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Comparison of Topical and Intravenous Tranexamic Acid on Blood Loss and Transfusion Rates in Total Hip Arthroplasty

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ABSTRACT

The objective of this study was to determine whether topical tranexamic acid (TXA) carried similar hemostatic effect compared with intravenous TXA in total hip arthroplasty (THA). Three hundred and three THA patients were enrolled and randomized into 3 groups: no TXA group, topical and intravenous TXA group. The results showed that the topical and intravenous TXA group had reduced but similar blood transfusion rates (5.88% v. s. 5.94%, $P = 0.816$). No significant difference was detected in total blood loss between the two TXA groups [(963.4 ± 421.3) ml vs. (958.5 ± 422) ml $P = 0.733$]. We conclude that topical use of TXA was equally effective and safe compared with intravenous TXA in reducing blood loss and transfusion rate following THA without substantial complications.

Total hip arthroplasty (THA) is one of the most common major operations in orthopaedic elective surgery. THAs can cause considerable blood loss and blood transfusions. Perioperative transfusions are associated with several risks, including transmission of infectious agents, hemolytic transfusion reaction, and short-term mortality [1–3]. To reduce the need for blood transfusion, a variety of techniques are used such as controlled hypotension [4], regional anesthesia [5], autologous blood transfusion [6,7], and antifibrinolytic agent - tranexamic acid (TXA) administration [8–18].

Intravenous (IV) use of TXA in THAs reduces blood loss and blood transfusion rates significantly [8–15,19]. Topical use of TXA could minimize systemic drug absorption, and thus reduce the potential complications of IV TXA administration [16,20–25]. However, it is still unknown if topical TXA has similar benefits in reducing blood loss and transfusion rate with IV TXA following THA. Therefore, to evaluate the effect of topical and IV TXA administration in THA, we performed this prospective randomized study to compare the outcomes of blood loss and the transfusion rate in patients in primary THA. We hypothesized that topical TXA produces similar efficient and safe outcome with IV TXA in reducing blood loss and the transfusion rate following THA.

Materials and Methods

Four hundred and seventeen patients in total consented to participate in the prospective randomized trial approved by the Hospital Ethical Committee (No. 201301025). One senior surgeon (BFW) performed all surgeries. Preoperative teaching and perioperative management were the same for patients in all groups. Patients were enrolled between September 2013 and January 2014. Patients were approached for participating in this trial once qualified to the following inclusion criteria.

1. Age 45–80 years
2. Preoperative hemoglobin values >11 g/dl
3. Normal international normalized ratio (INR), prothrombin time (PT), partial thromboplasin time (PTT) values
4. Consented to undergo unilateral cementless THA
5. Had no history of previous hip surgery

All enrolling patients were informed of the expectations of the trial, which were to reduce postoperative blood loss and transfusion rate. During this study, the senior surgeon (BFW) performed 417 THAs; 63 patients were excluded based on the exclusion criteria (shown as follows). Of the remaining 354 patients, 51 declined to participate, 303 were enrolled in this study.

Exclusion criteria were:

1. Had a documented history of thrombo-embolism
2. Had an allergy to TXA
3. Had a high risk of venous thrombosis for intravenous use of TXA according to the American Academy of Orthopaedic Surgeons Guideline [26].

Patients were assigned randomly into three groups: no TXA group (n = 100), topical TXA group (n = 102) and IV TXA group (n = 101). Randomization was achieved with the application of numbered,

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opaque and sealed envelopes after the patients arrived in the operating room. These envelopes were created using a computer-generated randomization list. The patients, surgeons and related nurses were blinded. The medications were handed out by a nurse not involved with this trial. All subject demographics including age, gender, height, weight, body mass index (BMI), prothrombin time, and hematocrit (Hct) values were found to be similar between the three groups, suggesting successful randomization (Table 1).

With the application of the same cementless prosthesis (Triology cup, Prolong polyethylene, Versys Fiber Metal Taper stem; Zimmer, Warsaw, IN, USA), all procedures were performed via the posterior approach. Physiological saline solution (0.85%) was used as placebo in no TXA group. Topical TXA was prepared and used according to the methods described by Konig et al. [24]. During the surgery, the acetabulum was bathed with 20 ml TXA solution (3 g TXA/100 ml saline) after preparation. Then the uncemented acetabular component was impacted. Adjunctive screw fixation was used in all cases with placement of screws in the safe posterior superior quadrant. Following femoral canal broach preparation, the femoral canal was filled with 20 ml TXA solution. Then the uncemented femoral stem was installed. The remaining 60 ml TXA solution was injected into the hip joint following fascia closure. IV TXA was given as a 3 g intravenous infusion 10 minutes prior to incision. A drain was placed in all groups and clamped for 30 min. The drain was removed in the next morning after the surgery.

The use of intraoperative blood transfusion was determined by the anesthesiologist following the physiologic requirement of maintaining the mean arterial pressure greater than 70 mmHg. Fluid need and intraoperative third-space loss were supplemented with balanced crystalloid solutions-hydroxyethyl starch. Packed RBC transfusion was performed following our unit protocol when patient Hb <9 g/dl measured at 24 h postoperatively. LMWH (low molecular weight heparin) was used for prophylaxis against deep vein thrombosis (DVT).

The primary outcomes include the nadir in-patient Hct, maximum Hct drop from preoperative levels, length of hospital stay, transfusion rates, wound complications and total blood loss (TBL). TBL was estimated with equations described by Gross et al. [27] and Nadler et al. [28].

$$TBL = PBV \times \left(Hct_{pre} - Hct_{post}\right)/Hct_{ave}.$$

$$PBV = k1 \times height(m) + k2 \times weight(kg) + k3;$$

k1 = 0.3669, k2 = 0.03219, and k3 = 0.6041 for men; and k1 = 0.3561, k2 = 0.03308, and k3 = 0.1833 for women.

Hct_{pre} = the preoperative Hct level.
Hct_{post} = the minimum postoperative Hct level.
Hct_{ave} = the average of the Hct_{pre} and Hct_{post}.
PBV = the patient's blood volume (PBV, ml)

If blood transfusion was used, the TBL equals to the loss estimated with the aforementioned formula plus the transfusion volume [29].

Presence of wound complications was observed by a single experienced medical staff. Any evidence of erythema, swelling of wound, wound drainage or surrounding cellulitis was considered as wound complication. Position of prosthesis components were measured using methods described by Ha et al. [30]. Each patient was routinely administered ultrasound examination for screening DVT before discharge. Symptomatic DVT and Pulmonary embolism (PE) after THAs were observed continuously by follow-up for three months by a single experienced medical staff.

This sample size was determined for a fixed effects one-way analysis of variance design. To detect a difference of 225 ml of total blood loss, with a power of 0.90 and the alpha level (two-tailed) of 0.05, the sample size needed for each group of this study was 97 patients. For statistical analysis, a one-way analysis of variance was used to detect differences between patients from each group for normal distributions. The Bonferroni test was used to compare the pairwise variable. The Pearson chi-square test was used to analyse qualitative comparative parameters. A P value of less than 0.05 was considered to be statistically significant (as per SPSS 20.0; SPSS Inc, Chicago, IL, USA).

Results

The surgical results are shown in Table 2. No significant differences in wound length, operation time, position of acetabular and femoral prosthesis were detected among the three groups. Nadir in-patient Hct, Hct drop, TBL, blood transfusion rate, length of hospital stay and wound complication are summarized in Table 3. All comparisons except length of hospital stay and wound complication were substantially positive in favor of TXA. The nadir in-patient Hct of no TXA group (0.272 ± 0.019) was lower than that in topical TXA group (0.302 ± 0.031) and IV TXA group (0.316 ± 0.024). And therefore no TXA group had more Hct drop (0.139 ± 0.021) than topical TXA group (0.101 ± 0.034) and IV TXA group (0.098 ± 0.026). (See Table 4.)

The TBL was (1364.2 ± 278.6) ml in no TXA group, which is significantly higher than the TXA groups [(963.4 ± 421.3) ml in topical TXA group and (958.5 ± 422.1) ml in IV TXA Group]. With regard to the blood transfusion rate, 26 of 100 patients (26.00%) received blood transfusions, as compared with 6 of 102 (5.88%) in topical TXA group and 6 of 101 (5.94%) in IV TXA group. Comparing topical TXA group with IV TXA group, we found no statistical differences in the parameters discussed above. The difference of length of hospital stay and wound complication was not significant

Table 1
Demographic And Preoperative Clinical Data.

	No TXA (n = 100)	Topical TXA (n = 102)	IV TXA (n = 101)	Significance[a]
Age (years)	63.9 ± 6.7	60.2 ± 6.5	63.6 ± 7.0	0.291
Gender (female/male)	61/100	67/102	62/101	0.684[b]
Height (m)	1.64 ± 0.055	1.63 ± 0.071	1.65 ± 0.061	0.089
Weight (kg)	67.8 ± 7.2	66.9 ± 5.7	66.1 ± 7.0	0.431
BMI (kg/m^2)	25.1 ± 3.6	25.3 ± 3.0	24.2 ± 3.1	0.558
Prothrombin time (s)	9.8 ± 1.2	9.4 ± 1.7	9.5 ± 1.6	0.542
Hct (dl/dl)	0.411 ± 0.035	0.403 ± 0.037	0.414 ± 0.038	0.476

Data shown as mean ± SD.
BMI = body mass index; Hct = hematocrit; IV = intravenous.
[a] ANOVA test unless otherwise stated.
[b] Pearson chi-square test.

Table 2
Surgical Results.

	No TXA (n = 100)	Topical TXA (n = 102)	IV TXA (n = 101)	Significance[a]
Wound length (cm)	9.5 ± 2.1	9.4 ± 2.2	9.1 ± 2.0	0.724
Operation time (minutes)	103 ± 23	107 ± 25	104 ± 22	0.583
Acetabular component				
Abduction (°)	41.9 ± 3.6	41.3 ± 3.7	42.9 ± 3.4	0.812
Anteversion (°)	14.0 ± 2.1	14.6 ± 2.8	13.9 ± 2.6	0.673
Femoral component Stem alignment (°)	0 ± 0.4	0 ± 0.6	0 ± 0.5	0.549
Canal fill ratio	0.96 ± 0.04	0.95 ± 0.06	0.98 ± 0.02	0.816

Data shown as mean ± SD. IV = intravenous.
[a] ANOVA test.