The Journal of Arthroplasty 31 (2016) 1442–1448

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Primary Arthroplasty

Topical vs Intravenous Tranexamic Acid in Reducing Blood Loss After Bilateral Total Knee Arthroplasty: A Prospective Study

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A R T I C L E I N F O

Article history:
Received 23 August 2015
Received in revised form
25 November 2015
Accepted 15 December 2015
Available online 21 December 2015

Keywords:
topical tranexamic acid
total knee arthroplasty
blood loss
blood transfusion
complications
clinical outcome

A B S T R A C T

Background: Total knee arthroplasty (TKA) results in substantial postoperative blood loss with increased morbidity. Despite various studies proving the efficacy of tranexamic acid (TXA), no consensus exists on the routes of administration.

Methods: Seventy consecutive patients with knee arthritis undergoing simultaneous bilateral TKA, who were eligible and fulfilled the criteria, were taken up for this study. They were randomly allocated by a computer-generated random number table, either to receive intravenous TXA (IVTXA; group 1) or topical TXA (TTXA; group 2) in a prospective, double-blinded study. The primary outcome measures were total blood loss and total drain output. The secondary outcome measures were number of blood units transfused and clinical and functional outcomes as evaluated by the Knee Society Score, Western Ontario and McMaster Universities Arthritis Index score, visual analog score, and wound score.

Results: Both groups were similar in age, sex, and body mass index, and no statistical significance was observed. There was statistically significant difference between IVTXA and TTXA groups in mean postoperative total blood loss ($P < .001$), postoperative hemoglobin ($P < .001$) with a higher drop of hemoglobin in the former, total drain output ($P < .001$), and allogeneic blood transfusion ($P < .001$). No complication was observed in either group. Significant difference was observed in the Western Ontario and McMaster Universities Arthritis Index score at 12 weeks and 6 months ($P = .015$ and .007) and Knee Society Score at 6 and 12 months ($P = .050$ and .045, respectively). However, no significant difference was found at 6 weeks.

Conclusion: TTXA is better than IVTXA in reducing blood loss and clinical outcome after simultaneous bilateral TKA.

A successful total knee arthroplasty (TKA) offers tremendous benefits and vastly enhances the quality of life. Painless knee movements allow patients to retain a wide range of daily activities, including climbing stairs, shopping, and getting in and out of chairs, thus enabling them to lead a normal life [1]. Significant amount of blood loss postoperatively after bilateral TKA requires the need of allogeneic blood transfusion. Owing to this, more patients will be at risk of anemia and associated morbidity such as hypovolemic shock, renal failure, breathlessness, fatigue, cardiac abnormality, syncope, delayed wound healing, and increased costs, as a result of an exponential increase in the number of TKAs done per year [1]. About 10%-38% patients require blood transfusion because of postoperative blood loss after TKA [2,3]. Average blood loss in TKA patients ranges from 1450 to 1790 mL leading to anemia in many patients [4-7].

Postoperative blood loss in TKA is due to surgical trauma that induces both the coagulation cascade and local fibrinolysis [8]. Tourniquet release further accentuates the local fibrinolysis thus causing further blood loss [9]. Many strategies have been tried to reduce blood loss and subsequent need of allogeneic blood transfusion [10-13]. Drugs such as tranexamic acid (TXA) and aminocaproic acid have been tried [4]. TXA has been found to reduce postoperative blood loss in various nonorthopedic surgeries such as dental [14] and cardiac [15] procedures. TXA reduces blood loss by around 30%-40% [16]. A few studies have found TXA useful in TKA when used in an injectable form [4,5]. However, there is lot of concern about the safety of intravenous (IV) TXA and the risk of thromboembolic events such as deep vein thrombosis (DVT) or

No benefits or funds were received in support of the study.

No author associated with this paper has disclosed any potential or pertinent conflicts which may be perceived to have impending conflict with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2015.12.033.

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http://dx.doi.org/10.1016/j.arth.2015.12.033
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pulmonary thromboembolism in high-risk patients. Recently, topical application of TXA has been tried to minimize these adverse effects [16-19]. Wong et al [16] reported favorable results of use of topical application of TXA in TKA for reducing perioperative blood loss. However, this method is still not very well established. Hence, we conducted a prospective, randomized, double-blinded study to compare the efficacy of topical use of TXA with the injectable form in reducing blood loss and adverse effects in 70 consecutive patients undergoing bilateral TKA for arthritis of the knee.

Material and Methods

The study was conducted in 70 consecutive patients admitted for primary, bilateral TKA between January 2012 and June 2014, who were eligible for the study and fulfilled the criteria. No patient satisfying the eligibility criteria was left out of the study. All those patients with severe arthritis of the knee with tricompartmental involvement requiring bilateral TKA were enrolled for this prospective, randomized, double-blinded comparative study. The study was approved by the institutional review board, and all patients provided written informed consent to participate in it. Inclusion criteria were patients of either sex who underwent primary bilateral simultaneous TKA and those who were willing and able to return for follow-up over at least a 6-month postoperative period. Patients with allergy to TXA, acquired disturbances of color vision [16], preoperative use of anticoagulants within 5 days of surgery, fibrinolytic disorders requiring intraoperative antifibrinolytics, coagulopathy, history of arteriolar or venous thromboembolic disease, pregnancy, breastfeeding, plasma creatinine of >115 μmol/L in males and >100 μmol/L in females or hepatic failure, and hemoglobin (Hb) <8 g/dL were excluded from the study. TXA is contraindicated in patients with acquired defective color vision because this prohibits measuring one end point that should be followed as a measure of toxicity [16]. In 1963, a new classification for acquired color vision defects was described by Verriest [20]. Pokorny and Smith in their article dealt with the controversy on acquired color vision defects [21].

Patients were allocated randomly into 2 groups by a computer-generated random number table as follows:

Group l (IVTXA; n = 35) received IV TXA in a dose of 15 mg/kg 30 minutes before tourniquet deflation. Another equivalent dose was repeated after 2 hours.

Group 2 (TTXA; n = 35) received 15 mg/kg of TXA in 100 mL of normal saline solution which was applied topically on to the joint surface and left in contact for 10 minutes followed by meticulous suturing.

Both groups were compared statistically on the parameter of age, sex, and body mass index to determine the level of significance.

The patient, assessor, and analyzer were blinded to the study. The surgeon was not blinded. There was a placebo (topical for the IV group and IV for the topical group). The surgeon was not the assessor. The surgeon was not the decision maker for transfusion postop. Blood transfusion was given if the postoperative blood loss was >20% of blood volume as assessed by measuring hematocrit (<25%) or postoperative Hb was <8 g/dL. The drain was clamped for both groups.

This study was conducted in the orthopedics operation theater of a tertiary care center. All the patients were operated by the senior author. All the surgeries were performed under regional spinal/epidural anesthesia. The patient was positioned supine on the operating table with a tourniquet on the thigh. All the surgeries were performed by medial parapatellar retinacular approach using a surgical technique standardized to the same design of cemented knee prosthesis (Scorpio+ single-axis system posterior stabilized; Stryker Howmedica Osteonics, Allendale, New Jersey). After all components were cemented in place, the joint was thoroughly irrigated with normal saline and suctioned out. The study medication in the dose mentioned previously was diluted in 100 mL of saline, applied to the open joint surface, and left in contact for 10 minutes. Wound was then closed without any irrigation or manipulation over suction drain. Negative suction drain was clamped for 2 hours for full effect of topical TXA and then charged. The tourniquet was deflated after the application of dressing and compression bandaging. Antibiotic prophylaxis was given perioperatively with IV injection of cefoperazone sodium (1 g) and sulbactam (1 g) 30 minutes before inflation of the tourniquet followed by every 8 hours for 3 days in all the patients. Antithrombolytic prophylaxis with oral aspirin (150 mg 1 day before surgery and 150 mg daily continued through the 10th postoperative day) was used. Ankle pumps, use of DVT stockings, and early mobilization were administered postoperatively to prevent thromboembolic phenomena. Hb level was measured on third postoperative day. Total drain output was also measured by emptying it in a measuring jar after which the drain was removed. Isometric exercises were enforced in the immediate postoperative period, with passive and active mobilization of the knee as soon as the pain became tolerable. All patients began walking with the support of a walker by the fourth postoperative day. After suture removal at 2 weeks postoperatively, walking with a cane was advised. Unguarded weight-bearing was encouraged after 3 months postoperatively. Patients were examined daily for any clinical symptoms of DVT and any other adverse effects of drugs.

Equivalent dose was given to the patients in group 1 intravenously and repeated after 2 hours irrespective of the second knee surgery. The surgical procedure and other protocols were similar in both groups.

Outcome Measures

Primary: The primary outcome measures evaluated were as follows:

1. Blood loss as calculated from the differences between the preoperative Hb and the lowest postoperative Hb during hospital stay or before blood transfusion. Because of use of a tourniquet, intraoperative blood loss was negligible in all patients. It was assumed that blood volume (BV in mL) on the third day after surgery was the same as that before surgery. BV was assessed according to the following formula of Nadler et al [22]:

$BV = k1 \times \text{height (m)}^3 + k2 \times \text{weight (kg)} + k3$ (where k is constant, whose values are, $k1 = 0.3669$, $k2 = 0.03219$, $k3 = 0.6041$ for men; $k1 = 0.3561$, $k2 = 0.03308$, $k3 = 0.1833$ for women).

Based on the Hb balance, the blood loss was calculated according to the formula described by Good et al [5] as follows:

The loss of Hb (g) was first calculated according to the formula:

$$\text{Hb loss} = BV \times (\text{Hbi} - \text{Hbe}) \times 0.001 + \text{Hbt}$$

where Hb loss (g) is the amount of Hb lost, Hbi (g/L) is the Hb concentration before surgery, Hbe (g/L) is the Hb concentration on the third day after surgery, and Hbt (g) is the total amount of allogeneic Hb transfused.

The blood loss (mL) was related to the patient's preoperative Hb value (g/L) and was calculated as follows:

$$\text{Blood loss} = 1000 \times \text{Hb loss}/\text{Hbi}$$

Calculated blood loss takes into account the uneven dilutional effects of differential amounts of IV fluid administered. This included the hidden blood loss and drain output.