Original Article

Comparative study of two dose regimen of tranexamic acid for control of blood loss in total knee arthroplasty

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Abstract

Background: Tranexamic acid (TXA) has been reported to reduce blood loss and be cost effective in many areas of orthopaedic surgery. TXA may be administered intra-venous (IV) or topically in the surgical wound or by intra-articular injection. There has been a growing attention of using TXA as intra-articular agent (IA-TXA) in total knee arthroplasty to avoid drug-induced venous thromboembolic (VTE) complication due to IV use of TXA. This study evaluates the efficacy of intra-articular and IV Tranexamic acid for reducing blood loss during Total Knee Arthroplasty (TKA) and objective is to evaluate post-operative total drain output. **Materials and Methods:** A prospective, clinical and comparative study was conducted in MGM Medical College and Hospital, Aurangabad, in 50 patients with osteoarthritis of knee joint and underwent TKR. Patients were divided in two groups, each receiving single dose of tranexamic acid either by intravenously (IV) or by intra-articular route. We evaluated post-operative total drain output. **Results:** Significant reduction in mean haemoglobin in both groups was seen post-operatively. Mean HTC was similar in both groups. Mean drain output was significantly lower on day 1 compared to day 0 in both the study groups. No change in BT, CT and PT/INR was observed in both groups. Significantly lower number of patients in group II required blood transfusion than group I patients. **Conclusion:** Intra-articular tranexamic acid application has better efficacy and is not only reduces blood loss but also decreases knee joint swelling after total knee Arthroplasty.
Keywords: Tranexamic acid, Total knee arthroplasty.

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INTRODUCTION

Since its introduction in the late 1960s, total knee Replacement (TKR) has become one of the most common operations in orthopaedic practice. Undergoing TKR may necessitate allogeneic blood transfusion[1,2] and patients remain concerned about the potentially serious complications of transfusion, although serological screening has reduced the risk for viral infection.[3,4] Allogeneic blood transfusion may be associated with other non-infectious complications, such as haemolysis, immunosuppression, transfusion-related acute lung injury and even death.[5] Technologies to minimize the need for blood transfusion include the use of ant fibrinolytic drugs such as aprotinin, tranexamic acid (TXA) and aminocaproic acid (EACA).[6,7] However, the use of these drugs remains controversial and in many centres is not routine. Tranexamic acid was previously used by other major surgeries like urosurgery, gynaecological and thoracic surgical procedures in order to reduce post-operative blood loss. TXA may be administered intra-venous (IV) or topically in the surgical wound. TXA has been reported to reduce blood loss and be cost effective in many areas of orthopaedic surgery, such as spinal surgery[8] as well as knee and hip Arthroplasty.[9] One significant concern with TXA however, is the possibility that it, as well as other antifibrinolytics, could increase the risk of developing thromboembolic complications such as deep vein thrombosis (DVT).[10] Regarding of the

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proven methods used for reducing post-operative blood loss in TKR, tranexamic acid (TXA), an anti-fibrinolytic agent, has been demonstrated ability to decrease post-operative blood loss and proportion of patients required postoperative blood transfusion and could be applied via either intravenous application[11] or intra-articular injection.[12] However, the intravenous application of TXA has a major disadvantage on uncertain risk of drug-induced venous thromboembolic (VTE) complication from prolonged high systemic drug level especially with multiple injections or continuous infusion regimens.[13] Thus, for safety concern of the VTE complication, there has been a growing attention of using TXA as intra-articular agent (IA-TXA) in TKR.[14]. The purpose of this study was to investigate the effect of TXA on early post-operative blood loss after TKR, as well as changes in adverse clinical outcomes such as re-operation or increases in complications such as deep-vein thrombosis (DVT), pulmonary embolism (PE), infection, ischemic heart disease and mortality.

MATERIALS AND METHODS

This was prospective, clinical and comparative study conducted in MGM Medical College and Hospital, Aurangabad, in the year 2012-2015. Population include all patients with osteoarthritis of knee joint and underwent TKR, attending Orthopaedic department of MGM hospital, Aurangabad with Sample size of 50 patients and this patients were categorized in 2 groups:

Group I: 25 Patients receiving single dose of tranexamic acid 10mg/kg 15 minute before release of tourniquet intravenously (IV)

Group II: 25 Patients receiving single dose of tranexamic acid 1.5gm in 100 ml NS intra-articular through drain after closure and drain clamp for 1 hr. All surgeries performed by senior surgeon using standard surgical technique, closure will be performed only after adequate haemostasis; intra-articular negative suction drain was used to measure post-operative blood loss. In this study, we evaluated post-operative total drain output.

Inclusion Criteria

- Patients considered for inclusion at the age of 30-80 years who diagnosed as primary and post traumatic knee osteoarthritis and underwent TKR.
- Patient should have an evident X-ray finding and clinical symptoms of Osteoarthritis of knee joint.

Exclusion Criteria

- Patients having thromboembolic disease
- Cerebrovascular disease
- Chronic liver or renal disease
- Patients having coagulation disorder.

Statistics Analysis

The collected data was compiled in EXCEL sheet and Master sheet was prepared. Data analyzed with SPSS (Statistical Software for social Sciences) software version 20. Quantitative Data was analyzed using t-test and for qualitative data chi-square test was applied. It was also represented in form of mean and SD etc.

OBSERVATIONS AND RESULTS

Table 1: Age and gender-wise distribution of study groups

Variables		Group I		Group II		Statistical test	P -Value
		No.	%	No.	%		
Age in years	<40	01	04	00	00	Unpaired t test Z-value=1.02	P=0.311 NS
	41-50	01	04	01	04		
	51-60	03	12	05	20		
	61-70	13	52	12	48		
	>70	07	28	07	28		
	Total	25	100	100	100		
	Mean ± SD	66.4±9.73		65.92±7.89			
Gender	Male	13	48.0	11	44.0	Chi-square test x^2=0.321	P=0.389 NS
	Female	12	52.0	14	56.0		
	Total	25	100	25	100		

Table 2: Comparison of Mean HB in two Groups at Pre and Post Treatment

Study Groups	Pre-Operative Mean ± SD	Post-Operative Mean ± SD	Mean Difference	t-value	p-value
Group I	11.92 ±1.65	9.77 ±1.88	2.16	6.90	P=0.000 S
Group II	11.44 ±1.45	9.83 ±1.44	1.6	11.55	P=0.000 S

Table 3: Comparison of Mean HTC in two Groups at Pre-operative stage

HTC	Group	Mean	SD	t-value	p-value
Pre-Operative	Group I	36.00	4.95	0.890	P=0.378
	Group II	34.88	3.87		NS

Table 4: Comparison of mean Drain Day 0, Drain Day 1 and Total Drain in groups

Study Groups	Day 0 Mean ± SD	Day 1 Mean ± SD	Total drain Mean ± SD	Mean Difference Day 0-Day 1	t-value	p-value
Group I	459.40 ± 31.43	219.80 ±46.46	678.60 ±55.10	240.40	12.25	P=0.000 S
Group II	304.00 ±35.79	197.00 ±38.37	500.20 ±64.84	107.0	9.67	P=0.000 S

Table 5: Comparison of Mean Bleeding Time and Clotting Time in two Groups

BT and CT	Group	Mean	SD	t-value	p-value
BT	Group I	2.87	0.449	0.975	P=0.384
	Group II	3.00	0.518		NS
CT	Group I	6.02	0.523	0.744	P=0.461
	Group II	5.91	0.495		NS

Table 6: Comparison of Mean PT/ INR in two Groups

Group	Mean	SD	t-value	p-value
Group I	1.19	0.0846	0.248	P=0.850
Group II	1.20	0.087		NS

Table 7: Blood Transfusion in Patients:[Chi-square test]

Blood Transfusion	Group I		Group II		Chi-square Value	P-value
	NO.	%	No.	%		
Given	11	44.0%	03	12.0%	6.34	P=0.012 S
Not Given	14	56.0%	22	88.0%		
Total	25	100%	25	100%		

RESULTS

Table 1 revealed that maximum subjects were in age group of 61-70 years while below 40 years subjects were minimum in both the study groups. No significant difference was observed in both the study groups with respect to age or gender.

Table 2 shows that post-operatively there was significant decrease in the mean haemoglobin level in both groups as compared to pre-operative level (p=0.000). Pre-operatively there was no significant difference in the mean HTC in both the study groups (Table 3). Table 4 revealed that the mean drain output was significantly lower on day 1 compared to day 0 in both the study groups. Table 5 shows that the mean BT and CT were almost similar in both the study groups. Mean PT/INR was almost equal in both the study groups (Table 6). Table 7 revealed that a significantly lower number of patients required blood transfusion in group II receiving TXA intra-articularly than group I patients receiving TXA intravenously.

DISCUSSION

A total of 50 patients were prospectively allocated to each of the groups (intravenous, intra-articular) and underwent unilateral TKA. During closing the operative wound, TXA (1.5g mixed in 100cc of saline) was administered intravenously or intra-articularly according to the enrolled group respectively. The amount of blood loss and transfusion, and changes in haemoglobin levels were documented accordingly in which 24 were male and 26 were female. In our study, 50 patients were prospectively allocated to 2 groups [intravenous (25), intra-articular (25)]. During closure, TXA 1.5g/100ml saline was administered intra-articularly or intravenously and results showed mean blood loss in intra-venous and intra-articular to be 678.60 +/-in group I, 500.20 +/-Group II respectively. About 44% of the intra-articular group, 12% of the intravenous group did not require transfusion for any reason, and the mean transfusion required in intra-articular group 12%, intravenous group 44%, respectively. We found better result in intra-articular group similar to Ishida K *et al*,[14] Seo *et al* [15] and Aguilera X *et al* [16] also showed better efficacy with intra-articular administration. Topical use of tranexamic acid may have

the potential of directly inhibiting fibrinolysis at the injured site and limit systemic effects of tranexamic acid; however, this benefit has not been proven yet intravenous use in total knee Arthroplasty has been extensively studied and has shown good results. [17-18] Topical use on the other hand is still up and coming, although early results are promising.[15] In a direct comparison between intravenous and intra-articular topical tranexamic acid application during unilateral total knee Arthroplasty. A study by Ishida K *et al*[14] showed that intra-articular tranexamic acid application not only reduces blood loss but also decreases knee joint swelling after total knee Arthroplasty. Although topical tranexamic acid has shown good results, further studies are needed to find the optimal application dose, timing, and frequency of administration. Furthermore since intra-articular tranexamic acid directly bathes polyethylene, its effects need further investigation. On a systemic level, high dose tranexamic acid (61-259mg/kg) has been shown to be associated with seizures during cardiac procedures.[19] It is unlikely for orthopaedic surgeons to use such high dosages, however further studies need to determine optimal dosing to minimize potential risks. Due to safety concerns with intravenous administration of tranexamic acid, there has been a growing interest in the topical use of tranexamic acid for prevention of bleeding in orthopaedics. Since topical application of tranexamic acid can directly target the source of bleeding, it can be considered to be a safer method of delivery while decreasing potential systemic effects. Similar to intravenous tranexamic acid, multiple studies and meta-analysis confirm the safety and efficacy of topical intraarticular administration of tranexamic acid.[8] Compared to intravenous administration, intra-articular administration of TXA seems to be more effective in terms of reducing blood loss and transfusion frequency. TXA may improve the general conditions of patients given TKA by maintaining a hemodynamically stable state, aiding in recovery, and reducing the chance of transfusion-associated side effects and complications.[15] In this study, we found better efficacy with intra-articular administration. Intra-articular tranexamic acid application not only reduces blood loss but also decreases knee joint swelling after total knee Arthroplasty.

CONCLUSION

We found that TXA leads to a statistically significant reduction in TBL and fewer patients requiring allogeneic transfusions, with no apparent increased risk of thromboembolic complications. Compared to intravenous administration, intra-articular administration of TXA seems to be more effective in terms of reducing blood loss and transfusion frequency.

REFERENCES

1. Benoni G, Carlsson A, Petersson C, Fredin H. Does tranexamic acid reduce blood loss in knee Arthroplasty? Am J Knee Surg1995; 8:88–92.
2. Hiippala ST, Strid LJ, Wennerstrand MI, *et al*. Tranexamic acid radically decreases blood loss and transfusions associated with total knee Arthroplasty. AnesthAnalg1997; 84:839–844.
3. Klein HG. Allogenic transfusion risks in the surgical patient. Am J Surg1995; 170 (Suppl):21–26.
4. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion transmitted viral infections: the Retrovirus epidemiology donor study. N Engl J Med 1996; 334:1685–1690.
5. Madjdpour C, Spahn DR. Allogeneic red blood cell transfusions: efficacy, risks, alternatives and indications. Br J Anaesth2005;95:33–42
6. Henry DA, Carless PA, Moxey AJ, *et al*. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 2007; 4:CD001886.
7. Zufferey P, Merquiol F, Laporte S, *et al*. Do antifibrinolytics reduce allogeneic blood transfusion in orthopedic surgery? Anesthesiology 2006; 105:1034–1046.
8. Wong J, Abrishami A, El Beheiry H, Mahomed NN, *et al*. Topical application of tranexamic acid reduces postoperative blood loss in total knee Arthroplasty: a randomized, double-blinded, placebo-controlled trial of efficacy. J Bone Joint Surg Am 2010; 92:2503–2513.
9. 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, 78:434–40.
10. Molloy DO, Archbold HAP, Ogonda L, McConway J, Wilson RK, Beverland DE. Comparison of topical fibrin spray and tranexamic acid on blood loss after total knee replacement. J Bone Joint Surge [Br] 2007; 89-B: 306–309.
11. Cid J, Lozano M. Tranexamic acid reduces allogeneic red cell transfusions in patients undergoing total knee Arthroplasty: results of a meta-analysis of randomized controlled trials. *Transfusion* 2005; 45:1302-1307.
12. Ipema HJ, Tanzi MG. Use of topical tranexamic acid or aminocaproic acid to prevent bleeding after major surgical procedures.*The Annals of pharmacotherapy* 2012;46**:**97-107
13. Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis**.** *BMJ* 2012; 344:e3054.
14. Ishida K, Tsumura N, Kitagawa A, Hamamura S, Fukuda K, Dogaki Y, Kubo S, Matsumoto T, Matsushita T, Chin T, *et al*. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee Arthroplasty. *IntOrthop* 2011; 35:1639-1645.
15. Seo JG, Moon YW, Park SH, Kim SM, Ko KR. The comparative efficacies of intra-articular and IV tranexamic acid for reducing blood loss during total knee Arthroplasty. Knee Surg Sports TraumatolArthrosc2013; 21:1869-1874.

16. Aguilera X, Videla S, Almenara M, Fernandez JA, Gich I, Celaya F. Effectiveness of tranexamic acid in revision total knee Arthroplasty. ActaOrthop Belg. 2012; 78:68-74.
17. Alshryda S, Sarda P, Sukeik M, Nargol A, Blenkinsopp J, Mason JM. Tranexamic acid in total knee replacement: a systematic review and meta-analysis. J Bone Joint Surg Br. 2011; 93:1577-1585.
18. 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. ClinOrthopRelat Res. 2013;471: 150-154
19. Murkin JM, Falter F, Granton J, Young B, Burt C, Chu M, *et al*. High-dose tranexamic Acid is associated with nonischemic clinical seizures in cardiac surgical patients. AnesthAnalg. 2010; 110:350-353.

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