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Original Research Article

Comparison of blood loss in total knee replacement surgery with and without tranexamic acid: a prospective, time framed and observational analytical study

Shaival Mandal[1], B. D. Chatterjee[1], Abheek Kar[1], Saumya Agarwal[2]*

[1]Department of Orthopaedics, Apollo Gleneagles Hospitals, Kolkata, West Bengal, India
[2]Department of Orthopaedics, Geetanjali Medical College & Hospital, Udaipur, Rajasthan, India

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***Correspondence:**
Dr. Saumya Agarwal,
E-mail: saumyathecalyx.agarwal@gmail.com

ABSTRACT

Background: Total knee replacement is one of the common orthopaedic procedures performed worldwide. Blood transfusion is one of the major requirements in TKR procedure due to the amount of blood loss during and after the procedure. We carried out a prospective study to determine the efficacy of tranexamic acid in controlling blood loss during TKR procedure.
Methods: Study was conducted at a tertiary care centre, involving cases operated by a single surgeon. Study included 140 patients undergoing primary TKR for advance degenerative disease of knee and were divided into two groups of 70 each, one group that received tranexamic acid before surgery and another group that did not receive tranexamic acid before surgery. Patient with allergy to the drug, hepato/renal dysfunction, DVT, abnormal PT and INR were not included. Tranexamic acid was given intravenously as well as intra-articular.
Results: Pre-operative haemoglobin ranged from 10.2 gm% to 14.4 gm% in the group getting tranexamic acid and from 10% to 14 % in the group not getting tranexamic acid. Post operatively haemoglobin varied from 8.4 gm% to 12.8 gm% in Group 1 and from 7.8 gm% to 12 gm% in Group 2. Difference of mean post-operative Hb (p=0.0045) and PCV (p=0.0024) in two groups was statistically significant.
Conclusions: We concluded that administration of tranexamic acid reduces the blood loss as well as need of blood transfusion in a patient undergoing total knee replacement.

Keywords: Blood loss, Blood transfusion, Haemoglobin, Total knee replacement, Tranexamic acid

INTRODUCTION

Total knee replacement (TKR) is one of the common orthopaedic procedures performed worldwide due to the predominance of knee arthritis population. According to Frost and Sullivan survey, approximately 70,000 joint replacement procedures were performed in India in 2011 and the requirement of arthroplasty was expected to increase at a compound growth rate of 26.7% (calculated annually) till 2017.[1] Blood transfusion is one of the major requirements in TKR procedure due to the amount of blood loss during and after the procedure.[2] However, the transfusion of blood carries a risk of transmitting viral infections along with the chances of antibody-antigen reactions making it an unsafe solution for maintaining the haemostasis.[3] Therefore, research to control the blood loss is being extensively conducted to decrease the requirement of blood transfusion. Use of bipolar cautery, hypotensive anaesthesia, tourniquet, ligation of larger vessels are a few conventional methods of reducing blood loss during surgeries. Pharmacological means of controlling blood loss has become popular with the introduction of anti-fibrinolytic agents such as tranexamic acid. These agents reduce the blood loss and requirement

of blood transfusion, apart from promoting the maintenance of haemostasis and does not create the risk of Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE).[4-6] Several studies have reported the efficacy of tranexamic acid in controlling blood loss during TKR procedure. However, reports on complications due to the administration of tranexamic acid have not been reported till date.[3] Studies taking into account the weight and Basal Metabolic Index of the patients (to monitor the anaemic condition) and the parameters such as intra- and postoperative blood loss in the Indian population are lacking. Therefore, the originality of this study lies in the variables and parameters selected for evaluating the efficacy of tranexamic acid in reducing blood loss during total knee replacement surgery in Indian population.

METHODS

A time framed prospective study of observational analytical design in 140 patients undergoing primary total knee arthroplasty, operated by a single surgeon and diagnosed with advance degenerative disease of knee joint, in a tertiary care centre was conducted between August 2017 and May 2020. The study protocol was approved by institutional ethical and scientific committee. Patients having allergy to tranexamic acid, or known hepato/renal dysfunction, DVT, hypercoagulable state, bleeding disorders or abnormal prothrombin time (PT), International normalized ratio (INR) were excluded from the study. Seventy patients were allocated into Group 1- i.e. those who received tranexamic acid prior to surgery. Seventy patients were allocated into Group 2- i.e. those who did not receive tranexamic acid prior to surgery. The number of subjects for this study was 140.4 ~ 140 with power 86% (From the different studies done, expected proportion of the patients, amongst the cases had been assumed to be 60%). 140 patients was taken and divided for two groups and calculations were done using sample size formula. Hemoglobin (Hb) levels measured pre-operatively (within 07 days prior to surgery) and on first post-operative day (cyanmethemoglobin method was be used to determine Hb levels.) Drain collection was noted for first and second post-operative day. Patients who satisfied the inclusion criteria and consented to participate in the study had their Hb levels measured within 24 hours prior to the planned procedure. For patients whose Hb level was below 10gm%, proper measures were taken like plasma red blood cells transfusion to raise it to 10 or above. In the comparative group labelled as 2, no tranexamic acid was administered and was identified retrospectively from chart review and matched for age and gender with subjects from Group 1. The pre-operative and post-operative Hb levels were recorded as a part of 'standard of care' in all charts and drain collection for first and second post-operative day was noted. The drop in hemoglobin post-operatively was compared between the two groups to determine the effectiveness of tranexamic acid.

Surgical technique

To avoid any discrepancy single surgeon cases were included in this study. Anterior midline incision was taken followed by medial parapatellar arthrotomy. Cautery and tourniquet was used in all cases to minimize the blood loss. Average time of procedure was 03 hours. 1 gram of tranexamic acid (dosage 10mg/kg body weight -max dose 1g) given as an Intravenous (IV) infusion in 100 ml of Normal Saline over fifteen minutes; 15 minutes before incision and then intra-articular tranexamic acid was injected in the operated knee joint at the time of closure of the wound. Tourniquet was deflated after cementation was done. The study was explained to the patient and those who consented were recruited in the study. All patients were informed about the administration of the drug prior to the surgery. All drug-related queries including the management of complications were clarified with the patients.

Statistical analysis

Data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0 and Graph Pad Prism version 5. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. P value ≤ 0.05 was considered statistically significant. Randomised allocation was done and sample size calculation formula was used to calculate the number of subjects.

RESULTS

The collected data was grouped into two as group 1 who received tranexamic acid prior to surgery and group 2 who did not receive tranexamic acid.

In this study, there were 47 females and 23 males in group 1 and 50 females and 20 males in group 2. Association of gender distribution in two groups was not statistically significant (p=0.5825) In group 1, the mean age (mean±SD) of patients was 64.7857±6.9007 years with range 49.00-78.00 years and the median age was 64.50 years and in group 2, the mean age (mean± SD) of patients was 64.9571±7.7337 years with range 51.00-85.00 years and the median age was 64.00 years. There was no statistically significant difference in age distribution between the groups. (p=0.8901). Table 1 shows distribution of mean pre-op Hb level in both the groups. Pre-operative haemoglobin ranged from 10.2 gm% to 14.4 gm% in the group getting tranexamic acid and from 10% to 14% in the group not getting tranexamic acid. Difference of mean Pre-operative Hb in two groups was not statistically significant (p=0.4249). Table 1 shows distribution of mean pre-op Packed Cell Volume (PCV) level in both groups. Difference of mean Pre-operative PCV in two groups was not statistically significant (p=0.6117).

Table 1: Distribution of mean pre-op Hb and mean pre-op PCV in two groups.

		Number	Mean	SD	Minimum	Maximum	Median	P value
Pre-op Hb	Group-1	70	11.6971	1.0427	10.2000	14.4000	11.4500	0.4249
	Group-2	70	11.8371	1.0269	10.0000	14.0000	11.8000	
Pre-op PCV	Group-1	70	38.1686	3.2999	30.2000	46.0000	37.5500	0.6117
	Group-2	70	38.4550	3.3599	31.5000	46.3000	38.3000	

Table 2: Distribution of mean post-op Hb and mean post-op PCV in two groups.

		Number	Mean	SD	Minimum	Maximum	Median	P value
Post-op Hb	Group-1	70	10.4557	1.0656	8.4000	12.8000	10.4500	0.0045
	Group-2	70	9.9186	1.1327	7.8000	12.0000	10.1000	
Post-op PCV	Group-1	70	33.8964	3.3589	25.6000	40.6000	34.0000	0.0024
	Group-2	70	31.6243	5.1541	3.4000	40.0000	32.0000	

Table 3: Distribution of mean fall Hb and mean fall in PCV in two groups.

		Number	Mean	SD	Minimum	Maximum	Median	P value
Fall in Hb	Group-1	70	1.2414	0.4372	0.3000	2.2000	1.2000	<0.0001
	Group-2	70	1.9186	0.6830	0.5000	4.2000	1.8000	
Fall in PCV	Group-1	70	4.2721	1.4406	1.3000	8.5000	4.2500	<0.0001
	Group-2	70	6.8307	4.5463	1.7000	39.8000	5.8500	

The distribution of mean post-op Hb levels in both groups is shown in (Table 2). Post operatively haemoglobin varied from 8.4 gm% to 12.8 gm% in Group 1 and from 7.8 gm% to 12 gm% in Group 2. Difference of mean post-operative Hb in two groups was statistically significant (p=0.0045). The distribution of mean post-op PCV level in both groups is shown in (Table 2). Difference of mean post-operative PCV in two groups was statistically significant (p=0.0024). Post-operative drain collection on first day was more in cases of Group 2 with median of 147.5 (maximum of 700 ml) as compared to Group 1 with median of 80 (maximum of 200ml). Difference of mean drain in both groups was statistically significant (p<0.0001). Post-operative drain collection on second day was again more in cases of Group 2 with median of 100 (maximum of 350ml) as compared to Group 1 with median of 60 (maximum of 150ml). Difference of mean drain 2 in both the groups was statistically significant (p<0.0001).

Table 3 shows distribution of mean fall in Hb levels in both groups. Difference of mean fall in Hb in two groups was statistically significant (p<0.0001). Table 3 shows distribution of mean fall PCV levels in both the groups. Difference of mean fall in PCVin two groups was statistically significant (p<0.0001).

DISCUSSION

The blood loss associated with unilateral TKR, as reported, ranges from 600 ml to 1550 ml depending on the clinical setting and study design.[7,8] Probably the main reason for this great variation is the different methods used to define and determine perioperative blood loss. Knee surgeons have increased efforts to reduce such complications and other complications associated with massive blood loss after TKR. Among different methods, tranexamic acid injection and drainage are most preferred and recent reports have documented successful outcomes of the method. Despite the possible differences in transfusion policies, the volume of transfused red cells, gives a more coherent and probably also a more objective picture of the total perioperative blood loss.[7,8]

The treatment results of TKR are satisfying, but it has been associated with massive blood loss compared to other orthopaedic operations. Mean blood loss of 1518 ml was reported by Lotke et al in their TKR patients, indicating the increased necessity of blood transfusion after TKR.[9] Major cause of blood loss includes resection of the bone or soft tissue during TKR. Besides such 'visible' blood loss, there is hidden blood loss due to bleeding into the soft tissue. Despite being non negligible in terms of the amount, it can cause underestimation of the total amount of blood loss. The mean postoperative blood loss calculated by Sehat et al in their study was 1,498 ml, and approximately 49% (735 ml) of which was hidden blood loss.[10]

Several studies have studied the effects of various operative techniques and different modalities on TKR associated blood loss, but until recently only one clinically relevant factor has been identified.[7,8] Use of cement reduces blood loss caused by TKR significantly.[7]

Application of a pneumatic tourniquet or venous occlusion enhances fibrinolytic activity several times above the basal level in the ipsilateral extremity. This is due to tissue plasminogen activator released from the vascular endothelium which is triggered by anoxia or venous distension.[11] Excessive fibrinolysis may increase blood loss caused by major orthopedic surgeries such as TKR. This theory is supported by the results of some recent studies that focused on the reduction of blood loss by the use of antifibrinolytic drugs. Thorpe et al conducted a study where aprotin in was given to TKR patients before inflation of the tourniquet.[12] Study concluded that the transfusion requirements and blood loss, decreased in the treatment group compared to controls. Transfusion requirements were reduced significantly by 43% with tranexamic acid and by 60% with aprotinin in one study.[13]

In a prospective, double-blind, placebo-controlled trial, conducted by Wong Jean et al, 124 patients were randomized to receive 1.5 or 3.0 g of tranexamic acid in 100 ml of normal saline solution or an equivalent volume of placebo (normal saline solution) applied into the joint for five minutes at the end of surgery.[14] The primary outcome was blood loss, calculated from the difference between the preoperative hemoglobin level and the corresponding lowest postoperative value or hemoglobin level prior to transfusion. Wong et al also used Doppler ultrasound in all patients and measurement of plasma levels of tranexamic acid was done one hour after release of the tourniquet.[14] They also concluded that there was no difference in the rates of deep-vein thrombosis or pulmonary embolism between the three groups.

In a study by Gomez-Barenna et al, a phase-3, single-centre, double blind, randomized, controlled clinical trial was performed to compare topical intra-articular tranexamic acid with two IV doses of same (15 mg/kg in 100 ml of physiological saline solution) in a multimodal protocol for blood loss prevention.[15] Topical administration according to the described protocol demonstrated non-inferiority compared with the IV tranexamic acid, with no safety concerns, as the transfusion rate was zero in both the groups. Similar study by Soni et al concluded that intra-articular tranexamic acid is equally effective as three dose intravenous regimen in reducing blood loss during total blood loss during TKR surgery.[16] There are quite a number of similar studies. However, we did not come across many studies conducted upon Indian population with more sample size, which was one of the reasons for us to do this study. As with patient awareness and technological advancement TKR is now a very common orthopaedics procedure.

In our study, we recruited 140 patients undergoing primary total knee arthroplasty into two groups. The data was collected from a single surgeon cases to avoid surgeon based difference in the tissue handling. Pneumatic tourniquet and cautery was used in all cases to minimize blood loss. Tranexamic acid was given by IV (before incision) as well as intra-articular (at the time of closure) routes. There is no consensus regarding which is the better route of administration of tranexamic acid and in what dose, we chose for the combined route. Study shows intra-articular tranexamic acid along with reducing blood loss also reduces knee swelling.[17] Intra-operative blood loss was checked by checking the intra-operative drain collection, weighing mops, post-operatively drain collection was checked till post-operative day 2nd. In few cases among the group not receiving tranexamic acid, drain collection on post-operative day 2nd was more than 150ml and we continued with drain till post operative day 3rd for such patients. Haemoglobin was checked on post-operative day 1st. The doses of tranexamic acid were planned according to the available pharmacokinetic data to ensure therapeutic concentrations of tranexamic acid during the first 12-14 postoperative hours.[18] Along with haemoglobin, PCV was also taken into consideration to determine the blood loss more precisely. There was significant decrease in the intraoperative as well as postoperative blood loss in the patients getting tranexamic acid. Only 2 patients in the group getting tranexamic acid needed blood transfusion postoperatively whereas the other group had 14 such patients. Intraoperative blood loss and postoperative drain collection was more in the patients who did not receive tranexamic acid.

Till date follow up of the patients, showed no evidence of DVT or PE among the patient receiving tranexamic acid. However the role of tranexamic acid in established thromboembolic condition remains debatable. It is also unknown how readily the findings of significant studies such as CRASH-2 can be translated to surgical patients, where the haemostatic picture may be very different.[19] The threshold for use may decrease in patients where intraoperative bleeding becomes significant or life-threatening. The evidence for relation between thromboembolic complications and tranexamic acid use is not strong but many studies did not measure the incidence of these phenomena, while others excluded patients judged at an increased risk. This is the reason why role of tranexamic acid in such patients is still unclear and there's no consensus upon the use of drug for the patients with existing risk factors (e.g. DVT, PE).

There is high overall strength of evidence for the use of intra-articular tranexamic acid injection and additionally topical and intravenous injections are recommended for reducing the proportion of patients transfused and units of red blood cell transfused in orthopedic and cardiac surgical adult patients.[20] Moreover, both intravenous and tropical tranexamic acid injections are recommended at the end of TKR surgery.[21]

This study will be continued with a view to increase the sample size and reassess the results. It was not possible to calculate blood loss accurately. Age and sex matching

were not done. Other minor coagulopathies were not taken into consideration. The size of the study group is not large enough to reliably account for all important variables or draw firm conclusions. Studies with larger sample size can be conducted to validate the findings of our study and draw conclusions for all parameters.

CONCLUSION

It is evident from this study that administration of tranexamic acid in patients undergoing total knee replacement decreases the blood loss as well as decreases the need for blood transfusion post operatively. We can safely conclude that there was a significant fall in hemoglobin following total knee replacement. The drop in hemoglobin was steeper in patients who did not receive tranexamic acid. Reduction in drop of hemoglobin levels with the use of tranexamic acid was statistically significant. Incidence of blood transfusion was more in the group that did not receive tranexamic acid.

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REFERENCES

1. Pachore JA, Vaidya SV, Thakkar CJ, Bhalodia HKP, Wakankar HM. ISHKS joint registry: A preliminary report. Ind J Orthopae. 2013;47(5):505.
2. Carling MS, Jeppsson A, Eriksson BI, Brisby H. Transfusions and blood loss in total hip and knee arthroplasty: a prospective observational study. J Orthop Surg Res. 2015;10(1):48.
3. Dakir A, BalakrishnanRamalingam VE, Dhanavelu P. Efficacy of tranexamic acid in reducing blood loss during maxillofacial trauma surgery–a pilot study. JCDR. 2014;8(5):ZC06.
4. Kazemi SM, Mosaffa F, Eajazi A, Kaffashi M, Besheli LD, Bigdeli MR, et al. The effect of tranexamic acid on reducing blood loss in cementless total hip arthroplasty under epidural anesthesia. Orthopedics. 2010;33(1).
5. Hourlier H, Reina N, Fennema P. Single dose intravenous tranexamic acid as effective as continuous infusion in primary total knee arthroplasty: a randomised clinical trial. Arch Orthopaed Trauma Surg. 2015;135(4):465-71.
6. Gillette BP, DeSimone LJ, Trousdale RT, Pagnano MW, Sierra RJ. Low risk of thromboembolic complications with tranexamic acid after primary total hip and knee arthroplasty. Clin Orthopaed Relat Res. 2013;471(1):150-4.
7. Mylod AG, France MI', Muser DE, Parsons JR. Perioperative blood loss associated with total knee arthroplasty. J Bone Joint Surg Am. 1990;72(7):1010-2.
8. Cushner FD, Friedman RJ. Blood loss in total knee arthroplasty. ClinOrth. 1991;269:98-101.
9. Lotke PA, Faralli VJ, Orenstein EM, Ecker ML. Blood loss aftertotal knee replacement. Effects of tourniquet release andcontinuous passive motion. J Bone Joint Surg Am. 1991;73(7):1037-40.
10. Sehat KR, Evans R, Newman JH. How much blood is really lost in total knee arthroplasty? Correct blood loss management should take hidden loss into account. Knee. 2000;7(3):151-5.
11. Petajl J, Myllynen I', Myllyla G, Vahtera E. Fibrinolysis after application of a pneumatic tourniquet. ActaChir Stand. 1987;153(11-12):647-51.
12. Thorpe CM, Murphy WG, Logan M. Use of aprotinin in knee replacement surgery. Br J Anaesth. 1994;73(3):408-10.
13. Dunn CJ, Goa KL. Tranexamic Acid: a review of its use in surgery and other indications. Drugs. 1999;57(6):1005-32.
14. Wong J et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. J Bone Joint Surg Am. 2010;92(15):2503-13.
15. Gomez-Barrena E, Ortega-Andreu M, Padilla-Eguiluz NG, Perez-Chrzanowska H, Figueredo-Zalve R. Topical intra-articular compared with intravenous tranexamic acid to reduce blood loss in primary total knee replacement: a double-blind, randomized, controlled, noninferiority clinical trial. J Bone Joint Surg Am. 2014;96(23):1937-44.
16. Soni A, Saini R, Gulati A, Paul R, Bhatty S, Rajoli SR. Comparison between intravenous and intra-articular regimens of tranexamic acid in reducing blood loss during total knee arthroplasty. J Arthropl. 2014;29(8):1525-7.
17. Ishida K, Tsumura N, Kitagawa A, Hamamura S, Fukuda K, Dogaki Y, et al. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee arthroplasty. Int Orthopaed. 2011;35(11):1639-45.
18. Hiippala ST, Strid LJ, Wennerstrand MI, Arvela JV, Niemela HM, Mantyla SK, et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. Anesth Analg. 1997;84(4):839-44.
19. Crash-2 Collaborators. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet. 2011;377(9771):1096-101).
20. Derzon JH, Clarke N, Alford A, Gross I, Shander A, Thurer R. Reducing red blood cell transfusion in orthopedic and cardiac surgeries with Antifibrinolytics: a laboratory medicine best practice systematic review and meta-analysis. Clin Biochem. 2019;71:1-3.

21. Zhou KD, Wang HY, Wang Y, Liu ZH, He C, Feng JM. Is topical or intravenous tranexamic acid preferred in total hip arthroplasty? A randomized, controlled, noninferiority clinical trial. PLoS One. 2018;13(10):e0204551.

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