

Role of intra-articular tranexamic acid in reducing blood loss in total knee arthroplasty

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Background

Total knee arthroplasty (TKA) is associated with postoperative blood loss. Tranexamic acid (TXA) administration is an effective strategy used to reduce the blood loss.

This study aimed to evaluate the effect of intra-articular injection of TXA on blood loss and transfusion rate after an elective TKA.

Patients and methods

This was a randomized controlled clinical trial adopted to fulfill the purpose of this study. The study was conducted at Benha Health Insurance Hospital and Benha University Hospitals. It was conducted on 42 adult patients who underwent an elective primary unilateral total knee arthroplasty (TKA) through midline incision with medial parapatellar approach after tourniquet application. Patients were categorized into two groups: control group (without TXA), and intra-articular (IA) group who received 1.5 gm of TXA in 10ml of normal saline injected into the joint after packing, lavage, hemostasis and closure of the muscle layer just before the deflation of the tourniquet to guarantee maintenance of the injected fluid inside the joint. Demographic data and age, sex, comorbidities, and preoperative hemoglobin levels were collected. The maximum hemoglobin decline was the primary outcome, while the drain's blood amount (cc/day), the rate of blood transfusion, and the duration of hospital stay were secondary outcomes.

Results

Patients who received Intra-articular TXA had statistically significant lower drop in hemoglobin level (0.99 ± 0.45 mg/dl) compared to their control group (2.14 ± 1.07 mg/dl) ($P < 0.001$).

Conclusion

TXA is a safe and efficient way to reduce overall blood loss in TKA patients, according to data from this study and the literature. Administration intraarticular seems to be significantly effective in reducing postoperative blood loss without increasing the risk of thrombotic events.

Keywords:

Hemoglobin drop; Hospital stay; Osteoarthritis; Total Knee Arthroplasty; Tranxamic acid

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Evidence level: Randomized controlled comparative study 'Level II'.

Introduction

Total knee arthroplasty is associated with postoperative blood loss necessitating allogeneic blood transfusion in 10% to 38% of patients [1].

The major causes of postoperative blood loss following total knee arthroplasty (TKA) can be attributed to surgical trauma that induces a considerable activation of both the coagulation cascade and local fibrinolysis; the latter is further enhanced by tourniquet release at the end of the surgical procedure [2].

Tranexamic acid (TXA) is an anti-fibrinolytic agent that reversibly binds to the lysine-blocking sites on

plasminogen as a synthetic derivative, which results in prevention of clot degradation [3].

Several studies have shown that intra-articular administration of the anti-fibrinolytic agent (TXA) reduces postoperative bleeding and the need of blood transfusion [4].

In view of these safety concerns, the usage of intra-articular injection of tranexamic acid in total knee arthroplasty was noticed to reduce postoperative bleeding, transfusion rate and relieve knee swelling. Yet,

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will not increase the hypercoagulable state associated with total knee arthroplasty [5].

The aim of the study was to evaluate the effect of intra-articular injection of TXA on blood loss and transfusion rate after an elective TKA, through a randomized clinical trial.

Patients and methods

This was a randomized controlled clinical trial. The study was conducted at Benha Health Insurance Hospital and Benha University Hospitals. It was conducted on 42 adult patients Who underwent an elective primary unilateral total knee arthroplasty (TKA)) through midline incision with medial parapatellar approach after tourniquet application.

Patients were randomly divided into two groups. The 1st group (21 patients) received intra-articular injection of TXA (1.5 gm). And the 2nd group (21 patients) with no intra-articular injection received. (Control group).

Patients included were adults 40 years old or more, primary osteoarthritis of the knee, post traumatic arthritis, rheumatoid arthritis, normal INR, APTT, PT values and Preoperative Hb level >10 gm/dl.

We excluded patients as Revision TKA, preoperative use of anticoagulant therapy within five days prior to surgery as aspirin 75 mg, history of arterial or venous thromboembolic disease such as (cerebrovascular accident, deep venous thrombosis, or pulmonary embolus), abnormal bleeding tendency or bleeding disorder as hemophilia, anemia, major comorbidities (ischemic heart disease, renal failure, hepatic failure, severe pulmonary disease and uncontrolled DM) and contra-indication for TXA use (active intravascular clotting process, acquired defective color vision, subarachnoid hemorrhage, hypersensitivity to TXA and hematuria).

After obtaining an informed consent, all patients were subjected to Pre-operative patient evaluation: All patients were fit and prepared for TKA.

Full present history was taken from patients: smoking, hypertension, diabetes, cardiac conditions, previous operation, DVT and the drugs regularly taken by the patients. For cardiac patients who are taking aspirin 5 mg. aspirin was stopped 5 days before operation day and shifted on low molecular weight heparin.

Preoperative full laboratory investigations is done for all patients as complete blood count, prothrombin time

and activity, partial thromboplastin time, INR, RBS, fasting and postprandial blood sugar, renal and liver functions and hepatitis markers.

This was done after approval of ethical committee of Benha University Hospital and Faculty of Medicine.

Forty two adult patients underwent an elective primary unilateral total knee arthroplasty were divided into two groups: First group (21 patients) received 1.5 gm of TXA in 10 ml of normal saline injected into the joint after packing, lavage, hemostasis and closure of the muscle layer just before the deflation of the tourniquet to guarantee maintenance of the injected fluid inside the joint (case group). And second group (21 patients) no intra-articular injection was received. (Control group).

Through a randomized controlled clinical trial; the results of the two groups are analyzed & compared in order to evaluate the efficacy of intra-articular TXA injections in reducing blood loss after TKA. All knees implanted with cemented knee replacement prosthesis for tibiofemoral articulation only (no patella replacement was done). Standard techniques of intra-operative hemostasis are used, ensuring adequate hemostasis.

Wounds were closed in layers over 16 gauge suction drain as shown in Fig. 1 and the drain is closed for 2 h in both groups.

Postoperative drain closure for 2 h after the operation, then the drain was opened for suction then removed on the third day. Patients were kept during the first 48 h

Figure 1



Wound closure over drain.

under observation, C.B.C was done 24 h and 48 h after surgery to evaluate Hb level, the lowest postoperative Hb level is recorded and continuous recording of the drain's output in patient's file. The assessor was blinded to the subject of study and randomization. A standard prophylaxis against venous thromboembolism in the form of subcutaneous injections of low molecular weight heparin is given to all patients once daily from day one postoperatively. During first visit in outpatient clinic evaluation of joint movement, overlying skin condition, clinical evaluation for DVT and X-rays were done.

Data were analyzed using statistical program for social science (spss) version 25.0. Paired sample t-test of significance was used when comparing between related samples. χ^2 test of significance was used in order to compare proportions between two qualitative parameters.

Results

A total of 42 patients were included in the study. The mean age of patients in the interventional group was 57.81 ± 13.80 years, while mean age of patients in the control group was 61.52 ± 4.18 years ($P=0.39$). Females formed 90.5% of the sample in the interventional group and 76.2% of the sample in the control group ($P=0.41$). one third of the patients in both groups had

chronic illnesses ($P=0.92$) mainly hypertension (four patients in the interventional group and five patients in the control group) and diabetes mellitus (three patients in the interventional group and two patients in the control group). (Table 1).

There was no statistically significant difference between hemoglobin level of the intervention group (12.31 ± 1.12) and control (12.66 ± 1.24) before receiving TXA. (Table 2).

Patients who received Intra-articular TXA had statistically significant lower drop in hemoglobin level (0.99 ± 0.45 mg/dl) compared to their control group (2.14 ± 1.07 mg/dl). (Table 3).

Patients who received Intra-articular TXA had statistically significant lower amount of redivac drainage (285 ± 64.718 ml) compared to their control group (540 ± 91.478 ml). (Table 4).

Patients who received intra-articular TXA had statistically significant lower need for blood transfusion (2 patients (9.5%)) compared to their control group (5 patients (23.8%)). Moreover, patients who received intra-articular TXA had statistically significant lower amount of transfusion units (1 ± 0.5 ml) compared to their control group (2.08 ± 0.61 ml). (Table 5).

Table 1 Baseline characteristics of studied patients

Variables	Type of injection		P value
	Intra-articular TXA control (n=21)	group (n=21)	
Age (years), mean*	57.81 ± 13.80	61.52 ± 4.18	0.39 ^a
Sex			
Male	2 (9.5)	5 (23.8)	0.41 ^b
Female	19 (90.5)	16 (76.2)	
Site of TKA			
Right	9 (42.9)	10 (47.6)	0.76 ^c
Left	12 (57.1)	11 (52.4)	
Comorbidities			
Absent	14 (66.7)	14 (66.7)	0.92 ^c
Present	7 (33.3)	7 (33.3)	
HTN	4 (19)	5 (23.8)	
DM	3 (14.3)	2 (9.5)	

P value are based on Man-Whitney U test. Statistical significance < 0.05.

P value are based on Fisher-Exact test. Statistical significance < 0.05.

P value are based on Chi square test. Statistical significance < 0.05.

Table 2 Comparison between two groups in regard to pre- operative Hb

Variables	Type of injection		P value
	Intra-articular TXA group (n=21)	control group (n=21)	
Preoperative Hb (mg/dl)			
Mean \pm SD	12.31 ± 1.12	12.66 ± 1.24	0.40 ^c
Median (range)	12.6 (10.3-14.3)	12.6	

P value are based on Man-Whitney U test. Statistical significance < 0.05.

Table 3 Comparison between the two groups in regard to amount of changes in Hb level

Variables	Type of injection		P value
	Intra-articular TXA group (n=21)	control group (n=21)	
Drop in Hb level			
Mean±SD	0.99±0.45	2.14±1.07	<0.001 ^a
Median (range)	0.8 (0.4 -2. 1)	3.2 (0.8 -5)	

Table 4 Comparison between the two groups in regard to total redivac drainage

Variables	Type of injection		P value
	Intra-articular TXA group	(n=21)control group (n=21)	
Amount of redivac drainage (ml)			
Mean±SD	285±64.718	540±91.478	<0.001 ^a
Median (range)	250–500	400–700	

P value are based on Man-Whitney U test. statistical significance 0.05.

Table 5 Comparison between the two groups in regard to total transfusion units

Variable	Type of injection		P value
	Intra-articular TXA group (n=21)	Control group (n=21)	
Blood transfusion			
No	19	16	0.001
Yes	2	5	
Amount of transfusion units(ml)			
Mean SD	1±0.5	2.08±0.61	<0.001
Median (range)	1 (0.5–1)	2 (1–3)	

2.08 Median (range) 1 (0.5- 1) 2 (1–3) up-value are based on fisher- exact test. Statistical significance < 0.05

P value are based on Man-Whitney U test. Statistical significance < 0.05.

Table 6 Multivariable linear regression analysis of postoperative Hb level

Predictors	Unstandardized Coefficients		Standardized 95% Coefficients		P value
	B	Std. Error	Beta	confidence interval	
(Constant)	7.710	0.532			<0.001*
Groups					
Study Vs. control (R)	810	0.337	0.648	(0.129–2.49)	<0.001*

ANOVA < 0.001.

+41.9%.

• Statistical significance at P<0.05.

Multivariable linear regression analysis was used to assess predictors of postoperative Hb level among patients who had total knee arthroplasty. R²—0.419, where 41.9% of the variability of among patients Who had total knee arthroplasty can be explained by this linear model (Table 6) It was found that patients received intra-articular TXA had significantly 1.8 mg/dl higher postoperative Hb level.

Discussion

This study is a randomized controlled trial on 42 patients, (21 patients) received 1.5 gm of TXA in 10 ml of normal saline injected into the joint just before the deflation of the tourniquet while the other group did not receive IA injection of TXA.

NO statistically significant difference obtained when comparing between the group according to demographic data (age, sex), side of operation and comorbidities (hypertension, DM, smoking).

The average total blood loss in the drain after 48 hrs., in the first group patients who received Intra-articular TXA had statistically significant lower amount of blood lost in drains in ml (285 + 64.718 ml) compared to the second group (540 + 91.478 ml), so it shows highly statistically significant difference between two groups with a (P value <0.001).

Patients who received Intra-articular TXA had Statistically significant lower drop in hemoglobin level (0.99 + 0.45 mg/dl) compared to their control group (2.14 + 1.07 mg/dl), so it shows highly statistically

significant difference between two groups with a (P value <0.001).

Patients in both groups had a decrease in Hb level postoperatively but it was found that the decrease in Hb level is less in the 1st group than in the 2nd group which indicate less postoperative anemia and blood loss in the first group.

Intra-articular injection at the surgical site provides direct and straightforward means of application before tourniquet releasing [6]. In addition, intra-articular TXA injection induces partial microvascular hemostasis by stopping fibrin clot dissolution in the affected area, once injected intra-articularly [7].

A concern exists on the use of TXA that anti-fibrinolytic effect of TXA may cause thromboembolic complications in patients underwent Total knee arthroplasty. Due to the concern, patients with a history of a cardiac problem or with a thromboembolic disease were excluded from this study enrolment. Furthermore, no thromboembolic complications such as DVT or pulmonary embolism have been encountered after intra-articular injection of TXA [8].

Our findings of reducing postoperative blood loss are consistent with the findings of previous studies of TXA application in patient underwent TKA. Generally, most of the previously mentioned studies show significant results in decreasing postoperative blood loss after TKA, which indicates the necessity of using TXA for reducing blood loss, and consequently less chance of blood transfusion with all of its hazards, also this permits early hospital discharge and rehabilitation of the patient [9]. However, The study has some limitations as the sample size needs to be increased, the follow up period was short and some patients escaped from post operative follow up appointment.

Conclusion

In TKA patients, TXA minimizes total blood loss efficiently and safely, according to the findings of this study and the literature. The IA protocol appear to be significantly much better than the other protocols.

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Conflicts of interest

None declared.

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