A comparative study of local application versus intravenous application of tranexamic acid preoperatively in cases of total hip arthroplasty

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Received: 12-May-2024
Revised: 02-Jun-2024
Accepted: 07-Jun-2024
Published: 13-Sep-2024

The Egyptian Orthopaedic Journal 2024, 59:261–265

Background
One of the biggest issues associated with total hip arthroplasties is the amount of blood loss and the need for blood transfusions. Tranexamic acid (TXA) has been proven to decrease the amount of blood loss associated with these operations. However, there is no consensus regarding the best method of TXA application. Classically, TXA had been given through the intravenous route, however, recent papers have advocated local usage. This study aimed to compare the outcomes between both local and intravenous applied TXA and determine which had less blood loss and adverse effects.
Results
Fifty patients were included in this study and were split into two groups. Group A was given local TXA, while group B took intravenous TXA. Blood loss showed no significant difference between the two groups. There were no significant differences in the incidence of adverse effects however, group B had one case of deep venous thrombosis and one case of superficial thrombosis.
Conclusion
Both local and intravenous applied TXA help decrease blood loss. There is no significant difference between the two groups in blood loss however deep venous thrombosis cases were observed in the intravenous group. In cases with a high risk of vascular thrombosis undergoing total hip arthroplasty, we would suggest applying TXA locally.

Keywords:
surgical blood loss, total hip arthroplasty, tranexamic acid

Egypt Orthop J 2024, 59:261–265

1110-1148

Introduction

Since its introduction in the 1960s, total hip arthroplasty (THA) has revolutionized the management of debilitating hip disorders, offering relief and improved quality of life with favorable long-term outcomes. In recent practice, an increasingly younger demographic seeks THA with the expectation of resuming high-demand activities, thereby elevating the functional demands placed on surgical intervention [1].

Despite advancements in surgical techniques, significant perioperative blood loss remains an inherent challenge of THA. Reports suggest an average intraoperative blood loss of ~1500 ml, underscoring the clinical importance of effective blood management strategies [2].

The administration of homologous blood transfusions, while a conventional response to blood loss, carries inherent risks, including the potential for immunologic reactions and transmission of infectious diseases [3]. Tranexamic acid (TXA) operates as an antifibrinolytic agent by inhibiting the activation of plasminogen to plasmin, the primary enzyme responsible for fibrin degradation. During total hip replacement surgery, TXA's mechanism of action helps maintain the integrity of the formed blood clot, thereby significantly reducing perioperative bleeding and the need for subsequent blood transfusions [4]. Several clinical trials have found TXA to be an effective method in decreasing blood loss [5–7]. However, there is still no consensus on the best method of application, whether it be injected locally intracapsular or intravenously. In light of these concerns, this study aims to conduct a comparative analysis of the efficacy of TXA when applied locally versus intravenously in THA. The primary objective is to ascertain which method is more efficacious in reducing blood loss, minimizing the necessity for blood transfusions, and mitigating the risk of thromboembolic complications associated with the procedure.

Patients and methods

Patients

This randomized comparative study was conducted from April 2022 to April 2023, encompassing 50 patients scheduled for total hip replacement. The participants were prospectively allocated into two equal groups of 25 based on the administration route of TXA.

Group A: local application group.

Group B: intravenous application group.

Randomization was achieved through a simple method, assigning patients to groups based on even and odd numerical order. Before inclusion, informed consent was obtained from each participant, detailing the study's nature, procedures, potential benefits, and risks. The study followed the CONSORT guidelines for randomized controlled trials, and the study protocol received approval from the Cairo Faculty of Medicine Ethics Committee.

Inclusion criteria

(1) Advanced osteoarthritis:
   (a) Primary osteoarthritis.
   (b) Secondary osteoarthritis (posttraumatic, osteonecrosis, and rheumatoid arthritis).
(2) Fracture neck of femur.
(3) Weight range: 60–110 kg.
(4) Age range: 40–60 years fracture neck of femur.

Exclusion criteria

(1) Patients with anemia or coagulation abnormalities.
(2) Patients with allergy to TXA.
(3) Patients who were medically unfit for surgery.

Preoperative preparation

Each patient provided written informed consent, which included comprehensive information about the surgical procedure, anticipated benefits, and potential risks and complications.

A prophylactic dose of 1 g cefoperazone was administered preoperatively to mitigate the risk of surgical site infection.

Surgical technique

All surgical procedures were performed using a lateral approach. The choice of implant, including the size of its components (cup, head, and stem) and whether it was cemented or cementless (press-fit), was tailored to the individual needs of the patient.

Methods of tranexamic acid administration

Patients were randomly divided into two groups:

(1) Group A: patients allocated to the topical TXA group received an instillation of 60 ml of isotonic sodium chloride solution, which was augmented with 3 g of TXA. This solution was applied to saturate the hip joint cavity for a minimum duration of three minutes before its aspiration after the surgical procedure.
(2) Group B: intravenous application of TXA consisted of a dose of 30 mg/kg in 100 ml saline, administered intravenous over 15–20 min preoperatively.

The surgical technique, surgical team, preoperative, and postoperative management, and transfusion criteria were standardized across both groups.

Postoperative management

(1) Anticoagulant: enoxaparin 40 mg was administered subcutaneously as anti-thromboembolic prophylaxis daily for 2 weeks in both groups.
(2) Antibiotics: postoperative management included intravenous cefoperazone 1 g every 12 h for 2 days, followed by oral administration until suture removal. Antibiotic therapy was extended if signs of infection persisted.
(3) Drain: a suction drain was employed in all cases and removed after 48 h.
(4) Wound condition: wound assessment occurred during the initial 2 weeks postsurgery, with suture removal on day 14, permitting bathing and showering.

Method of evaluation

Outcome measures included:

(1) The volume of blood transfused.
(2) Variations in hemoglobin (Hb) levels over the postoperative period.
(3) Fluctuations in hematocrit levels over the postoperative period.

The estimated total blood loss was calculated as follows:

We estimated the initial patient blood volume (PBV) and employed the formula described by Nadler *et al.* [8]. The formula is as follows: PBV=k_1 times height^3+k_2 times weight+k_3 where (k_1), (k_2), and (k_3) are constants that differ based on sex and age, and height is in meters and weight in kilograms. Once the PBV was determined, we applied the method described by Liu *et al.* [9] to calculate the total blood loss. This method has been replicated in various peer-reviewed articles and is considered a reliable approach

for such measurements. The total blood loss was calculated using the following equation: total blood loss=PBV times ({Hb_{pre}−Hb_{post}} divided by {Hb_{ave}}). Where (Hb_{pre}) is the preoperative Hb concentration (Hb_{post}) is the lowest postoperative Hb concentration, and (Hb_{ave}) is the average of the two. This approach allowed us to accurately estimate both the Hb levels and the total blood loss, which are critical parameters for evaluating the efficacy of TXA in reducing perioperative blood loss in THA patients.

Additional evaluations encompassed the incidence of thromboembolic complications and infections.

Results

A total of 50 patients were included in our study. The demographic data is presented in Table 1. The mean patient age was 48.32 years in the local TXA group, while the intravenous group was 47.81 years. This study included 15 males and 10 females in the local TXA group, whereas the intravenous group included 14 males and 11 females. The mean BMI in the local TXA group was 27.68, while it was 28.12 for the intravenous group, which showed no significant variations between the two groups There were no significant differences between both groups in terms of smoking or associated comorbidities such as diabetes or hypertension (Table 1).

The group that received local TXA had a relatively larger Hb drop compared to the intravenous group both at 2 h and 2 days postoperatively. However, the difference was not statistically significant (Table 2).

The amount of estimated blood lost was found to have no significant difference although the local TXA group still had more blood loss compared to the intravenous group. Hematocrit level changes showed no significant difference between both groups either (Table 2).

The complication rate did not show any significant difference between the two groups, however, there was a case of deep venous thrombosis and a case of minor thromboembolism that were recorded in the intravenous TXA group (Table 2).

Discussion

TXA has consistently demonstrated efficacy in diminishing postoperative hemorrhage and the

Table 1 The demographic data and the distribution of comorbidities between the two groups

Variables	Local TXA (*N*=25)	Intravenous TXA (*N*=25)	*t*	*P*
Age (years) (mean±SD)	48.32±6.54	47.81±6.49	0.277	0.783
BMI (kg/m^2) (mean±SD)	27.68±2.76	28.12±2.83	0.557	0.581
Sex [*n* (%)]				
Female	10 (40)	11 (44)	0.082	0.775
Male	15 (60)	14 (56)		
Comorbidities [*n* (%)]				
Smoking	7 (28)	8 (32)	0.095	0.758
DM	2 (8)	4 (16)	0.758	0.384
HTN	4 (16)	5 (20)	0.136	0.713

DM, diabetes mellitus; HTN, hypertension; TXA, tranexamic acid.

Table 2 Hemoglobin and hematocrit levels preoperatively, 2 h and 2 days postoperatively as well as the amounts of blood loss and associated complications of each group

	Local TXA (*N*=25)	Intravenous TXA (*N*=25)	*t*	*P*
Hb levels preoperative (mean±SD)	12.25±0.413	12.17±0.532	0.594	0.555
Hb levels 2 h postoperatively (mean±SD)	11.48±1.63	11.61±1.84	0.264	0.793
Hb levels 2nd day postoperatively (mean±SD)	9.88±1.56	10.19±1.49	0.719	0.476
HCT preoperative (mean±SD)	40.82±3.72	41.13±3.57	0.301	0.765
HCT 2 h postoperatively (mean±SD)	37.4±4.56	38.1±4.32	0.557	0.580
HCT 2nd day postoperatively (mean±SD)	34.63±3.68	33.24±4.1	1.26	0.213
Blood loss 2 h (ml) (mean±SD)	469.3±108.7	427.2±94.3	1.46	0.150
Blood loss 2nd day (ml) (mean±SD)	615.45±145.6	594.82±123.4	0.541	0.591
Blood transfusion rate [*n* (%)]	5 (20)	2 (8)	1.5	0.222
Complications [*n* (%)]				
DVT	0	1 (4)	1.02	0.315
Minor thromboembolism	0	1 (4)	1.02	0.315
Allergy	0	0	–	–
Superficial infection	2 (8)	1 (4)	0.355	0.552

Hb, hemoglobin; HCT, hematocrit; TXA, tranexamic acid.

necessity for blood transfusions in the context of hip and knee arthroplasty, as evidenced by a multitude of studies [5–7,10,11]. Recent scholarly attention has been captivated by the exploration of topical TXA application in these surgical procedures [12,13]. Our investigation sought to compare the topical and intravenous administration of TXA, exploring closely the topical approach compared to the more substantiated systemic TXA's effectiveness.

TXA, a synthetic analog of the amino acid lysine, exerts its antifibrinolytic effect by obstructing the lysine binding sites on plasminogen molecules, thereby impeding the formation of plasmin and curtailing fibrinolysis [4]. Comprehensive reviews and meta-analyses have corroborated the role of intravenous TXA in reducing transfusion frequencies and blood loss in THA [10]. Nevertheless, the danger of thromboembolic events in patients at elevated risk undergoing arthroplasty casts a shadow over the safety profile of systemic TXA administration. In this view, topical TXA application emerges as a potentially safer modality, offering efficacy akin to its systemic counterpart but with markedly diminished systemic absorption, ostensibly reducing the likelihood of thromboembolic sequelae.

In our study, topical TXA was deployed, conferring the advantage of direct application at the surgical site, ensuring peak TXA concentration at the joint without associated systemic complications. Despite this, the literature remains scant on the utilization of topical TXA in THA, even as recent meta-analyses advocate for intravenous TXA to curtail postoperative blood loss in such procedures [5].

Our primary endpoint, estimated blood loss, revealed that patients receiving intravenous TXA exhibited an average reduction of ~20 ml in blood loss compared to their counterparts receiving local TXA. This is almost a very minimal difference. Notably, thromboembolic events were exclusively documented in the intravenous TXA cohort. This suggests that individuals predisposed to cardiac and thromboembolic complications could find an advantage in topical TXA. Topical TXA administration may not only serve as a viable alternative but could potentially be deemed superior for all patients undergoing hip replacement. This assertion is bolstered by the findings of Alshryda *et al.* [14] in a double-blind, randomized controlled trial, which attested to the effectiveness of topical TXA in mitigating blood loss and transfusion requirements in THA patients. Similarly, Yue *et al.* [13] conducted a randomized double-blind controlled study, unveiling that 3 g of topical TXA can significantly reduce blood loss, drainage output, transfusion rates, and Hb levels. Our study, however, showed that there is no significant difference in blood loss between the two groups. We recommend either method to be performed based on the surgeons' preference.

However, our study is not without its limitations. The efficacy of topical TXA is heavily dependent upon the watertight closure of the capsulotomy, which, if not achieved, could lead to an underestimation of blood loss. Furthermore, our estimation of blood loss is predicated on an indirect methodology, reliant on preoperative Hb levels and serial postoperative Hb measurements. Also recent methods for the application of TXA have developed for THA in the form of both combined systemic and topical TXA, which has shown to have promising results in reducing blood loss, which should be compared with further trials [15,16].

Acknowledgements

Author contributions: M.G. and A.O.S. took part in writing the main manuscript. A.S. took part in designing the study and writing the drafts. M.Y. and M.S. revised the manuscript and analyzed the data. A.A.A. collected data and proofread the work.

Financial support and sponsorship

Nil.

Conflicts of interest

None of the authors have anything to disclose.

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