The Reduction of Blood Loss by Using of Tranexamic Acid During Total Knee Arthroplasty

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Abstract

Background: Blood loss is the main complication associated with total knee arthroplasty with its risks of transfusion. Strategies are mandated to decrease blood loss and to reduce its consequence risks and costs of blood transfusion.

Objective: To find out the effect of tranexamic acid in reduction of blood loss intra and postoperatively blood loss and lowering the rates of homologous blood transfusions in total knee arthroplasty.

Patients and Methods: A non-randomized controlled clinical trial was conducted on 40 patients having total knee arthroplasty. In the first study group (20 patients) given tranexamic acid intra-articularly just before the tourniquet was deflated and the drain was locked. External postoperative blood loss was recorded together with the estimated amount of blood lost intraoperatively. The patients whom given blood transfusion with the number of packed red cells given was recorded also; any thromboembolic event postoperatively was investigated.

Results: Reduction in the total drain output, total blood loss and in the need of homologous blood transfusion was observed in first group whom given tranexamic acid, as compared to the second control group which were statistically significant ($p<0.001$). In the control group the postoperative hemoglobin and hematocrit levels were significantly lower ($p=0.001$ and 0.036, respectively) which were recorded at fifth postoperative day.

Conclusion: Intra-articular injection of tranexamic acid is associated with significantly marked reduction in both blood loss and the need of blood transfusion in patients undergoing total knne arthroplasty **.**

Key words: Antifibrinolytic drugs, blood loss, hemoglobin, Knee arthroplasty, ranexamic acid.

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Received: 6th December 2016

Accepted: 14th May 2017

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Introduction

A remarkable postoperative blood loss is usually seen after total knee arthroplasty. Application of a pneumatic tourniquet minimizes intraoperative bleeding and guarantees a dry surgical field [1][2][3]. In total knee arthroplasty an increase in the bleeding postoperatively had been described after pneumatic tourniquet removed most probably due to the activation of the fibrinolytic system stimulated by surgical trauma in the first hours after surgery[2][4][5][6].

The blood which lost postoperatively may reach such a level that it necessate the administration of homologous blood transfusion with its entire list of associated

consequences and hazards. High morbidity ratio postoperatively is seen in such patients whom are in the matter of increase the need of blood transfusion. This fact is true regarding in the developing countries where the blood transfusion is only allogenic, with absence of facilities and modern equipments for autologous retransfusion and harvesting blood intraoperatively in nearly all centers[3][7][8].

Local administration of antifibrionlytic agent reduces blood loss post operatively and the need for allogenic blood transfusion. Tranexamic acid (TEA) action is by locally inhibition of fibrinolysis and is a synthetic analog to aminoacid lysin, it shows no effect on fibrinolysis from plasma which is derived from peripheral venous system [9][10[11].

With the usage of TEA in patients undergoing total knee arthroplasty a redudtion in total blood loss and blood transfusion need was shown as previously proven by multiple studies[6][12][13][14][15][16]. Although few researches, in patients undergoing concurrent bilateral total knee arthroplasty there was a significant reduction of blood loss after use of TEA [17][18][19]. increase the need of blood transfusion is expected in these patients and thus they are more likely to get the benefit of TEA usage.

As far as we know this study was the first to evaluate the effect of TEA on blood loss postoperatively and homologous blood transfusion requirement in patients with unilateral total knee arthroplasty in Erbil city-Kurdistan region. This study's objective was, therefore, to find out the antifibrinolytic effect in patients with TEA administration in regards to reduce blood loss postoperatively and decreasing homologous blood transfusion need in unilateral cemented total knee arthroplasty surgery.

Patients and Methods

A non-randomized, controlled clinical trial was done on two surgically parallel groups. A total of 40 patients with osteoarthritis or rheumatoid arthritis who needed unilateral, bi-compartmental, primary, cemented TKA and were in same risk groups of American Society of Anesthetists (ASA) classification groups I to III were involved in the study.

Twenty patients in the first group received TEA as antifiblolytic agent and the control group of 20 patients did not receive any antifibrolytic agent. Patients and controls were matched for age and sex. The study was done between Jan 2014 and Jan 2015 on patients admitted to the department of orthopedic surgery of Erbil teaching hospital. Exclusion criteria were if creatinine plasma level peroperatively was greater than 130 mmol /litre, history of ischemic heart disease, history of unstable angina in the last one year and history of dementia. All patient are asked in advance to stop taking drugs containing any forms of antithrombotic agents. The use of other non-steroidal anti-inflammatory drugs was not prevented before admission to the hospital.

Complete blood count including hemoglobin (Hb) level, hematocrit (Hct) and platelet count was done to all patients together with template bleeding time, activated partial thromboplastin time and prothrombin time were measured preoperatively the day before the operation after 24 hour postoperatively and in day five (usually at time of discharge) post operative days.

An inflated pneumatic tourniquet with a pressure of 420 mmHg was applied around the thigh after elevating and draining the lower extremity with a sterile rubber bandage. This pressure is the usual tourniquet pressure used by the orthopedic surgeons because in 99% of all cases this pressure enabled a dry bloodless surgical field. A standard midline skin and parapatellar capsular incision was made to show the knee joint. A knee cemented prosthesis (NexGen

II) of an accurate size was inserted and fixed with bone cement. All surgical operations were performed by the same senior author, using a surgical procedure which is standardized to the same designed knee cemented prosthesis (Zimmer).

Intra-articular drain attached to a suction negative drain system was placed and kept for 2 days for patients of two groups postoperatively and the drain output was measured for 0 day and 1st post-operative day. The drain system was locked and intra-articular injection of 10-20 mg/kg of TEA was given to the first group. The tourniquet deflated 10-15 mins after closure of the wound by water tie suturing. The drain system was unlocked after one hour of the injection to prevent drug escape. The control group did not receive any antifibrinolytic drug.

Packed red cell was the form of homologous blood transfusion which was given to all patients with a Hb level less than 9 gm / dl or an Hct less than 28%. The requirement for blood transfusion was also estimated on the basis of blood loss in both intra and postoperatively which was measured by calculating the quantity in the suction and/or drainage container, and by a qualitative description of the blood stained surgical gauzes and/or swaps. The number of packed red cell units which was transfused were recorded.

All patients given subcutaneous injection of LMWH (enoxaparin) 4000 i.u as a thromoprophylaxis drug, started after 6 hours postoperatively and continued for 2 weeks postoperatively. Postoperative physiotherapy was started after 24 hours. Postoperatively usage of DVT stockings and early mobilization were also involved as a part of antithrombotic measures.

The study was approved by the research ethics committee of the college of medicine of Hawler medical university, and an informed written consent was taken from each patient before being involvement in the study.

Statistical analysis

Statistical analysis was achieved by SPSS software version 22. On analysis, the independent t-test, Chi-square test and Fischer's exact test were used for statistical analysis as appropriate. statistically significant P value less than 0.01 was considered.

Results

The sociodemographic specifics and clinical variables of both study groups are shown in Table 1. No significant distinctions were demonstrated between the two study groups for any of the sociodemographic characteristics and clinical variables.

Table (1): Sociodemographic specifics and clinical variables of both study groups.

Variables	First TEA group (n.=20)	Second Control group (n.=20)	*P* value
		Age (years)	
Range	51-75	52-82	
Mean ±SD	60.75 ±6.00	60.15 ±7.50	0.78
Gender			
No. (%) of females	18 (90.0)	19(95.0)	0.50
Weight (Kg)			
Range	70-94	75-114	
Mean ±SD	83.00 ±6.00	85.00 ±9.75	0.43
Right knee involvement			
No. (%)	13 (65.0)	12 (60.0)	0.50
ASA* risk [No. (%)]			
ASA I ASA II ASA III	1(5.0) 13(65.0) 6(30.0)	1(5.0) 15(75.0) 4(20.0)	0.76
Method of anesthesia [No. (%)]			
General Epidural Spinal	4(20.0) 2(10.0) 14(70.0)	3(15.0) 2(10.0) 15(75.0)	0.91
Mean surgery duration (min.)	100.4 ±15.1	103.2±12.3	0.50
Mean ischemia time (min.)	90.0±11.2	89.0±13.5	0.79

*ASA= American Society of Anesthetists

No statistically significant difference (P=0.11) between the means of intra operative blood loss in the first (TEA) group (325±51ml) and the second (control) group (348 ±37 ml). The TEA group showed a significantly lower drain output in both first 24 hours and 1st postoperative day than the control group (P<0.001). The mean of total blood loss was significantly (P<0.001) lower in the TEA group (611±25.0 ml) than in the control group (1286 ± 64.0 ml), as shown in table 2.

Table (2): Drain output and total blood loss in both study groups**.**

Variable	TEA group Mean ± SD	Control group Mean ± SD	*P* value
Blood loss intraoperatively (ml)	325.0±51.0	348.0±37.0	0.11
Drain output in 1st 24 hours (ml)	214.7±71.3	687.9±175.2	<0.001
Drain output in 1st P O day (ml)	71.3±35.3	250.3±97.4	<0.001
Total drain output (ml)	286.0±139.8	938.3±272.7	<0.001
Total blood loss (ml)	611.0±52.0	1286.0±64.0	<0.001

The reduction in both HB level and Hct level between admission and 5th post-operative day was significantly (P<0.001) less in the TEA group than the control group (Table 3).

Table (3): Reduction in hemoglobin level and Hct at the 5th postoperative day in both study groups**.**

Variable	TEA group Mean ±SD	Control group Mean±SD	*P* value
Preoperative Hb(g/dl)	12.68±1.75	12.93±1.64	0.64
Preoperative Hct(g/dl)	36.90±2.50	36.90±3.20	1.00
Hb at 5th PO day	10.20±1.40	9.30±2.30	0.14
Hct at 5th PO day	29,89±9.6	27.69±9.7	0.47
Reduction of Hb at 5th PO day	2.60±1.10	3.40±1.10	0.001
Reduction of Hct at 5th PO day	7.00±2.90	9.20±3.50	0.036

Only 10% of patients in TEA group required homologous blood transfusion (one pint) whereas 90% of the control group required blood transfusion, of whom 13 patients needed single pint and 5 patients needed two pints,

with a statistically significant difference (P< 0.001) between the two groups (Table 4).

Table (4): Homologous blood transfusion in both study groups.

Study group	No. of patients	Blood transfusion	*P* value
		No. (%)	
TEA group	20	2 (10.0)	< 0.001
Control group	20	18 (90.0)	

No one of the 40 patients of both groups developed DVT or any systemic clinical thromboembolic conditions.

Discussion

An average blood loss ranging from 761-1784 ml was reported following unilateral total knee arthroplasty postoperatively [6][20][21][22]. In this study the mean of total blood loss in the second (control) group was 1286 ml. In single stage bilateral total knee arthroplasty the range of blood loss expected to be higher thus the need for blood transfusion increases [17][18][19].

The effects of various operative procedures and techniques have been evaluated in several studies to reduce postoperative blood loss in total knee arthroplasty. Reduction in blood loss in TKA significantly achieved by the use of bone cement [1][2]. This blood sparing effect has been confirmed in many clinical studies and appears have direct relationship with the number of cemented components [1][23][24].

Aprotinin, e-aminocaproic acid, and TEA as different antifibrinolytic drugs can help lowering blood loss in TKA. TEA acts by competitive inhibition of the conversion of plasminogen to plasmin, and by inhibiting the binding of plasminogen to fibrin, which retards fibrinolysis, thus reducing blood loss by clot stabilization rather than clot formation promotion [9][10[25].

Our study showed a statistically significant decrease in the total drain output and total blood loss postoperatively in patients whom given tranexamic acid, in comparison to the second (control) group. In addition to that, the reductions in the haemoglobin and haematocrit levels at the 5th PO day were markedly lower in the TEA group than control group. The number of cases whom given blood transfusions, and the number of units transfused were markedly lower in the study group in comparison to the control group. Our study showed that TEA reduced postoperative blood loss by almost half in patients with TKA, and reduced blood transfusion demand in these cases by almost 80%. These findings are similar to those found in other clinical studies [16][26][27]. And to those of meta-analysis studies[13][14][28][29].

Regarding dosage of TEA, previous studies [6][17][30]. Similarly have demonstrated that 10-20 mg / kg of TEA given intra-articularly was the least dosage needed to obtain the required antihemorrhagic effect. The timing of the initial dose may be crucial in the safety of TEA therapy [20][29]. Starting the injection before inflating the tourniquet would leads to interaction between thrombosis against the natural defense mechanisms [19]. Thorpe *et al* [31]. Gave aprotinin in that way and decided to seize their study after a case lost his lower extremity due to massive arteriovenous thrombosis. In this study, the intra articular injection of TEA was given after the tourniquet was inflated.

No cases of thromboembolic complications and DVT for both groups in our study were reported, a finding which is similarly reported by Lindoff *et al* [32]. This finding in addition to the low cost and the high safety

[11][28][33]. Makes TEA the preferred antifibrinolytic agent.

The first strength point of this study is that all cases in both groups were operated by same surgeon authors who lead to exclusion of the possibility of surgeon dependent factors affecting the study; the relatively large sample size of our study adds the second strength point.

In conclusion, intra-articular injection of tranexamic acid is associated with marked reduce in blood loss in cases undergoing total knee replacement, reflected in a lowering in the need of number of blood transfusions.

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