

## Research Article

# Tranexamic acid - cost effective method in preventing blood loss in total knee replacement

C. K. Sreehari, S. Nithin\*, Mangesh Shenoy, A. J. Shareef

Department of Orthopaedics, Pariyaram Medical College, Kannur, Kerala, India

**Received:** 23 August 2014

**Accepted:** 06 September 2014

### \*Correspondence:

Dr. S. Nithin,

E-mail: drsnithin@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. 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.

### ABSTRACT

**Background:** Total joint replacement is a frequently done procedure in modern day practice of any orthopedics unit. Limiting blood loss both postoperatively and intraoperatively presents a challenge to the surgeon. Use of tranexamic acid (TA) reduces perioperative blood loss and need for allogenic blood transfusion in patients undergoing total knee replacement.

**Methods:** This is a randomized controlled study that involved 105 patients who underwent primary total knee arthroplasty at our institute. A total of 105 consecutive patients underwent total knee replacement (TKR) between 2009 and 2014 at our institute. No patients who had primary TKR were excluded from the study. The information was collected prospectively but reviewed retrospectively. Patients were allocated to either the TA group (TA,  $n = 55$ ) or the control group ( $n = 50$ ).

**Results:** The results were analyzed and no significant differences between the groups were found in the demographic data. Our results demonstrate significant reduction in blood loss with the use of TA.

**Conclusions:** We can conclude that TA use might be a good solution to the problem of massive allogenic transfusion requirements especially in developing countries. A meta-analysis which looked at double-blinded randomized controlled trial also found that TA was useful in reducing blood loss in major orthopedic procedures.

**Keywords:** Tranexamic acid, Total knee replacement, Blood transfusion

## INTRODUCTION

Total joint replacement is a frequently done procedure in modern day practice of any orthopedics unit. Limiting blood loss both postoperatively and intraoperatively presents a challenge to the surgeon.<sup>1-3</sup> Postoperatively, blood continues to ooze from the cut ends of bone, the open intra-medullary canal and the raw, dissected soft tissues. This can amount to significant bleeding with figures ranging from 600 to 1500 ml. Perioperative bleeding is a major concern in orthopedics and is associated with additional risks and costs to the procedure. In addition, the rapid discharge of patients after surgery has increased the emphasis on blood conservation to enhance patient outcomes.

Patients undergoing total knee arthroplasty (TKA) are transfused at rates of 11-21%. Antifibrinolytics have been

used in orthopedic surgery via an intravenous (IV) route, resulting in a 50% reduction in the rate of transfusions.<sup>5</sup>

Considering the high risks associated with the use of allogenic blood, we think that this drug can be very beneficial to patients undergoing both unilateral and simultaneous bilateral total knee replacements. The aim of this study was to determine: If the use of tranexamic acid (TA) reduces perioperative blood loss and need for allogenic blood transfusion in patients undergoing total knee replacement.<sup>7,8</sup>

Hip fracture is commonly encountered clinical problems, which are associated with a 1 year mortality rate of about 25%. In recent years, studies have documented a rapidly increasing incidence of hip fractures especially in elderly

patients. Surgery for hip fractures frequently requires blood transfusion, despite recent advances in techniques of orthopedic surgery and mechanical improvements of implants. Blood may be transfused before, during or following surgery.<sup>9,10</sup>

## METHODS

This is a randomized controlled study that involved 105 patients who underwent primary TKA at our institute. A total of 105 consecutive patients underwent total knee replacement (TKR) between 2009 and 2014 at our institute. No patients who had primary TKR were excluded from the study. The information was collected prospectively but reviewed retrospectively.

A total of 105 patients with 135 knee joints was included in the study. Patients were randomized using a random number technique. Caring personnel, both the staff of the operating room and the Intensive Care Unit (ICU) were blinded regarding the type and nature of treatment; the correct treatment option was assured by means of coded infusion syringes, prepared by a personal of the hospital pharmacy, not involved otherwise in the study. Patients were allocated to either the TA group (TA,  $n = 55$ ) or the control group ( $n = 50$ ).

In the TA group, a single bolus dose of 15 mg/kg was administered IV at induction of anesthesia. In control group, the same volume of saline solution was infused.

Transfusions were given on a case-by-case basis with regard to age, cardiovascular status, hemoglobin concentration, and blood loss. Most patients who had blood transfusions received these at a hemoglobin concentration between 80 and 100 g/L.

No transfusions were administered after the second post-operative day. Perioperatively, in ICU, routine hematological (hemoglobin, hematocrit, platelet count, prothrombin time, partial thromboplastin time) and hematochemical parameters like creatinine were analyzed in all patients.

## RESULTS

The data related to hematochemical are summarized in Table 1. No significant differences between the groups were found in the demographic data. Mean age of our study

**Table 1: Baseline and hematochemical data.**

Characteristic	Group 1 ( $n=50$ )	Group 2 ( $n=55$ )
Age	65.8	68.1
Weight	83.8	84.3
Sex (M/F)	33/67	46/54
Hemoglobin		
Preoperative	11.3	11.5
Postoperative	10.9	10.3

population was 67 years. Indication for surgery in 71% of the patients was osteoarthritis while in 29% of the patients it was rheumatoid arthritis.

There was no difference between two groups regarding thrombotic complications, pulmonary dysfunction and neurological deficits. The data related to blood loss are summarized in Table 2. This difference between the two groups in the number of units of blood transfused is statistically significant ( $p < 0.001$ ). A statistically significant ( $p < 0.01$ ) difference in transfusion requirement for patients with osteoarthritis and rheumatoid arthritis was also noted. No untoward side effect of TA was noted in our patients.

## DISCUSSION

The most noticeable and extensively explored options available are preoperative blood donation, acute normovolemic hemodilution, perioperative red cell salvage, and certain anesthetic techniques (deliberate hypotension, normothermia). Certain pharmacological interventions that have been used with success are recombinant human erythropoietin, TA, and aprotinin.<sup>4,6</sup>

Extensive blood loss in relation to surgery is associated with a high risk for patients, especially due to cardiovascular complications; allogenic blood transfusion carries the risk of immunological and non-immunological adverse effects, such as transfusion reactions and transmission of infectious agents (AIDS and hepatitis viruses). Allogenic blood transfusion has, furthermore a high medical cost.<sup>15-17</sup>

Antifibrinolytics are a class of drugs that have been in use since the 1960s. TA is an analog of the amino acid lysine. It competitively inhibits plasminogen activation and plasmin binding to fibrin, thus inhibiting fibrin degradation. Since it works by reducing breakdown of fibrin once formed, it is not procoagulant *per se*, but rather supportive of coagulation already in progress.<sup>18-20</sup> This makes it potentially well-suited for use in reducing post-operative bleeding, where surgical hemostasis has been achieved and fibrinolytic activity needs to be suppressed to help maintain hemostasis without promoting venous thrombus formation.<sup>8,9,22</sup>

The fact that all the patients in both the groups were operated by the same team of surgeons excluded the possibility of surgeon dependent factors affecting the results and in turn added strength to our study.

Reinfusion autotransfusion, although an excellent modality, is not available at most of the centers in our country. Thus, simultaneous bilateral TKA is usually associated with massive allogenic blood transfusion requirements. This may, in turn predisposes to various complications such as electrolyte imbalance, deranged coagulation, and hypersensitivity reactions in already compromised patients.

**Table 2: Perioperative and postoperative blood loss.**

	Group 1 (TA group)	Group 2 (Control group)	p value
Mean postoperative drainage			
Unilateral	826 ml	1828 ml	<0.001
Bilateral	1288 ml	2695 ml	<0.001
Mean drop in postoperative hemoglobin			
Unilateral	1.49 g/dl	1.79 g/dl	0.0005
Bilateral	1.94 g/dl	2.21 g/dl	<0.0005
Mean number of packed cells transfused			0.043
Unilateral	0.1	1.24	
Bilateral	0.9	2.6	
Number of patients requiring transfusion	6	18	

TA: Tranexamic acid

## CONCLUSION

We can conclude that TA use might be a good solution to the problem of massive allogenic transfusion requirements, especially in developing countries.

Our results demonstrate significant reduction in blood loss with the use of TA. Other studies have also had similar results. A meta-analysis which looked at double-blinded randomized controlled trial also found that TA was useful in reducing blood loss in major orthopedic procedures. No adverse effects were seen in our population with the use of TA.<sup>20,23</sup>

*Funding: No funding sources*

*Conflict of Interest: None declared*

*Ethical approval: Not required*

## REFERENCES

- Cushner FD, Friedman RJ. Blood loss in total knee arthroplasty. Clin Orthop Relat Res. 1991;98-101.
- Fragen RJ, Stulberg SD, Wixson R, Glisson S, Librojo E. Effect of ketorolac tromethamine on bleeding and on requirements for analgesia after total knee arthroplasty. J Bone Joint Surg Am. 1995;77(7):998-1002.
- Burkart BC, Bourne RB, Rorabeck CH, Kirk PG, Nott L. The efficacy of tourniquet release in blood conservation after total knee arthroplasty. Clin Orthop Relat Res. 1994;147-52.
- Karnezis TA, Stulberg SD, Wixson RL, Reilly P. The hemostatic effects of desmopressin on patients who had total joint arthroplasty. A double-blind randomized trial. J Bone Joint Surg Am. 1994;76(10):1545-50.
- Mylod AG Jr, France MP, Muser DE, Parsons JR. Perioperative blood loss associated with total knee arthroplasty. A comparison of procedures performed with and without cementing. J Bone Joint Surg Am. 1990;72(7):1010-2.
- Faunø P, Suomalainen O, Rehnberg V, Hansen TB, Krøner K, Soimakallio S, et al. Prophylaxis for the prevention of venous thromboembolism after total knee arthroplasty. A comparison between unfractionated and low-molecular-weight heparin. J Bone Joint Surg Am. 1994;76(12):1814-8.
- Goodnough LT, Verbrugge D, Marcus RE. The relationship between hematocrit, blood lost, and blood transfused in total knee replacement. Implications for postoperative blood salvage and reinfusion. Am J Knee Surg. 1995;8(3):83-7.
- Klenerman L, Chakrabarti R, Mackie I, Brozovic M, Stirling Y. Changes in haemostatic system after application of a tourniquet. Lancet. 1977;1(8019):970-2.
- Benoni G, Carlsson A, Petersson C, Fredin H. Does tranexamic acid reduce blood loss in knee arthroplasty? Am J Knee Surg. 1995;8(3):88-92.
- Petäjä J, Myllynen P, Myllylä G, Vahtera E. Fibrinolysis after application of a pneumatic tourniquet. Acta Chir Scand. 1987;153(11-12):647-51.
- Martin JW, Whiteside LA, Milliano MT, Reedy ME. Postoperative blood retrieval and transfusion in cementless total knee arthroplasty. J Arthroplasty. 1992;7(2):205-10.
- Lane GJ, Hozack WJ, Shah S, Rothman RH, Booth RE Jr, Eng K, et al. Simultaneous bilateral versus unilateral total knee arthroplasty. Outcomes analysis. Clin Orthop Relat Res. 1997;106-12.
- Nozoe T, Miyazaki M, Saeki H, Ohga T, Sugimachi K. Significance of allogenic blood transfusion on decreased survival in patients with esophageal carcinoma. Cancer. 2001;92(7):1913-8.
- McClelland B, Contreras M. Appropriateness and safety of blood transfusion. BMJ. 2005;330(7483):104-5.
- Spahn DR, Casutt M. Eliminating blood transfusions: New aspects and perspectives. Anesthesiology. 2000;93(1):242-55.
- Hedlund PO. Antifibrinolytic therapy with Cyklokapon in connection with prostatectomy. A double blind study. Scand J Urol Nephrol. 1969;3(3):177-82.
- Dunn CJ, Goa KL. Tranexamic acid: A review of its use in surgery and other indications. Drugs. 1999;57(6):1005-32.
- Békássy Z, Astedt B. Treatment with the fibrinolytic

- inhibitor tranexamic acid –Risk for thrombosis? *Acta Obstet Gynecol Scand.* 1990;69(4):353-4.
19. Katsaros D, Petricevic M, Snow NJ, Woodhall DD, Van Bergen R. Tranexamic acid reduces postbypass blood use: A double-blinded, prospective, randomized study of 210 patients. *Ann Thorac Surg.* 1996;61(4):1131-5.
  20. Hiippala ST, Strid LJ, Wennerstrand MI, Arvela JV, Niemelä HM, Mäntylä SK, et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesth Analg.* 1997;84(4):839-44.
  21. Hiippala S, Strid L, Wennerstrand M, Arvela V, Mäntylä S, Ylinen J, et al. Tranexamic acid (Cyklokapron) reduces perioperative blood loss associated with total knee arthroplasty. *Br J Anaesth.* 1995;74(5):534-7.
  22. Benoni G, Fredin H. Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: A prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg Br.* 1996;78(3):434-40.
  23. Rosenblatt MA. Strategies for minimizing the use of allogeneic blood during orthopedic surgery. *Mt Sinai J Med.* 2002;69(1-2):83-7.
  24. Zufferey P, Merquiol F, Laporte S, Decousus H, Mismetti P, Auboyer C, et al. Do antifibrinolytics reduce allogeneic blood transfusion in orthopedic surgery? *Anesthesiology.* 2006;105(5):1034-46.
  25. Ip PP, Lam KW, Cheung CL, Yeung MC, Pun TC, Chan QK, et al. Tranexamic acid-associated necrosis and intralesional thrombosis of uterine leiomyomas: A clinicopathologic study of 147 cases emphasizing the importance of drug-induced necrosis and early infarcts in leiomyomas. *Am J Surg Pathol.* 2007;31(8):1215-24.

DOI: 10.5455/2349-3933.ijam20141107

**Cite this article as:** Sreehari CK, Nithin S, Shenoy M, Shareef AJ. Tranexamic acid - cost effective method in preventing blood loss in total knee replacement. *Int J Adv Med* 2014;1:196-9.