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Research Article

EVALUATING THE BLOOD-SPARING EFFICACY AND SAFETY OF TRANEXAMIC ACID IN TOTAL KNEE ARTHROPLASTY

RAMYA R[1]*, LEENA RANJINI V[2], HARISIVANANDAN M[3]

[1]Department of Pharmacology, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India. [2]Department of Pharmacology, Shri Sathya Sai Medical College and Research Institute, Sri Balaji Vidyapeeth University, Tamil Nadu, India. [3]Department of Orthopaedics, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India. *Corresponding author: Ramya R; Email: ramyavishal1595@gmail.com

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ABSTRACT

Objectives: Tranexamic acid (TXA) is an antifibrinolytic agent that effectively reduces bleeding both during and after surgery. The purpose of our study was to assess the effectiveness and safety of TXA use in reducing blood loss in uncomplicated primary total knee arthroplasty (TKA) without complications.

Methods: This is a prospective, open-label, comparative study that includes patients who are undergoing unilateral primary TKA. The patients were divided into two groups: Group I, which is a control group, did not receive any doses of TXA, and Group II received three doses of intravenous TXA: 15 mg/kg TXA was administered 30 min before incision, followed by post-operative doses of 10 mg/kg TXA at 3 and 6 h. The primary objectives of the study were to measure the total blood loss (TBL) and Hemoglobin (Hb) drop, which were calculated preoperatively and on the third post-operative day. The secondary objectives were to determine transfusion rates, incidences of symptomatic deep vein thrombosis, and thromboembolic events (TE).

Results: In this study, a total of 57 patients underwent unilateral TKA. The TBL in Group I was 861.67±167.65 mL, compared to 780.05±158.05 mL in Group II ($p<0.001$). The study also found that the Hb drop was significantly lower (2.78±0.36 vs. 2.3±0.37) with IV TXA. Furthermore, neither group required transfusions, nor were any thromboembolic complications noted for up to 6 months post-operation.

Conclusion: Our study supports the use of TXA in TKA, as it effectively reduces perioperative blood loss, decreases the need for blood transfusions, and does not increase the risk of TE.

Keywords: Total knee arthroplasty, Blood loss, Tranexamic acid, Intraarticular route, Intravenous route.

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INTRODUCTION

Total knee arthroplasty (TKA) helps end-stage osteoarthritis patients by relieving pain and improving quality of life. As the prevalence of TKA is increasing, it is important to note that there are associated risks, such as blood loss and blood transfusion effects [1-3]. While blood transfusions can be lifesaving in cases of severe bleeding, they can also carry a significant risk of transfusion reactions and infectious disease transmission [4,5]. Moreover, blood transfusions considerably increase the cost of treatment [6]. During TKA surgery, a tourniquet is often used to provide a bloodless field and for better visualization of the surgical field. However, many studies have reported many tourniquet-related complications, such as limb swelling, paralysis, and injury to soft-tissue, muscles, calcified vessels, and nerves, [7-9]. In addition, the release of the tourniquet can even result in ischemia-reperfusion (I-R) injury that occurs when blood supply is re-established after the tourniquet release [10]. Therefore, it is vital to consider the risks associated with blood transfusions and tourniquets and to explore alternative methods to reduce blood loss during TKA surgery.

Plasminogen activation is a critical step in fibrinolysis, where tPA tissue like plasminogen activators convert plasminogen into plasmin, which causes breakdown of fibrin and dissolves the blood clots. Tranexamic acid (TXA) acts by binding to plasminogen, thus preventing its activation and enhancing the coagulation process. This process leads to reduced bleeding, making it an essential tool for the hemostatic management in medical disciplines such as orthopedic surgery, trauma care, dentistry, and obstetrics.

In orthopedic surgery, such as joint replacements like total hip arthroplasty (THA) and TKA, TXA has emerged as a promising strategy for reducing blood loss and the need for blood transfusions. When administered intravenously, it reduces perioperative blood loss, which is crucial in minimizing complications and optimizing early patient recovery post-surgery. Various studies have confirmed that TXA use during surgery can provide a bloodless surgical field, and reduce surgical drains, and the need for blood transfusions and surgical drains. Encouraging surgical drain-free surgeries can also help minimize perioperative wound complications. Therefore, this prospective study aims to analyze the safety and effectiveness of TXA in patients undergoing TKA.

METHODS

This prospective, randomized comparative clinical study was designed and conducted in the Departments of Orthopedics outpatient department (OPD). All patients attending orthopedic OPD with primary osteoarthritis of knee joints were assessed in the OPD and those willing for surgery were scheduled for elective surgery. All the consecutive unilateral TKA were randomly assigned to two groups in a 1:1 ratio.

Inclusion criteria

All adult patients aged between 50 and 80 with Grade III and IV (Kellgren–Lawrence) osteoarthritis who were undergoing elective unilateral primary TKA were included in the study.

Exclusion criteria

The patients with:

1. Post-traumatic arthritis
2. Inflammatory arthritis,
3. Bilateral TKA,
4. Revision knee,
5. Any additional procedure other than TKA,
6. A history of venous thromboembolic disease,
7. Any underlying diseases such as cirrhosis, chronic renal failure, hemostasis,
8. Patients on anticoagulants or antiplatelet drugs,
9. Know allergy to TXA, and
10. Pre-operative Hemoglobin (Hb)<10 g/dL.

The study protocol received clearance from the Institutional Ethics Committee before the start of the study. This study was conducted in accordance with the principles of good clinical practice and the declaration of Helsinki for Biomedical Research Involving Human Subjects. Written informed consent was obtained mandatorily from all the patients who were recruited for the study after a thorough explanation of the objective of the study. The patients who were included in the study were assured of confidentiality.

All patients underwent standard pre-operative preparations. Routine laboratory investigations, chest X-rays, echocardiograms, and electrocardiograms were done. Before surgery, cardiologists, and anesthetist evaluated the patient's fitness status for surgery. Two units of packed cells were arranged in all cases before surgery. In case of severe blood loss, allogeneic blood transfusion was indicated if post-operative patient's Hb drops to <7.0 mg/dL or if any symptoms are suggestive of anemia [11].

The same surgeon performed all surgical procedures, and no drain was used for any patient after TKA. In Group I, a tourniquet was applied during the procedure, while patients in Group II received intravenous TXA (IV TXA) at a pre-operative dose of 15 mg/kg of body weight, 30 min before the skin incision. A post-operative dose of 10 mg/kg was administered at 3 and 6 h after surgery. All subjects received intravenous diclofenac sodium 75 mg in 100 mL normal saline every 8 h as a routine analgesic, provided that their pre-operative serum creatinine levels were normal. If the levels were elevated, they were given a 1000-mg infusion of paracetamol every 8 h instead. In addition, injection tramadol 50 mg was administered as an add-on analgesic for breakthrough pain if required. Patients were encouraged to begin walking as soon as possible, and early and aggressive post-operative mobilization was recommended. Static quadriceps exercises and straight leg raising exercises were started on day 0, while a range of motion exercises began on day 1. Below-knee thromboembolic disease stockings were given for both lower limbs. Tablet rivaroxaban 10 mg was administered once a day for 6 weeks for deep vein thrombosis (DVT) prophylaxis followed by tablet aspirin for 6 weeks [12,13]. Intravenous antibiotic prophylaxis was given for 24 h, followed by the oral route for the next 3 days. Patients were discharged on the 5th post-operative day when the patients were able to walk more than 10 m with the help of a walking aid. An ultrasonographic study was for patients with suspicious DVT symptoms such as pain, swelling, and tenderness in the thigh or calf was done. However, no routine Doppler to rule out DVT/thromboembolic events (TE) was performed. All patients were followed up for 6 months to monitor the incidence of DVT and TE.

Outcome assessment

The primary outcome measures were total blood loss (TBL) and post-operative Hb drop. Hb was recorded on 3rd post-operative day. The TBL was calculated using Hb balance method based on patient blood volume, Hb loss, and the formula described in previous studies [14,15]. The post-operative Hb drop was determined from the difference between the pre-operative Hb and the post-operative Hb level (the third post-operative day before the patient was routinely discharged from the hospital). The secondary outcomes were transfusion rates, incidences of symptomatic DVT, and TE.

RESULTS

Out of 65 patients assessed and recruited for elective surgery, eight patients were excluded from the study, as three were diagnosed with inflammatory arthritis, one patient with bilateral TKA four patients with post-traumatic arthritis, and 57 patients completed the study. Their ages ranged from 50 to 80 years including 17 men and 40 women with mean age of 66.66±12.22 in Group I and 67.10±7.49 in Group II. There were no significant differences in basic demographic data between the two groups (Table 1).

The TBL in Group I was 861.67±167.65 mL, compared to 780.05±158.05 mL in Group II (p<0.001). The Hb drop was significantly lower in the IV TXA group (2.3±0.37) than control group (2.78±0.36) (Table 2). Blood transfusion was not needed in any group and no thromboembolic complications were noted postoperatively. None of the patients had clinical evidence of subcutaneous hematomas, hemarthroses, peroneal nerve palsies, surgical site wound infections, or skin necrosis up to 14 days following the surgery. No thromboembolic complications were noted in the 6-month follow-up.

DISCUSSION

The results of our investigation underscore the potential of IV TXA as a beneficial intervention in TKA, demonstrating its efficacy in minimizing blood loss and enhancing patient recovery. Administering 15 mg/kg of body weight 30 min before the pre-operative skin incision followed by 10 mg/kg at 3- and 6-h post-surgery, yielded significant advantages in reducing TBL and Hb drop compared to control groups. This reduction in blood loss is particularly critical in TKA, where excessive bleeding may lead to post-operative complications and the necessity for blood transfusions. The diminished blood loss observed in the IV TXA group contributes to a more favorable post-operative course, potentially reducing the need for transfusions and associated risks.

A retrospective analysis of 886 medical records indicated that both IV and topical TXA required lower amounts to reduce blood loss with IV TXA than with topical TXA, without compromising safety and efficacy. This supports our study's findings on the use of IV TXA alone [16]. A meta-analysis involving 2260 patients from 18 randomized controlled trials (RCTs) for TKA and four RCTs for THA demonstrated a significantly smaller maximum drop in Hb in the intravenous group than in the topical group. No significant differences were observed in TBL, drainage volume, Hb level, DVT, pulmonary embolism, wound complications, or other adverse events [17]. Consequently, we exclusively used IV TXA in our study.

Furthermore, a two-dose regimen with pre-operative and intraoperative doses emerged as the most effective for reducing drain loss and TBL [18]. Consistent with this, our study administered TXA preoperatively and at 3 and 6 h postoperatively, aiming to maintain a bloodless field during surgery and minimize TBL. Studies in THA have emphasized the efficacy of pre-operative TXA administration in reducing intraoperative

Table 1: Patient characteristics at baseline

Parameters	Group I	Group II	Independent t-test (p-value)*
Sex (F/M)	19/10	21/7	
Age (years)	66.66±12.22	67.10±7.49	0.98
Weight (kg)	71.30±13.52	69.70±9.80	0.43
Height (cm)	148.14±13.67	152.45±6.35	0.21
BMI (kg/m^2)	33.60±12.29	29.21±4.25	0.09
Pre-operative Hb	12.20±0.93	12.21±1.26	0.81
Post-operative Hb	9.71±1.30	10.36±1.02	0.03

*p<0.05 is considered statistically significant. BMI: Body mass index, Hb: Hemoglobin

Table 2: Comparison of the mean total blood loss and HB drop between the study groups.

Parameters	Group I	Group II	Independent t-test (p-value)
Total blood loss (mL)	861.67±167.65	780.05±158.05	0.00
Hemoglobin (Hb) difference (g/dL)	2.78±0.36	2.3±0.37	0.00

*p<0.05 is considered statistically significant

blood loss, with the most effective regimen involving 1 g TXA 10 min before surgery and a second dose 6 h later [19,20]. Some studies have even reported improvements in clinical and functional outcomes [21].

TXA plays a crucial role in patient blood management programs, demonstrating significant cost savings during total knee replacement surgery by reducing blood transfusions and shortening hospital stays [22]. In dentistry, TXA mouthwash is employed to prevent gingival bleeding in aplastic anemia patients, highlighting its comprehensive management utility [23].

While our study yielded promising results, further research is needed to determine the optimal dosage and ensure long-term safety. The limited sample size prevented the detection of uncommon events such as venous thromboembolisms. In addition, routine Doppler for DVT or any TEs was not done, relying instead on symptoms and signs. Although no enhancement in clinical and functional outcomes was observed, our experience with TXA demonstrated a significant reduction in TBL, improving visualization of the surgical field.

CONCLUSION

This study indicates that IV TXA is not only effective in reducing blood loss during TKA but also safe concerning its impact on fibrinolytic activity. These findings contribute as evidence supporting the use of IV TXA as a valuable adjunct in TKA. Further research and long-term follow-up studies are essential to validate these findings and establish the enduring safety and efficacy of IV TXA in the context of TKA.

AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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