

The effect of Tranexamic Acid on Blood Loss and Hospital-Stay after Knee Replacement Surgery

Abstract

Background: Total knee arthroplasty (TKA) is widely used as an effective treatment for end-stage osteoarthritis and other knee diseases to relieve pain and improve quality of life. While the benefits of TKA are reduced pain and an improved function there are also risks, such as hemorrhage, thromboembolic events, infection and the need for additional surgical procedures. Tranexamic acid (TXA) is effective in reduction of hemorrhage after such major surgical procedure. Abundant literature confirms that intravenous (IV) and intra-articular (IA) administration of tranexamic acid (TXA) reduces blood loss in total knee arthroplasty (TKA).

Methods and Material: The study is a retrospective cross-sectional study of 152 male and female patients aged 45 to 85 years who underwent Total knee replacement. They were divided into two groups. 72 patients received tranexamic acid during the operation and 80 patients did not.

Hemoglobin, transfused packed cell, hospital time, Visual analogue pain scale, Knee range of motion and cardiovascular accident were determined and compared between the two groups.

Results: Comparing the result of hemoglobin drop, post op hemoglobin, transfused packed cell and hospital stay time showed significant difference between experimental and control group when pre op hemoglobin, range of motion, VAS score for pain measurement and cardiovascular effects were not significantly different.

Conclusions: We found that the administration of tranexamic acid can reduce the complications of knee replacement surgery due to bleeding, as well as decreasing the need for blood transfusion. In addition, the administration of tranexamic acid can reduce the length of hospital stay after knee replacement surgery; that in turn significantly reduces the cost of hospitalization.

Keywords: Knee Arthroplasty, joint Replacement, Surgical Blood loss, Blood Transfusion, Tranexamic Acid

Received: 2 months before printing; Accepted: 1 Months before printing

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Introduction

The most common indication of total knee arthroplasty (TKA) is the treatment of cases of severe knee osteoarthritis^[1]. TKA is considered to be one of the orthopedic surgeries with the highest estimated bleeding,^[2] with values ranging from 300 to 2000 ml^[3]. Several studies show a high incidence of transfusion in the postoperative period^[2,4]. According to Wong et al.,^[5] these rates vary from 10% to 38%.

With an increased life expectancy and a large incidence of osteoarthritis (OA) in older people, the demand for TKA as ultimate treatment option for advanced knee OA will rise within the next 25 years^[6]. Total knee arthroplasty is already one of the most frequent surgical procedures performed worldwide^[7]. While the benefits of TKA are reduced pain and an improved function, it is associated with risks, such as hemorrhage, thromboembolic events, infection and the need for additional surgical procedures. Especially, older people with co-morbidities are at risk for complications. Due to hemorrhage up to one third receive blood transfusions which adds additional risks and costs^[8,9,10,11,12].

Previous studies reported a transfusion rate ranging from 10 to 38% after standard TKA ^[13,14,15]. Transfusion carries significant risks of cardiopulmonary embarrassment, disease transmission, immunological reaction, and postoperative infection ^[13,16,17].

In order to reduce the number of blood transfusions in TKA, some precautions are taken to try to minimize perioperative and postoperative bleeding, such as occlusion of the femoral intramedullary canal with bone graft, use of pneumatic tourniquet and suction drain, improvement of surgical technique, ^[18,21] anaesthesia combined with hypotension, ^[22] cryotherapy and Jones bandage, ^[23] postoperative drainage clamping, ^[24] local application of fibrin glue, ^[25] use of tranexamic acid, ^[26] local infusion with norepinephrine, ^[27] and the placement of platelet gel in the operative wound. ^[28]

Tranexamic acid (TXA), as an antifibrinolytic agent, is a synthetic lysine derivative that reduces blood loss through reversible competition for the lysine-binding site on the plasminogen with fibrin. This further inhibits activation of the plasminogen and prevents degradation of fibrin by the plasmin ^[29]. Therefore, TXA is not only effective in inhibiting the systemic fibrinolysis reaction after surgical trauma but also inhibits the local fibrinolytic activity caused by the use of a tourniquet. In recent decades, growing evidence has demonstrated the beneficial effects of TXA in reducing blood loss and the transfusion rate in several orthopaedic surgeries. In the literature, it has been reported that the application of TXA in conventional TKA lowers the blood loss by 300–500 ml on average, resulting in a reduction in the transfusion rate from 4.3% to 0.4% ^[30,31].

Methods

This study was done after obtaining permission from the Ethics Committee, is a retrospective study of 152 male and female patients (56 female and 96 male), aged 45 to 85 years who underwent total knee arthroplasty. The surgery was performed for severe DJD between 2015 and 2018 .

The patients in question were called after extracting their demographic information from the visiting hospitals. A total of 174 cases were examined, of which 72 patients who received tranexamic acid during the operation (28 female and 44 male) and 80 patients who did not receive (28 female and 52 male), were evaluated and extracted according to the criteria for entering and leaving the study and Laboratory results of hemoglobin one day before and 24hr after surgery were obtained.

All the patients underwent knee replacement surgery in the same way. Midline skin and medial joint incision were used for arthrotomy. ZIMMER cemented prosthesis with polyethylene liner was used for all patients. Pneumatic tourniquet in all patients with pressure 100 mm /Hg above systolic blood pressure was set and was activated 2 minutes after raising the leg and 15 minutes after the venous injection of tranexamic acid.

The anaesthesia technique is chosen by the anaesthesiologist depending on the patient's medical condition.

The tranexamic acid injection was administered intravenously: 20 mg / kg TXA ,15 minutes before activation of the tourniquet. At the end of the operation, the tourniquet was deflated and electrically coagulation of homeostasis was performed. Finally, after closing the joint capsule and before suturing the skin,

15 mg / kg of tranexamic acid was injected into the joint capsule.^[32]

After repairing the joint capsule, the wound was sutured in two layers as subcutaneous and skin.

No drain was used in any patient after surgery. LMWH was used in all patients for DVT prophylaxis.

The day after the operation, patients sit next to the bed and begin active knee movements. Partial weight bearing is allowed 24 hours after surgery. Patient physiotherapy begins on an outpatient basis after the first week.

Patients' data were evaluated separately and based on the information in the files and laboratory results, the patient's blood hemoglobin level based on mg / dl, before and 24 hr after surgery, the amount of

blood products received during surgery based on anaesthesia and operation room sheets and nursing-recorded data, as well as after surgery and the hospital stay was extracted and recorded.

We used the first Hb level obtained (actually 24hrs after surgery) for post op Hb comparison, not after blood transfusion. Furthermore, our threshold for blood transfusion was the Hb level of 8mg/dl for usual patient and 10mg/dl for patient with cardiac problem or haemoglobin drop more than 2 grams.

Patient follow-up was performed within two weeks, 6 and 12 weeks after surgery. The same rehabilitation, graphic and examination protocols were performed in follow-up visits.

Table 1- Statistical data obtained from patients

	Groups	Mean	Standard deviation	t value	Significant level
Hemoglobin level before operation (mg/dl)	Experimental	12.68	1.14	-0.051	0.96
	Control	12.69	1.67		
Hemoglobin level after operation (mg/dl)	Experimental	11.23	1.26	2.954	0.004
	Control	10.54	1.58		
Hemoglobin drop (mg/dl)	Experimental	1.456	0.85	-4.583	0.001
	Control	2.15	1.02		
Injected Paced cell (unit packed cell)	Experimental	0.15	0.522	-2.907	0.004
	Control	0.42	0.632		
Hospital Time (number of days)	Experimental	1.29	0.54	-3.191	0.002
	Control	1.60	0.65		
VAS Score	Experimental	7.25	1.29	0.859	0.392
	Control	7.72	4.52		
Knee ROM (degree)	Experimental	108.45	7.28	1.035	0.303
	Control	107.25	7.11		

After the visit, the patients underwent a clinical examination for knee ROM (flexion and extension). Knee pain was also assessed in patients based on the VAS (Visual Analogue Scale).

Thromboembolic events following TXA administration in both groups was based on the patient's history and the physician's examination performed one week after the operation. If suspected, the Doppler ultrasound of the lower limb was performed.

Final follow up time for all the patients of the two groups was 12 weeks.

Quantitative data were analysed by mean and standard deviation and qualitative data were analysed by frequency and percentage of extraction. To compare the quantitative data obtained in the last follow-up, the parameter t test for independent groups (Independent t-test) was used and for qualitative data, the Chi-square test was used. Data were analysed using SPSS 22 statistical software and a significance level of less than 0.05 was considered significant.

Results

The treatment results of 152 patients in the age groups of 45 to 85 years were evaluated under two groups: Intravenous and intra-articular injection of tranexamic acid in 72 and control group with no TXA injection in 80 patients.

Age

The age distribution in the experimental group was 54_73, mean (62.89) with standard deviation (5.94) and for the control group was 55-65, mean (64.23) with standard deviation (5.46) were obtained. The results of the independent t-test show that there was no significant difference between the two groups, in

terms of age. The distribution of sex was also similar in both groups.

The mean Hb level before surgery was 12.58 for experimental and 12.69 for control group- Showing no inter-group statistical difference.

The mean Hb level after surgery was 11.23 for experimental and 10.54 for control group-Showing statistical difference between two groups in the post operative Hb level.

Comparison of hemoglobin loss, shows also a significant difference between the two groups.

For the mean number of injected packed cell, the significance level of the test is less than (0.05), and so there is a significant difference between the two groups.

Comparing the mean hospital-stay time shows a significant difference between the two groups.

For VAS SCORE at 3 months post surgery, there was no significant difference between the two groups.

The knee range of motion in 3 months showed no difference in the two groups.

No confirmed thromboembolic complications was reported in the control or experimental group.

Discussion

In this retrospective study, the affect of tranexamic acid injection during total knee joint replacement, in reducing bleeding and need for blood transfusion was investigated. The treatment results of 152 patients in the age groups of 45 to 85 years were evaluated under two groups by intravenous and intra-articular injection of tranexamic acid in 72, and no drug injection in 80 patients.

In a 2009 study by Mosaffa et al., Transaxamic acid injection reduced hemoglobin drop 6 hours and 24 hours

after hip arthroplasty and reduced the need for blood transfusions, which is consistent with our study.^[33]

In another study conducted by Sarzaeem et al. In 2013, intravenous and intra-articular injection of tranexamic acid in patients with TKA was studied and compared, which in both methods reduced the hemoglobin drop after surgery. Simultaneous intravenous and intra-articular injections were not performed, but the results were consistent with our study.^[34]

In a 2017 study by Marra et al., the effect of transgenic acid administration on three different intravenous, interaarticular methods and a combination of the two was studied in postoperative knee replacement patients. There was no significant difference in the three groups and all three methods reduced postoperative hemoglobin loss, which is consistent with the results of our study on concomitant intravenous and interaarticular administration and decreased blood loss.^[35]

The study, conducted by Fernandes et al. on the effect of tranexamic acid prescribing on knee replacement, found that intra-articular tranexamic acid was not effective in reducing hemoglobin loss 24 hours after, which is not consistent with our study that this difference can be due to using method of tranexamic acid which was just intra-articular but we administered intra-articular and intravenous together. However, in this study, the administration of tranexamic acid reduced the decrease in hemoglobin 48 hours after surgery. In addition, in that study, the administration of tranexamic acid had no effect on reducing postoperative pain on days 7, 21 and two months after surgery, but reduced postoperative pain in the first 24 and 48 hours. We didn't however measure the pain score on the post operative datas,

except the 12 week after surgery. Another factor considered in Fernandes et al. study is the amount of knee flexion after knee replacement surgery following the administration of tranexamic acid, which was not significantly different on days 7, 21, and two months after surgery from a group that did not receive medication. This finding is consistent with our study.^[36]

In a 2019 study by Tille et al.^[37] the effect of intra-articular tranexamic acid administration on reducing haematocrit, hemoglobin and the need for blood transfusion after knee replacement surgery was studied. Their findings were similar to the present report.

In another meta-analysis conducted by Guo et al. in 2018 looking at 5 studies, the oral administration of tranexamic acid reduced hemoglobin loss after TKA, but did not reduce the need for blood transfusion, which is different from our findings. Oral TXA administration did not have a significant affect on thrombo-embolic complications, a findings also confirmed by our study.^[38]

Conclusion

Administration of tranexamic acid reduces bleeding during knee replacement surgery , the need for blood transfusion and may reduce the complications of knee replacement surgery from bleeding and blood transfusion. It also reduces the length of hospital stay. Significantly reduces the cost of hospitalization and treatment of patients and the complications of blood transfusion.

We faced some limitation in this study: This was a retrospective study and information was mainly collected from hospital charts, the amount of fluid received by patient in addition to blood products was not exactly recorded in patients, file during and after operation.

Another limitation was VAS SCORE presentation and poor reporting by very old patients. We did not use any drain after surgery and could not evaluate the amount of blood loss after surgery. Another limitation of our study is using Hb level 24 hours after surgery which would not reflect exact level of drop.

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