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Comparison of the tranexamic acid use with tourniquet and drain application in 170 primary total knee prosthesis cases

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Abstract

Objective: In our study, we compared the use of tranexamic acid (TXA) with tourniquet and Hemovac drain application in terms of bleeding, deep vein thrombosis (DVT), infection development and functional scores following total knee arthroplasty (TKA).

Methods: Our TKA cases were evaluated retrospectively. The group that was not applied a tourniquet or Hemovac drain but administered TXA was designated as the study group (TXA group) and the group that was applied a tourniquet or Hemovac drain but was given no TXA was designated as the control group. The age, gender, operated side, body mass index, comorbid diseases, anesthesia type, duration of operation, perioperative blood pressure values of patients from both groups were recorded. Perioperative blood loss, the difference between preoperative and postoperative Hb and Hct values, need for transfusion, infection, DVT development and the WOMAC scores of both groups were compared.

Results: The duration of surgery in the TXA group was 82.5±7.1 minutes and 75.2±4.2 minutes in the control group ($p<0.05$). Perioperative bleeding was higher in the TXA group (112.77±12.82 ml) than the control group (146.14±40.54 ml) ($p<0.05$). The difference between the preoperative and postoperative Hb levels was 2.9±0.7 g/dl in the control group compared to 1.5±0.5 g/dl in the TXA group. The need for transfusion, DVT and infection development in the postoperative period were significantly higher in the control group ($p<0.05$). In terms of functional scores, the only significant difference between the groups was detected in the WOMAC pain scores ($p<0.05$).

Conclusion: A lower bleeding, transfusion, infection, DVT development rate and pain scores can be obtained with IV TXA application and without the use of a tourniquet or drain in TKA.

Keywords: Deep vein thrombosis, hemovac drain, postoperative bleeding, total knee arthroplasty, tourniquet

Introduction

In our day, total knee arthroplasty (TKA) is one of the most common orthopedic surgeries performed successfully. However, perioperative blood loss is still important; hemorrhages exceeding 1000 ml may be encountered [1, 4]. Hypotensive or spinal anesthesia, autologous transfusion, tourniquet and antifibrinolytic agents are used to reduce blood loss [5, 6].

A tourniquet is often used for better visualization of the surgical field, attainment of short surgery time, low perioperative blood loss and better bone-cement integration [7, 9]. However, thigh pain, nerve paralysis, cardiovascular problems, flexion problems, wound complications and venous thromboembolism are frequently encountered due to tourniquet use [10, 13]. Deep vein thrombosis (DVT), which may cause serious problems, can be seen in 40 to 84% of the cases following TKA [14, 15]. Closed drainage systems (Hemovac drainage) have been used for a long time to prevent hematoma development, reduce the risk of infection and achieve faster wound healing and functional return [16, 18]. However, in an increasing number of studies, it has been reported that drainage systems are bacterial entry pathways which increase the need for postoperative blood loss and transfusion, increase costs and thus are not advantageous [19, 22].

Tranexamic acid (TXA) is an antifibrinolytic inhibiting the formation of plasmin, which acts by competitively blocking the lysine-binding sites of plasminogen, and reduces blood loss and The need for transfusion without increasing the risk of postoperative venous thromboembolism [2, 23, 25].

In our study, we retrospectively evaluated the risks and benefits of using tourniquets and drains in TKA by evaluating the results of the group which was given TXA. We believe that our work will contribute to these practices that are still debatable.

Patients and Methods

Our study was performed with the approval of the institutional ethics committee. Patients who had undergone revision TKAs, bilateral cases, patients with a history of DVT or pulmonary embolism (PE), patients with renal or hepatic dysfunction, patients with ischemic heart disease, blood clotting disorders and secondary osteoarthritis were excluded from the study. 170 patients were evaluated in two groups. The first group was given TXA IV but was not applied a tourniquet or Hemovac drain (TXA group). The second group consisted of cases who were applied a tourniquet and Hemovac drain but were administered no TXA (control group).

Surgical technique and patient care

The decision for performing anesthesia was given jointly by the patient and anesthesiologist. Prophylactic cefazolin sodium 2g was administered to all patients preoperatively. The patients were operated by the same surgical team using the same brand knee prosthesis (NexGen LPS-Flex Knee; Zimmer Biomet, Warsaw, IN, USA).

The measured resection technique was applied by performing a midline skin incision via medial parapatellar approach. An extramedullary incision guide was used for the tibia and an intramedullary guide for the femur. Denervation was performed without patellar resurfacing. Autologous bone was used to fill the femoral medullary canal before implant cementation. Closure was routinely done with the knee positioned in flexion.

No blood salvage system was used. Electrocautery and routine hemostasis were performed in all cases during surgery. The duration of surgery and the perioperative amount of blood loss were recorded. The amount of intraoperative blood loss was measured in all cases based on the suction volume and weight of the sponges.

The duration of surgery was defined as the period starting from surgical incision to skin closure.

In the TXA group, 15 mg/kg TXA was given 15 minutes before and two hours after the surgery intravenously with 100 ml of saline. Attention was paid to not exceed the rate of 100 ml/min during administration to avoid hypotension. In the control group, a 10.5 cm-wide thigh tourniquet was padded and inflated up to 150 mmHg over the systolic pressure with simple elevation and was not deflated during the whole surgery. The Hemovac drain was removed on the first postoperative day.

All patients were given prophylactic antibiotherapy and analgesia for two days after surgery and antithrombotic enoxaparin 4000 IU was administered subcutaneously 12 hours after surgery. Cold-pack and compression socks were applied in both groups. Range of motion (ROM) and strengthening exercises were started to all patients in the early period. Patients in the TXA group were mobilized on the same day and patients in the control group were mobilized after removal of the drain. Total blood loss in TKA is the total of the measured blood loss and hidden blood loss.[2,3] In order to evaluate hidden blood loss, Hb values should be referred to as done by George *et al.* [3] The postoperative change in Hb was taken as the primary evaluation criterion in

our study.

Blood transfusion was performed in cases with a postoperative Hb value below 7 g/dl or in symptomatic cases with a postoperative Hb value of 7-10 g/dl. Patients were discharged and were given a daily dose of 4000 IU of enoxaparin sodium for one month postoperatively.

All patients were evaluated with Doppler ultrasonography for DVT at the first postoperative month or when they had a complaint.

Age, gender, operated side, body mass index (BMI), comorbid diseases of the patients and the anesthesia type applied were recorded in each group. The hemoglobin (Hb) and hematocrit (Hct) values, liver and kidney functions and WOMAC scores of all cases were evaluated preoperatively and at the first postoperative month. Duration of surgery, perioperative arterial blood pressure, perioperative bleeding amount and the maximum amount of decrease in the postoperative Hb values (difference between the preoperative Hb level in the sample drawn closest to the time of the surgery and the lowest Hb level recorded postoperatively during hospitalization or prior to any blood transfusion) were recorded. Patients were followed up for a minimum of one year for postoperative complications.

Statistical method

Mean, standard deviation, median, minimum, maximum, frequency and ratio values were used in descriptive statistics of the data. Distribution of the variables was measured with the Kolmogorov-Smirnov test. The independent samples t-test and Mann-Whitney U test were used for the analysis of quantitative independent data. The paired samples t-test and Wilcoxon's test were used to analyze the dependent quantitative data. The chi-square test was used for the analysis of qualitative independent data; Fischer's test was used when the chi-square test conditions were not met. The SPSS 22.0 software was used in the analyses. The level of significance was set at $p < 0.05$.

Results

A total of 230 patients who underwent primary TKA in our clinic between 2014 and 2017 were evaluated retrospectively. 170 cases (mean age: 65.8 ± 8.4) were included in the study after exclusion.

There was no significant difference between the groups in terms of age, gender, operated side, BMI, anesthesia type, comorbidity and preoperative Hb. The TXA group consisted of 96 patients and the control group consisted of 74 cases (Table 1).

Perioperative mean systolic and diastolic blood pressures, surgical time, perioperative bleeding amount, maximum changes in Hb-Hct, transfusion requirement, changes in the WOMAC and WOMAC pain scores are presented in Table 2. The duration of surgery was significantly longer in the TXA group (82.5 ± 7.1 vs 75.2 ± 4.2 minutes) ($p < 0.05$). Perioperative bleeding was higher in TXA cases (112.77 ± 12.82 ml) than in the control group (146.14 ± 40.54 ml) ($p < 0.05$). The difference between the preoperative and postoperative Hb levels was 2.9 ± 0.7 g/dl in the control group compared to 1.5 ± 0.5 g/dl in the TXA group. The change in the control group was statistically significant ($p < 0.05$). The change between the preoperative and postoperative Hct levels was $4.3 \pm 2.0\%$ for the TXA group and $8.0 \pm 3.0\%$ for the control group ($p < 0.05$). WOMAC pain scores were statistically lower in the TXA group ($p < 0.05$). The need for transfusion was significantly higher in the control group ($p = 0.028$) (Table 2) (Figures 1 and

2). Superficial infection developed in four patients in the control group, whereas no infection was observed in the TXA group ($p < 0.05$). Proximal DVT was seen in two patients in the TXA group versus eight cases in the control group (Table 3).

Table 1: Patient characteristics.

	TXA group (n=96)	Control group (n=74)	p
Age	66.1±8.8	65.3±7.9	0.525*
Gender			
Male	20 (20.8%)	15 (20.3%)	0.928†
Female	76 (79.2%)	59 (79.7%)	0.928†
Operated side (R/L)	55/41	40/34	0.673†
BMI (kg/m ²)	32.7±5.7	32.8±5.8	0.863*
Anesthesia type			
Spinal	81 (84.4%)	69 (93.2%)	0.075†
General	15 (15.6%)	5 (6.8%)	0.075†
Comorbidity			
HT	35	30	0.587†
DM	20	15	0.542†
Preoperative Hb (g/dl)	12.9±1.4	13.1±1.2	0.430*

*Mann-Whitney U test, †chi-square tes

Table 2: Perioperative and postoperative data of the patients.

	TXA group (n=96)	Control group (n=74)	p
Perioperative blood pressure (mm/Hg)			
Systolic	21.40±9.53	122.97±7.01	0.128*
Diastolic	72.5±9.6	71.6±10.2	0.291*
Surgical time (min.)	82.5±7.1	75.2±4.2	0.000*
Perioperative bleeding (ml.)	146.14±40.54	112.77±12.82	0.000*
Max. Hb change (gr/dl)	1.5±0.5	2.9±0.7	0.000*
Max. Hct change (%)	4.3±2.0	8.0±3.0	0.000*
Transfusion (1U)	4 (4.2%)	10 (13.5%)	0.028†
WOMAC score			
Preoperative	72.1±10.1	70.1±9.6	0.146*
Postoperative	27.9±9.5	29.4±10.6	0.380*
Intragroup change (p)	0.000‡	0.000‡	
WOMAC pain score			
Preoperative	14.5±3.6	13.8±3.4	0.219*
Postoperative	4.4±2.1	6.6±3.1	0.000*
Intragroup change (p)	0.000‡	0.000‡	

*Mann-Whitney U test, †chi-square test, ‡Wilcoxon test

Table 3: Complications encountered.

	TXA group (n=96)	Control group (n=74)	p
Superficial infection	0	4 (5.4%)	0.034*
DVT	2 (2.1%)	8 (10.8%)	0.022*

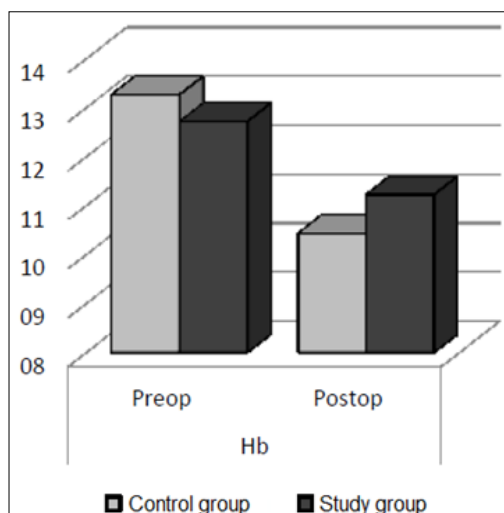


Fig 1: Preoperative versus postoperative Hb values (g/dl).

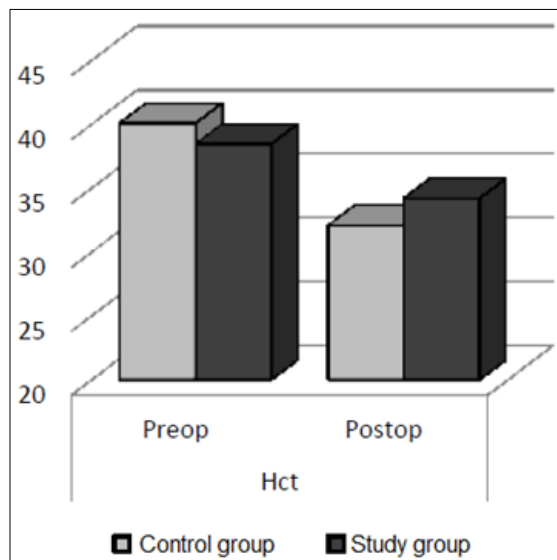


Fig 2: Preoperative versus postoperative Hct levels.

Discussion

Bleeding, infection, and thromboembolism are major complications of TKA [26, 27]. Bleeding is undesirable as it may lead to hemodynamic instability, complications due to transfusion, increased risk of infection due to accumulation of the blood in the joint, declining function scores and for cost reasons [28, 29].

Perioperative bleeding in TKA is due to surgical trauma and hyperfibrinolysis enhanced by tourniquet application [30, 32]. Postoperative hyperfibrinolysis is the cause of hidden bleeding into the joint and surrounding tissues [33]. TXA reduces blood loss by inhibiting fibrinolysis [34, 35]. All available meta-analyses suggest identical outcomes between IV-IA routes 10-8, 10-9. We did not intend to evaluate the dose and route of TXA. For this reason, TXA was applied intravenously in doses proportioned to the body weight, as it has been during almost the last decade. In a recent meta-analysis, it was reported that preoperative and postoperative (double) application, as we did, is more effective on bleeding than a single dose IV application [1].

Despite the presence of more recent techniques, tourniquet and closed drainage systems are frequently used in TKA [16, 36, 38]. Despite numerous studies, the issue is still a hot matter of debate [29, 39, 41].

In a recent meta-analysis involving randomized controlled trials, it was stated that the use of closed drainage systems does not provide a positive contribution or advantage in infection, blood loss, DVT, pain scores or ROM [42]. In another meta-analysis, the decrease in the Hb values were even higher in TKA cases in which closed drainage systems were used [43]. This situation was associated with the disappearance of self-limiting effect of bleeding [44, 45]. Increased blood losses paved the way for the modification of traditional drain applications. In two studies, it was reported that blood loss was reduced without complications using intermittent clamping instead of continuous drain [41, 46]. The total bleeding and infection rates in our study was high in the control group where we used the drainage system.

Tourniquet application has been preferred in TKAs as it reduces perioperative bleeding, improves the cement-bone integration and shortens the duration of surgery [47, 48]. The amount of postoperative bleeding was higher than the amount of perioperative bleeding with tourniquet application in Mutlu *et al.*'s study, however, the hidden blood loss was not evaluated [49]. In a recent meta-analysis by Smith and Hing, it

was reported that total blood loss was not reduced despite the decrease in the amount of perioperative bleeding in the tourniquet groups, and there was no evidence of interdigitation of the cement [7]. Pfitzner *et al.* reported that the tibial cement thickness showed a small difference with a questionable clinical significance [50]. According to Ledin *et al.*'s randomized controlled study, the use of a tourniquet does not contribute to cement-bone fixation [51]. In their prospective study, Bilgen and Yilmaz did not recommend the use of tourniquet in TKA as they asserted that tourniquet application increased the bleeding amount and delayed the postoperative rehabilitation process [52]. In our study, cement-bone integration was not evaluated. However, we did not observe the positive effect of tourniquet application on total blood loss despite the reduced duration of surgery and perioperative bleeding.

Peersman *et al.* stated that the surgical time was a risk factor independent from the presence of a superficial infection in total joint prosthetic surgeries, and that there was a close relationship between superficial infections and deep infections [53]. The duration of TKA surgery was 94 ± 28 minutes in cases which did not develop a postoperative infection and 127 ± 45 minutes in those who developed an infection [54]. In their retrospective study, Mutlu *et al.* [49] recorded a distinctively low but statistically insignificant surgical time in the tourniquet group of TKA patients. The authors detected a superficial infection rate of 9.4% in the tourniquet group and 2.8% in the control group. Frisch *et al.* noted a transfusion rate of 9.27% following arthroplasty [55]. Rosencher *et al.* detected an 11% infection rate in patients who underwent arthroplasty and 8% in those who did not [56]. In our study, the surgical time between cases who developed an infection versus those who did not was not significantly different. In the TXA group, 4.16% of the cases required transfusion, while the rate was 13.51% in the control group. Both groups were similar in terms of comorbidity, BMI and the source of arthrosis. Despite this, the reason why we encountered infection more frequently in the control group can be attributed to the conditions that increased the use of tourniquets and drains or the need for transfusions.

Tourniquet application increases the risk of symptomatic DVT and PE [12, 57, 58]. In a recent prospective randomized controlled study where anticoagulants were not used, Mori *et al.* did not find a statistically significant difference in the duration of surgery, but observed higher prevalences of distal and proximal DVT in the tourniquet group (distal DVT 52.9%-23.1%, proximal DVT 5.9%-3.8%) [39]. In their study on 153 patients in which DVT development was investigated with venography, Chang *et al.* [59] stated that there was no need for a preoperative DVT scan, since DVT was a rare condition and did not exhibit a clinical importance. The authors detected DVT development in 9.8% of their patients and of them one developed PE.

In their prospective randomized study where they used a drain, Huang *et al.* [9] encountered the most frequent bleeding after TKA in the group applied a tourniquet alone and the least blood loss in the group given TXA alone. Infection was observed in groups where TXA was administered combined with tourniquet and where tourniquet was used alone. No infection was detected in the TXA group. Similarly, Akgül *et al.* found a lower prevalence of blood loss in the TXA group compared to the control group where they applied a tourniquet [60]. Schnettler *et al.* [40] treated their patients without drain application and observed the most frequent bleeding in the group that was applied tourniquet alone, and

the least bleeding in the group that was administered TXA alone. The patients who were given TXA had also less bleeding compared to the patients who were treated with the combination of tourniquet application and TXA. The prevalence of DVT was similar in all three groups, however, the authors failed to state whether these were proximally or distally located.

These studies support the reduction of the effectiveness of TXA by tourniquet application. We did not conduct a preoperative DVT scan in our study but rather evaluated the proximal veins that we thought were of clinical relevance for DVT. In our study, we detected proximal DVT in 10.81% of the control group and 2.08% of the TXA group. Our results show that the use of TXA is a good alternative to tourniquet application regarding the risk of DVT in TKA.

In terms of pain and functional scores, lower VAS values were observed postoperatively in the non-tourniquet group than in the tourniquet group in various studies [50, 51, 61]. Huang *et al.* [9] found higher VAS values up to the third postoperative month and lower patient satisfaction scores in the tourniquet group compared to the TXA group. The authors stated that the differences between the groups disappeared after the sixth month. In our study, we did not find any significant difference between the groups in terms of WOMAC global scores in the first month, but observed lower WOMAC pain scores in the TXA group, in accordance with the literature. This situation was evaluated in accordance with the VAS values from the literature.

Our study had several limitations. First, our sample size was relatively small and our cases were retrospectively evaluated. Although it was not a reference method for the diagnosis of DVT, we preferred to employ Doppler ultrasonography as it was a noninvasive and practical method.

Our failure to check the presence of DVT with preoperative ultrasonography may be considered a limitation. However, it is known that preoperative DVT has not been frequently observed and has a low clinical importance [59].

Our study investigated the efficacy of drain and tourniquet on bleeding, DVT and infection, revealed all variables related to patients and the procedure, considered the Hb change in order not to overlook the hidden bleeding and compared the groups with respect to functional scores.

Conclusion

Our study demonstrated that TKA can be performed with administration of TXA in absence of drain and tourniquet application, and lower bleeding, less infection and DVT rates, and low pain scores in the early period can be achieved. Physicians who perform TKA should question the use of tourniquet and drains, which are widely used in our day, considering both their expected benefits and potential risks. We believe our findings will contribute to improvements in procedural recommendations for knee replacement surgery.

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