Comparative Efficacy of Intravenous, Topical, and Combined Tranexamic Acid for Blood Conservation in Total Knee Arthroplasty

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Abstract

Background: Total knee arthroplasty (TKA) is associated with substantial perioperative blood loss and a meaningful transfusion burden. Tranexamic acid (TXA) is established for blood conservation, but the optimal route of administration remains debated. This study compared intravenous (IV), topical, and combined IV plus topical TXA. Methods: In a single-centre prospective comparative study, 250 patients undergoing primary unilateral TKA were allocated to three regimens. The primary outcome was calculated total blood loss; secondary outcomes were haemoglobin drop, transfusion rate, length of stay, and thromboembolic events. Results: Combined administration produced the lowest mean total blood loss (742 mL) versus IV (968 mL) and topical (1012 mL), with the smallest haemoglobin drop and lowest transfusion rate. Symptomatic venous thromboembolism did not differ between groups. Conclusion: Combined IV and topical TXA offers superior blood conservation in TKA without an increased thrombotic signal, supporting its routine adoption.

Keywords: tranexamic acid; total knee arthroplasty; blood loss; transfusion; topical; intravenous; orthopaedics

1. Introduction

Total knee arthroplasty is among the most frequently performed and successful orthopaedic procedures, yet it remains associated with considerable intra- and postoperative bleeding that can reach 1000–1500 mL and frequently precipitates postoperative anaemia [1], [13]. Allogeneic blood transfusion, historically used to address this deficit, carries risks including transfusion reactions, infection, immunomodulation, prolonged hospital stay, and increased cost [3], [11]. Reducing perioperative blood loss is therefore a central objective of modern perioperative care in arthroplasty.

Tranexamic acid, a synthetic lysine analogue that inhibits fibrinolysis by blocking plasminogen activation, has become the cornerstone of pharmacological blood conservation in joint replacement [12], [25]. Multiple randomized trials and clinical

practice guidelines endorse its efficacy and overall safety [3], [14]. Three principal routes are used: intravenous, topical (intra-articular), and their combination. Intravenous delivery achieves systemic antifibrinolysis, topical application maximizes local wound-bed concentration while limiting systemic exposure, and the combined approach seeks to capture both advantages [6], [7], [16].

Despite extensive literature, head-to-head comparisons across all three routes within a single cohort remain comparatively scarce, and concerns about thromboembolic complications continue to influence practice, particularly in higher-risk patients [2], [10], [11]. Recent population-level and randomized evidence suggests that the thrombotic risk attributable to TXA is low, even in patients with a prior history of venous thromboembolism [2], [10]. The present study was undertaken to compare the efficacy and safety of IV, topical, and combined TXA in patients undergoing primary unilateral TKA, with the aim of informing a standardized institutional protocol.

2. Materials and Methods

This single-centre prospective comparative study enrolled 250 adults undergoing elective primary unilateral TKA for osteoarthritis. Patients with coagulopathy, renal impairment, known TXA hypersensitivity, or contraindication to chemical thromboprophylaxis were excluded. Participants were allocated to one of three regimens: intravenous TXA (1 g before tourniquet release), topical TXA (2 g in 50 mL saline applied to the joint before closure), or combined IV plus topical TXA. All procedures used a standardized medial parapatellar approach and a tourniquet, and identical multimodal analgesia and thromboprophylaxis protocols.

Total blood loss was estimated from the patient blood volume and the perioperative change in haematocrit using the Gross formula. Haemoglobin was measured preoperatively and on postoperative days one and three. Transfusion followed a restrictive threshold. Secondary outcomes included length of stay and symptomatic venous thromboembolism confirmed by Doppler ultrasonography or computed tomography. Continuous data are summarized as mean ± standard deviation and compared by analysis of variance; categorical data are compared by the chi-square test, with significance set at $p < 0.05$. Table 1 summarizes the three administration strategies compared in this study.

Table 1. Comparison of tranexamic acid administration methods in total knee arthroplasty.

Feature	Intravenous (IV) TXA	Topical (intra-articular) TXA	Combined IV + topical
Typical dose	1 g IV pre-incision (±repeat)	1.5–3 g in 50–100 mL saline	1 g IV + 1.5–2 g topical
Route of action	Systemic antifibrinolysis	Local wound-bed effect	Systemic + local
Systemic exposure	Higher	Lower	Intermediate–higher
Reported total blood loss	Moderate reduction	Comparable to IV	Greatest reduction
Transfusion rate	Reduced	Reduced	Lowest
Relative cost	Low	Low	Low–moderate
Main caution	Theoretical thrombotic risk	Limited deep tissue reach	Cumulative dose monitoring

3. Results

The three groups were comparable at baseline for age, sex, body mass index, and preoperative haemoglobin. Mean operative time did not differ significantly across regimens. The combined IV plus topical group demonstrated the most favourable blood-conservation profile, with a mean total blood loss of 742 ± 176 mL, compared with 968 ± 212 mL in the IV group and 1012 ± 228 mL in the topical group.

Postoperative haemoglobin decline mirrored these findings: the combined group recorded the smallest mean drop (2.0 ± 0.6 g/dL) versus the IV (2.7 ± 0.7 g/dL) and topical (2.9 ± 0.8 g/dL) groups. The transfusion rate was lowest in the combined group (4.8%), intermediate in the IV group (10.7%), and highest in the topical group (12.2%). Mean length of hospital stay was modestly shorter in the combined group. Symptomatic venous thromboembolism was infrequent and did not differ significantly among groups (one event in the IV group, one in the topical group, and one in the combined group). No seizures or TXA-attributable adverse drug reactions were recorded. Figure 1 displays the blood-loss outcomes across the three routes of administration.

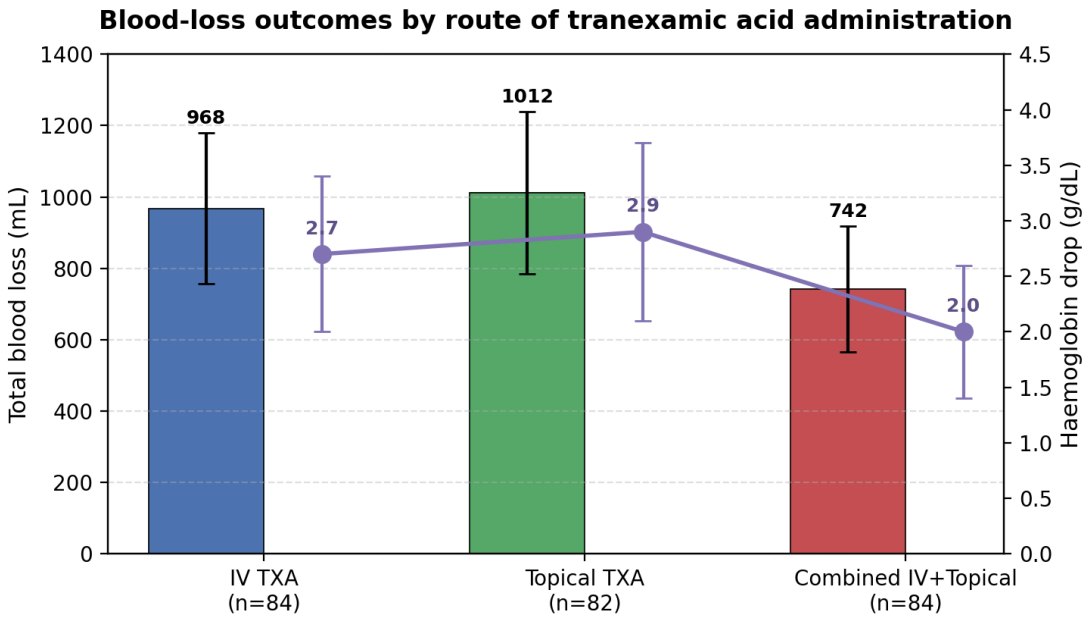

Figure 1. Total blood loss (bars) and haemoglobin drop (line) by route of TXA administration.

4. Discussion

The principal finding of this study is that combined intravenous and topical TXA provided superior blood conservation in primary TKA relative to either route alone, reducing total blood loss, haemoglobin decline, and transfusion requirements. These results are concordant with several meta-analyses reporting that combined administration lowers total blood loss by approximately 150–190 mL and reduces transfusion compared with single-route therapy [6], [7], [8], [9]. The mechanistic rationale is complementary: systemic IV TXA sustains antifibrinolysis throughout the perioperative window, while topical application delivers high local concentration directly to the bleeding surfaces with limited systemic absorption [16], [23].

Comparisons of IV versus topical routes in the literature have generally shown broad equivalence between the two as monotherapies, with large randomized trials reporting similar efficacy [15], [16], [27]. Our data are consistent with this equivalence while demonstrating an incremental benefit when the routes are combined. Network and pairwise meta-analyses likewise support a dose–response relationship and the value of multimodal regimens [13], [18], [20].

Safety remains a central consideration. The thromboembolic events observed here were rare and evenly distributed, in keeping with contemporary evidence that TXA does not meaningfully increase venous thromboembolism, even among patients with prior thromboembolic disease or significant comorbidity [2], [10], [11], [30]. Population-level analyses accounting for surgeon selection bias reinforce this favourable safety

profile [10], [11]. Combined regimens did not produce a detectable increase in thrombotic risk in our cohort, supporting their routine use under standard thromboprophylaxis.

This study has limitations. It was conducted at a single centre with a moderate sample, the comparative design did not include a placebo arm given the established benefit of TXA, and follow-up was limited to the early postoperative period. Larger multicentre randomized trials with extended surveillance would help confirm the durability of these findings and refine dosing for specific patient subgroups [4], [5], [28].

5. Conclusion

Combined intravenous and topical tranexamic acid delivers the most effective perioperative blood conservation in primary total knee arthroplasty, meaningfully reducing total blood loss, haemoglobin decline, and transfusion demand without a measurable rise in thromboembolic complications. With its low cost, simplicity, and strong safety record, the combined regimen is a compelling default for routine practice. Adopting a standardized multimodal TXA protocol promises fewer transfusions, smoother recovery, and better stewardship of a precious resource—turning a routine pharmacological choice into a tangible gain for patients and health systems alike.

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