



A Study on Efficacy of Tranexamic Acid in Reducing Blood Loss in Total Hipreplacement Surgery

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Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 03 Nov 2023	Background: The purpose of this study was to assess tranexamic acid effectiveness in lowering perioperative blood loss in total hip arthroplasty. Materials and Methods: Two groups with a total of sixty patients were created. tranexamic acid was administered preoperatively to patients in Group A. patients in Group B did not receive tranexamic acid. Intraoperative blood loss, preoperative, postoperative hemoglobin were monitored and documented. Results: The following observations were made: patients in the study were in the age group of 20-70 years age. Majority patients belonged to 20-50 years of age (N=45, 75%). Male to female ratio of the study population was 13:1. mean weight of the study population was 57.35 kg. Out of the various preoperative diagnosis majority of the patients were diagnosed with avascular necrosis with secondary osteoarthritis (55%). 37 patients underwent Non cemented total hip replacement, 21 underwent cemented total hip replacement and 2 patients underwent Hybrid total hip replacement. Conclusion: Intraoperative blood loss was less in tranexamic acid group compared to control group (172 ml) p value (0.001). Postoperative fall in hemoglobin was less in tranexamic acid group compared to control group (0.510 g/dl) p value (0.016). Keywords: Hip replacement, Surgery, Post-operative, tranexamic acid, blood loss, Avascular necrosis.
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1. Introduction

Total hip replacement is a commonly performed reconstructive hip surgery in adults (1). Substantial blood loss is associated with this procedure leading to acute anemia and other ailments therefore increasing the requirement for blood transfusion (2). However, transfusion can be costly as well as a scarcely available resource. blood transfusion also carries a probability of transfusion reaction which in turn may increase cost of treatment (3). It also exposes patient to the risk of post-transfusion infective disorders, like *Human Immunodeficiency Virus (HIV)*, *Hepatitis B Virus (HBV)*, *Cytomegalovirus*, *Epstein-Barr Virus (EBV)*, etc. (3,4).

The positive end result of Total hip arthroplasty needs adequate intra operative haemostasis in order to prevent haematoma formation. Achieving soft tissue haemostasis is also vital for postoperative rehabilitation. Continuous hemorrhage after operative procedure can lead to ache, wound haematoma, seroma formation and arthrofibrosis causing sub optimal outcomes after surgical procedure (5). Regardless of the best effort of the surgical team, complications are sometimes encountered after Total Hip replacement.

Clinically substantial loss of blood often occurs insidiously. The subcutaneous fat content of the surrounding tissue around the hip joint, can cause substantial blood loss which can often be overlooked during and after the procedure. Use of tourniquet in THA is not a viable option as opposed to Total Knee arthroplasty due to location of incision. However local tamponade effect of prosthesis substantially decreases the amount of loss of blood. in absence of a blood coagulation process persistent haemorrhage could be of enough severity to requisite transfusion of blood (6).

Tranexamic. acid is an artificial analogue of lysine, which is a competitive inhibitor of lysine receptor on plasminogen and plasmin causing fibronolysis inhibition (5). tranexamic acid when compared with other pharmacological agents such as aprotinin aminocaproic acid is much cheaper and has better

efficacy. Moreover, concentration of tranexamic acid is higher in joint fluid in comparison to plasma levels of the drug (7,8).

This study aims to assess and bring out the efficacy of intravenous tranexamic acid in reducing blood loss in total hip arthroplasty.

2. Literature Review

Over the years with improvement of surgical techniques various method of controlling bleeding or cauterization have been popularized which includes the use of tourniquet, cauterization, antifibrinolytic agents Epsilon amino caproic acid an artificial analogue of lysine having a strong inhibiting effect on plasminogen and Trans 4 amino methylcyclohexane carboxylic acid well known as tranexamic acid, have been widely used clinically over last few years to control bleeding. The efficacy of tranexamic acid has been reported to be 10 times more than Epsilon amino caproic acid and more tolerable when compared to Epsilon aminocaproic acid (9).

Kazi et al. in the year 2012 assessed the tranexamic acid efficacy in reducing transfusions required in patients that underwent revision hip replacement surgery. Analysing the effect of tranexamic acid given in 30 subjects compared to 30 subjects that were not given the drug. blood loss was measured intra operatively, perioperative hemoglobin values measured and postoperative values also recorded. The mean post-operative hemoglobin was 9.50 gm% in the tranexamic acid group and 8.20 gm% in the other group. The average hemoglobin change was 2.70 gm% in the tranexamic acid group and 3.40 gm% in the other group. Average blood products that were required in the study were 2.760 in the tranexamic acid group while 4.0 were required in the group not given the drug (10).

In 2018 a network meta-analysis by Yoon et al. on optimum use of tranexamic acid in total hip replacement surgery in which a cumulative number of 2227 subjects were divided into 5 categories: 564 Intravenous single, 319 multiple-intravenous, 398 local, 120 local and intravenous, and 826 placebo trials. Most optimal treatment was classified on basis of reduction in requirement of transfusion in following manner: (a) Local and intravenous = 98.2%, (b) Intravenous single = 54.0%, (c) Intravenous multiple 78.6%, local = 66.1%, (d) placebo = 0%. Compared with placebo, intravenous single, intravenous multiple, local, local plus intravenous treatment groups revealed no statistically significant difference in the frequency of occurrence of DVT and emboli formation. Concluding that local plus intravenous tranexamic acid was efficacious in reduction of transfusion requirement after hip replacement compared with intravenous or local alone (11).

In a 2-phase retrospective matched-pair study published in the year 2018 by El Beheiry et al. (12) of patients who were operated for THR between 2007–2013. In the initial phase, 58 subjects aged more than or equal to 65 years who were administered tranexamic acid were matched with subjects that had not administered tranexamic acid for age and sex, American Society of Anesthesiologists grading and B.M.I. In the later phase, 58 subjects that were older than equal to 65 years were administered tranexamic acid were matched with subjects <65 years of age who were administered tranexamic acid for sex, ASA grade and BMI. Initial outcomes that were recorded were percent maximum decrease in hemoglobin level and estimated blood loss post arthroplasty.

3. Materials And Methods

This study was conducted in the Department of Orthopaedics, Himalayan Institutes of Medical Sciences, Swami Rama Himalayans University, Swami Ram Nagar, Dehradun over a period of 12 months. patients presenting in Orthopaedic OPD / Emergency, were recruited for the study after taking written and informed consent.

Study Design:

Type of study: Quasi experimental study.

Sample size:

Sample size of 60 was taken for this study (30 patients in each group). Group A (intravenous) (n) Administered preoperatively 15 minutes prior to incision over the course of 10-15 minutes, a bolus dose of tranexamic acid (20 mg/kg) diluted in 100 ml of normal saline is given. Group B (Those who did not receive the drug). Sample size calculation using the formula:

$$\frac{4pq}{e^2}$$

where, p is prevalence of hip osteoarthritis (11.5 per 100,000), q is 100- p and e is relative error taken as 10%.

Sampling method: All cases of primary total hip arthroplasty.

Selection of Subjects

Inclusion Criteria:

1. patients undergoing primary total hip replacement.
2. Pre-operative Haemoglobin > 10 g/dl for males and > 9 g/dl for females.

Exclusion Criteria:

1. Having a history of coagulopathies, deep vein thrombosis, pulmonary embolism, convulsions, arterial thromboembolism, conditions like medical contraindication to using tranexamic acid (angina, myocardial infarction, stroke, acute lower limb ischemia).
2. Coagulopathy i.e., preoperative platelet counts < 150,000 mm³, international normalized ratio (INR) > 1.4 and prolonged prothrombin time (PT) > 1.4 s.
3. Perioperative anaemia defined as a haemoglobin (Hb) level lower than 10 g/dL in males and 9 g/dL in females.
4. patients with associated bony pathology or tumour.

Study Tools:

1. Case reporting form.
2. Inj. tranexamic acid
3. Digital weighing machine
4. suction machine.

Study Protocol:

This study was conducted after obtaining approval from the Institutional Ethical Committee of Swami Rama Himalayan University. Whenever a patient fitting in the inclusion criteria presented to orthopedics OPD /emergency, a written informed consent was sought from him/her after explaining the objectives of the study. Those patients giving written consent were included in the study. first of all, baseline characteristics (like age, sex, weight, IPD number, preoperative hemoglobin) were noted followed by the surgery required/planned as per the discretion of the operating surgeon based on patient requirements and clinical indication, tranexamic acid was administered to the patients

Drug Preparation and Administration:

The nursing personnel in the operation room prepared the drug. In the intravenous group (Group A), the anaesthetist administered tranexamic acid at a dosage of 20 mg/kg diluted in 100 ml of ordinary saline. given as an infusion 15 minutes before surgery, over the course of 10 to 15 minutes.

Method of calculation of blood loss:

During surgery (intraoperatively)

1. The average weight of a dry mop (b) was determined before sending them to the autoclave for sterilization this was the benchmark used for all dry mops.
2. Digital weighing scale to measure the weight of a dry mop and compare it to the weight of a used, blood -soaked mop (b)used during the surgery.
3. Soakage weight (S.W.) is computed as the difference between the weights of the wet and dry mop, shown as $S.W. = a - b$. 2. blood loss in suction (B.S.) is equal to total output in suction container (c) minus normal saline used to wash the surgical site (d) ($B.S. = c - d$). this corresponds to total output in suction container (c) minus the quantity of fluid (Normal Saline) used to wash the surgical site (d).
4. Spillage recorded by the operating surgeon.
5. Post operatively: On post-operative day 2, haemoglobin and packed cell volume were assessed.

Data Management & Statistical Analysis:

Statistical analysis using statistical package for social sciences (SPSS) version 22.0. Interpretation and analysis of obtained results will be carried out using following tests of significance:

1. Data was presented as arithmetic mean \pm standard deviation (SD) for parametric data, median (range), or number (%) for non-parametric data unless specified.

- Student unpaired 't' test was to analyse the total blood loss among the two groups.
- Mann Whitney test was used to analyse the Haemoglobin and (Haematocrit) PCV difference between the two groups.

3. Results and Discussion

The following observations were made: patients in the study were in the age group of 20-70 years age. Majority patients belonged to 20-50 years of age (N=45, 75%). Male to female ratio of the study population was 13:1. mean weight of the study population was 57.35 kg (Table 1 – Table 3).

Table 1 Age distribution of the study population (N=60)

Age group	Group A N (%)	Group B N (%)	Total N (%).
21 - 30 years	9 (30)	8 (26.7)	17 (28.3)
31 - 40 years	9 (30)	9 (30)	18 (30)
41 - 50 years	4 (13.3)	6 (20)	10 (16.7)
51 - 60 years	4 (13.3)	1 (3.3)	5 (8.3)
61 to 70 years	4 (13.3)	6 (20)	10 (16.7)
Total	30 (100)	30 (100)	60 (100)
Mean age (mean \pm S.D)	41.87 \pm 14.38	41.93 \pm 15.61	p value = 0.98

The age distribution in the tranexamic acid group was not significantly different from the control group and hence both the groups were comparable.

Males and females were equally distributed in tranexamic acid group and the control group (Table 2).

Table 2: Gender distribution of the study population (N=60)

Gender	Group A (30) N (%)	Group B (30) N (%)	Total (60) N(%)
Male	25 (83.3)	27 (90)	52 (86.7)
Female	5 (16.7)	3 (10)	8 (13.3)
Chi-square	p value:	0.571	

The mean weight of patients in tranexamic acid group and control group was comparable and the minor difference between the groups was not statistically significant (Table 3).

Table 3: Weight among subjects in tranexamic acid group and the control group(n=60)

Group	mean weight	Std. Deviation	p value	95% confidence interval
Group A	57.47	5.99	0.621	-3.682 to 2.216
Group B	58.20	5.39		

The mean pre-operative hemoglobin levels of tranexamic acid group and control group was comparable and the minor difference between the groups was not statistically significant (Table 4).

Table 4: Comparison of pre-operative hemoglobin levels among subjects in tranexamic acid group and the control group (n=60)

Group	mean Hb(gm%)	Std.Deviation	p value	95% confidence interval
Group A	11.92	0.97	0.743	-0.543 to 0.390
Group B	12.00	0.82		

Majority of the subjects had AVN Hip with secondary OA (55%) and the difference in the surgical diagnosis between the groups was not statistically significant (Table 5).

Table 5: Distribution of the study subjects according to indication for surgery (N=60)

Diagnosis	Group A N (%)	Group B N(%)	Total N (%)
AVN Hip with secondary OA	17 (56.7)	16 (53.3)	33 (55)
Rheumatoid arthritis with Bilateral hip secondary OA	5 (16.7)	1 (3.3)	6 (10)
Post TB Hip with secondary OA	6 (20)	12 (40)	18 (30)
OA Bilateral Hip	2 (6.7)	1 (3.3)	3 (5)
Total	30 (100)	30 (100)	60 (100)
Chi-square p value: 0.170			

Majority of the subjects (61.7%) underwent Non cemented THR followed by Cemented THR (35%). The minor difference in proportion of surgical procedure done between the groups was not statistically significant and hence both the groups were comparable (Table 6).

Table 6: Distribution of the study subjects according to surgical procedure done (N=60)

Surgical procedure	GroupA N (%)	GroupB N (%)	Total N (%)
Non cemented THR	20 (66.7)	17 (56.7)	37 (61.7)
Cemented THR	9 (30)	12 (40)	21 (35)
Hybrid THR	1 (3.3)	1 (3.3)	2 (3.3)
Total	30 (100)	30 (100)	60 (100)
Chi-square p value: 0.715			

Subjects who received tranexamic acid had lesser intra-operative blood loss (approximately 170ml) than the control subjects and this difference was found to be statistically significant ($p < 0.05$).

Subjects who received tranexamic acid had higher post-operative day 2 (after 48 hours) than the control subjects and this difference was statistically significant ($p < 0.05$) (Table 7).

Table 7: Comparison of post-operative hemoglobin between the groups (N=60)

Hemoglobin (gms %)	Group	Hb mean (gms %)	Std. Deviation	Mean difference	p value
Post-operative 48 Hour	A	11.440	0.3802	0.343	0.003
	B	11.097	0.4642		

Subjects who received tranexamic acid had lesser fall (approximately 0.510 gm %) in hemoglobin at day 2 than the control subjects and this difference was statistically significant ($p < 0.05$).

Our study included patients of diverse age group. patients in the study were divided into two groups, one group received intravenous tranexamic acid preoperatively while the other group did not receive the drug. The patients in both the groups were of age groups ranging from 20-70 years of age, with mean age of tranexamic acid group being 41.87 ± 14.38 years while that of non-tranexamic acid group being 41.93 ± 15.61 years. The age demographics of our study were significantly different from study conducted by Wong et al., as the mean age in their study was 67 ± 8.88 years in the control group while that for tranexamic acid group being 67.46 ± 7.124 years (13).

In the present study the intraoperative blood loss was measured for the tranexamic acid group as well as the non-tranexamic acid. The mean intraoperative blood loss in tranexamic acid group was 685 ml mean difference in both groups being 172 ml with p value of < 0.001 . The study conducted by Benoni et al., (14) in the year 2021 on patients (N = 123) that underwent for primary unilateral THA were divided into 3 treatment groups: control group; TXA, systemic, repeated 1gm bolus; TXA, topically intra-articularly, 2gm in 50 mL saline. According to the author the recorded intraoperative blood loss in the control group was 300.0 ± 100.0 mL, in the systemic tranexamic acid group 287.5 ± 103.1 ml. The observations of the study showed significantly less blood loss as compared to our study this observational difference could be due the use of multiple doses of tranexamic acid used in the study as compared to single dose methodology used in our study.

In a single center retrospective analysis by Nicoleta et al., conducted a retrospective chart review of 564 primary and revision THAs performed at a single academic center. surgical patients received either no tranexamic acid or 1g IV tranexamic acid at the beginning of surgery followed by a second bolus just before the surgical wound closure differences in hemoglobin (Hb), estimated blood loss (EBL) following surgery were analysed (15).

With a direct anterior approach, median estimated blood loss (EBL) retrieved from operatory notes was 500.00 mL in both study groups (P value.3222); in the postero-lateral approach, median EBL was 400.00 mL for the tranexamic acid group and 325.00 mL for the no- tranexamic acid group (P value.8158); for those undergoing a revision, median EBL was 500.00 mL in the tranexamic acid group and also 500.00 mL in the no- tranexamic acid group ,while in our study the mean blood loss in tranexamic acid group was 513 ml in tranexamic acid group while that of non-tranexamic acid group

was 685 ml mean difference in both groups being 172 ml with p value of <0.001 the mean blood loss in our study was comparable to the observations of this study the difference in blood loss according to approach was not taken as a variable in our study (16).

In a randomized, placebo- controlled clinical trial by Lopez-Picado et al., (17) that included 108 patients undergoing unilateral total hip replacement surgery. Total blood loss volumes up to day 2 were 1377 ± 689 , 1308 ± 641 , and 2215 ± 1136 mL in the single-dose, 2-dose and control groups, respectively ($P < 0.001$ between the placebo and the experimental groups). The blood loss volume recorded were significantly larger than our current study (mean blood loss 513ml. In tranexamic acid group, and that for control group 685ml. mean difference being 172ml. p value <0.001. Subjects receiving tranexamic acid had roughly 170ml lesser intraoperative blood loss than the control subjects and this difference was statistically significant ($p < 0.05$) but the difference in case and control group were consistent with our findings of reduced blood loss associated with tranexamic acid use.

In our study subjects who received tranexamic acid preoperatively had mean hemoglobin concentration difference between preoperative and post operative day 2 hemoglobin concentration of 0.420 gm% while the difference in non-tranexamic acid group was 0.930 gm %. the mean difference in post operative fall in hemoglobin concentration between the groups was 0.510 gm % which was statistically significant p value (<0.05). In a prospective, controlled, randomized study by Schiavone et al., (18) with randomized controlled feasibility study prospective, randomised, double blind placebo- controlled trial in 140 patients, aged 45 years or older, undergoing elective primary or revision hip or knee joint replacement. Subjects were randomised to receive intravenous (IV) TA or a placebo. The fall in Hb concentration from preoperative levels to the lowest level recorded in hospital was significantly greater in patients who received the placebo compared to those who received tranexamic acid (19). The mean difference between lowest and preoperative Hb concentration (95% CI) was 0.46 (0.43 to 0.50) g/dl in those receiving the placebo compared with 0.32 (0.29 to 0.35) g/dl for those receiving tranexamic acid with $p < 0.0001$. The difference between fall in Hb concentration in our study was considerably more as compared to this study highlighting the efficacy of tranexamic acid in reducing blood loss in total hip replacement surgery (20).

4. Conclusion

From this study consisting of 60 subjects undergoing primary total hip arthroplasty which were divided into two groups one group consisting subjects receiving preoperative tranexamic acid while the other group did not receive the drug it is concluded that the perioperative blood loss can be effectively reduced by using tranexamic acid. There was significantly less intraoperative blood loss observed in the tranexamic acid group (0.460LSD 0.228) compared with the control group (0.687L SD 0.283L) ($p < 0.001$). The estimated blood loss was also significantly less in the tranexamic acid group (1.084L SD 0.440) compared with the control group (1.394 L SD 0.426. these observations were comparable to the observations made in our study highlighting the efficacy of tranexamic acid in reducing blood loss in total hip replacement surgery.

References:

1. James W. Harkess, John R. Crockarell Jr. arthroplasty of the hip. In: Frederick M. Azar, James H. Beaty, S. Terry Canale, editors. Campbell's operative orthopaedics: 13th ed. Canada: Elsevier. 2017. p. 167.
2. Charoencholvannich K, Siri Wattanasakul P. tranexamic acid Reduces blood loss and blood Transfusion after TKA: A Prospective Randomized Controlled Trial. Clin Orthop Relat Res. 2011 Oct;469(10):2874-80.
3. Bursi F, Barbieri A, Politi L, Di Girolamo A, Malagoli A, Grimaldi T, et al. Perioperative Red blood Cell Transfusion and Outcome in Stable patients after Elective Major Vascular Surgery. European Journal of Vascular and Endovascular Surgery. 2009 Mar;37(3):311-8.
4. Saravanan R, Venkatraman R, Karthik K, Pushparani A. Efficacy of different doses and timing of tranexamic acid in major orthopedic surgeries: a randomized trial. Revista Brasileira de Anestesiologia. 2020 Sep 21;70:311-7.
5. Goodman, L. S., Brunton, L. L., Chabner, B., & Knollmann, B. C. Goodman & Gilman's pharmacological basis of therapeutics: 13th ed. New York: McGrawHill: 2011. p. 596
6. Nadeau, Richard P. blood Conservation in Total Hip arthroplasty: Interim Analysis of the tranexamic acid Comparison in Hip Replacement (TeACH-R) Trial. Electronic Repository. <https://ir.lib.uwo.ca/etd/2504> . Accessed Nov 16 2020
7. Henry DA, Moxey AJ, Carless PA et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. The Cochrane Library, Oxford. 2002 Issue 4.
8. Sleman AM, Kakai SS, Karim OA. The Reduction of Blood Loss by Using of Tranexamic Acid During Total Knee Arthroplasty. Diyala Journal of Medicine. 2017;12(2):13-9.
9. Chaudhary D, Kumar P, Mehrotra R, Bhathal M. Role of intravenous tranexamic acid for the reduction of blood loss in total knee arthroplasty. International Journal of Orthopaedics. 2017;3(4):553-5.

10. Kazi HA, Fountain JR, Thomas TG, Carroll FA. The Effect of Bolus Administration of tranexamic acid in Revision Hip arthroplasty. *HIP International*. 2012 Nov;22(6):615-20.
11. Yoon B, Kim T, Ko YS, Lee Y, Ha Y, Koo K. Optimal use of tranexamic acid for total hip arthroplasty: A network meta-analysis. *PLoS ONE*. 2018 Oct 31;13(10):e0206480.
12. El Beheiry H, Lubberdink A, Clements N, Dihllo K, Sharma V. tranexamic acid administration to older patients undergoing primary total hip arthroplasty conserves hemoglobin and reduces blood loss. *CJS*. 2018 Jun 1;61(3):177-184.
13. Wong, J., Abrishami, A., Beheiry, H., Mahomed, N.N. & Roderick, D.J. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, double-blinded, placebo-controlled trial of efficacy. *The Journal of Bone and Joint Surgery America*. 2010;92:2503–2513.
14. Benoni G, Lethagen S, Nilsson P, Fredin H. tranexamic acid, given at the end of the operation, does not reduce postoperative blood loss in hip arthroplasty. *Acta Orthopaedica Scandinavica*. 2000 Jan;71(3):250-204.
15. Thippampall AK, Gurajala I, Gopinath R. The effect of different dose regimens of tranexamic acid in reducing blood loss during hip surgery. *Indian Journal of Anaesthesia*. 2017 Mar;61(3):235.
16. Husted H, Blønd L, Sonne-Holm S, Holm G, Jacobsen T, Gebuhr P. tranexamic acid reduces blood loss and blood transfusions in primary total hip arthroplasty A prospective randomized double-blind study in 40 patients. *Acta Orthopaedica Scandinavica*. 2003 Jan;74(6):665-9.
17. Lopez-Picado A, Barrachina B, Remón M, Errea M. Cost-benefit analysis of the use of tranexamic acid in total replacement hip surgery. *Journal of Clinical Anesthesia*. 2019 Nov;57:124-8.
18. Schiavone A, Bisaccia M, Inkov I, Rinonapoli G, Manni M, Rollo G, Meccariello L, Vicente CI, Ceccarini P, Ruggiero C, Caraffa A. Tranexamic acid in pertrochanteric femoral fracture: is it a safe drug or not?. *Folia medica*. 2018;60(1):67-78.
19. Bradley KE, Ryan SP, Penrose CT, Grant SA, Wellman SS, Attarian DE, et al. tranexamic acid or epsilon-aminocaproic acid in total joint arthroplasty? A randomized controlled trial. *The Bone & Joint Journal*. 2019 Sep;101-B(9):1093-9.
20. Pérez-Chrzanowska H, Padilla-Eguiluz NG, Gómez-Barrena E. Defining the Most Effective Patient blood Management Combined with tranexamic acid Regime in Primary Uncemented Total Hip Replacement Surgery. *JCM*. 2020 Jun 22;9(6):1952.