TKA (5). Odum et al. reported that minor and major hospital complications and mortality rate were higher in bilateral simultaneous TKA (6). Fu et al. determined that the need for perioperative blood transfusion and the risk of embolism were more frequent in bilateral simultaneous TKA (7). As it can be seen, the discussions on bilateral simultaneous TKA and unilateral TKA are mostly focused on complication rates. It is well-known that bilateral TKA leads to more blood loss, and therefore the patient requires more blood transfusion compared to unilateral TKA (8-9). The excess amount of blood transfusion due to the amount of bleeding is a predisposing factor for possible complications. Reducing the amount of postoperative blood loss and therefore the need for blood transfusion may reduce the complication rates and improve the early functional outcomes. Accordingly, the aim of this study was to investigate whether intra-articular topical tranexamic acid administration at the end of the surgery can reduce the bleeding, need for blood transfusion, morbidity rate and improve functional outcomes by this way.

Material and method

Between January 2015 and September 2018, the medical history files of the patients who underwent simultaneous bilateral TKA by the same surgeon were reviewed retrospectively and 40 patients who

sequential bilateral TKA were included in the study. Patients who had bilateral primary knee osteoarthritis, patients who diagnosed with secondary osteoarthritis (Rheumatoid Arthritis, posttraumatic osteoarthritis) and patients with a history of deep vein thrombosis and pulmonary embolism were excluded from the study. The groups were created based on demographic data (age, gender). The patients were divided into two groups: treated with tranexamic acid (group 1) and untreated (group 2). 5 patients (3 in Group 1 and 2 in Group 2) who underwent TKA due to secondary osteoarthritis were excluded from the study. All patients underwent simultaneous sequential surgery. Patient who had high complaints firstly underwent the surgery. The tourniquet was inflated before the surgery and tranexamic acid was administered from the topical drain tip in Group 1 after the surgical wound was closed, the tourniquet was opened and the drain was held for 30 minutes before opening. In the meantime, the other knee joint surgery was started. The tourniquet was inflated on the other extremity. After the surgery, the medicine was administered from the drain following the closing of the surgical wound. The tourniquet and the drain were opened after 30 minutes. In the group treated with tranexamic acid, the solution was prepared to contain 4 ampules (1 g) tranexamic acid in 100cc saline. It was administered into the each joint from the hemovac drain after surgical wound closure for topical administration. In the group without tranexamic acid administration, the tourniquet and the hemovac drain were opened after the routine closure of the surgical wound. Both groups received 40 mg enoxaparin for 10 days for pulmonary embolism prophylaxis. In both groups, the daily amount of bleeding from the drains until postoperative 2nd day, the total amount of bleeding and the amount of blood transfusions on the 3rd day until being discharged from the hospital were measured. A blood transfusion administration criterion was considered as hemoglobin levels lower than 10g/dl. Postoperative complications were examined retrospectively from the file data and then from the data during follow-ups.

In order to evaluate the functional outcomes, amount of knee range of motions and walking cadence were measured. Amount of flexion range of motion was measured three times: post-operative second day, 15th, and 90th day for each group. The measurement of range of motion was done manually with the help of the goniometer. To evaluate the cadence for ambulation, , the number of steps taken in 1 minute was recorded for both groups on postoperative 2nd and 3rd day in a safe hospital corridor under supervision of a physical therapist.

The study was approved by the SANKO University Ethics Committee for Clinical Research Trials and was conducted in accordance with the principles in the Declaration of Helsinki. All participants gave their written informed consent before their participation in the study and were free to withdraw from the study at any time.

Statistical analysis. The statistical package SPSS 21.00 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All continuous variables were evaluated for normality using Kolmogorov–Smirnov test. Descriptive statistics for continuous data including mean and standard deviation (mean$\pm SD$) or median and minimum-maximum (min-max) values were calculated. Independent samples t-test was used to compare the two groups if the continuous data showed normal distribution, if not the Mann-Whitney U test was used. Fisher's exact chi-square test was used to compare the qualitative data. The level of significance was set at $p<0.05$.

Results

40 patients with bilateral sequential TKA were included in the study. Twenty patients were administered with topical tranexamic acid after the surgery while the other 20 patients were not. There was no statistically significant difference between the two groups in terms of age, sex,
hemoglobin ratio, and platelet count (Table I). In Group 1, the mean amount of hematoma from the hemovac drain was 592.5 (250-900) cc on the 1st day; 291.25 (250-900) cc on 2nd day and total blood loss was 881.25 (400-1350) cc; In Group 2, the mean amount of hematoma was 1360 (1200-1600) cc on the 1st day, 412.50 (300-650) cc on the 2nd day and 1770 (1450-2200) cc in total. An average of 1.5 (0-4) units of blood was transferred in Group 1 while Group 2 received 4 (2-5) units. There was a statistically significant difference between the two groups in terms of the mean amount of hematoma on the 1st day, the 2nd day and the total amount of bleeding (Table II). There was a significant difference between the two groups in terms of mean blood transfusion ($p<0.001$) (Table III). No infection or pulmonary embolism complication occurred in either group.

In the group I, the median walking cadence was 38 (36-41) on the 2nd day, was 57 (55-60) on the 3th day whereas it was 35 (33-39) on the 2nd day, 56 (53-60) on the 3th day in Group II. In the group I, the mean range of motion (ROM) of both knee flexion was 86 ± 22,7 on the 2nd day, was 115 ± 22,7 on the 15th day, was 130,25 ± 14,1 on 90th day.

Table I. Comparison of two groups according to age, gender and preoperative hemoglobin levels and platelet counts

Group	Age (yrs)	Gender (M/F)	Preop. Hb (g/dL)	Preop. Plt (x10^3/μL)
1	64,35±6,9	4/16	12,02±1,54	249,17±64,88
2	65,25±7,6	5/15	12,22±1,52	238,89±66,97

Preop.: Preoperative; Hb: Hemoglobin level; Plt: Platelet Count

For the patients in group II, the mean range of motion (ROM) of both knee flexion was 87 ± 23,4 on the 2nd day, was 114 ± 21,4 on the 15th day, and was 128,3 ± 10,4 on 90th day.
There were no significant differences in terms of walking cadence and ROM of knee flexion between the two groups (p>0.05) (Table IV). The total erythrocyte suspension requirement in group 2 was higher than that of Group I and this difference was statistically significant (p <0.001).

Table II. Comparison of two groups according to drainage volume

Group	DV(mm^3), Day 1	DV(mm^3), Day 2	Total
1	592,50±200,18	291,25±145,83	881,25±288,24
2	1360,00±124,18	412,50±97,16	1770,00±183,81
p value	<0,001	=0,004	<0,001

DV: Drainage Volume

Table III. Comparison of two groups according to erythrocyte suspension requirement

Group	median	minimum	maximum
1	1,5	0	4
2	4,0	2	5

Table IV. Comparison of two groups according to cadence and range of motion

Variables		Group 1 (n=20)		Group 2 (n=20)		p
		Mean ± SD		Mean ± SD		
		Right Knee	Left Knee	Right Knee	Left Knee	
Amount of flexion (degree)	Second day	86 ± 22,7	86 ± 22,7	87 ± 23,4	87 ± 23,4	0.05
	15th day	115 ± 22,7	115 ± 22,7	114 ± 21,4	114 ± 21,4	
	90th day	130,25 ± 14,1	130,25 ± 14,1	128,3 ± 10,4	128,3 ± 10,4	
Cadance (step/min)	Second day	38±2		35±1		
	Third day	57±2		56±2		

Discussion

Tranexamic acid is known to reduce postoperative bleeding with oral, intravenous or topical use (10-12). Several studies showed that tranexamic acid is effective to reduce bleeding after TKA, total hip replacement and fracture (10-14). The use of tranexamic acid in unilateral TKA was also reported (10-12). Some studies reported that the sequential bilateral TKA surgery is safe and its clinical outcomes are good. However, it is a well-known that single-session bilateral TKA surgery causes an increased bleeding and morbidity. In the literature, the mean bleeding rate after unilateral TKA has been reported in the range of 761-1784 cc (15-19). In the bilateral single-session TKA, theoretically, bleeding would be 2 times the average, meaning serious blood loss. The reported rate of blood loss for unilateral TKA is a tolerable bleeding for the patient, while bleeding in the bilateral TKA surgery is hard to tolerate. In this case, the need for blood transfusion increases with increasing other risks for patients. Reducing bleeding decreases the need for blood transfusion, thereby reducing also complication and morbidity rate. In our study, the mean blood loss was found to be significantly lower in the group treated with tranexamic acid group and therefore, the blood transfusion was limited in this group.

Hedge et al. used oral, intravenous, and intra-articular tranexamic acid in patients who underwent simultaneous bilateral TKA, and compared their effects on blood loss and need for blood transfusion. They found that intra-articular administration was more effective (20). In our study, the use of intra-articular tranexamic acid was also found to be an effective method for reducing bleeding.

In another study, Kim et al. investigated the effect of topical tranexamic acid on transfusion rate and reported that the use of topical tranexamic acid decreased the need for transfusion. In aforementioned study, they prepared a solution using 2 g of tranexamic acid in 30 cc saline. They stated that they made the final wash with this solution before the tourniquet was opened, sucked in the fluid with an aspirator, and they closed the surgical wound. The mean loss of hemoglobine was determined as 4.1 g/dl in the patients administered with tranexamic acid and the mean hemoglobine loss was found as 6.2 g/dl ($p<0.001$) in the patients not receiving it (21). In the study of Safeer Ahmad et al., they evaluated the rate of blood loss between the use of intravenous and intra-articular topical tranexamic acid in patients treated with unilateral TKA and concluded that topical use was more effective. In the study, 1.5 g of tranexamic acid was prepared in 100 cc saline (22). In their study, Yamaguchi et al. (23) studied the dose optimization of topical tranexamic acid use to reduce bleeding in total hip arthroplasty. They reported no difference between 1 and 2 g tranexamic acid in terms of effectiveness (23). In our study, the intra-articular solution was prepared through mixing 1 g of tranexamic acid with 100 cc saline and the surgical wound was closed without opening the tourniquet. The prepared solution was administered to the joint from the end of the drain and then the tourniquet was opened. However, the drain was not operated. After half an hour, the drain was taken to negative pressure and operated. Mean blood loss was found to be 881 in group 1 and 1770 in group 2. With such administration way, we achieved the same effect using 1 g tranexamic acid.

Tengborn et al. reported that the use of topical tranexamic acid was contraindicated in patients with a history of pulmonary embolism and deep vein thrombosis due to possible risk of embolism (24). However, there are also several studies suggesting that topical tranexamic acid administration does not increase the risk of complications of deep vein thrombus or pulmonary embolism (25,26). In our study, patients with a history of pulmonary embolism and deep vein thrombus were not included. No complications of pulmonary embolism or deep vein thrombus were therefore observed in either of the study groups.

Limited studies reporting on the effect of tranexamic acid on functional results have been available in the literature. Meteo et al and Wang's et al showed that functional scores improved in postoperative 1-2 months but there was no difference in ROM with tranexamic acid (27,28). In the study of Grosso et al, postoperative functional outcomes were improved with tranexamic acid but there was no difference on ROM and visual analogue scores (VAS) between the two groups (29). In our study, we did not find any difference on functional results and ROM on the bilateral TKA patients between the patients receiving tranexamic acid and patients not receiving.

Given the fact that one of the disadvantage of bilateral simultaneous TKA is the increased bleeding and need for blood transfusion, bilateral TKA surgery can be performed safer in a single session with reducing the number of the complications and morbidity rate through the use of topical tranexamic acid. Tranexamic acid doesn't improve functional outcomes on bilateral simultaneous TKA.

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