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Topical Tranexamic Acid May Improve Early Functional Outcomes of Primary Total Knee Arthroplasty

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ABSTRACT

Introduction: The use of tranexamic acid (TXA) reduces postoperative anemia and blood transfusion requirements. We investigated if these beneficial effects improve the early outcomes of primary total knee arthroplasty (TKA).

Methods: We retrospectively studied 166 consecutive patients (179 TKAs) who received topical TXA (3 g before tourniquet deflation). This "study group" was compared with a "control group" of 197 consecutive patients (209 TKAs) in whom no TXA was used. We captured outcomes during the first 4 postoperative months. Knee Society score (KSS) was determined preoperatively, 6 weeks, and 4 months postoperatively. The outcomes were compared using univariate analysis. Multiple logistic regressions were calculated to assess differences between groups in KSS at 6 weeks and 4 months, controlling for age, sex, body mass index, and preoperative KSS.

Results: Postoperative hemoglobin was significantly higher in the study than that in the control group on day 1, day 2, and at discharge ($P < .0001$). Blood transfusions were required in 5% and 22% of patients ($P < .001$), respectively. Six weeks postoperatively, the functional KSS and its 5 categories (ability to walk, negotiate stairs up and down, stand up from a chair, and the use of support) were significantly higher in the study than those in the control group ($P \leq .001$). Four months postoperatively, there was no difference in the KSS between the groups.

Discussion: Our study suggests that the clinical benefit of topical TXA administration extends beyond the hospitalization period. Its use may improve knee function during the first 6 postoperative weeks. This beneficial clinical effect seems to be negligible afterward.

The use of intravenous or topical tranexamic acid (TXA) has revolutionized orthopedic surgery. In the last few years, there has been evidence supporting its use to diminish intraoperative and postoperative bleeding, postoperative anemia, and transfusing requirements in patients undergoing joint arthroplasty surgery [1-5].

Patients undergoing total knee arthroplasty (TKA) are among those who may benefit the most from these perioperative effects as postoperative bleeding is high and postoperative anemia is routinely observed. Without the use of TXA, the estimated blood loss ranges from 330 [6] to 1725 cc [7], hemoglobin drop ranges from 2.9 [7] to 4.5 g/dL [4,8], and blood transfusion is required in 2% [9,10] to 58% [11] of patients. In the historic experience of the senior author (AGDV), the mean postoperative drain output is 578.9 cc, hemoglobin drop averages 3.29 g/dL, and postoperative transfusion is needed in 21% of patients.

The substantial reduction of postoperative bleeding and anemia may have additional advantages during the recovery period. Such favorable effects may include but are not limited to improved pain,

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range of motion (ROM), and functional outcomes. To our knowledge, such potential benefits have not been widely studied [6,7]. The purpose of this study was to determine if the use of topical TXA is associated with improved local and functional outcomes in patients undergoing TKA surgery.

Material and Methods

We conducted an Institutional Review Board-approved, retrospective review of the senior author's (AGDV) prospective primary, elective TKA database. All 365 patients who underwent 390 TKAs between December 2012 and January 2015 were considered for this study. Two patients who died before the fourth postoperative month were excluded: 1 patient received unfractionated heparin after being diagnosed with an upper extremity deep venous thrombosis 3 weeks postoperatively. She developed heparin-induced thrombocytopenia and thrombosis and a secondary intracranial bleed for which she required a decompression craniotomy. She died 3 months postoperatively. The second patient suffered a cardiopulmonary arrest and died 2 months postoperatively. No autopsy was performed. The remaining 363 patients (388 TKAs) were included in the analysis.

The first 197 consecutive patients (209 TKAs) underwent surgery between October 2012 and November 2013 and constituted the "control group." No TXA was used. The remaining 166 patients (179 TKAs) underwent surgery between December 2013 and January 2015 and receive 3 g of topical TXA before tourniquet deflation and wound closure. No intravenous TXA was used. They constituted the "study group."

All surgeries were performed by a single surgeon using standardized surgical technique and perioperative care [12,13]. Surgeries were performed using a combined spinal/epidural anesthetic and a tourniquet inflated at a pressure ranging from 250 to 300 mm Hg. A standard midline incision and medial parapatellar arthrotomy were used. The tibial cut was made using an extramedullary guide referencing off the most normal side. The femur was prepared with an intramedullary guide, and the distal femoral canal opening was routinely closed with a bone plug. Measured resection and posterior referencing instruments were used. All implants were cemented, and the patella was routinely resurfaced.

After final component implantation, 3 g of nondiluted TXA were poured into the articular cavity in study group patients. After 5 minutes, the solution was suctioned from the knee, the tourniquet was deflated, and hemostasis was achieved with electrocautery. Routine arthrotomy, subcutaneous, and skin closure were performed. A surgical drain was placed. The patients in the control group received an identical protocol but without the use of TXA.

Postoperative pain control was achieved with an epidural patient-controlled anesthetic and fentanyl for the first 24 hours postoperatively, progressing to oral analgesics as tolerated. Drains were removed on the first postoperative day. Rehabilitation was initiated on the day of surgery with a continuous passive motion machine, and patients were weight bearing as tolerated. All patients received antibiotic prophylaxis. Pharmacologic thromboprophylaxis was determined by preoperative risk stratification: most of the patients who had no additional risk factors for venous thromboembolism received aspirin. Those who were at a higher risk or received anticoagulation for medical reasons before surgery received Coumadin, and those deemed to be at a very high risk, received Coumadin combined with low molecular weight heparin. The latter was discontinued when the International Normalized Ratio reached a target goal between 1.8 and 2 (Table 1).

We captured in-hospital outcomes, transfusion requirements, thromboembolism, and other life-threatening complications. Hemoglobin and hematocrit values were recorded preoperatively, on the first, second day postoperatively, and on the discharge day. Transfusions were given to patient based on the clinical judgment of individuals involved in patient care and based on hemoglobin levels, medial history, and vital signs. Patients were discharged home or to an inpatient rehabilitation unit within 3-4 days after surgery and were seen in the surgeon's office at 6 weeks and 4 months postoperatively. Gravity-assisted ROM, functional (patient reported), and knee-specific (physician-reported) Knee Society score (KSS) [14] were obtained by the operating surgeon (AGDV) at each visit.

Table 1
Comparison of the Preoperative Characteristics in the Study and Control Groups.

Variable	Study[a]; N = 179	Control[a]; N = 209	*P* value
Sex			
Male	59 (33)	66 (31.6)	.77
Female	120 (67)	143 (68.4)	
Age	65.87 ± 9.72	67.44 ± 9.94	.12
BMI	30.93 ± 6.67	31.18 ± 6.47	.72
Diagnosis			
Osteoarthitis	168 (93.9)	204 (97.6)	.09
Post-traumatic arthritis	6 (3.4)	1 (0.5)	
Rheumatoid arthritis	5 (2.8)	4 (1.9)	
Hypertension			
No	115 (64.2)	117 (56)	.1
Yes	64 (35.8)	92 (44)	
Coronary artery disease			
No	164 (91.6)	189 (90.4)	.68
Yes	15 (8.4)	20 (9.6)	
Congestive heart failure			
No	176 (98.3)	209 (100)	.1
Yes	3 (1.7)	0	
Smoking			
No	163 (91.1)	196 (93.8)	.28
Yes	11 (6.1)	6 (2.9)	
Ex-smoking	5 (2.8)	7 (3.3)	
Chemoprophylaxis			
Aspirin	117 (65.4)	147 (70.3)	.35
Warfarin	48 (26.8)	52 (24.9)	
Enoxaparin	9 (5)	4 (1.9)	
Others	5 (2.8)	6 (2.9)	
Preoperative hemoglobin	13.47 ± 1.45	13.59 ± 1.29	.41
Preoperative hematocrit	40.23 ± 4.16	40.61 ± 3.51	.34
Preoperative FKSS	50.1	48.8	.49
Preoperative KKSS	37.8	35.7	.12

BMI, body mass index; FKSS, functional knee society score.
[a] Percentage (%) or standard deviation (±) shown.

Demographics, preoperative functional KSS (FKSS), and knee-specific KSS (KKSS) were assessed to assure comparability between the groups. Postoperative differences between groups were compared using 2 sample *t* test for continuous variables, and chi-square or Fisher exact test for categorical variables. Multivariate analysis was performed using multiple logistic regressions looking at the difference between groups in FKSS and KKSS at 6 weeks and 4 months, controlling for age, sex, body mass index, preoperative FKSS, and KKSS. Group sample sizes of 179 and 209 achieve 80% power to detect a difference of 10 points in the KSS between groups 4 months postoperatively, with an estimated group standard deviation of 35 and a significance level of 0.05 using a 2-sided 2-sample *t* test.

Results

There were no significant preoperative differences between the groups (Table 1).

Postoperative hemoglobin was significantly higher in the study group than that in the control group on the first postoperative day (11.2 and 10.1, respectively; $P < .0001$), on the second postoperative day (10.7 and 9.6, respectively; $P < .0001$), and at discharge (10.6 and 9.7, respectively; $P < .0001$). Blood transfusions were required in 5% and 22% of patients ($P < .001$), respectively. Two