ORIGINAL ARTICLE

Efficacy of tranexamic acid in reducing blood loss in total knee replacements

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Abstract

Objective: To assess the efficacy of tranexamic acid in reducing blood loss in total knee replacement.

Methods: The retrospective study was conducted at Quaid-e-Azam International Hospital, Islamabad, Pakistan, and comprised data of patients who underwent total knee replacement between January 2012 and December 2014. The effect of tranexamic acid on postoperative haemoglobin, hematocrit and number of blood units transfused was noted and compared between cases who had received standard dose of tranexamic acid with those who had not received it. SPSS 19 was used for data analysis.

Results: A total of 416 knee replacement surgeries were conducted during the study period and involved 254 patients; 76(30%) men and 178(70%) women. The overall mean age was 62.2±9.6 years (range: 36-87 years). Tranexamic acid was used in 162(74%) patients and was not used in 92(36%). When it was used, only 26(16%) patients required blood transfusion, but when it was not used, 35(39.1%) required transfusion ($p<0.05$).

Conclusion: Tranexamic acid was able to reduce total blood loss and transfusion requirements.

Keywords: Total Knee Replacement, Joint Replacement, Transexamic acid, Blood Loss. (JPMA 65: S-210 (Suppl. 3); 2015)

Introduction

Total knee replacement (TKR) is a commonly performed orthopaedic reconstructive procedure in order to relieve pain and improve mobility of patients suffering from advanced degenerative arthritis secondary to osteoarthritis, rheumatoid arthritis (RA) and other arthritis.[1,2] TKR is a major surgical procedure involving extensive dissection of soft and bony tissues and it is associated with increased risk of local fibrinolytic activity due to use of tourniquet for prolonged period of time.[3-6] Due to nature of procedure it is associated with significant amount of blood loss after surgery. Blood transfusion carries a substantial risk of immunological reaction and transmission of disease.[7-10] Blood transfusion also involves additional cost, and, therefore, a reduction in its use is important.

A large number of patients require blood transfusions after unilateral and bilateral knee replacement surgeries. Some measures are commonly done to reduce transfusion rate which include autologous blood transfusion,[11-13] intra-operative blood salvage,[14,15] use of Jones Dressing,[16] use of regional anaesthesia[17] intraoperative controlled hypotensive anaesthesia,[17] use of fibrin tissue adhesives,[18] and use of anti-fibrinolytic agents[19-23] etc.

Tranexamic acid (TXA), a synthetic anti-fibrinolytic agent that is approximately 7-10 times more potent than epsilon-aminocaproic acid, competitively blocks the lysine-binding site of plasminogen, plasmin, and tissue plasminogen activator which prevents their association with fibrin.[5,24] As a result, the conversion of plasminogen to plasmin is greatly retarded, and the proteolytic action of plasmin on fibrin monomers and fibrinogen is inhibited. Adverse effects of TXA are rare and mainly limited to nausea, usually elicited by rapid intravenous (IV) infusion.[25]

The currents study was planned to evaluate the efficacy of single preoperative bolus dose of TXA on reduction in blood loss and red blood cell (RBC) transfusion in patients undergoing TKR and untoward effects with the use of TXA.

Material and Methods

The retrospective study was conducted at Quaid-e-Azam International Hospital, Islamabad, Pakistan, and comprised data of patients who underwent TKR between January 2012 and December 2014. All consecutive unilateral and bilateral TKRs were included, while cases of revision knee; additional procedures done other than TKR; and those with incomplete data were excluded.

All patients presenting with advanced arthritis of knee joints were assessed in the outpatient department (OPD) and those willing for surgery were scheduled for elective surgery. Patients were sent to cardiologist to review cardiac status and fitness for anaesthesia. Routine laboratory workup, chest X-rays, electrocardiogram (ECG) and echo-cardiogram were done in all cases. Preoperative anaesthesia assessment was done routinely in all cases.

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Two units of packed cells were arranged in all cases prior to surgery. All patients were admitted a day prior to scheduled surgery.

Patients were kept Nil per Oral (NPO) from midnight as surgery was scheduled early morning as a first case of the day. Combined spinal and epidural anaesthesia was given in majority of patients unless contraindicated because of haematological or biochemical reasons or because of local factors such as history of back surgery.

All surgeries were done by same surgical team in the operation theatre reserved for Joint Replacement Surgeries where advanced measures were being utilised to achieve germ-free environment.

An appropriate sized tourniquet was applied in proximal thigh and pressure was maintained between 350 to 400mmHG using Automatic Digital Tourniquet System. A single dose of 250mg of TXA was given IV before tourniquet inflation. Surgery was done using standard Medial Parapatellar Arthrotomy. Tibial, femoral and patellar precise bony cuts were made using standard jigs. Soft tissue balance was checked before proceeding to final cuts. Wound was thoroughly irrigated with normal saline and final implantation of appropriate sized components (Zimmer NexGen Flex, or Biomet Vanguard Knee) were done systematically using bone cement. However, in some cases, additional procedures were required to achieve soft tissue balance. Some of the cases required reconstruction of deficient bone.

All visible blood vessels in the field were coagulated. No drain was applied in any case. Meticulous closure was done in 3 layers. Jones Dressing was applied and tourniquet was deflated.

In case of bilateral TKR, sequential surgical technique was used with surgery performed on left side first followed by surgery on right knee.

Preoperatively any patient taking clopidogrel were instructed to stop this platelet lowering drug 72 hours before surgery and this drug was restarted after 72 hours after surgery, but aspirin was only stopped on day of surgery and was resumed after surgery. TXA (250mg of Inj. Transamin) was given in majority of the patients before inflation of tourniquet and incase of bilateral TKR another dose of TXA was given before inflation of second tourniquet.

Postoperatively patients were managed according to TKR pathway. In the first 24 hours pain management was done using epidural anaesthesia which was supervised by anaesthesia team. Later on, oral and IV analgesics were given. Ambulation was started on 1st postoperative day and joint range of motion (ROM) was started on 2nd postoperative day after dressing was removed. Postoperative haemoglobin (Hb) and haematocrit (Hct) were done routinely on 1st, 3rd postoperative days in all patients but in case of bilateral TKR it was also done on 5th postoperative day. If the Hb was below 8gm/dl, then 2 unit-packed cells were transfused in the next 24 hours followed by repeat measurement of Hb and Hct values. Postoperatively, all patients were daily given Inj. Enoxaparin 20mg during their stay. Physical examination was done to detect deep vein thrombosis (DVT) and in suspected cases Doppler scan was ordered.

Patients were discharged after surgery when they were able to walk with walker comfortably and were able to bend knees up to 90 degrees. Some of the patients due to medical comorbid conditions were discharged when their condition was stable.

All data was gathered from the files of the patients from our medical record department and was assessed using SPSS 19. Results were analysed and $p<0.05$was considered significant.

Results

A total of 426 knee replacement surgeries were conducted, but 10(2.3%) had to be left out of the analysis because of insufficient data. As such, the study sample had 416(97.7%) knees and involved 254 patients; 76(30%) men and 178(70%) women (Table-1). Of the total,, 324(78%) knees were operated as bilateral simultaneous procedures, while 92 (22%) surgeries were done as unilateral procedures (47[51%] Right and 45[49%] left TKRs).

The overall mean age of the sample was 62.2±9.6 years (range: 36-87 years). Mean hospital stay in unilateral TKR

Table-1: Gender distribution.

Gender	Frequency	Percent
Male	76	29.9
Female	178	70.1
Total	254	100

Table-2: Transfusion requirement in unilateral vs. bilateral surgery.

Type of Surgery	Transfusion		Total
	No	Yes	
Unilateral	86	6	92
Bilateral	107	55	162
Total	193	61	254

Table-3: Effect of tranexamic acid (TXA) on transfusion rate.

Type of Surgery	Transfusion		Total
	No	Yes	
TXA - Not Used	57	35	92
TXA - Used	136	26	162
Total	193	61	254

Table-4: Effect of tranexamic acid (TXA) on transfusion rate (unilateral vs. bilateral total knee replacement [TKR]).

Type of Surgery	Use of TXA	Transfusion		Total
		No	Yes	
Unilateral TKR	No	27	0	92
	Yes	59	66	162
Bilateral TKR	No	30	35	65
	Yes	77	22	97
Total	193	61	254	

was 5.2±3 days, while in bilateral surgery, it was 6.9±1.7 days.

A total of 61(24%) patients were given blood transfusion after surgery, while 193(76%) had no transfusion, and 55(90%) of the transfusions were seen in bilateral TKRs (p=0.001) (Table-2).

TXA was used in 162(74%) patients and was not used in 92(36%).Only 26(16%) of the patients with TXA required transfusion, but when TXA was not used, 35(39.1%) patients required transfusion(p<0.05) (Table-3).

Besides, a statistically significant relationship existed between the use of TXA in patients undergoing bilateral TKR (Table-4).

Mean drop of Hb on 1st postoperative day was 2.5gm/dl (SD 1.2 with range: -0.6 to 8). Mean drop in Hct on 1st postoperative day was 7.5 (SD 3.6 with range: -7.9 to 23.9). Mean drop of Hb on 3rd postoperative day compared to preoperative Hb was 3.13 (SD 1.4), while mean drop of Hct was 9.4 (SD 4.3).

Preoperative Hb value had a statistically significant relationship with number of transfusion (p<0.05). A value of less than 12gm/dl was associated with transfusion after surgery in 38/76 patients (50%), while a value of 12-15gm/dl was associated with transfusion in 13(17%) patients, while patients having a value above 15gm/dl had no transfusions. Preoperative Hb value <12gm/dl had stronger association with blood transfusion after bilateral TKR surgery (p<0.05) though a less strong but still statistically significant relationship was also found in unilateral TKR surgery (p<0.05).

While assessing the effect of number of procedures on transfusion, there was no statistically significant relationship between the number of procedures and requirement of transfusion (p>0.05).

There was no statistically significant association between blood transfusion after surgery with the type of arthritis, number of comorbid conditions,total stay in hospital or surgery duration (p>0.05 each).

Nine (11.5%)male patients required transfusion, while 52(29.5%) female patients required it (p<0.05).

Clinical assessment did not reveal any thromboembolic complications.

Discussion

TKR surgery is associated with considerable blood loss and patients are often subjected to risk of transfusion, including reactions and disease transmission. The reported incidence of blood loss after TKR ranges from 500ml to 1500ml depending on patients and surgery variables.[26-31] Blood transfusion after surgery increases the cost of surgery which is a concern for patient and hospital alike. However, the main cause for decreasing the number of blood transfusion was to reduce risk associated with transfusion, including reactions, transmission of diseases, coagulopathy, and volume overload. Therefore, every healthcare professional involved in managing these patients tries to reduce these potentially harmful effects, and uses safer methods to avoid complications. Several methods reportedly reduce postoperative blood loss and avoid homologous blood transfusions.

Control of bleeding with anti-fibrinolytic agents may be a preferable alternative. TXA is a safe drug and is not associated with significant side effects. Role of TXA in blood loss reduction has also been confirmed in major General Surgery and Gynaecological procedures as well.[32,33] Keeping this in mind, we started using TXA in TKR few years back at our institution. However, due to concerns that it may cause increased incidence of venous thromboembolism, a low dose was given to the patients.

Our current study confirms the role of TXA in reducing blood loss associated with TKR. Single dose of TXA in unilateral surgery and 2 doses of TXA in bilateral surgery were able to reduce blood transfusion by 2.5 times. The number of patients requiring blood transfusion would have been even lower if transfusion trigger would have been lowered.

In one regional study[34] where effect of single dose of TXA

on transfusion rate after knee replacement surgery was assessed, it was observed that even a single dose reduced blood loss by more than two thirds compared to controls among whom no TXA was used. Similarly transfusion requirements were radically reduced as seen in our study.

The use of TXA in this study was not associated with increased incidence of thromboembolic phenomenon which is one of the feared complications associated with TXA use. Similarly, any significant wound drainage and haematoma formation were not seen with the use of TXA along with enoxaparin. No major thromboembolic complication occurred in our patients, corroborating earlier studies reporting the same.[4,35] This also confirms the safety profile of TXA in our population undergoing major orthopaedic surgical procedures.

In two case-control regional studies[36,37] where TXA was used in 2 doses 3 hours apart, the results showed significant reduction in blood loss and requirement of any transfusion in patients undergoing bilateral TKR surgeries compared to the control group where no TXA was used.

Although a number of studies have concluded that use of a single dose of TXA before tourniquet inflation is not as effective as repeating the dose of TXA after tourniquet deflation,[38] but our study showed that even a single dose of TXA significantly reduced blood transfusion requirements in patients undergoing TKR. In order to find out the true efficacy of single dose before tourniquet inflation, further prospective studies shall be done to compare its efficacy with 2 or more doses of TXA. Nevertheless the cost-benefit ratio of the short-term TXA therapy to reduce TKA-associated blood loss is extremely rewarding.

Conclusion

Single bolus dose of TXA before tourniquet inflation significantly reduced blood loss caused by TKR surgery performed with a tourniquet, without increasing the risk of thromboembolic complication.

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