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Original article

INTRAVENOUS TRANEXAMIC ACID REDUCES PERIOPERATIVE BLOOD LOSS AND TRANSFUSION REQUIREMENTS IN TOTAL HIP ARTHROPLASTY: A PROSPECTIVE COMPARATIVE STUDY

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Abstract

Introduction: Total hip arthroplasty (THA) remains one of the most commonly performed and effective orthopedic procedures, but it continues to be associated with substantial perioperative blood loss and a persistent need for allogeneic transfusion. Tranexamic acid (TXA), a synthetic antifibrinolytic agent, has been proposed as a simple and inexpensive means of reducing this burden, although consensus on its routine use in some healthcare settings remains incomplete.

Materials and methods: This prospective, single-center comparative study included 80 patients undergoing primary uncemented THA for coxarthrosis treated at the University Clinic for Orthopedic Diseases in Skopje (2023-2025). Patients were allocated to an experimental group (40 patients) who received 1 g intravenous TXA before skin incision, or a control group (40 patients) who did not receive antifibrinolytic agent. Total blood volume was calculated using the Nadler formula and total blood loss using the Mercuriali formula. Groups were compared with Student's t-test, chi-square test, and repeated-measures ANOVA, with significance set at $p<0.05$.

Results: The two groups were homogeneous for sex, age, body mass index, and preoperative hematological parameters. Total blood loss was significantly lower with TXA (1327.92±553.6 mL *vs*. 2144.47±727.4 mL, $p<0.001$), as was erythrocyte volume loss (486.05±198.5 mL *vs*. 765.07±254.7 mL, $p<0.001$) and total drain output (564.45±210.7 mL *vs*. 679.80±207.6 mL, $p=0.016$). Only 9 blood units were transfused in the TXA group in comparison with 39 in the control group, and the proportion of patients transfused was significantly lower with TXA at every perioperative interval in which transfusion occurred. Transfusion-independent hemoglobin and hematocrit values were significantly higher in the TXA group from 3 hours postoperatively onward. No thromboembolic events occurred in either group.

Conclusion: A single preincision 1 g intravenous dose of TXA significantly reduced blood loss, drainage, and transfusion requirements after uncemented THA without any observed increase in thromboembolic risk. These findings support incorporating intravenous TXA as a standard component of the perioperative blood management protocol for THA.

Keywords: tranexamic acid; total hip arthroplasty; perioperative blood loss; blood transfusion; antifibrinolytic agents; coxarthrosis.

Introduction

Hip osteoarthritis is one of the most common degenerative joint diseases and a leading cause of chronic pain, disability, and reduced quality of life worldwide, affecting an estimated 5-10% of people over 60 years of age[1,2]. The lifetime risk of developing symptomatic hip osteoarthritis approaches one in four, and approximately one in ten affected individuals will eventually require total hip arthroplasty (THA)[2,3]. Total hip arthroplasty is the only definitive treatment for advanced hip osteoarthritis and has been described as "the operation of the century" because of its reliability in restoring function and quality of life [4]. More than one million THA procedures are performed globally each year, a number projected to keep rising with population ageing[4,5].

Despite advances in prosthetic design, surgical instrumentation, and minimally invasive technique, THA remains associated with substantial perioperative blood loss, frequently exceeding 1000-2000 mL depending on the estimation method used[6,7]. Reported rates of allogeneic transfusion after THA vary widely, from roughly one-fifth to more than two-thirds of patients across published series[8-10], and allogeneic transfusion carries recognized risks including transfusion reactions, immunomodulation, pathogen transmission, and surgical site or periprosthetic infection[11,12].

Tranexamic acid (TXA) is a synthetic lysine analogue that competitively inhibits plasminogen activation, thereby limiting fibrinolysis at sites of vascular injury. It has a long track record of reducing blood loss and transfusion requirements in cardiac and other major surgery[13], and a growing body of orthopedic literature now supports its efficacy in THA[14,15]. However, published trials differ considerably in dosing, route, and timing of administration, and utilization patterns vary substantially across institutions, indicating that a single, universally accepted protocol has not yet been established[16,17].

We designed the present study to prospectively evaluate the effect of a single preincision intravenous dose of TXA on perioperative blood loss, transfusion requirements, and postoperative hematological recovery in patients undergoing primary uncemented THA, using a within-institution control group treated with an identical surgical protocol but without TXA.

Materials and methods

Study design and setting

This was a prospective, single-center comparative clinical study conducted at the University Clinic for Orthopedic Diseases, Skopje, within the University Clinical Center for Traumatology, Orthopedics, Anesthesiology, Reanimation, Intensive Care and Emergency Center (TOARILUC), between 2023 and 2025. The study compared perioperative blood loss and related outcomes between patients who received intravenous TXA during THA and patients who underwent an identical procedure without TXA.

Participants

Eighty adult patients with a clinical and radiographic diagnosis of coxarthrosis, indicated for primary elective unilateral uncemented THA, were enrolled and randomly stratified into an experimental group (EG, n = 40, receiving TXA) and a control group (CG, n = 40, no TXA). Inclusion criteria were: adult patients of either sex undergoing unilateral primary elective uncemented THA for hip osteoarthritis; American Society of Anesthesiologists (ASA) physical status I–III; normal hematological, electrolyte, and hemostatic status; and written informed consent. Exclusion criteria included known TXA allergy, coagulopathy, any prior thromboembolic event, receipt of fresh frozen plasma or other hemostasis-altering products within 24 hours preoperatively, severe cardiac, renal, or hepatic

insufficiency, active joint infection or osteomyelitis, known malignancy, rheumatoid arthritis, planned use of bone cement, a history of seizures, and current oral contraceptive use.

Surgical technique and TXA protocol

All procedures were performed under spinal anesthesia with the patients in supine position, using a modified Watson-Jones anterolateral approach. Patients in the control group did not receive antifibrinolytic agent. Patients in the experimental group received 1 g (2 × 5 mL ampoules) of intravenous TXA by slow infusion (1 mL/min) before skin incision, corresponding to standard local fibrinolysis-prevention dosing rather than weight-based dosing. All patients received a single active Redon drain and standardized antibiotic and thromboprophylactic regimens (third-generation intravenous cephalosporin 1 hour preoperatively; subcutaneous low-molecular-weight heparin from 24 hours postoperatively, weight-adjusted).

Data collection and blood loss calculation

Height, weight, and body mass index (BMI) were recorded preoperatively. Erythrocyte count, hemoglobin (Hgb), and hematocrit (Hct) were measured preoperatively and at 3 hours, 2 days, and 5 days postoperatively; values were additionally recalculated to remove the contribution of any transfused units, using the assumption that one unit of packed red blood cells raises Hgb by approximately 1 g/dL and Hct by approximately 3% [18,19]. Drain output was measured on the day of surgery and the first postoperative day using a digital scale. Total blood volume (TBV) was calculated using the Nadler formula [20], and total blood loss (TBL) using the Mercuriali algorithm, which multiplies TBV by the difference between preoperative and 5th postoperative day hematocrit and adds the volume of any transfused erythrocytes [21]. The indication for intraoperative transfusion was determined by the anesthesiologist; postoperative transfusion was indicated for Hgb below 9 g/dL or clinical signs of anemia (fatigue, palpitations, pallor, tachycardia, tachypnoea, hypotension).

Statistical analysis

Data were analyzed with SPSS, version 25.0 (IBM Corp., Armonk, NY). Distribution normality was assessed with the Kolmogorov–Smirnov and Shapiro–Wilk tests. Qualitative variables are presented as absolute and relative frequencies and were compared with the chi-square test; quantitative variables are presented as mean ± standard deviation (minimum–maximum) and were compared between groups with Student's t-test. Repeated-measures ANOVA with Bonferroni post-hoc correction was used to compare hematological values across the four perioperative time points within each group. Statistical significance was defined as $p<0.05$.

Results

Eighty patients were included (mean age 61.9±8.4 years, range 32-76; 39 men [48.75%], 41 women [51.25%]), 40 per group. The experimental group (EG, TXA) and control group (CG, no TXA) were statistically homogeneous for all baseline characteristics (Table 1).

Total blood loss, erythrocyte volume loss, and drain output were all significantly lower in the TXA group (Table 2). The between-group difference in total blood loss (mean difference 816.6 mL) and erythrocyte loss (mean difference 279.0 mL) were the largest and most significant effects observed.

Table 1. Baseline demographic and clinical characteristics

Characteristic	EG (TXA), n = 40	CG (no TXA), n = 40	p-value
Male sex, n (%)	19(47.5)	20(50.0)	0.823
Age, years (mean ± SD)	62.1±8.5	61.6±8.4	0.800
BMI, kg/m² (mean ± SD)	29.47±3.8	30.12±5.2	0.525
Total blood volume, mL (Nadler)	4637.7±698.1	4797.9±846.3	0.360
Preop. erythrocytes, $\times 10^{12}$/L	4.62±0.44	4.68±0.39	0.496
Preop. hemoglobin, g/L	136.90±12.9	138.77±12.8	0.516
Preop. hematocrit, %	41.29±4.0	40.98±4.0	0.717

EG-experimental group (received TXA), CG-control group, BMI-body mass index, SD-standard deviation

Table 2. Perioperative blood loss and drainage outcomes

Outcome	EG (TXA)	CG (no TXA)	p-value
Drain volume, day 0, mL	346.3±147.9	446.9±170.1	0.006
Drain volume, day 1, mL	220.6±106.8	233.6±119.4	0.610
Total drain volume, mL	564.5±210.7	679.8±207.6	0.016
Erythrocyte volume loss, mL	486.1±198.5	765.1±254.7	<0.001
Total blood loss (Mercuriali), mL	1327.9±553.6	2144.5±727.4	<0.001

Values are mean ± SD. Total blood loss calculated with the Mercuriali algorithm

A total of 48 red-cell transfusions were administered across both groups; only 9(18.8%) were given to EG patients, *versus* 39(81.2%) to CG patients (Table 3). Significantly fewer EG patients required transfusion intraoperatively (5% *vs*. 37.5%, p<0.001) and postoperatively (17.5% *vs*. 60%, p<0.001).

Total units transfused reflects the sum across all patients in each group and was not subjected to a separate significance test.

Table 3. Blood transfusion requirements

Transfusion outcome	EG (TXA)	CG (no TXA)	p-value
Intraoperative transfusion, n (%)	2(5.0)	15(37.5)	<0.001
Postoperative transfusion, n (%)	7(17.5)	24(60.0)	<0.001
Any transfusion, day 0, n (%)	1(2.5)	12(30.0)	<0.001
Total units transfused, n	9	39	—

Because raw (non-adjusted) hemoglobin and hematocrit values were confounded by unequal transfusion rates between groups, we additionally analyzed transfusion-independent values (i.e., values recalculated as if no transfusion had occurred). These values were significantly higher in the TXA group from 3 hours postoperatively through postoperative day 5 (Table 4), confirming a true pharmacological effect independent of replacement therapy.

Table 4. Transfusion-independent hemoglobin and hematocrit values

Time point	Parameter	EG (TXA)	CG (no TXA)	p-value
3 h postop.	Hgb, g/L	119.60±12.1	112.95±14.9	0.031
3 h postop.	Hct, %	36.0±3.8	33.0±4.4	0.002
Day 2	Hgb, g/L	106.95±13.8	99.55±13.2	0.016
Day 2	Hct, %	31.55±4.0	29.41±4.0	0.023
Day 5	Hgb, g/L	106.20±11.9	94.80±13.0	<0.001
Day 5	Hct, %	31.44±3.7	27.86±3.9	<0.001

Hgb-hemoglobin, Hct-hematocrit. Values recalculated to remove the estimated contribution of transfused units.

The overall decline in Hgb from preoperative baseline to postoperative day 5 (uncorrected for transfusion) was similar between groups in relative terms (-20.8% in EG *vs*. −24.7% in CG), reflecting the fact that the apparent recovery in the control group was

substantially supported by a far greater volume of transfused blood. No intraoperative or postoperative thromboembolic complications were recorded in either group.

Discussion

In this prospective comparative study, a single preincision 1 g intravenous dose of TXA was associated with substantially lower total blood loss, erythrocyte loss, drain output, and transfusion requirements after primary uncemented THA, with no observed increase in thromboembolic complications. These findings are consistent with the broader literature on antifibrinolytic use in arthroplasty. The 2011 systematic review and meta-analysis by Sukeik *et al*., pooling 11 randomized trials, found that TXA significantly reduced intraoperative and postoperative blood loss and transfusion requirements in THA without increasing thromboembolic risk[14]. Similarly, the 2018 network meta-analysis by Fillingham *et al*., commissioned to support combined clinical practice guidelines of several North American orthopedic and anesthesia societies, concluded that TXA reduces blood loss and transfusion in primary THA regardless of the specific dosing regimen used[15].

Our transfusion rates (18.8% in the TXA group *vs*. 81.2% in the control group, expressed as a share of all transfusions administered) are broadly consistent with, if numerically more pronounced than, previously reported reductions. Gómez Barbero *et al.,* in a prospective randomized study comparing intravenous and intra-articular TXA in THA, likewise found significantly reduced postoperative drainage with intravenous administration, although their absolute drain volumes were lower than ours, which the authors attributed to weight-based (15 mg/kg) rather than fixed-dose administration[22]. This raises the possibility that a weight-adjusted regimen could further improve hemostatic control in some patients, a question our fixed-dose protocol cannot address.

The safety profile observed here is consistent with recent large-scale evidence. Thapaliya *et al*., in a matched cohort analysis of 144,344 THA patients, found no increase in venous thromboembolic events associated with TXA use[16]. Richardson *et al*., analyzing a large administrative database including patients with a prior history of venous thromboembolism, similarly found that TXA use was not associated with increased postoperative pulmonary embolism, stroke, or myocardial infarction, even in this higher-risk subgroup[23]. While our sample size is too small to detect rare thromboembolic events, the complete absence of such events across 80 patients is consistent with, and does not contradict, this reassuring safety signature.

Beyond clinical outcomes, reduced transfusion needs carry economic and systemic implications. Gillette *et al*., found that routine TXA use in primary hip and knee arthroplasty reduced mean direct hospital costs by several hundred US dollars per patient, driven by reduced blood and laboratory costs that outweighed the modest additional pharmacy expense[24]. Although cost data specific to our healthcare system were not collected, the substantial reduction in transfused units we observed (9 *vs*. 39 units) suggests a comparable resource-sparing effect, with the additional benefit of preserving blood bank inventory for patients in more urgent clinical need.

This study has several limitations. It was conducted at a single center with a fixed, non-weight-adjusted intravenous dosing regimen, limiting generalizability to other dosing strategies (topical, oral, or weight-based intravenous). The sample size, while adequate to detect the primary blood loss outcomes, is underpowered to assess rare adverse events such as venous thromboembolism. Follow-up was limited to the early postoperative period, precluding assessment of longer-term functional or safety outcomes. Finally, although allocation was stratified and groups were well balanced at baseline, this was a comparative rather than a formally blinded and centrally randomized trial, which may introduce a degree of allocation-related bias.

Future research should compare single-dose against repeated-dose intravenous regimens, directly compare intravenous, topical, and combined administration within the same population, and extend follow-up to capture functional recovery, thromboembolic events, and cost-effectiveness over a longer horizon, including patients with renal impairment or a prior thromboembolic history who remain underrepresented in the TXA literature.

Conclusion

A single preincision 1 g intravenous dose of tranexamic acid significantly reduced total blood loss, erythrocyte loss, drain output, and transfusion requirements in patients undergoing primary uncemented total hip arthroplasty, with a favorable safety profile and no observed thromboembolic complications. These results support the incorporation of intravenous TXA as a standard, low-cost component of perioperative blood management protocols for THA.

Declarations

Ethics approval and consent to participate: All patients provided written informed consent for both the surgical procedure and study participation, in accordance with the principles of good clinical practice. [Institutional ethics committee name and approval number to be inserted by the authors.]

Author contributions: D.D. designed the study, collected data, and drafted the manuscript. A.S. contributed to [role to be confirmed by the authors, e.g., study conception, data analysis, or manuscript review]. V.M. supervised the study as mentor, contributed to study design, and critically revised the manuscript. All authors approved the final version. Author order and specific contributions should be confirmed against ICMJE authorship criteria before submission.

Conflict of interest statement. None declared.

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