SHORT REPORT

Lower red cell transfusion rates with use of tranexamic acid in single-stage bilateral total knee arthroplasty: A retrospective audit

Muhammad Aziz,[1] Salman Bin Mahmood,[2] Riaz Hussain Lakdawala,[3] Tashfeen Ahmad[4]

Abstract

Bilateral total knee arthroplasty (BTKA) patients may require blood transfusion which has its risks. Anti-fibrinolytic drugs such as aprotinin, aminocaproic acid and tranexamic acid (TXA) have reduced transfusion requirements in major surgery. This retrospective audit was performed to assess effectiveness of TXA in reducing blood transfusion rate in single-stage sequential BTKA cases operated by a single surgeon. Records of 91 patients given TXA and 80 controls who were operated before 2012 and not given TXA were reviewed. TXA was given 15mg/kg intravenously (IV) before tourniquet deflation and 3 hours postoperatively.Blood transfusion was done in 9(10%) patients in the TXA group compared to 20(25%)in the control group ($p<0.01$). One (1.25%) patient in the control group had non-fatal pulmonary embolism.TXA appeared to be effective in decreasing post-operative blood loss and requirement for blood transfusion after single-stage BTKA.

Keywords: Bilateral total knee arthroplasty, Tranexamic acid, Blood loss, Haemoglobin drop, Transfusion.

Introduction

As the proportion of geriatric people increases with improvements in healthcare, the proportion of people with osteoarthritis is also expected to increase, with a corresponding increase in knee arthroplasty procedures. This procedure,like other major orthopaedic reconstructive procedures, carries a risk of blood loss necessitating blood transfusions.[1] Allogeneic blood transfusion has its own risks, such as risk of infection transmission, immunomodulation, transfusion reactions and increase in cost.[2] Different strategies are being employed to reduce the need for allogenic transfusions, such as autologous blood transfusion, cell savers, haemo-dilution and hypotensive anaesthesia.[3] As hyperfibrinolysis is considered a major cause of postoperative bleeding in total knee arthroplasty (TKA)[4] another modality is the use of antifibrinolytic agents, including aprotin, aminocaproic acid and tranexamic acid (TXA). TXA has already been used for more than 20 years in cardiac, gynaecological and liver transplant surgeries, among other procedures, and its benefits have been reported in orthopaedic surgeries as well.[5] It acts by reversibly inhibiting fibrinolysis by blocking lysine binding sites on the plasmin and plasminogen activator molecules.[4]

The use of TXA came into routine use in TKA at our institution in January 2012 following the emergence of substantial evidence supporting its utility in limiting blood loss postoperatively in a variety of procedures. This study was planned to assess effectiveness of TXA in reducing blood loss and rate of blood transfusion in cases operated by a single surgeon for sequential bilateral TKA (BTKA).

Methods and Results

The retrospective study was conducted at Aga Khan University Hospital, Karachi, and comprised record of patients who underwent BTKA in a single stage by the same surgeon between January 2012 and June 2014. To compare the data, a historic cohort of patients who were operated between January 2009 and December 2011 and had not received TXA was included. Patients with a recorded history of bleeding disorder, chronic anticoagulant therapy or with a history of previous thromboembolism, and those who received intra-operative or immediate post-operative blood transfusion for any reason were excluded.

TXA administration protocol was 15mg/kg intravenously (IV) before tourniquet deflation and 3 hours postoperatively. All patients received epidural anaesthesia as per the standard practice. All procedures were conducted using standard cemented technique and implants from the same company in both groups (Zimmer Inc., NexGen Legacy and NexGen Flex).

Haemoglobin (Hb) levels were measured

[1,2]Medical College, [3,4]Section of Orthopedics, Department of Surgery, Aga Khan University, Karachi, Pakistan.

Correspondence: Riaz Hussain Lakdawala. Email: riaz.lakdawala@aku.edu

Table-1: Comparison of control and tranexamic acid groups.

	Control Group (n = 80)	Tranexamic Acid group (n = 91)	P value
Demographic, disease and initial laboratory data			
Age (years)	64±8	64±9	0.850
BMI (kg/m2)	32.2±5.0	31.7±5.2	0.519
Gender(M/F)	13 / 67	12 / 79	NS
Osteoarthritis (n)	79	91	NS
Rheumatoid arthritis (n)	1	0	NS
INR	0.99±0.07	0.97±0.08	0.304
Haemoglobin (g/dl)	12.4±1.2	12.6±1.1	0.388
Haematocrit (%)	37.7±3.7	38.4±3.4	0.195
Outcome measures			
Torniquet time (mins)	189±36	183±22	0.199
Post-operative Hb at 24 hours	9.6±1.1	10.4±1.1	<0.001
Drop in Hb post-operative	2.8±1.1	2.1±0.9	<0.001
Post-operative Hct at 24 hours	28.9±3.3	31.7±3.2	<0.001
Units of packed red cells transfused	0.59±1.1	0.14±0.46	0.001
Number of patients requiring transfusion (n)	20	9	0.009

Numbers indicate counts, or mean±SD. NS=not significant
BMI: Body mass index
INR: International normalised ratio
Hb: Haemoglobin
Hct: Haematocrit.

Table-2: Comparison of different studies evaluating the effect of TXA in BTKR.

Study	Type of Study	Sample (n) (Control/ Treatment)	Tranexamic Acid Dose (mg/kg)	Mean Hb drop (control/treatment) mg/dl	No. of patients transfused (Control/Treatment)	No. of Units transfused (Control/Treatment)
MacGillivray et al. (2009)	Double blind RCT	(20/40)	(a) 10 mg/kg IV before Tourniquet inflation and after 3 h (b) 15 mg/kg IV before Tourniquet deflation and after 3 h	2.62 / (a) 1.93 (NS) / (b) 1.32 (p <0.01)	10 / 13 (NS)	0.95 / 0.65 (NS)
Dhillon et al. (2011)	Retrospective cohort	(56/52)	10 mg/kg IV before Tourniquet inflation and after 3 h	2.79 / 0.99 (p <0.001)	56 / 27 (p <0.001)	3.17 / 0.80 (p <0.001)
Sepah et al. (2011)	Retrospective cohort	(14/15)	1 g IV before Tourniquet inflation and after 3 h	2.21 / 1.94 (p <0.001) 1.46 / 1.29 (p 0.02)	-------- 18 / 7	2.6 / 0.9 (p 0.04) 0.31 / 0.09 (p 0.02)
Raviraj et al. (2012)	RCT	(87/88)	10 mg/kg IV before Tourniquet inflation and after 3 h			
Karam et al. (2014)	Retrospective cohort	(50/37)	20 mg/kg IV before Tourniquet inflation only	4.64 / 3.58 (p <0.001)	25 / 4 (p <0.001)	0.90 / 0.16 (p <0.001)
Aziz et al. (2015)	Retrospective cohort	(80/91)	15mg/kg IV before Tourniquet deflation and after 3 h	2.80 / 2.14 (p <0.001)	20 / 9 (p 0.01)	0.59 / 0.14 (p 0.001)

TXA: Tranexamic acid
BTKR: Bilateral total knee replacements.

preoperatively and 24 hours postoperatively. The number of packed red cells transfused during the hospital stay was recorded.

In the practice of the surgeon, factors that are considered for the decision to transfuse blood are: postoperative Hb of<10 mg/dl in patients who have known co-morbids, for example, diabetes or coronary heart disease, or<8 mg/dl in patients with no prior co-morbids; and the presence of physiological signs of inadequate oxygenation such as haemodynamic instability or symptoms of myocardial ischemia.

Additionally, patient's charts were reviewed for

thromboembolic complications, like deep vein thrombosis (DVT), pulmonary embolism (PE.) etc., to evaluate the safety of TXA in thestudy population.

SPSS 21 was used for data analysis. Means were compared using the student's t-test and p<0.05 was taken as significant.

There were 91(53%) cases and 80(47%) controls. Demographic data, primary disease and initial Hb levels were comparable in both groups (Table-1). Mean post-operative Hb concentration evaluated at 24 hours was significantly higher in TXA group (p=<0.001), while mean Hb drop at 24 hours was significantly lower (p<0.001).

Nine(10%) patients required blood transfusion in the TXA group compared to 20(25%) who received packed cell transfusion in the control group (p=0.009) with relative risk (RR) reduction of 60% and absolute risk (AR) reduction of 15%. Mean number of packed cells transfused was higher for control group compared to TXA group (p=0.001).

Post-operative thromboembolic complications of TXA were not detected in any of our patients. However, one (1.25%) patient in the control group developed pulmonary embolism, and was managed accordingly. He recovered and was discharged.

Conclusion

TKA surgeries involve significant blood loss, frequently leading to autologous blood transfusions. Different strategies to reduce the need for transfusion have been reported, including, though not limited to, minimally invasive techniques, releasing tourniquet after wound closure, and local infiltration with vasoconstrictor drugs as well as anti-fibrinolysis. TXA is a fibrin clot stabiliser that works by inhibiting the conversion of plasminogen to plasmin, thereby preventing degradation of the fibrin clot.[4] Substantial data is available about the use of TXA in unilateral knee arthroplasties and a number of meta-analyses illustrate its effectiveness in reducing blood loss and the rate of transfusion.[6] In concurrent bilateral knee arthroplasty procedures, a larger amount of blood loss is expected compared to unilateral surgery, thus the use of TXAto reduce post-operative blood loss becomes more relevant. However, there are only a limited number of studies showing such data for bilateral simultaneous TKAs.

A recent trial compared blood loss after bilateral TKAs with administration of two IV doses of TXA (10 or 15 mg/kg) versus placebo.[7] A significant reduction in blood loss was observed in the 15mg/kg treatment group compared to the placebo group and the number of total transfusions was similar to our study. A case-control study employed a protocol of administration of two doses of TXA, 10mg/kg each.[8] A 48% reduction in the mean number of units transfused per patient was also observed, which can be compared to the 76% reduction shown in our study. A recent article showed that a 20mg/kg dose of TXA before incision led to a significant reduction of 82% in the rate of units transfused.[9] A retrospective study at our institution showed significant reduction in post-operative drainage and drop in Hb.[10] These results (Table-2) are consistent with our findings when a dose of 15 mg/kg was administered.

There is a theoretical risk of hypercoagulability associated with anti-fibrinolytic effects of TXA which is frequently a cause of concern prior to such use. In our study no thromboembolic events were observed in any patient receiving TXA, which was in line with a recent meta-analysis on TXA use in unilateral knee arthroplasty.[6] However, we may have missed subclinical thromboembolic diseaseas venous ultrasonography was not performed for screening. We excluded those patients who had a history of any bleeding disorder, hypercoagulable states, or previous history of thromboembolic disease.

A limitation of our study is its retrospective nature which compares the treatment group with historical controls. However, the control selection seemed appropriate considering the similarity in the baseline demographic variables across the two groups. On the other hand, the strength of the study is that the procedure was performed by a single surgeon with a single technique and the same implants were used throughout the time period in which both groups were operated upon. Also, to our knowledge, this study has one of the highest numbers of patients undergoing bilateral TKAs.

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