



Comparison of Intravenous, Intra-articular, and Combined Tranexamic Acid Use in Primary Total Knee Arthroplasty without a Tourniquet and a Drain

Turnike ve Dren Olmadan Primer Total Diz Artroplastisinde İntravenöz, İntra-artiküler ve Kombine Traneksamik Asit Kullanımının Karşılaştırılması

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ABSTRACT

Objective: We assessed the effect of tranexamic acid (TXA) route of administration on the estimated blood loss (EBL) in patients undergoing primary total knee arthroplasty (TKA) without tourniquet and drain use.

Methods: One hundred fifty three patients who underwent primary TKA with use of TXA, between December 2012 and February 2016 were evaluated retrospectively. The patients were divided into three groups according to the route of TXA use: group I, 2 g of intravenous (IV; n=50); group II, 2 g of intraarticular (IA, n=50); and group III, 1 g of IV and 1 g IA combined use (n=53). We recorded the body mass indexes, the platelet counts, haemoglobin, haematocrit levels, prothrombin time, partial thromboplastin time, and international normalized ratio, preoperatively and at 1st and 7th days, postoperatively. EBL was calculated using Meunier's formula.

Results: On the first day, the mean EBLs for groups I to III were 286.3±128.8 mL, 342.7±176.0 mL, and 379.7±228.9 mL, respectively (p=0.029 for group I vs. group III). On 7th day postoperatively, they were calculated as 823±619.3 mL, 1175.1±970.5 mL, and 1092.2±766.7 mL (p=0.073) During the first 90 days postoperatively, we did not see any symptomatic thromboembolic complications, delayed haemorrhage, or surgical site or periprosthetic infections.

ÖZ

Amaç: Turnike ve dren kullanmadan primer total diz artroplastisi (TDA) geçiren hastalarda traneksamik asit (TXA) uygulama yolunun tahmini kan kaybı (EBL) üzerindeki etkisini değerlendirdik.

Yöntemler: Aralık 2012-Şubat 2016 tarihleri arasında TXA kullanılarak primer TDA uygulanan 103 hasta retrospektif olarak incelendi. Hastalar TXA kullanım yoluna göre üç gruba ayrıldı: grup I, 2 g intravenöz (IV; n=25); grup II, 2 g intraartiküler (IA, n=25); ve grup III, 1 g IV ve 1 g IA kombine kullanım (n=53). Vücut kitle endeksleri, platelet sayımı, hemoglobin, hematokrit seviyeleri, protrombin zamanı (PT), parsiyel tromboplastin zamanı (PTT) ve international normalized ratio (INR) preop, postop 1. ve 7. günde değerlendirdik. EBL, meunier formülü kullanılarak hesaplandı.

Bulgular: İlk gün I ila III. grupların ortalama EBL'leri sırasıyla 286,3±130,15 mL, 342,7±177,87 mL ve 379,7±228,85 mL idi ve istatistiksel olarak farklı değildi (p=0,152). Ameliyat sonrası 7. günde 823±625,75 mL, 1175,1±980,6 mL ve 1092,2-766,7 mL (p=0,250) ameliyattan sonraki ilk 90 gün boyunca herhangi bir semptomatik tromboembolik komplikasyon, gecikmiş kanama veya cerrahi bölge veya periprostetik enfeksiyon görülmedi.

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Conclusion: IV, IA or combined uses of TXA are effective and safe for reducing blood loss and transfusion requirements in primary TKA without a tourniquet and drain.

Keywords: Tranexamic acid, total knee arthroplasty, blood loss

Sonuç: IV, IA veya TXA'nın kombine kullanımları, turnike ve drenaj olmadan primer TKA'da kan kaybını ve transfüzyon gereksinimlerini azaltmak için etkili ve güvenlidir.

Anahtar Sözcükler: Traneksamik asit, total diz artroplastisi, kan kaybı

Introduction

Total knee arthroplasty (TKA) is the surgical option used most frequently in the treatment of symptomatic knee osteoarthritis and it usually results in patient satisfaction. However, it is prone to several complications related to the 800-1500 mL blood loss involved and the requirement for intraoperative and early postoperative allogeneic blood transfusions in 10-30% of patients (1-8). Decreasing the rate of blood loss and the need for allogeneic blood transfusion is very important in TKA for improving functional recovery and decreasing transfusion-related risks and costs (9). Tranexamic acid (TXA) is a potent antifibrinolytic agent that decreases bleeding in TKA by preventing fibrinolytic activity. It acts by binding to the lysine-binding area of plasminogen, consequently blocking the attachment of plasminogen to fibrin. The half-life of TXA, which has been used safely since 1964, is 1.9-2.7 h and a large amount of TXA is excreted in urine without being metabolised when used intravenously (10,11). Recent meta-analyses have revealed that antifibrinolytics are safe and cost-effective, and they decrease the need for blood transfusion and shorten the hospital stay (1,12).

The literature contains no reports on adverse thromboembolic events related to the intravenous (IV) administration of 1-3 g TXA in TKA, but there are potential advantages in terms of tolerability and decreased costs (13). Topical TXA use decreases the plasma TXA concentration ten-fold compared with an IV dose and has 70% less systemic absorption, which decreases the likelihood of adverse effects (14). In addition, to maintain microvascular haemostasis, it is important to reach maximum concentrations at the surgical site (15). The effectiveness of intra-articular (IA) TXA compared to IV administration has not been proven. In some studies, IA TXA reduced postoperative swelling around the knee compared with placebo (16,17). However, there is still no clear evidence whether IA administration has similar effects with IV application.

The literature on the combined IV and IA use of TXA is limited; almost all of the available studies involved tourniquet use, which stimulated fibrinolysis and consequently bleeding (18-20). Therefore, this comparative retrospective study assessed the effect of TXA route of administration (IV, IA, or combined) on the estimated blood loss in patients undergoing primary TKA without tourniquet and drain use.

Methods

This retrospective study included 103 patients with tricompartmental osteoarthritis who underwent primary TKA between December 2012 and February 2016. Patients using

anticoagulant or anti-aggregant medications (such as enoxaparin, fondaparinux, clopidogrel, Factor Xa, or thrombin inhibitors) and oral contraceptives, having thrombophilia, oncological disease, hepatic or renal dysfunction, a history of myocardial infarction, deep venous thrombosis (DVT), and alcohol abuse were excluded. The patients were divided into three groups according to the route of TXA use: Group I, 2 g IV [n=50; 46 females, 4 males; mean age, 65.9 (range=46-77) years]; group II, 2 g IA [n=50; 40 females, 10 males; mean age, 70 (range=59-80) years]; and group III, 1 g IV and 1 g IA together [n=53; 46 females, 7 males; mean age, 66.3 (range=54-87) years].

All of the surgeries were performed by three arthroplasty surgeons under spinal anaesthesia and without use of a tourniquet and Hemovac drains. We administered 2 g of IV cefazolin for infection prophylaxis, 30 min before the incision. All patients underwent cemented, cruciate-retaining, tricompartmental TKA using a medial parapatellar approach. Group I was given 2 g TXA in 100 mL of saline, intravenously. Group II was given 2 g of TXA in 30 mL of saline injected intra-articularly after closing the joint capsule. Group III was given 1 g of TXA in 100 mL saline intravenously and 1 g in 15 mL of saline intra-articularly. During the postoperative period, we administered 1 g IV cefazolin for infection prophylaxis for 24 h and 0.4 mL of enoxaparin for DVT prophylaxis for 2 days. On the third day, the patients were discharged and advised to take 100 mg oral aspirin daily and to use anti-embolic socks for the next 6 weeks.

We recorded the body mass index (BMI) preoperatively, and the platelet count, haemoglobin level (Hb), haematocrit (Hct) and international normalised ratio (INR), preoperatively and on 1st and 7th days, postoperatively. The blood loss was estimated using the Meunier's formula: (21)

Estimated blood loss volume (EBV)= $BV \times (Hb_i - Hb_f) / Hb_f$, where BV is the estimated blood volume [=weight \times average blood volume (75 mL/kg for males, 65 mL/kg for females)], Hb_i is the initial preoperative Hb, and Hb_f is the Hb on a given day postoperatively.

The estimated blood losses of the three groups were compared. Patients were investigated for thromboembolic complications, delayed haemorrhage, and periprosthetic infection for 3 months postoperatively.

Statistical Analyses

The data were analysed using one-way analysis of variance (ANOVA) with post hoc tests, using the program SPSS. A p value <0.05 was defined as statistically significant with 95% confidence interval.

Results

The mean BMI and its range in groups I to III were 34.4 (23-47), 33.2 (26-43), and 33.7 (23-50) kg/m², respectively (p=0.537). The demographic information for the three groups and preoperative Hb, Hct, and EBV values are shown in Table 1. On the first day, the mean EBV and its standard deviation in groups I to III were 286.3 (128.8), 342.7 (176.0), and 379.7 (228.9) mL, respectively, and did not differ statistically among the groups. The mean EBV was significantly lower in the group I than the group III (p=0.029). There was no significant difference between group I and II (p=0.277) and between group II and III (p=0.564). On the 7th postoperative day, the EBV values were 823 (619.3), 1175.1 (970.5), and 1092.2 (766.7) mL, respectively (p=0.073) (Table 2).

During the first 90 days postoperatively, we did not see any symptomatic thromboembolic complications, delayed haemorrhage, or surgical site or periprosthetic infections.

Discussion

There is still no consensus on the dosage and route of administration of TXA in orthopaedic surgery. Adequate

blockage of fibrinolysis in the tissues requires an approximately 80% decrease in plasminogen activity. For this reason, the plasma TXA concentration should be 10 ng/mL and this plasma concentration can be obtained with a 10 mg/kg dose of IV TXA in 3 h (22). In the literature, TXA decreased the need for blood transfusion by up to 38% in orthopaedic, cardiovascular, cranial, and general surgeries (23). The estimated blood loss in groups I and III showed that both dosages were sufficient for reaching the effective plasma concentration.

Topical TXA has less systemic absorption and higher local concentrations compared with IV administration, which means it has fewer systemic side effects. It also decreases the need for transfusion 13-fold compared with placebo (10,15,24). Wang et al. (15) reported that IV TXA was not superior to IA administration in reducing blood loss or the need for transfusion. Maniar et al. (22) showed that a single 3 g IA TXA dose is as effective as single 10 mg/kg IV TXA dose. A review by Pantelli et al. (25) compared topical TXA application of less than 2 g and more than 2 g with placebo and found that both dosages decreased the rate of transfusion need, although the decrease was not significant in the group who received less

Table 1. Demographic data and preoperative blood counts

	IV group	IA group	Combined group	P value
No. of patients (M/F)	50 (4/46)	50 (10/40)	53 (7/46)	
Age (SD)	65.9 (8.3)	70.1 (6.7)	66.3 (8)	0.101
BMI (kg/m ²) (SD)	34.4 (6.5)	33.2 (4.5)	33.7 (5.3)	0.537
Preop. Hb (g/dL)	12.6 (1.6)	12.7 (1.4)	12.8 (1.4)	0.741
Preop. HcT (%)	37.6 (4.3)	38.8 (3.5)	39.4 (3.7)	0.061
Preop platelet count X1000	267.7 (73.6)	254.7 (62.5)	271.4 (98)	0.541
Preop INR	1.05 (0.10)	1.14 (0.21)	1.05 (0.21)	0.131
Estimated blood volume (mL) (SD)	5666.7 (1019)	5727.8 (779.7)	5648.1 (1046.4)	0.908

SD: Standard deviation, HcT: Haematocrit, Hb: Haemoglobin, INR: International normalised ratio

Table 2. Summary of the data on the first and seventh postoperative days

	Intravenous group (SD)	Intra articular group (SD)	Combined group (SD)	p value
Hb (g/dL) (first day)	11 (1.6)	10.9 (1.3)	10.7 (1.3)	0.541
HTC (%) (first day)	32.4 (4.5)	32.2 (3.8)	32.6 (3.6)	0.879
Hb (g/dL) (7 th day)	11 (1.2)	10.7 (1.6)	10.8 (1.3)	0.576
HTC (%) (7 th day)	32.4 (3.4)	32.8 (4.9)	34.1(4.7)	0.296
Estimated blood loss (first day)	286.3 (128.8)	342.7 (176)	379.7 (228.9)	0.037 (group I vs III)
Estimated blood loss (7 th day)	823 (619.3)	1175.1 (970.5)	1092.2 (766.7)	0.073

SD: Standard deviation, Hb: Haemoglobin, HTC: Hematocrit

than 2 g topical TXA. In their topical TXA group, the decrease in the postoperative Hb level was around 1 g/dL. In our study, the means of decrease in the Hb level on the first postoperative day in groups I to III were 1.6 ± 0.6 , 1.9 ± 0.9 , and 2.1 ± 1.0 g/dL, respectively ($p=0.009$). On day 7, the differences between the pre- and postoperative Hb levels in groups I to III were 1.6 ± 1.1 , 2.0 ± 1.4 , and 2.0 ± 1.2 g/dL, respectively ($p=0.133$). Although there was a statistically significant difference in terms of the mean Hb loss in the first postoperative day between groups I and III, which might not have a clinical importance, no statistical difference was seen in the 7th postoperative day. Postoperatively, no symptomatic anaemia or need for blood transfusion was seen in any patient.

Although TXA is expected to increase the rates of DVT and pulmonary embolism due to its antifibrinolytic activity, Astedt et al. (26) reported that TXA did not exert its antifibrinolytic activity on the walls of veins and it protected against thrombosis. Moreover, several studies have proven that TXA decreases blood loss without increasing the incidence of DVT or thromboembolic events (10,27,28). We did not see a symptomatic DVT or pulmonary embolism in any patient and in parallel with the literature, we think that this is a consequence of using TXA and not using a tourniquet in our study.

This study had some limitations. First, it was a retrospective study with a limited number of patients. It would have been better if we had groups with tourniquet or drain use or combined use of them. Lastly, we could not compare the results of different dosages of TXA.

Conclusion

Intravenous, intra-articular, or combined use of TXA is effective and safe for reducing blood loss and transfusion requirements in primary TKA without using tourniquet and drains.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: G.U., F.Y., İ.T., V.U., J.A., Concept: F.Y., İ.T., Design: İ.T., F.Y., Data Collection or Processing: V.U., J.A., G.U., Analysis or Interpretation: İ.T., G.U., F.Y., Literature Search: R.B., G.U., Writing: G.U., F.Y.

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