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Do We Concern Ourselves with Blood Loss and Blood Transfusions of the Peri-articular Injection of Tranexamic Acid after Unilateral Total Knee Arthroplasty?

Tek Taraflı Total Diz Artroplastisi Sonrası Traneksamik Asit Peri-artiküler Enjeksiyonunun Kan Kaybı ve Kan Transfüzyonları ile İlgili Endişemiz Var mı?

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(Bu makale bir önceki sayımızada hatalı olarak yayınlandığı için bu sayıda tekrar yayınlıyoruz.)

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Abstract

Objective: The means of peri-articular (PA) administration of tranexamic acid (TXA) is not examined sufficiently in unilateral total knee arthroplasty (TKA). The primary purpose of this study was to evaluate postoperative blood loss and transfusions rates after the administration of PA injection of TXA in TKA. In addition, PA TXA may decrease pain owing to reduced hemarthrosis after TKA.

Materials and Methods: In this retrospective study, 113 patients who underwent a primary unilateral TKA with or without a PA injection of TXA were included. A total of 1500 mg/50 ml TXA was injected into the extra-articular soft tissue around the medial, lateral capsules and muscular soft tissue around the quadriceps tendon immediately after cementation the prothesis, but before capsular closure and 15 minutes before the deflation of the tourniquet. A total of 56 patients in the control group did not receive TXA. The surgical procedure was standardized in all of the patients.

Results: There was a statistically significant reduction in hidden blood loss, estimated blood loss, and receiving a postoperative allogeneic blood transfusion in the TXA group compared with the control group (p=0.0001). We found a significant correlation between blood transfusion and the length of hospital stay (p=0.0001). No significant difference was found regarding pain VAS score after postoperative 1st day and postoperative 3rd day (p=0.597 and p=0.183, respectively). 1500 mg/50 ml (30 mg/ml) TXA was a relatively optimal dose to minimize the cytotoxic effects on the soft tissue around the knee compared with 50 mg/ml. No patients encountered any thromboembolic and wound complications.

Conclusion: The PA administration of TXA may offer a significant reduction in postoperative blood loss and transfusions rates as well as the length of hospital stay without increasing the risk of thromboembolic complications and cytotoxic effects on cartilage and peri-articular soft tissue. However, we did not observe a significant reduction in postoperative pain VAS score.

Keywords: Total Knee Arthroplasty, Tranexamic Acid, Peri-Articular Injection, Blood Loss

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Öz

Amaç: Tek taraflı total diz artroplastisinde (TDA) traneksamik asidin (TXA) peri-artiküler (PA) uygulama şekli yeterince incelenmemektedir. Bu çalışmanın birincil amacı, TDA'da TXA'nın PA enjeksiyonunun uygulanmasından sonra postoperatif kan kaybı ve transfüzyon oranlarını değerlendirmekti. Ek olarak, PA TXA, TDA sonrası hemartrozun azalması nedeniyle ağrıyı azaltabilir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya TXA PA enjeksiyonu olan veya olmayan primer tek taraflı TDA uygulanan 113 hasta dahil edildi. Protezin simante edilmesinden sonra, ancak kapsül kapanmadan ve turnike indirilmeden 15 dakika önce, medial, lateral kapsüller ve kuadriseps tendonu çevresindeki kas yumuşak doku çevresindeki eklem dışı yumuşak dokuya toplam 1500 mg/50 ml TXA enjekte edildi. Kontrol grubundaki toplam 56 hasta TXA almadı. Tüm hastalarda cerrahi prosedür standardize edildi.

Bulgular: Kontrol grubuna kıyasla TXA grubunda gizli kan kaybında, tahmini kan kaybında ve postoperatif allojenik kan transfüzyonu almada istatistiksel olarak anlamlı bir azalma vardı (p=0,0001). Kan transfüzyonu ile hastanede kalış süresi arasında anlamlı bir ilişki bulduk (p=0,0001). Postoperatif 1. gün ve postoperatif 3. günden sonra ağrı VAS skoru açısından anlamlı bir fark bulunmadı (p=0,597 ve p=0,183, sırasıyla). 1500 mg/50 ml (30 mg/ml) TXA, 50 mg/ml. ile karşılaştırıldığında diz çevresindeki yumuşak doku üzerindeki sitotoksik etkileri en aza indirmek için nispeten optimal bir dozdu. Hiçbir hastada herhangi bir tromboembolik ve yara komplikasyonu görülmedi.

Sonuç: TXA'nın PA uygulaması, tromboembolik komplikasyon ve kıkırdak ve periartiküler yumuşak doku üzerinde sitotoksik etki riskini artırmadan, postoperatif kan kaybı ve transfüzyon oranlarında ve hastanede kalış süresinde önemli bir azalma sağlayabilir. Ancak postoperatif ağrı VAS skorunda anlamlı bir azalma gözlemlemedik.

Anahtar Kelimeler: Total Diz Artroplastisi, Traneksamik Asit, Periartiküler Enjeksiyon, Kan Kaybı

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Introduction

One of the most common problems related to total knee arthroplasty (TKA) is intraoperative and postoperative blood loss leading to anemia-related complications, such as the increased risk of infection, cardiovascular complications, hemarthrosis and decreased patient's satisfaction (1,2). To avoid excessive blood loss and transfusion-related complications, various methods have been proposed, such as spinal anaesthesia, careful surgical electrocautery, drain clamping, intraoperative autologous blood transfusion, intraoperative blood saving, hypotensive anesthesia and antifibrinolytic therapy (3,4).

One of the pharmacological agents is tranexamic acid (TXA) which has been well established in a variety of surgical procedures, mostly in TKA (5). Trauma or surgery results in the release of tissue plasminogen activator, which triggers fibrinolysis (6). TXA is an antifibrinolytic agent that acts by competitively blocking a lysine-binding site of plasminogen and thereby inhibiting the formation of plasmin (7,8). The optimal administration means of TXA in TKA is still controversial (8,9). In the literature, most of the studies have suggested that the use of IV TXA is effective in reducing postoperative blood loss and the necessity of an allogenic blood transfusion (9). Many surgeons are, however, concerned that patients who have several comorbidities, such as a history of thrombosis, myocardial infarction, and severe renal dysfunction, may experience thromboembolic problems as the result of major surgery and the use of IV TXA (6,10). Moreover, only a small percentage of the IV TXA diffuses into the target location of soft tissue (8,11). Therefore, some studies focused on the topical application of TXA in the TKA (11,12). The administration of intra-articular (IA) TXA has been documented in many studies in which TXA was found effective and safe for diminishing blood loss after arthroplasty surgery (12,13,14). Nevertheless, Mao et al. thought that the volume of IA TXA solution might be insufficient to reach the anterior soft tissues of the knee joint while the patient is in a supine position until they walk (11). Moreover, IA TXA may have the potential to be cytotic to cartilage (15). Benoni et al. indicated that the positive effects of TXA on blood loss in knee arthroplasty were exerted mainly by inhibition of the fibrinolytic activity locally in the surgical field (16). Hence, some studies suggested the peri-articular (PA) application of TXA in TKA (17,18). However, the means of PA administration of TXA is not examined sufficiently.

We determined that the use of TXA in the way of peri-articular (PA) injection may promise some advantages, including lead to reach sites of soft tissue release and incisal edge, no systemic effects of TXA, reduced thromboembolic events, and decreased cytotoxic effects on cartilage and peri-articular tissue. The primary purpose of this study was to evaluate postoperative blood loss and transfusions rates due to the administration of PA injection of TXA in patients who encountered unilateral TKA. In addition, we hypothesize that PA TXA may decrease pain owing to reduced hemarthrosis after TKA.

Materials and Methods

After approval of the local ethics committee of Medipol University (no, E-10840098-772.02-2616; date, 27/01/2021), a cohort of 113 consecutive patients who performed between November 2017 and January 2021 with unilateral TKA was retrospectively assessed. We commenced applying for PA TXA in the middle of 2019. The patients who met the inclusion criteria in this study were divided into two groups. A total of 57 patients received 1500 mg/50 ml TXA in the TXA group, while 56 patients did not receive TXA in the control group. We excluded the patients who had rheumatoid arthritis, revision TKA, simultaneous bilateral TKA, American Society of Anaesthesiologists (ASA) Level 4, severe allergic history to local anesthetics or TXA, bleeding or clotting disorders, and desperate renal failure. All patients stopped the anticoagulant and non-steroidal anti-inflamatory agents (NSAID) 7 days before the surgery. Written informed constent was obtained from all patients.

All knees were performed according to comorbidity and prefence of the patient under general anesthesia or spinal anesthesia combined with epidural block. All patients were performed through a standard medial

prepatellar approach without patellar eversion to expose the surgical site of the knee joint under tourniquet control. The technique included cemented posterior stabilized NexGen (Zimmer, LPS-Flex Mobile, Warsaw, Indiana and USA) prosthesis without patellar replacement was utilized in all patients. TXA (Transamine, 250 mg/5 ml; Pharmacia, Teva, Turkey) with 50 ml saline solution was prepared in the TXA group. A total of 1500 mg/50 ml TXA was injected into the medial, lateral capsules and muscular soft tissue around the quadriceps tendon immediately after performing knee prosthesis, before capsular closure and 15 minutes before the deflation of the tourniquet (Figure 1). The tourniquet was inflated before the skin incision at 300 mmHg during the procedure. After 15 minutes of injection of the TXA and the cement was completely polymerized, the tourniquet was deflated immediately. When the touniquet was deflated we asked the anesthesiologist to reduce the blood pressure in safe zone. We aimed hypotension during the last period of the surgery until closed the wound. We calculated peroperative blood loss. No patients received any local injection into the knee joint, such as ropivacaine with epinephrine during the procedure. In both groups, the sole drain was placed and clamped for two hours in both groups. We monitored suction drainage blood volume and removed it when the drain 24-h volume of drainage was less than 50 ml after the surgery. All of the patients received the same physical rehabilitation program in which continuous passive machine motion was initiated within 12 h after the surgery and continued on postoperative day 1. After removing the drain, all of the patients began full weight bearing walking with the use of a walker postoperative day 1.

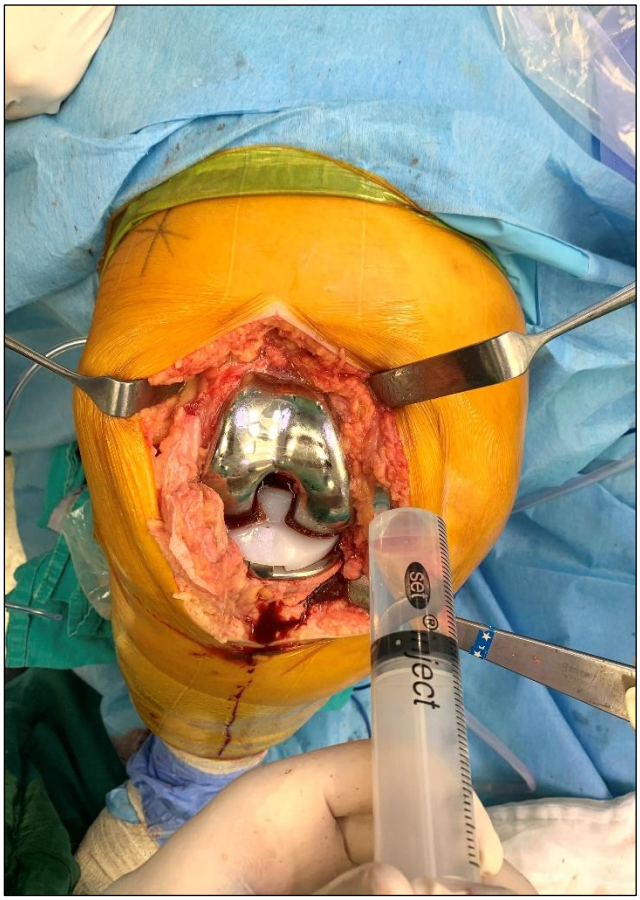

Figure 1. The way of applying PA-TXA

All of the patients were administered a standard course of an antithrombotic agent, which was low molecular-weight heparin (enoxaparin sodium, 40 mg) at eight hours postoperatively and continued three weeks after the surgery. Prophylactic antibiotic (cefazolin sodium, 1000 mg) was administered to all patients 30 minutes before the tourniquet inflated and continued postoperatively over the 24 h.

We recorded the levels of preoperative and postoperative hemoglobin, hematocrit and its drop during the procedure. Laboratory measures were determined from venous blood samples postoperative day 1, 2, and 3. Criteria of allogenic blood transfusion were a postoperative hemoglobin level of ≤ 8 g/dL or a postoperative hemoglobin level between 8 and 10 g/dL with the clinical signs of hemodynamic instability, including light-headedness, presyncope, palpitation or shortness of breath not owing to other causes. Pre-donation of autologous blood was not administered for any patients.

We calculated total blood volume (TBV) using the Nadler method (19). Estimated blood loss (EBL) was monitored using Gross's formula (20), which considers the initial hematocrit before surgery, the minimum postoperative hematocrit level, and the average of the initial and minimum hematocrit levels. Measured blood loss (MBL) was calculated as the sum of the intraoperative blood loss plus the total drain output. Hidden blood loss (HBL) was calculated using Sehat's formula (21), which subtracts the total MBL from the EBL and adds the volume of blood transfused (each packed red blood cell unit contains 200 ml).

We evaluated the two groups regarding blood loss in the volume of intraoperative blood, the volume of drain output, the volume of HBL, the volume of EBL, hemoglobin and hematocrit concentrations, the necessity of allogeneic transfusion, total operation time, pain visual analog score (VAS), the risk of the thromboembolic complications, length of hospital stay, age, sex, body mass index (BMI) and ASA. The surgical procedures and data collection processes were performed by the two authors who participated in this study.

All of the statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA). Data description was based on the mean ± standard deviation (SD). The Shapiro-Wilk test was used to test for normality. The one–way analysis of variance (ANOVA) test was used to detect differences between patients from each group for normal distributions. Groups were compared using the Student t-test for normally distributed continuous variables. Subgroups were compared with the Newman-Keuls test. The Chi-square test was used to analyse qualitative comparative parameters. A value of $p < 0.05$ was considered to be statistically significant.

Results

In this study, 117 patients were assessed retrospectively from medical records in our institution. No statistically significant differences were found in the demographic variables except for body mass index between the two groups (Table 1).

We found a statistically significant reduction in section drainage blood loss in the TXA group compared with the control group (320.09 ± 89.74 ml and 413.39 ± 118.34 ml, respectively). The hidden blood loss was significantly lower in the TXA group than in the control group (386.78 ± 108.05 ml and 581.87 ± 198.29 ml, respectively). Estimated blood loss was less in the TXA group than in the control group (812.58 ± 134.66 ml and 1025.64 ± 247.08 ml, respectively). Furthermore, hemoglobin reduction was significantly lower in the TXA group compared with the control group at three days postoperatively ($p = 0.0001$). However, there was no significant difference between the TXA and the control group concerning intraoperative blood loss ($p = 0.343$) (Table 2).

In terms of receiving a postoperative allogeneic blood transfusion, there was a highly significant difference between the TXA and the control group ($p = 0.009$) (Table 3). Whereas the TXA group received 6 units, the control group received 20 units. In addition, no patients in the TXA group received more than one unit erythrocyte suspension.

A significant reduction in length of hospital stays was found in the TXA group compared with the control group ($p = 0.01$) (Table 4). No significant difference was observed between the two groups regarding pain VAS score after postoperative 1st day and postoperative 3rd day ($p = 0.597$ and $p = 0.183$, respectively)

(Table 5). However, postoperative pain declined daily in both groups. No patients encountered any thromboembolic and wound complications.

Table 1

Demographic Characteristics Of The Patients.

Variable	TXA group (n = 57)	Control group (n= 56)	P value
Age (years)	67.19 ± 6.86	67.98 ± 7.16	0.551*
Sex (female/male)	47/10	48/8	0.636+
BMI (kg/cm³)	30.11 ± 3.66	32.45 ± 3.38	0.001*
Side (left/right)	30/27	33/23	0.500+
ASA class (I/II/III)	11/36/10	14/30/12	0.583+
Type of anesthesia			
Spinal + epidural	43 (75.44%)	45 (80.36%)	
General + epidural	14 (24.56%)	11 (19.64%)	0.529+
Operation time (min)	73.54 ± 6.33	72.20 ± 6.26	0.258*
Tourniquet time (min)	58.19 ± 5.99	57.86 ± 5.91	0.765*
Hospital stay (day)	3.09 ± 0.29	3.27 ± 0.45	0.01*
Total blood volume (ml)	4405.57 ± 507.89	4411.71 ± 518.53	0.949*

Values presented as mean (standard deviation) and p calculated by using the Student t test (*) and the chi-square test (+).

Table 2

Blood Loss Calculation (ml)

Variable	TXA group (n = 57)	Control group (n= 56)	P value*
Intraoperative blood loss (ml)	103.41 ± 20.69	106.98 ± 19.15	0.343
Drainage blood loss (ml)	320.09 ± 89.74	413.39 ± 118.34	0.0001
Hidden blood loss (ml)	386.78 ± 108.05	581.87 ± 198.29	0.0001
Estimated blood loss (ml)	812.58 ± 134.66	1025.64 ± 247.08	0.0001
Hemoglobin (g/dl)			
Preoperative	12.96 ± 0.97	12.91 ± 0.95	0.794
Postoperative 1st day	11.71 ± 0.86	11.28 ± 0.97	0.014
Postoperative 2nd day	11.03 ± 0.77	10.60 ± 0.95	0.01
Postoperative 3rd day	10.49 ± 0.77	10.14 ± 0.85	0.027
p†	0.0001	0.0001	
Hemoglobin reduction (g/dl)	2.49 ± 0.49	2.85 ± 0.56	0.0001
Hematocrit (%)			
Preoperative	38.92 ± 2.63	38.63 ± 3.05	0.590
Postoperative 1st day	35.69 ± 2.39	34.21 ± 3.01	0.004
Postoperative 2nd day	33.80 ± 2.25	32.10 ± 2.85	0.001
Postoperative 3rd day	32.36 ± 2.19	30.77 ± 2.59	0.001
p†	0.0001	0.0001	
Hematocrit reduction (%)	6.62 ± 1.10	8.02 ± 1.62	0.001

Values presented as mean (standard deviation, range) and p calculated by using the Student t test (*) and the one–way analysis of varience (ANOVA) test (†).

Table 3

The Number of Blood Transfusions

Variable	TXA group (n = 57)	Control group (n= 56)	P value*
Number of patients (%)	6 (10.53%)	17 (30.36%)	0.009
Transfusion (in unit)	6	20	-

Values presented as n (%); *p calculated by using the chi-square test

Table 4

The Correlation Of Blood Transfusion and The Length of Hospital Stay

Variable	TXA group (n = 57)	Control group (n= 56)
Hospital stay in BT (-)	3.08 ± 0.27	3.11 ± 0.31
Hospital stay in BT (+)	3.17 ± 0.41	3.65 ± 0.49
p*	0.0001	0.479

Values presented as mean (standard deviation, range) and p* calculated by using the Student t test. BT= Blood transfusion.

Table 5

Visual Analogue Score (VAS) for pain

Variable	TXA group (n = 57)	Control group (n= 56)	P value*
Preoperative	6.96 ± 0.79	7.09±0.74	0.391
Postoperative 1st day	5.09 ± 0.72	5.02 ± 0.72	0.597
Postoperative 3rd day	3.96 ± 0.71	3.79 ± 0.67	0.183
p†	0.0001	0.0001	

Values presented as mean (standard deviation, range) and p calculated by using the Student t test (*) and the one–way analysis of varience (ANOVA) test (†).

Discussion

The current study suggested that patients who underwent TKA could obtain some advantages, such as smaller reduction of hemoglobin and hematocrit level, less drainage volume, less hidden blood loss, and less transfusion rate without an increase in the risk of thromboembolic disease and cytotoxic effects on cartilage and peri-articular tissue through PA administration of TXA.

Some studies focused on the use of IA TXA (11,12,13). In a recent randomized controlled trial performed by Meshram et al. demonstrated that there was no difference between IA alone and combined IA plus IV regimen of TXA administration (13). In addition, to avoid potential complications associated with systemic administration, they recommended that IA alone is sufficient to reduce blood loss and blood transfusion rates for routine TKA. In contrast, IA TXA may have some disadvantages, such as TXA leakage owing to soft tissue release and cytotoxic impact on chondrocytes (11,22). Therefore, some studies suggested the peri-articular (PA) application of TXA owing to the need to administer a sole dose, its easy employment, and maximum concentration of TXA at the surgical site in TKA (17,18,23).

Few studies have analyzed the effects of PA TXA administration on blood loss in TKA. In the literature, the means of PA administration of TXA is not examined sufficiently. Mao et al. performed a study that provided a significant reduction in the EBL (11). However, they did not calculate intraoperative blood loss and HBL. Pinsornsak et al. compared IV TXA and PA TXA without a control group and calculated only blood loss in the hemovac drain, which is insufficient to evaluate total blood loss (17). Yozawa et al. and Hirose et al. assessed the efficacy of PA TXA after TKA, in which EBL in the PA group was significantly lower than in the control group (18,23). Nevertheless, they did not search for intraoperative blood loss and HBL. Furthermore, there is a lack of consensus on the optimal dose of PA TXA. Mao et al. utilized 2000 mg PA TXA; Pinsornsak et al. used 750 mg; Yozawa et al. and Hirose et al. utilized 1000 mg after TKA (11,17,18,23). We injected 1500 mg PA TXA into the knee after TKA. At the end of the current study, the outcomes revealed that PA injection of 1500 mg TXA obtained a significant reduction in not only the EBL but also the HBL in the TXA group compared with the control group.

According to some reports, intramuscular administration of a single 1 g dose of TXA reaches its maximum plasma concentrations in 30 minutes and then rapidly diffuses into the joint fluid and synovial membranes (24,25). We employed TXA in the way of PA injection technique before 15 minutes tourniquet deflation to gain more soft tissue concentrations of the edge of the bleeding sites before closing the capsule. We found that although the mean calculated postoperative blood loss significantly diminished in the TXA group compared with the control group, intraoperative blood loss was similar in all patients. We concluded that we could employ TXA 30 minutes before tourniquet release.

When we analyzed the data, the PA administration of TXA effectively diminished the need for blood transfusion in the patients who underwent TKA (11,17,18). Yozawa et al. found that only two of 44 (4.5%) cases in the control group received postoperative an allogeneic blood transfusion, whereas no case in the TXA group received a transfusion (18). However, they used an autologous blood transfusion that is not utilized widely in the orthopaedic field and in our institution and did not consider this. In our present study, allogeneic blood transfusions administered to patients in the TXA group were less than those in the control group. This outcome is crucial concerning allogeneic blood transfusion.

We found similar outcomes concerning the length of hospital stay compared with other studies in which the length of hospital stay was higher in patients who did not receive TXA (1,14). The possible reason for this phenomenon is that the patients who administrated blood transfusion owing to intra- and postoperative blood loss needed to stay more days at the hospital. We found a significant correlation between blood transfusion and the length of hospital stay. The control group received more blood transfusion and stayed longer at the hospital compared with the TXA group in the present study.

Huang et al. indicated that the most important findings of their study were significant reduced postoperative knee pain and severity of knee swelling by combing a total dose of 3000 mg IV and topical application of TXA (1). The same conclusion was drawn by Ishida et al., who revealed that 2000 mg IA TXA decreased knee swelling and pain VAS score after TKA (8). Therefore, we hypothesized that PA TXA might decrease pain owing to reduced hemarthrosis after TKA. We found no significant difference with respect to pain between the two groups using a total of 1500 mg TXA, which was low-dose in our study compared with the two previous studies. Likewise, Hirose et al. demonstrated that although a PA injection of 1000 mg TXA was effective for promoting early recovery of knee range of motion (ROM) after TKA, there was no significant difference in pain VAS score (23). However, they injected ropivacaine with epinephrine in both the TXA knee and the control knee. Hence, according to previously reported studies, we assume that the PA TXA dose (1500 mg) used in our study was insufficient to reduce the VAS pain score. In contrast, Wong et al. conducted a randomized and controlled trial that compared the low-dose (1500 mg) and high-dose (3000 mg) topical TXA with a placebo (26). Their report revealed that there was no difference among the three groups in terms of postoperative VAS pain scores. Thus, further study is necessary to optimize dozes and timings to obtain more advantages from the PA technique of TXA.

Reale et al. indicated that TXA did not lead to the risk of thromboembolic complications (27). We observed similar results with no thromboembolic events, such as pulmonary emboli (PE) or deep venous thromboembolism (DVT) in both groups. The means of PA TXA injection around the soft tissue of the knee may suggest minimal TXA resorption into the systemic circulation. Moreover, Astedt et al. showed that TXA tranexamic acid did not suppress the fibrinolytic activity in the vessel walls, which may explain why previous studies and our study have not indicated a higher incidence of thromboembolic complications in patients given TXA (28).

In the literature, effective doses for the topical TXA ranging from 250 mg to 3 g have been applied by most surgeons (22-Goderecci). Although TXA provides a significant reduction of blood loss in total joint arthroplasty, one of the major concerns about the use of topical TXA is that TXA has the potential to be cytotic to cartilage, tendon and synovium, especially in an enclosed joint space (15,22,29,30). Tuttle et al. showed that 50 mg/ml TXA led to cytotoxic effects on cartilage, whereas 25 mg/ml did not result in a cytotoxic impact on chondrocytes (15). We may deal with this problem through PA injection because we do not apply TXA directly into the joint area. Moreover, Mc Lean et al. investigated the interaction between human periarticular tissues and TXA and found that 50 mg/ml or 100 mg/ml of topical TXA triggered significant periarticular tissue toxicity (29). Çıraklı et al. evaluated the effects of 50 mg/ml TXA injected into the soft tissue around Achilles tenotomy surgical sites in rats (30). At the end of the study, they revealed that topical TXA caused a long-term adverse effect on tendon healing. PA injections are partly intramuscular injection, administrating into the muscular soft tissue around the quadriceps tendon. We did not inject TXA directly into the quadriceps tendon, which has poor regenerative capacities. Furthermore, we employed 1500 mg/50 ml (30 mg/ml) TXA to minimize blood loss and the cytotoxic effects on the soft tissue around the knee, which was a relatively optimal dose compared with 50 mg/ml used by Çıraklı et al (27).

The main limitation of this study is its retrospective design. Secondly, IV or IA TXA use should have been chosen as the control group in this study. Another limitation of this study is that we did not evaluate the leg swelling. Postoperative leg swelling is affected by multiple factors, such as cardiovascular or renal dysfunction, soft tissue inflammation, and deep venous thromboembolic complications. Furthermore, we did not monitor TXA in the blood test. Finally, we searched only symptomatic DVT after surgery. We did not search asymptomatic DVT. Thus, we do not know the exact number of DVT in the patients administered TXA.

One of the strengths of our study is that this study has involved a consecutive group of patients who were performed through the same approach and the same implants and standardized perioperative procedure at a single institution. Furthermore, both groups were comparable about demographic characteristics, and preoperative levels of hemoglobin and hematocrit were not significantly different between the two groups.

In conclusion, the PA administration of TXA after unilateral TKA may offer a significant reduction in postoperative blood loss and transfusions rates as well as the length of hospital stay without increasing the risk of thromboembolic complications and cytotoxic effects on cartilage and peri-articular soft tissue. However, we did not observe a significant reduction in postoperative pain VAS score.

Ethics Committee Approval: The study was approved by the Ethics Committee Medipol University (date: 27.01.2021 and approval number: E-10840098-772.02-2616).

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

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