International Journal of Orthopaedics Sciences

ISSN: 2395-1958
IJOS 2019; 5(1): 123-127

www.orthopaper.com
Received: 05-11-2018
Accepted: 09-12-2018

Basoya N
Postgraduate Student
Department of Orthopedics, Himalayan Institute of Medical Sciences, Doiwala, Uttarakhand, India

Chauhan VD
Professor Department of Orthopedics, Himalayan Institute of Medical Sciences, Doiwala, Uttarakhand, India

Correspondence
Chauhan VD
Professor Department of Orthopedics, Himalayan Institute of Medical Sciences, Doiwala, Uttarakhand, India

Intravenous versus topical tranexamic acid as a blood conservation intervention in hip joint replacement surgeries

Basoya N and Chauhan VD

DOI: https://doi.org/10.22271/ortho.2019.v5.i1c.23

Abstract
Background: Hip arthroplasty is associated with substantial blood loss intraoperatively as well as postoperatively. The objective of the present experimental study was to compare the effectiveness of topical tranexamic acid with intravenous tranexamic acid in reducing blood loss in hip joint replacement surgeries.
Methods: The experimental study comprised of 60 cases undergoing hip joint replacement surgeries who were randomly assigned to the intravenous group (n=30) and topical group (n=30). Tranexamic acid was used in the dose of 15 mg/kg. All Patients undergoing hip joint replacement surgeries and preoperative Hb > 10 g/dl for males and > 9 g/dl for females were included in this study. Patients having a known history of thromboembolic disease, myocardial infarction, cerebrovascular disease, angina, coagulopathy, any liver or renal disease or any other source of active bleeding were excluded from the study.
Results: In hemiarthroplasty the blood loss in the topical and intravenous group was 547.8±178.11ml and 617.73±192.51ml with a p value of 0.298. The haemoglobin and PCV was 2.01±1.18 mg/dl, 6.22±4.08% and 2.41±1.74 mg/dl, 6.69±5.03 with a p value of 0.521 and 0.865. Similarly in total hip replacement the blood loss in the topical and intravenous group was 620.80±160.33ml and 745.30±152.67ml with a significant p value of 0.046. The haemoglobin and PCV was 2.75±1.60 mg/dl, 6.15±7.05% and 2.80±1.84 mg/dl, 8.52±5.47 with a p value of 0.534 and 0.214.
Conclusion: Tranexamic acid can be given by intravenous or topical route as both the routes are equally effective in reducing the intraoperative blood loss.

Keywords: Hip joint replacement, blood loss, tranexamic acid

Introduction
Extensive orthopedic surgeries like hip replacements are usually associated with substantial blood loss and may need blood transfusions. Bleeding in these surgeries can be due to many factors eg. Increase fibrinolytic activity [1-3]. It has also been observed that there is an increase in mortality in patients associated with anaemia resulting due to such bleedings [4]. Further, the severity of anaemia is also associated with reduced functional recovery [5].
Blood transfusion compensates for blood loss but blood transfusion itself is associated with complications such as transfusion reaction, risks of transmission of viral diseases, post-operative surgical site infection, high medical costs and prolonged hospital stay. Thus creating the need for new modality of blood conservation [6].
Various available techniques of controlling bleeding like hypotensive anesthesia, blood salvage and reinfusion and autologous blood transfusions are costly and associated with complication [7]. The use of tranexamic acid in joint replacements has led to reduction in blood loss and blood transfusion [8, 9]. Tranexamic acid is a synthetic derivative of the amino acid lysine (4-aminoethyl cyclohexane carboxylic acid); it produces antifibrinolytic effect by forming a reversible complex with plasminogen, thus blocking the dissolution of haemostatic fibrin and in turn reduces the blood loss secondary to fibrinolysis [3, 10, 11].
Tranexamic acid finds its usage in neurosurgery, orthopedic, cardiac, spine and maxillofacial surgeries with good results [9]. The regimen of tranexamic acid used differs from one study to another, since the optimal regimen in orthopedics has not been defined. The use of tranexamic acid is associated with a significant reduction of blood transfusion requirement in whatever

Regimen used; however greater effect was seen with the higher dosages [12].

We have extensive literature demonstrating the safety and efficacy of tranexamic acid. However, there are concerns of the development of deep vein thrombosis after its use intravenously. Hence topical usage may be an alternative [13]. The drug can be administered intravenously in dosages 10-20 mg/kg at the start of surgery and repeated 8 hourly for next two doses [14]. When used intravenously, the maximum plasma concentration levels of tranexamic acid reaches in 5-15 minutes [15].

The combined usage of tranexamic acid (intravenous and topical) in large joint replacements led to significant lowering of blood loss and transfusions and it was devoid of complications like deep vein thrombosis or pulmonary embolism [8].

This study was undertaken study to compare the effectiveness of topical versus intravenous administration of tranxemic acid in patients undergoing hip joint replacement surgeries.

Material and Methods

The present study was an Experimental study conducted from January 2017 to January 2018. It included 60 patients who underwent hip joint replacement surgery. Patients were randomized into Intravenous and Topical groups. Patients having a known history of thromboembolic disease, myocardial infarction, cerebrovascular disease, angina, coagulopathy, any liver or renal disease or any other source of active bleeding were excluded from the study. Patients with pre-operative hemoglobin more than 10mg/dl for males and 9mg/dl for females were included in this study after an informed and written consent.

The Intravenous group included 30 patients out of which 17 underwent Hemiarthroplasty and 13 Total Hip Arthroplasty. The Topical group consisted of 30 patients out of whom 15 underwent Hemiarthroplasty and 15 Total Hip Arthroplasty.

Drug Preparation and Administration

Drug was prepared by operating room nursing staff.

- In Intravenous group (Group A), tranexamic Acid was administered by the anesthetist in the dose of (15 mg/kg) which was diluted in 100 ml of normal saline. It was given preoperatively 15 minutes prior to incision over a period of 10-15 minutes as an infusion. The second dose (15 mg/kg diluted in 100 ml normal saline) of tranexamic acid was given as an infusion just before closure of wound.
- In topical group (Group B), tranexamic Acid (15 mg/kg) was diluted in 100ml normal saline and the surgical wound was packed with the mop soaked in this solution for 5 minutes after opening of surgical site. The second packing of the wound was done for 5 minutes with the mop soaked with tranexamic acid in the same concentration before closure of the wound.

Method of calculation of blood loss

- During surgery (intraoperative)

I. Average weight of a dry mop was calculated before sending them to autoclave for sterilization by using a sensitive digital weighing machine (American Weigh – AWS 100). This was used as a standard for all dry mops. Soakage weight (S.W.) was calculated as soaked mops weight (a) minus dry mops weight (b) and depicted as : S.W. = a - b

II. Blood loss in suction was calculated as : Total output in suction container (c) minus normal saline used to wash the surgical site (d) and is represented as (B.S. = c - d)

III. Spillage was recorded by the operating surgeon.

IV. Total blood loss = (i)+ (ii) + (iii)

Post operatively on post-operative day 2, hemoglobin and packed cell volume were assessed.

Statistical analysis was carried out using statistical package for social sciences (SPSS) version 22.0. Mann Whitney test was used to analyze the blood loss, hemoglobin and (hematocrit) PCV difference between the two groups.

Results

- The demographic distribution between the two groups is as shown in Table 1.
- Distribution of cases on the basis of diagnosis is as shown in Table 2.
- Difference in intra-operative bleeding in topical and intravenous groups is as shown in Table 3.
- Difference in pre-operative and post-operative Hemoglobin in Joint Replacement Surgeries is as shown in Table 4.
- Difference in pre-operative and post-operative PCV in Joint Replacement Surgeries is as shown in Table 5.

Table 1: Demographic distribution

Hip Joint Replacement	Intravenous Group (n=30)	Topical Group (n=30)
Hemiarthroplasty	17 cases	15 cases
• Mean Age (years)	71.70±12.77	68.26±10.42
• Sex Ratio (m:f)	8:9	11:4
• Mean Surgical Time (min)	128.23±18.48	130.27±11.78
Total Hip Replacement	13 cases	15 cases
• Mean Age (years)	45.76±13.38	43.2±12.41
• Sex Ratio (m:f)	10:3	11:4
• Mean Surgical Time (min)	175.76±15.31	171.66±20.93

Table 2: Distribution of cases based on diagnosis

Diagnosis	Hemiarthroplasty N = 32		Total Hip Replacement N = 28	
	Cases	Percentage	Cases	Percentage
Avascular necrosis	0	0.00	18	64.29
Fracture Neck of femur	32	100	8	28.57
Arthritis (OA, RA)	0	0.00	2	7.14

Table 3: Difference in intra-operative bleeding between the two groups

Group	Hemiarthroplasty (n=32)			Total Hip Replacement (n=28)		
	Mean	SD	P value	Mean	SD	P value
Topical	547.98	178.11	0.298	620.80	160.33	0.046
Intravenous	617.73	192.51		745.30	152.67	

*p values calculated using student unpaired't' test

Table 4: Difference in pre-operative and post-operative Hemoglobin between the two groups

Group	Hemiarthroplasty (n=32)			Total Hip Replacement (n=28)		
	Mean	SD	P value	Mean	SD	P value
Topical	2.01	1.18	0.521	2.75	1.60	0.534
Intravenous	2.41	1.74		2.80	1.84	

*p values calculated using student Mann Whitney test

Table 5: Difference in pre-operative and post-operative PCV between the two groups

Group	Hemiarthroplasty (n=32)			Total Hip Replacement (n=28)		
	Mean	SD	P value	Mean	SD	P value
Topical	6.22	4.08	0.865	6.15	7.05	0.214
Intravenous	6.69	5.03		8.52	5.47	

*p values calculated using Mann Whitney test

Discussion

Our study included patients of diverse age group. Patients of hemi arthroplasty ranged between 52-92 years with the mean age being 70.09±11.67 years with M: F ratio of 19:13. Similarly patients of total hip replacement ranged between 25-62 years with mean age being 44.39±12.69 years with M: F ratio of 3:1.

In a study done by Emara WM *et al* [16] the mean age for hemiarthroplasty was 56.5±3.1 years with M:F ratio of 3:2 and in a study done by Bawani VS *et al* [3] the mean age for total hip replacement was 49.3±19.5 years with M:F ratio of 12:35.

Age and sex in our study was not comparable to other studies may be because in our study hemiarthroplasty was done in cases of fracture neck of femur which is more common in old age and total hip replacement was done for avascular necrosis which was found in young adults.

Difference in intra-operative bleeding in topical and intravenous groups

We compared the mean difference in intra-operative bleeding in hemiarthroplasty and found that the intraoperative blood loss in topical group was 547.98± 178.11 ml and intravenous group was 617.73± 192.51 ml. No significant difference in intra-operative bleeding in topical group compared to intravenous group was observed (p value = 0.298). Similar results were also obtained by Emara WM *et al* [16].

The intraoperative blood loss in total hip replacement in our study in the topical group was 620.80± 160.33 ml and in the intravenous group it was 745.30± 152.67 ml. The topical group was better with a significant p value of 0.046. Our results are comparable to the metanalysis done by Xie J [17] for comparison of intravenous versus topical tranexamic acid in primary total hip arthroplasty. Similar results were also obtained by Ueno M *et al* [18] and Wei W *et al* [19].

However in a study done by North WT *et al* (20) tranexamic when given intravenously the blood loss was 1195±485.9 ml and when applied topically it was 1442.7±562.7 ml, with a statistically significant p value of 0.006. They concluded that intravenous tranexamic acid was better in reducing the intraoperative bleeding when compared to the topical tranexamic acid.

Hemoglobin

In our study, patients who underwent hemiarthroplasty, the mean difference between pre-operative hemoglobin and post-operative hemoglobin in topical group was 2.01± 1.18gm/dl and in intravenous group it was 2.41± 1.74 gm/dl. There was no significant difference in drop in hemoglobin post-operatively compared to pre-operative hemoglobin in intravenous group and topical group (p value = 0.521). Similar results were obtained by Emara WM *et al* [16] in patients who underwent hemiarthroplasty; they observed that the fall in hemoglobin in the topical group was 2.1±0.6g/dl and in the intravenous group it was 2.8±0.4g/dl. There was no significant difference in drop in hemoglobin post-operatively compared to pre-operative hemoglobin between the two groups with a p value >0.05.

In total hip replacement, the mean difference between pre-operative hemoglobin and post-operative hemoglobin in topical group was 2.75±1.60gm/dl and in intravenous group it was 2.80±1.84 gm/dl. There was no significant difference in drop in hemoglobin post-operatively compared to pre-operative hemoglobin in intravenous group and topical group with a p value of 0.534 in our study. Similar results were obtained by Ueno M *et al* [18] and Luo ZY *et al* [21]. They had drop in hemoglobin of 3.66gm/dl in patients who received topical tranexamic acid and 3.58 gm/dl in patients who received intravenous tranexamic acid in patients of total hip replacement. There was no statistical difference in fall of hemoglobin between the two groups with a p value of 0.73.

On the other hand North WT *et al* [20] found that the change in hemoglobin was -3.1±1.2g/dl in the intravenous group and -3.5±1.2g/dl in topical group in the patients undergoing total hip replacement. They concluded that the intravenous group demonstrated higher postoperative hemoglobin when compared to the topical group with a significant p value of 0.014.

Hemotocrit (PCV)

In hemiarthroplasty, the mean difference between pre-operative PCV and post-operative PCV in topical group was 6.22± 4.08% and in intravenous group it was 6.69± 5.03%. There was no significant difference in drop in PCV post-operatively compared to pre-operative PCV in intravenous group with a p value = 0.865. Similar results were also obtained by Emara WM *et al* [16] on patients who underwent

hemiarthroplasty. They observed that the hematocrit fall in patients who received intravenous tranexamic acid was 9.0±1.2% and in patients who received topical tranexamic acid 7.7±0.9% with a statistically non-significant P value of >0.05.

In total hip replacement, the mean difference between pre-operative PCV and post-operative PCV in topical group was 6.15± 7.05% and in intravenous group it was 8.52± 5.47%. There was no significant difference in drop in PCV post-operatively compared to pre-operative PCV in intravenous group and topical with a p value 0.214.Similar results were observed by Wei W *et al* [19] and Luo ZY *et al* [21].

Complications

Pharmacopia of tranexamic acid mentions very strongly the complications associated with tranexamic acid like thromboembolism and deep vein thrombosis, since it acts by blocking the fibrinolysis and preventing clot dissolution. Kakar PN *et al* [22], Duncan CM *et al* [23], Rajesparan K *et al* [24], Kazemi SM *et al* [25], Singh J *et al* [26], Sukeik M *et al* [27] Zhou XD *et al* [28], Sun X *et al* [29] and Wei W *et al* [19] found no thromboembolic effect after using tranexamic acid in their study. Our results were consistent with their study. We did not have any complications in the intravenous or the topical group. Similarly Xie J [17] did a meta-analysis to compare the efficacy and safety of intravenous tranexamic acid in approximately 2,262 patients of total knee arthroplasty and total hip arthroplasty involving 18 randomized controlled trials of total knee arthroplasty and 4 randomized controlled trials involving total hip arthroplasty and did not find any significant difference in complications in the intravenous or topical group in terms of deep vein thrombosis and pulmonary embolism. On the other hand Emara WM [16] had 30% increase of thromboembolic event in the intravenous group compared to the topical group which was 0%.

It appears that both the intravenous and topical are safe if given in the permissible dosages. Theoritically topical application of tranexamic acid appears to be more-safer in comparison to intravenous administration.

Luo ZY *et al* [21] had mentioned of a probability of periprosthetic infection due to contamination occurring during needle aspiration and when the drug is being diluted but if all aseptic precautions are taken this can be easily eliminated.

We agree with Georgiev GP *et al* [30] that topical tranexamic acid could be a reasonable alternative in patients with contraindications for intravenous application of tranexamic acid.

Conclusion

Tranexamic acid can be given by intravenous or topical route as both the routes are equally effective in reducing the intraoperative blood loss.

References

1. Mannucci PM, Levi M. Prevention and treatment of major blood loss. N Engl J Med. 2007; 356:2301-11.
2. Sculco TP. Global blood management in orthopedic surgery. Clin Orthop Relat Res. 1998; 357:43-9.
3. Vijay BS, Bedi V, Mitra S, Das B. Role of tranexamic acid in reducing postoperative blood loss and transfusion requirement in patients undergoing hip and femoral surgeries. Saudi Journal of Anaesthesia. 2013; 7(1):29-32.
4. Scott Beattie W, Karkouti K, Wijeysundera D, Tait G. Risk associated with preoperative anemia in non-cardiac surgery. Anesthesiology. 2009; 110:574-58.
5. Lawrence VA, Silverstein JH, Cornell JE, Pederson T, N oveck H, Carson JL. Higher Hb level is associated with better early functional recovery after hip fracture repair. Transfusion. 2003; 43:1717-22.
6. Perel P, Ker K, Morales Uribe CH, Roberts I. Tranexamic acid for reducing mortality in emergency and urgent surgery. Cochrane Database of Systematic Reviews, 2013, 1.
7. Sabatini L, Trecci A, Imarisio D, Uslenghi MD, Bianco G, Scagnelli R. Fibrin tissue adhesive reduces postoperative blood loss in total knee arthroplasty. Journal of Orthopaedics and Traumatology. 2012; 13(3):145-51.
8. Jun-feng L, Hang L, Zhao H, Wang J, Liu S, Song Y *et al*. Combined use of intravenous and topical versus intravenous tranexamic acid in primary total knee and hip arthroplasty: a meta-analysis of randomized controlled trials. JOSR. 2017; 12:22-8.
9. Reed MR, Woolley LT. Uses of tranexamic acid. Continuing Education in Anaesthesia, Critical Care & Pain. 2014; 15(1):32-7.
10. Nilsson IM. Clinical pharmacology of aminocaproic and 55 tranexamic acids. J Clin Pathol Suppl (R Coll Pathol) 1980; 14:41-7.
11. Dunn CJ, Goa KL. Tranexamic acid. Drugs. 1999; 57(6):1005-32.
12. Zufferey P, Merquiol F, Laporte S, Decousus H, Mismetti P, Auboyer C *et al*. Do anti-fibrinolytics reduce allogeneic blood transfusion in orthopedic Surgery? Anesthesiology. 2006; 105:1034-46.
13. Wong J, Abrishami A, El Beheiry H. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. J Bone Joint Surg Am. 2010; 92:2503-13.
14. Thipparampall A, Gurajala I, Gopinath R. The effect of different dose regimens of tranexamic acid in reducing blood loss during hip surgery. IJA. 2017; 61(3):235-9.
15. Sabatini L, Atzori F, Revello S, Scotti L, Debiasi F, Massè A. Intravenous use of tranexamic acid reduces postoperative blood loss in total knee arthroplasty. Archives of Orthopaedic and Trauma Surgery. 2014; 134(11):1609-14.
16. Emara WM, Moez KK, Elkhouly AH. Topical versus intravenous tranexamic acid as a blood conservation intervention for reduction of post-operative bleeding in hemiarthroplasty. Anesthesia, essays and researches. 2014; 8(1):48-52.
17. Xie J, Hu Q, Huang Q, Ma J, Lei Y, Pei F. Comparison of intravenous versus topical tranexamic acid in primary total hip and knee arthroplasty: an updated meta-analysis. Thrombosis Research. 2017; 153:28-36.
18. Ueno M, Sonohata M, Fukumori N, Kawano S, Kitajima M, Mawatari M. Comparison between topical and intravenous administration of tranexamic acid in primary total hip arthroplasty. Journal of Orthopaedic Science. 2016; 21(1):44-7.
19. Wei W, Wei B. Comparison of topical and intravenous tranexamic acid on blood loss and transfusion rates in total hip arthroplasty. The Journal of Arthroplasty. 2014; 29(11):2113-6.
20. North WT, Mehran N, Davis JJ, Silverton CD, Weir RM, Laker MW. Topical vs intravenous tranexamic acid in primary total hip arthroplasty: A double-blind, randomized controlled trial. The Journal of Arthroplasty.

2016; 31(5):1022-6.
21. Luo ZY, Wang HY, Wang D, Zhou K, Pei FX, Zhou ZK. Oral vs intravenous vs topical tranexamic acid in primary hip arthroplasty: A prospective, randomized, double-blind, controlled study. The Journal of Arthroplasty. 2018; 33(3):786-93.
22. Kakar PN, Gupta N, Govil P, Shah V. Efficacy and Safety of Tranexamic Acid in Control of Bleeding Following TKR: A Randomized Clinical Trial. Indian J Anaesth. 2009; 53:667-71.
23. Duncan CM, Gillette BP, Jacob AK, Sierra RJ, Sanchez-Sotelo J, Smith HM. Venous thromboembolism and mortality associated with Tranexamic Acid use during total hip and knee arthroplasty. J Arthroplasty. 2015; 30(2):272-6.
24. Rajesparan K, Biant LC, Ahmad M, Field RE. The effect of an intravenous bolus of tranexamic acid on blood loss in total hip replacement. The Journal of Bone and Joint Surgery (Br). 2009; 91(6):776-83.
25. Kazemi SM, Mosaffa F, Eajazi A, Kaffashi M, Besheli LD, Bigdeli MR, *et al*. The effect of tranexamic acid on reducing blood loss in cement less total hip arthroplasty under epidural anesthesia. Orthopedics. 2010; 33(1):21-9.
26. Singh J, Ballal MS, Mitchell P, Denn PG. Effects of tranexamic acid on blood loss during total hip arthroplasty. Journal of Orthopaedic Surgery. 2010; 18(3):282-6.
27. Sukeik M, Alshryda S, Haddad FS, Mason JM. Systematic review and meta-analysis of the use of tranexamic acid in total hip replacement. The Journal of Bone and Joint Surgery (Br). 2011; 93(1):39-46.
28. Zhou XD, Tao LJ, Li J, Wu LD. Do we really need tranexamic acid in total hip arthroplasty? A meta-analysis of nineteen randomized controlled trials. Archives of Orthopaedic and Trauma Surgery. 2013; 133(7):1017-27.
29. Sun X, Dong Q, Zhang YG. Intravenous versus topical tranexamic acid in primary total hip replacement: a systemic review and meta-analysis. International Journal of Surgery. 2016; 32:10-8.
30. Georgiev GP, Tanchev PP, Zheleva Z, Kinov P. Comparison of topical and intravenous administration of tranexamic acid for blood loss control during total joint replacement: Review of literature. Journal of Orthopaedic Translation. 2018; 8:11-9.