

# Effects of Tranexamic Acid on Perioperative Blood Loss Associated with Total Knee Arthroplasty: A Randomized Double Blinded Prospective Study

Lalit Kumar<sup>1\*</sup>, Simple Chahar<sup>2</sup>

<sup>1\*</sup>Associate Professor, Department Of Orthopaedics,  
Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India.

<sup>2</sup>Junior Resident, Department of Anaesthesia,  
Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India.

## ABSTRACT

**Introduction:** Total knee arthroplasty is usually associated with minimal intra-operative, but extensive postoperative blood loss, also because of the application of pneumatic tourniquet application there are theoretical risk of thrombotic complications. In this prospective randomized double blinded study we try to find out effect of tranexamic acid on hemostasis, bleeding and thrombotic incidences.

**Materials and Methods:** 30 patients were allocated randomly to receive either 15mg/kg tranexamic acid or equal volume of placebo a few min before tourniquet deflation.

**Results:** Mean blood loss during surgery was 659 (285) ml in the tranexamic acid group, and 1245 (623) ml in the control group ( $p < 0.001$ ).

In the recovery room, tranexamic acid group lost 131(98) ml, and the control group lost 645 (300) ml ( $p < 0.001$ ), whereas in the ward tranexamic acid group lost 295 (220) ml, and the control group lost 600 (275) ml  $p < 0.01$ .

**Conclusion:** We found that there was less blood loss in the

tranexamic acid group, during total knee arthroplasty with pneumatic tourniquet.

**Keywords:** Perioperative Blood Loss, Total Knee Arthroplasty, Tranexamic Acid.

## \*Correspondence to:

**Dr. Lalit Kumar,**  
Associate Professor,  
Department Of Orthopaedics,  
Muzaffarnagar Medical College,  
Muzaffarnagar, Uttar Pradesh, India.

## Article History:

**Received:** 17-02-2017, **Revised:** 05-03-2017, **Accepted:** 22-03-2017

Access this article online	
Website: <a href="http://www.ijmrp.com">www.ijmrp.com</a>	Quick Response code 
DOI: 10.21276/ijmrp.2017.3.2.020	

## INTRODUCTION

Total knee arthroplasty is associated with significant blood loss, and a number of methods have been applied to reduce the perioperative bleeding e.g. cemented prosthesis, fibrinogen concentrates, use of tourniquet, and cold compressive dressing;<sup>1-5</sup> as avoidance of post-operative anemia and blood transfusion is always one of the targets of the surgery. Studies have shown that when a pneumatic tourniquet has been used to minimize the blood loss, there is increase in fibrinolytic activity in the bloodless area and this increase in the fibrinolytic activity results in increased incidence of deep vein thrombosis (DVT).<sup>6-8</sup>

In this prospective, randomized double blinded study we examine the effect of tranexamic acid, an antifibrinolytic agent on blood loss, transfusion requirement and incidence of deep vein thrombosis in pneumatic tourniquet applied total knee arthroplasty.

## MATERIAL AND METHODS

This prospective double-blinded randomized study was conducted on 30 ASA 1 and 2 grade patients, undergoing total knee arthroplasty. After approval from the institutional ethical committee, written informed consent from all the patients taken.

All the acetylsalicylic acid containing medications were stopped 1 week before surgery, while non-steroidal anti-inflammatory medications were continued until the day before surgery.

Hemoglobin concentrations, platelets counts, bleeding times, clotting times, activated partial thromboplastin time (aPTT), and INR were measured day before surgery.

Enoxaprin 40 mg S.C. was given evening before surgery, to prevent DVT, and was continued once a day until patient was discharged or sufficiently mobilized.

Operation was conducted under spinal anesthesia using 0.5% levo-bupivacaine, and epidural catheter was placed for post-operative analgesia. During the post-operative period a constant infusion of fentanyl 10µg/ml+ levo-bupivacaine 0.1% was started. Using the formula based on weight, height and sex of the patient, blood volume of each patient was estimated.<sup>9</sup>

For blood transfusion and replacement in the perioperative periods, following formula was considered; if hemoglobin was less than 10% packed RBCs were used, otherwise Ringer's Lactate was used as the replacement fluid. Besides this, 2 liters of balanced glucose solutions were given by evening of the first post-operative day. All the fluids given till the morning of the second

post-operative day was recorded, all the blood transfusion till the hospital stay was recorded too.

All the surgeries were performed by the same operating surgeon. Before the surgery the limb to be operated was drained of blood by using a sterile rubber bandage, and a pneumatic tourniquet was applied on the upper thigh of the operating thigh and inflated to a pressure of 300 mmHg.

Surgical approach was as described: to expose the knee joint; skin incision was midline and parapatellar capsular incision was medial; knee prosthesis was fixed with cement, appropriate in size and sparing the posterior cruciate ligament.

Before deflating the pneumatic tourniquet, the joint was stuffed with moisturized surgical gauzes, and a compressive bandage was applied around the extended knee. The tourniquet was deflated and the knee was compressed manually for up to 10 min after which the gauzes were removed and electrical cauterization was used to achieve adequate haemostasis. Before closure, medium-sized intra- and extra-articular wound drains were inserted and connected jointly to a single drain reservoir which exerted a maximum vacuum pressure of 115 mm Hg. After closure of the wound, dressings and an elastic bandage were applied, and in the recovery room the extremity was rested on a wedge-shaped support. Passive physiotherapy was started on the first postoperative day.

5 minutes before deflating the tourniquet, the patients were given either a bolus of tranexamic acid 15mg/kg or an equal volume of placebo (0.9% sodium chloride solution) i.v. within 1 min. Randomization was carried out by a person not involved in the operation using a ticket drawn from an envelope containing an equal number of tranexamic acid and placebo tickets. The operating team was unaware of the contents of the solution administered.

During operation, blood loss was assessed by measuring the weight change of surgical swabs and the volume in the suction reservoir.

In the recovery room and on the surgical ward, the contents of the drain reservoir were measured and recorded. The drains were removed in the evening of the first postoperative day. The number of units of concentrated red cells transfused during the hospital stay was recorded, and any thromboembolic and other complications were documented.

Haemoglobin concentration, packed cell volume and platelet count were measured when the patient entered and left the recovery room, on the day of operation at 20:00, and on the first and second mornings after operation.

All continuous data are expressed as mean (SD) and two sided t tests were used for statistical analysis. Fisher's exact test was used for nominal data.  $P < 0.05$  was considered significant.

**Table 1: Data of present study**

Data/groups	Tranexamic acid group	Control group
age	32±10.5	33±8.7
Sex (male: female)	9:6	8:7
weight	57.2±9.8	62.8±6.8
ASA 1/2 grade	10/5	9/6
Duration of operation(min)	110 (18)	105(17)
Duration of tourniquet(min)	80 (16)	78(18)

**Table 2: Preoperative haemostatic mean (SD) status**

Parameters	Tranexamic acid group	Control group
Bleeding Time	315(100)	385(205)
Platelet Count	300(98)	302(99)
aPTT	34(5)	32(4)
Prothrombin time	106(21)	103(19)

**Table 3: Preoperative data mean (SD)**

Parameters	Tranexamic acid group	Control group
Duration of Operation (min)	120(18)	121(17)
Duration of Tourniquet Inflation (min)	85(18)	76(16)

## RESULTS

A total of 30 patients were randomly assigned to one of the two groups. The demographic data i.e. age, gender, and weight were comparable in both the groups. The tourniquet times and the duration of the surgery were also comparable in both the groups. [Table 1]

Per-operative blood loss was almost equal in both the group [tranexamic acid group 528 (289) ml vs control group 515 (246) ml]), whereas there was significant difference in the blood loss in the post-operative periods.

In the recovery room the tranexamic acid group lost 131 (98) ml and the control group 645 (300) ml ( $p < 0.001$ ).

The amount of blood loss in the surgical ward was: tranexamic acid group 295 (220) ml; control group 600 (275) ml ( $p < 0.01$ ).

Total blood loss was 659 (285) ml in the tranexamic acid group, and 1245 (623) ml in the control group ( $p < 0.001$ ).

The control group had to receive significantly more fluid replacement and packed RBCs transfusion, whereas the hemoglobin concentrations changes were similar in both the groups.

Two patients in the control group had a DVT, but none had suffered from the pulmonary embolism. There were four minor non-thrombotic complications in the control group and one in the tranexamic group, all these were statistically non-significant.

## DISCUSSION

During the surgery the blood loss was comparable in both the groups, as tranexamic acid being an antifibrinolytic agent has no role in primary hemostasis and coagulation per se. Once tourniquet was deflated significant hemostasis was achieved in the tranexamic acid group.

Patients in both the groups achieved hemostasis and the total blood loss within the normal range as reported by other studies.<sup>1-5</sup> The most significant difference in the blood loss was during the recovery phase when the tranexamic acid drug concentration was supposed to be within the therapeutic range. Even in the surgical wards the tranexamic acid group bled less than the control group but this difference was less significant as the effect of the drug was waning.

Application of the pneumatic tourniquet causes release of tissue type plasminogen activator from the vascular endothelium induced by anoxia and acidosis; this enhances the fibrinolytic activity of the blood in the area distal to the tourniquet.<sup>6-8</sup>

Tranexamic acid is an antifibrinolytic agent that inhibits the conversion of inactive plasminogen to active proteolytic enzyme plasmin by competitive blocking of a high affinity lysine binding site of plasminogen. This prevents plasmin from binding to fibrinogen and fibrin structures after clot formation. The therapeutic effect of tranexamic acid is apparent when the haemostatic system has produced a fibrin clot which is prematurely dissolved by the proteolytic action of plasmin. According to pharmacokinetic data the single i.v. dose of 15 mg/kg given in this study was expected to maintain a therapeutic drug concentration for a minimum of 2 h.

The major concern with the use of antifibrinolytic agents is their thrombogenic nature. However, Lindoff, Rybo and Astedt did not find any increase in thromboembolic complications in their retrospective study on tranexamic acid in obstetric patients,<sup>10</sup> a population susceptible to thrombotic consequences.

In our study there were two patients with thrombotic events, both in the control group. If tranexamic acid had been given before inflation of the tourniquet, the natural thrombolytic mechanism would have been disturbed. It is believed that the antifibrinolytic therapy timing modulates the excessive fibrinolysis without increasing the risk of deep venous thrombosis.

Leclerc and co-workers started thromboprophylaxis with low molecular weight heparin after operation in their double-blind study of deep venous thrombosis in patients undergoing total knee arthroplasty and tibial osteotomy.<sup>11</sup> In this study, we started enoxaparin in the evening before surgery and continued until the patient was discharged or sufficiently mobilized.

In this study it was found that tranexamic acid when given as single dose, 5 min before tourniquet deflations, significantly reduced perioperative blood loss. The treatment was safe as there was no apparent increase in thrombotic incidence.

However, a larger study is required to reconfirm the results, and another study to check the effect of a second dose of tranexamic acid on bleeding and thrombotic complications.

## REFERENCES

1. Mylod AG, France MP, Muser DE, Parsons JR. Perioperative blood loss associated with total knee arthroplasty. A comparison of procedures performed with and without cementing. *Journal of Bone and Joint Surgery* 1990; 72A: 1010-1012.
2. Cushner FD, Friedman RJ. Blood loss in total knee arthroplasty. *Clinical Orthopaedics and Related Research* 1991; 269: 98-101.
3. Marmor L, Avoy DR, McCabe A. Effect of fibrinogen concentrates on blood loss in total knee arthroplasty. *Clinical Orthopaedics and Related Research* 1991; 273: 136-1.
4. Burkart BC, Bourne RB, Rorabeck CH, Kirk PG, Nott L. The efficacy of tourniquet release in blood conservation after total knee arthroplasty. *Clinical Orthopaedics and Related Research* 1994; 299: 147-152.
5. Healy WL, Seidman J, Pfeifer BA, Brown DG. Cold compressive dressing after total knee arthroplasty. *Clinical Orthopaedics and Related Research* 1994; 299: 143-1.
6. Nakahara M, Sakahashi H. Effect of application of a tourniquet on bleeding factors in dogs. *Journal of Bone and Joint Surgery* 1967; 49A: 1345-1351.
7. Klenerman L, Mackie I, Chakrabarti R, Brozovic M, Stirling Y. Changes in haemostatic system after application of a tourniquet. *Lancet* 1977; 1: 970-972.
8. Petaja J, Myllynen P, Myllyla G, Vahtera E. Fibrinolysis after application of a pneumatic tourniquet. *Ada Chirurgia Scandinavica* 1987; 153: 647-651.
9. Nadler SB, Hidalgo JU, Bloch T. Prediction of blood volume in normal human adults. *Surgery* 1962; 51: 224-232.
10. Nielsen HJ. Detrimental effects of perioperative blood transfusion. *Br J Surg* 1995; 82: 582±87.
11. Leclerc JR, Geerts WH, Desjardins L, Jobin F, Laroche F, Delorme F, Haviernick S, Atkinson S, Bourquoin J. Prevention of deep vein thrombosis after major knee surgery—a randomized, double-blind trial comparing a low molecular weight heparin fragment (Enoxaparin) to placebo. *Thrombosis and Haemostasis* 1992; 67: 417-423.

**Source of Support:** Nil. **Conflict of Interest:** None Declared.

**Copyright:** © the author(s) and publisher. IJMRP is an official publication of Ibn Sina Academy of Medieval Medicine & Sciences, registered in 2001 under Indian Trusts Act, 1882.

This is an open access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Cite this article as:** Lalit Kumar, Simple Chahar. Effects of Tranexamic Acid on Perioperative Blood Loss Associated with Total Knee Arthroplasty: A Randomized Double Blinded Prospective Study. *Int J Med Res Prof.* 2017; 3(2):99-101. DOI:10.21276/ijmrp.2017.3.2.020