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INTRAARTICULAR APPLICATION OF TRANEXAMIC ACID VERSUS CONTROL IN PRIMARY POSTERIOR SACRIFICE CEMENTED TOTAL KNEE REPLACEMENT

[*1]Muthanna Al-Hifadhi, [2]Salam Abbas Mizher and [3]Bassam Majeed Hameed

[1]Al-Rusafa Health Directorate, Baghdad, Iraq.
[2]Al-Abayachi, Al-Rusafa Health Directorate, Baghdad, Iraq.
[3]Al-Rusafa Health Directorate, Baghdad, Iraq.

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***Corresponding Author: Muthanna Al-Hifadhi**
Al-Rusafa Health Directorate, Baghdad, Iraq.

ABSTRACT

Background: Blood loss during and after total knee arthroplasty (TKA) can result in significant morbidity and often necessitates blood transfusions. Various strategies are employed to reduce perioperative bleeding. Among these, the use of anti-fibrinolytic agents such as tranexamic acid (TXA) has gained attention, particularly in joint replacement surgeries. Several studies have demonstrated a reduction in blood loss with TXA use, without a corresponding increase in thromboembolic events. **Aim of the Study:** This study aimed to evaluate the efficacy of topical tranexamic acid in reducing blood loss and transfusion requirements during and after cemented unilateral primary TKA. **Method:** A prospective randomized controlled trial was conducted involving 45 patients undergoing primary cemented TKA. Patients were randomized into two groups: one received 1.5 g of TXA in 35 ml of saline applied intraarticularly for five minutes at the end of surgery, and the other served as the control. Data collected included demographic variables, operation time, hospital stay duration, serial hemoglobin levels (preoperative, 24 and 48 hours postoperative), blood loss through superficial and deep drains, transfusion rates, and postoperative complications. **Results:** Patients in the TXA group demonstrated significantly smaller drops in hemoglobin levels at both 24 and 48 hours postoperatively. Drain output in both superficial and deep drains was significantly lower in the TXA group at all measured time points ($p<0.05$). Although fewer patients in the TXA group required transfusions (28% vs. 45%), this difference was not statistically significant. No thromboembolic complications were reported. **Conclusion:** Topical intraarticular tranexamic acid is a safe and effective method for reducing blood loss in TKA, with a trend toward reduced transfusion need.

KEYWORDS: Total knee arthroplasty, tranexamic acid, anti-fibrinolytic, intraarticular application.

INTRODUCTION

Total knee arthroplasty (TKA) is one of the most frequently performed orthopedic procedures and remains the gold standard for treating advanced knee osteoarthritis. Despite its high success rates, TKA is associated with significant perioperative blood loss, leading to common complications such as postoperative anemia, swelling, pain, prolonged hospital stay, and delayed rehabilitation.[1,2] Bierbaum et al. reported that patients undergoing TKA experience considerable blood loss and are transfused at rates between 11–21%.[3] Other studies have shown that intraoperative and postoperative bleeding, often reaching volumes of 600–1500 ml, increases transfusion rates up to 50% and contributes to extended hospital stays and patient morbidity.[4] The risk of bleeding has also been amplified by the widespread use of antiplatelet and anticoagulant medications to reduce thromboembolic complications in TKA patients. This is particularly concerning in individuals with limited tolerance to anemia, who may require transfusions, thereby increasing the risk of complications such as infections or graft-versus-host disease.[5] Blood transfusions have also been associated with prolonged recovery times and increased healthcare costs.[6] Therefore, minimizing perioperative blood loss is crucial for improving TKA outcomes. To address these challenges, several blood conservation strategies have been adopted, including the use of anti-fibrinolytic agents. Eubanks reported that intravenous tranexamic acid (TXA), a synthetic lysine analog, reduces the need for transfusion by up to 50% in orthopedic procedures.[7] TXA inhibits fibrinolysis by blocking the conversion of

plasminogen to plasmin, thus stabilizing clots.[8] Its effectiveness has been well documented across various surgical fields including cardiac, dental, gynecological, and trauma surgeries.[9] TXA can be administered intravenously or topically. While intravenous use is effective, topical (intra-articular) application is gaining favor due to its localized effect, reduced systemic absorption, and simplified administration.[10] Studies have consistently demonstrated that topical TXA reduces blood loss and transfusion requirements without increasing the risk of thromboembolic complications.[11] In a randomized controlled trial, Georgiadis et al. found no statistically significant difference in rates of DVT or PE between patients treated with topical TXA and controls.[12] Similarly, meta-analyses and randomized controlled trials have shown that TXA, when used intra-articularly, is both safe and effective.[11,13] Given the clinical importance of minimizing perioperative blood loss and the growing evidence supporting TXA's benefits, this study aims to evaluate the efficacy of intra-articular TXA application in reducing blood loss, maintaining postoperative hemoglobin levels, and limiting transfusion needs in patients undergoing primary TKA.

METHOD

This study was designed as a prospective randomized therapeutic trial conducted between July 1st, 2014 and October 1st, 2015 at Medical City Teaching Hospitals, specifically Shaheed Ghazi Al Hariri Teaching Hospital for Surgical Specialties and the Nursing Home Hospital. The study population included patients diagnosed with osteoarthritis scheduled for primary unilateral total knee arthroplasty (TKA) using a posterior-stabilized prosthesis through a conventional approach. A total of 70 patients were screened, and 45 eligible patients were randomized based on the day of hospital admission—odd days to the treatment group and even days to the control group. Data were collected using interviews, clinical and laboratory assessments, Doppler ultrasonography, and structured follow-up. The questionnaire covered demographic and clinical characteristics, operation time, hemoglobin levels (preoperative, 24 and 48 hours postoperative), drain output (superficial and deep) at multiple time points, blood transfusion needs, and postoperative complications. Doppler ultrasound was used selectively in patients with clinical suspicion of deep vein thrombosis (DVT), and all complications within six weeks postoperatively were recorded. Inclusion criteria were patients with osteoarthritis undergoing unilateral primary TKA and normal preoperative coagulation profiles. Patients were excluded for thromboembolic history, coagulopathies, renal or liver dysfunction, recent myocardial infarction, retinopathy, or if a constrained prosthesis was indicated. Antiplatelet agents were discontinued seven days preoperatively. Surgical procedures were performed under general anesthesia with a standard midline approach. Tourniquets were inflated to 350 mmHg and released approximately 60 minutes into the procedure. After implanting the cemented prosthesis, deep and superficial drains were placed. In the treatment group, 1.5 g of tranexamic acid (TXA) diluted in 35 ml of saline was injected intra-articularly via the deep drain, which was clamped for 6 hours. All patients received postoperative thromboprophylaxis with low molecular weight heparin for 10 days. Data were analyzed using SPSS version 20. Statistical tests included independent and paired t-tests, Mann-Whitney, Chi-square, and Fisher's exact test, with $p < 0.05$ considered significant. **Limitations:** Blood loss was measured only via drains, not accounting for total blood loss, and the TXA dosage used was not optimized across regimens, necessitating further study.

RESULTS

Both groups did not differed significantly regarding their age and weight, where the mean age of group received topical tranexamic acid was 61.4 ±7years and control group was 59.5±7 years. With regards to weight of the patients, the results reported that the weight of the group received topical TXA was 72.3±7kg and that of control group was 73.7±7 kg as shown in table 1.

Table 1: Mean of age and weight of both groups.

	Study groups	N	Mean	Std. Deviation
Age(years)	TXA	25	61.4	7.0
	Control	20	59.5	7.7
Weight(kg)	TXA	25	72.4	7.3
	Control	20	73.7	8.8

Gender distribution was not significantly different in both groups as shown in table 2.

Table 2: Gender distribution of studied groups.

			Gender	
			Male	Female
Study groups	TXA	Count	11	14
		% within Study groups	44.0%	56.0%
	Control	Count	9	11
		% within Study groups	45.0%	55.0%

The results of present study demonstrated there was no significant difference with regard to the operation time or days of stay in the hospitals, the mean time of operation for treatment group was 2.3±0.4 hours, and of control group was 2.4±0.3 hours. The days of stay in hospital were 5.2±1.1 days for treatment group and 5.3±1.0 days for control group as seen in table 3.

Table 3: Mean of operation time and hospitalization days of studied groups.

	Study groups	N	Mean	Std. Deviation
Operation time (hours)	TXA	25	2.3	0.4
	Control	20	2.4	0.3
Hospitalization (days)	TXA	25	5.2	1.1
	Control	20	5.3	1.0

Our finding revealed that there was no significant difference of mean hemoglobin level between groups at baseline (preoperative), where the mean values were 13.4±0.9 mg/dl, 13.3±0.7 mg/dl for therapeutic and control group respectively (table 4).

Table 4: Serial mean values of hemoglobin in both groups.

Time	Study groups	N	Mean mg/dl	Std. Deviation
Baseline	TXA	25	13.4	0.9
	Control	20	13.3	0.7
24 hours	TXA	25	12.1	0.8
	Control	20	11.1	0.6
48 hours	TXA	25	12.5	0.7
	Control	20	11.9	0.8

At twenty-four hours post operation, the mean value of hemoglobin was significantly reduced from baseline in control group in comparison to treatment group (11.1±0.6 mg/dl,12.1±0.8 mg/dl) respectively with mean difference from baseline for control group of 2.2±0.9 mg/dl and for treatment group of 1.3 ±0.8 mg/dl respectively and this difference was statistically significant (p=0.04,0.03 respectively). After forty-eight hours of operation the results also revealed significant difference between groups with regards to hemoglobin level, where the mean level of hemoglobin for control group was 11.9±0.8 mg/dl and for group received TXA was 12.5 ± 0.7 mg/dl with mean difference of 0.8 ±0.7, 0.4±0.4 mg/dl respectively from twenty-four hours of operation. As shown in table 5.

Table 5: Mean difference of hemoglobin level at 24, 48 hours' post-operative of both groups.

	Mean difference mg/dl	Std. Deviation	p-value
Baseline-24 hours(TXA)	1.3	0.8	0.03
Baseline-24hours(control)	2.2	0.9	
24-48 hours(TXA)	0.4	0.4	0.04
24-48 hours(control)	0.8	0.7	

On further analyses of presented data of both groups with regard to hemoglobin level at different time post operatively according to the gender of the patients, the results demonstrated no significant difference between groups according to the gender of the patients($p \geq 0.05$). The blood drained during the first 6 hours was significantly lower in the treatment group (40.8±34.1 *vs* 105±66.6 ml; (p=0.001), the significant difference also recorded on first and second day post-operative between groups and the blood drained by superficial drain was lower in treatment group in comparison to control group (p value=0.001, 0.002) respectively as shown in table 6. No significant difference was reported on further analyses of data according to the sex of the patients.

Table 6: Mean of superficial drain output on serial time for both groups.

Superficial drain	Study groups	N	Mean/cc	Std. Deviation	p-value
After 6 hours	TXA	25	40.8	34.1	0.001
	Control	20	105.0	66.6	
After 24 hours	TXA	25	68.8	44.1	0.001
	Control	20	190.0	109.2	
After 48 hours	TXA	25	106.5	80.8	0.002
	Control	20	210.0	113.0	

The blood drained by deep drain during the first 6 hours was significantly lower in the treatment group (106.6±76.5 *vs* 175±1111.5 ml; (p=0.01), the difference become highly significant on first and second day of post-operative days between groups and the blood drained by deep drain was much lower in treatment group in comparison to control group (p value=0.001, 0.001) respectivelyas shown in table 7. Also no significant difference was reported on analyses of data according to the sex of the patients as seen in table 7.

Table 7: Mean of serial output of deep drain for both groups.

Time	Study groups	N	Mean/cc	Std. Deviation	p-value
After 6 hours	TXA	25	106.6	76.5	0.01
	Control	20	175.0	111.5	
After 24 hours	TXA	25	141.6	90.6	0.001
	Control	20	345.0	117.9	
After 48 hours	TXA	25	197.6	107.7	0.001
	Control	20	425.0	116.4	

The results revealed a reduced the rate of blood transfusions in the tranexamic acid groups in comparison to control group, the results showed that only 16% of treatment group were need blood transfusion intraoperatively in comparison to 40% of control group, but this difference not reach the significant association (p=0.7) as seen in table 8.

Table 8: Rate of Intra-operative blood transfusion of both groups.

			Inter-operative transfusion of blood		P
			Yes	No	
Study groups	TXA	Count	4	21	0.7
		% within Study groups	16.0%	84.0%	
	Control	Count	8	12	
		% within Study groups	40.0%	60.0%	

Present study showed that 32% of treatment group need post-operative transfusion in comparison to 55% of control group, no significant association was reported (p=0.1) as seen in table 9.

Table 9: Rate of post- operative blood transfusion of both groups.

			post-operative transfusion of blood		P- value
			Yes	No	
Study groups	TXA	Count	8	17	0.1
		% within Study groups	32.0%	68.0%	
	Control	Count	11	9	
		% within Study groups	55.0%	45.0%	

DISCUSSION

Total knee arthroplasty (TKA) is frequently associated with significant intraoperative and postoperative blood loss, often necessitating blood transfusions.[14] Various blood conservation strategies, including use of pneumatic tourniquets, hypotensive anesthesia, cryotherapy, and local hemostatic agents, have been explored to minimize this loss.[15] Among these, tranexamic acid (TXA), an antifibrinolytic agent, has gained attention due to its ability to inhibit plasminogen activation and stabilize fibrin clots, thereby reducing bleeding. In this study, topical intraarticular application of TXA demonstrated a notable reduction in blood loss, as evidenced by higher postoperative hemoglobin levels and lower drain outputs compared to the control group. These findings align with previous reports by Mutsuzaki et al.[16], who showed that TXA administration through the drain with clamping significantly reduced total blood loss and transfusion rates. Although our study did not find a statistically significant reduction in transfusion rates (p≥0.05), the trend was clearly favorable for the TXA group. The concept of directly applying TXA into the surgical site has been supported since Akizuki et al.[17] reported its effectiveness in TKA as early as 1997. The rationale is that local application targets the bleeding surfaces, enhances clot stability, and reduces systemic absorption, potentially minimizing the risk of thromboembolic complications.[18,19] Ishida et al.[20] further supported this by showing reductions in joint swelling with intraarticular TXA use. Although intravenous TXA is effective, concerns about systemic thrombotic risk persist.[21] Wong et al. [11] demonstrated that topical TXA has up to 70% lower systemic absorption, suggesting it as a safer alternative. Studies by Seo et al.[10] and others have shown superior or equivalent efficacy of intraarticular TXA compared to intravenous routes. This localized delivery maintains therapeutic levels in the joint fluid for extended periods (up to 17 hours), enhancing hemostasis while minimizing systemic exposure.[22] Cost and simplicity also make topical TXA

attractive. Compared to fibrin sealants or erythropoietin, TXA is more cost-effective and easier to administer.[23] Moreover, avoiding transfusions is essential, as they are associated with postoperative infections (10–20% of cases) and increased morbidity and hospital stay.[11,24] Despite the overall safety, some studies have reported rare complications such as seizures with high-dose systemic TXA, especially in cardiac surgery.[25] Thus, the topical route may provide a safer alternative, particularly in elderly or high-risk patients. Interestingly, Chen et al.[26] noted that intraarticular TXA might be more effective in TKA than in total hip arthroplasty (THA), possibly due to tourniquet use in TKA, which concentrates bleeding postoperatively. Oral TXA has also shown promising results in reducing transfusion rates without increasing thrombotic risk.[27] Our findings support the growing body of evidence that topical TXA is an effective and safe strategy in TKA. With no thromboembolic events observed and significant reductions in blood loss, we advocate for its continued use. Nonetheless, further studies are needed to define the optimal dose, timing, and frequency of administration. Given the minimal thrombotic risk observed in the literature, wider adoption of TXA in TKA seems justified.[28]

CONCLUSION

Topical application of tranexamic acid into the surgical wound of patients undergoing total knee arthroplasty reduces postoperative bleeding in comparison to controls, resulting in to less decline in postoperative hemoglobin values.

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