Original Research Paper

Volume-8 | Issue-3 | March-2018 | PRINT ISSN No 2249-555X

Orthopedics

WHETHER COMBINEDLY ADMINISTERED TRANEXAMIC ACID IN TKR IS MORE EFFECTIVE THAN ONLY INTRAVENOUS ADMINISTRATION ?

Dr. Satyen Joshi	Associate Professor, Department of Orthopedics, Dr Vasantrao Pawar Medical college, Adgaon, Nashik-422003 (India)
Dr. Brijbhushan Mahajan	Assistant Professor, Department of Orthopedics, Dr Vasantrao Pawar Medical college, Adgaon, Nashik-422003 (India)
Dr. Nitish Agrawal*	Post Graduate Resident, Department of Orthopedics, Dr Vasantrao Pawar Medical college, Adgaon, Nashik- 422003 (India) *Corresponding Author
Dr. Bhalchandra Bhalerao	Post Graduate Resident, Department of Orthopedics, Dr Vasantrao Pawar Medical college, Adgaon, Nashik- 422003 (India)

ABSTRACT **Introduction:** The aim of our study is to compare efficacy of 3 doses of intravenous (IV) Tranexamic acid (TXA) versus combined IV and intraarticular TXA in reducing blood loss and transfusion requirement in patients who underwent primary total knee arthroplasty.
Methods: Group A patients were administered 3 IV doses of TXA. Group B patients were administered 1 gram of IV and 2 grams of IA dose.
Results: The mean 48 hrs drain collection was 238.33 ml in group A and 149 ml in group B. Mean hemoglobin drop is 2.39 gm% in group A and 1.74 gm% in group B. Post operative blood transfusion was required in 12 patients (40%) of group A and 5 patients (16.67%) of group B.
Conclusion: IA with IV TXA is more beneficial than IV TXA in reducing blood loss in primary total knee arthroplasty.

KEYWORDS : Total knee arthroplasty, Tranexamic acid, Route of administration

Introduction

Total knee arthroplasty (TKA) is well established treatment modality for severe Osteoarthritis knee. Patients requiring TKA is likely to increase in the near future due to increase in life expectancy. Substantialperioperative blood loss with systemiccomplications remains a concern [1, 2]. Many methods are used to manage blood loss such as tourniquet application, blood transfusion, administration of haemostatic agents and autologous transfusion [3]. Allogenic blood transfusion increases the risk of adverse events, and adds to the financial burden on the patients [4].

The use of Tranexamic acid (TXA) is proven as an effective method to minimize the blood loss and transfusion rates in total knee arthroplasty (TKA) without increasing the risk of thromboembolic events (TEE) [5]. Many studies have been done using TXA intravenously as well as topically to prove its efficacy [6,7]. In these studies, different dosing regimens have been used for both IV and topical TXA. Some studies have demonstrated better results with two IV doses over single dose [8,9] while some have compared single topical dose to one or two IV doses [10,11,12]. However, the available studies have shown mixed results, hence the aim of this study is to compare the effectiveness and safety of combined and isolated IV route of TXA administration in TKA.

Material and Methods

Institutional ethical committee approval was taken and the study was conducted in a Tertiary Medical Institue. This study includes patients who got operated between May 2014 and August 2017 for Total knee Arthroplasty. The inclusion criteria was patients operated for Total knee Arthroplasty who had normal preoperative platelet count, prothrombin time, partial thromboplastin time and international normalized ratio. The exclusion criteria were a known allergy to tranexamic acid; preoperative hepatic or renal dysfunction; serious cardiac or respiratory disease; congenital or acquired coagulopathy; and a history of thromboembolic disease. Patients taking antiplatelet agents were asked to stop them at least 7 days before surgery.

This is a retrospective study to investigate the effects of IV TXA vs IV plus topical TXA. Sixty patients were assigned to two groups with thirty patients in each group.

(I) Group A- Patients were administered,
1st dose- 1 gram TXA IV 20 minutes prior to tourniquet deflation
2nd dose- 1 gram TXA IV 3 hrs after 1st dose and
3rd dose- 1gram TXA IV 6 hrs after 1st dose.

(II) Group B- Patients were administered
1st dose- 1 gram TXA IV 20 minutes prior to tourniquet deflation
2nd dose- 2 grams TXA in 100 milliliters (mL) normal saline topically after arthrotomy closure.

A tourniquet was utilised in all cases which was inflated prior to skin incision and deflated after implantation. Compression bandage was given with eschmarch bandage for 5 min in both the groups. Intraarticular drain was inserted in each of the patients of both the groups. None of the patients had thromboembolic instability in intra-operative as well as post operative period. No incidence of Pulmonary embolism was noted in any of the patients.

We studied postoperative hemoglobin (Hgb) levels, Hgb drop, total drain output, total intraoperative blood loss, and transfusion rate. A transfusion was provided for any Hgb less than 9.0 grams/deciliter (g/dL).

The established practice of transfusion in our unit is that patients are transfused if:
1. Postoperative Hgb is < 9 mg/dl
2. Physiological signs of inadequate oxygenation such as hemodynamic instability or symptoms of myocardial ischemia occur
3. Drainage of more than 1 liter of blood in the first 24 hours.

Results-

Mean age of study population was 64 years [Figure 1]. 70% were females and 30% were male patients. Indication for surgery in all the patients was osteoarthritis knee.

In Group A patients, the intra-operative bleeding ranged from 150ml to 400ml (Mean 262.33ml), drain ranged from 100ml to 400ml (Mean 238.33ml) (Figure no. 1), Hgb drop ranged from 0.7 to 4.6 g/dl (Mean 2.39) (Figure no. 2). 12 of the 30 patients (40%) required blood transfusion post- operatively.

In Group B patients, the intra-operative bleeding ranged from 200ml to 350ml (Mean 248.00 ml), drain ranged from 100ml to 250ml (Mean 149.00ml) (Figure no. 1), Hgb drop ranged from 0.7 to 3.3 g/dl (Mean 1.74) (Figure no. 2). 5 of the 30 patients (16.67%) required blood transfusion post-operatively.

We observed a significant decrease in Hgb drop (Table no. 1) and total drain amount with the Group B compared to Group A. Group B also

had a significant decrease in total blood loss and transfusion rates (Table no. 2)compared to Group A (Table no. 3).

Discussion-

TXA is a synthetic anti-fibrinolytic agent that competitively inhibits the activation of plasminogen to plasmin, an enzyme that degrades fibrin clots, fibrinogen, procoagulant factors V and VIII. At higher concentration, TXA also acts directly to inhibit plasmin activity. Consequently, there is a decrease in proteolytic action on the fibrin monomers and fibrinogen, which results in clot stabilization. The trauma of surgery activates fibrinolysis by promoting the release of tissue plasminogen activator. Although the body naturally inhibits fibrinolysis by 24 hours after surgery, anti-fibrinolytic agents such as TXA can block the activation of plasminogen to plasmin earlier and thereby decreasing the perioperative blood loss.

TXA can be given as preoperative, intraoperative or postoperative dose; or various permutations combining these three doses. TXA, when given intravenously, has a wide distribution throughout the extracellular and intracellular compartments. It diffuses rapidly into the synovial fluid. Dose of 10-20 mg per kg body weight intravenously is used. Its biological half-life is 3 hours in the joint fluid and 90% of it is eliminated within 24 hours by glomerular filtration. Meta-analyses have shown that intravenous TXA effectively reduces the perioperative blood loss and incidence of blood transfusion after TKR, without increasing the risk of thromboembolic events (TEE) [12-16].

TXA can be given as a topical wash or infused into the knee joint after arthrotomy closure. Topical administration of TXA induces microvascular hemostasis via preventing dissolving the fibrin clot. Compared to intravenous administration, its benefits include ease of administration, ability to achieve maximum concentration at the bleeding site and minimal systemic absorption. Wind et al. compared the two forms of TXA and reported decreased transfusion requirements with both forms of TXA compared to placebo [17]. However, many common medical conditions including renal impairment, cardiovascular diseases, cerebrovascular conditions and the concurrent presence of hormonal treatment may preclude the use of intravenous TXA at the time of surgery [18].

Most intravenous regime of TXA advocates use of minimum two doses. Maniar et al. noted that a single regimen of IV TXA cannot be recommended as the most effective regimen. The three-dose IV regimen of Pre operative, Intra operative and Post operative doses produced maximum effective reduction of drain loss and total blood loss [8]. Seo et al. [19] and Sarzaeem et al. [11] in their study noted decreased postoperative Hb drop with intravenous administration as compared to intra-articular administration.

Soni et al. concurred with Maniar et al. and concluded that intra-articular regimen of TXA is as effective as three doses IV regimen in preventing blood loss without any difference in thromboembolic complications [20].

A recent study by Gomez-Barrena et al [21]compared topical IA TXA (3 g) with 2 IV doses (15 mg/kg each) of TXA in preserving blood loss in patients undergoing primary unilateral TKA. They analyzed 39 patients in each group (78 total) and reported no inferiority of topical TXA to IV TXA when analyzed for transfusion rate, blood loss, and Hb drop. Another study which compared 3.0 g of IA TXA with 3 doses of IV TXA (10 mg/kg) involved 40 patients in each group and concluded that IA TXA is equally effective as a 3-dose IV regimen in reducing blood loss during TKA [19]. In another recent study by Patel et al., Hb level drop was 3.06 in the IV group and 3.42 mg/dL in the topical group. They showed that two groups were statistically the same with regard to Hb drop, drain output, and rate of transfusion [10]. In a recent meta-analysis, Wang et al. showed that topical TXA is similar to IV TXA in reducing blood loss and rate of transfusion without compromising patient safety [22].

In contrary, some studies have found that intra-articular administration of TXA leads to better results. Recently, Hamlin et al. showed that topical TXA diminished the rate of transfusion compared to IV TXA in patients who underwent primary TKA (0% versus 2.4%) [23]. In a systematic review and meta-analysis, Alshryda et al. showed that the indirect comparison of topical and IV TXA indicated that topical administration is a more appropriate route [12]. Similarly, Ishida et al. reported intra-articular administration of TXA not only decreased blood loss but also decreased joint swelling after TKA [24].

Despite several studies proving the efficacy of both intra-articular and intravenous TXA in reducing blood loss after TKR, the ideal route of administering TXA will remain a topic for ongoing debate and controversy in the upcoming years.

The conflicting findings across these studies are possibly contributed by: (I) the variation in surgical techniques using conventional intra- and extramedullary jigs or computer-assisted surgery; (II) the variation in dosing regimen for intravenous TXA, with some studies giving one dose while others giving three doses; (III) the variation in indications for blood transfusion across hospitals.

Conclusion

IA with IV TXA is more beneficial than IV TXA in reducing blood loss in primary total knee arthroplasty. Topical administration of TXA had better efficacy than intravenous administration in reducing total blood loss, drain output, blood transfusion and haemoglobin drop, without any increase in thromboembolic complications.

Declaration of conflicting interests

Nil

Table no. 1-

HB DROP (g/dl)		
	Group A	Group B
MEAN	2.39	1.74
MEDIAN	2.25	1.75
STANDARD DEVIATION	0.96	0.67
p- VALUE	0.003	

Table no 2-

BLOOD TRANSFUSION		
Groups	Yes	No
Group A	12	18
Group B	05	25
Chi square statistics	4.022	
p-value	0.045	

Table no 3-

Parameter	Group A (n=30)	Group B (n=30)	p-value
Age (Mean±SD)	63.97±7.65	63.63±8.79	0.876
Sex (M/F)	12/18	06/24	0.091
Intra-op Bl. loss (Mean±SD)	262.33±74.86	248.00±47.01	0.378
P/O drain (Mean±SD)	238.33±70.91	149.00±43.18	0.000
Hgb drop (Mean±SD)	2.39±0.96	1.74±0.67	0.003
Need for BT	12/30	05/30	0.045

References-

1. Mannucci PM, Levi M. Prevention and treatment of major blood loss. N Engl J Med. 2007;356(22):2301–11.
2. Sculco TP. Global blood management in orthopaedic surgery. Clin Orthop Relat Res. 1998;357:43–9.
3. Bilgili MG, Ercin E, Peker G, Kural C, Basaran SH, Duramaz A, Avkan C. Efficiency and cost analysis of cell saver auto transfusion system in total knee arthroplasty. Balkan Med J. 2014;31(2):149–53.
4. Conteduca F, Massai F, Iorio R, Zanzotto E, Luzon D, Ferretti A. Blood loss in computer-assisted mobile bearing total knee arthroplasty. A comparison of computer-assisted surgery with a conventional technique. Int Orthop. 2009; 33(6):1609–13.
5. Yang ZG, Chen WP, Wu LD. Effectiveness and safety of tranexamic acid in reducing blood loss in total knee arthroplasty: a meta-analysis. J Bone Joint Surg Am 2012;94:1153-9.
6. . Wong J, Abrishami A, El Beheiry H, 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;92:2503-13.
7. Panteli M, Papakostidis C, Dahabreh Z, et al. Topical tranexamic acid in total knee replacement: a systematic review and meta-analysis. Knee 2013;20:300-9.
8. Maniar RN, Kumar G, Singhi T, et al. Most effective regimen of tranexamic acid in knee arthroplasty: a prospective randomized controlled study in 240 patients. Clin Orthop Relat Res 2012;470:2605-12.
9. Tanaka N, Sakahashi H, Sato E, et al. Timing of the administration of tranexamic acid for maximum reduction in blood loss in arthroplasty of the knee.J Bone Joint SurgBr 2001;83:702-5.
10. Patel JN, Spanyer JM, Smith LS, et al. Comparison of intravenous versus topical tranexamic acid in total knee arthroplasty: a prospective randomized study. J Arthroplasty 2014;29:1528-31.
11. Sarzaeem MM, Razi M, Kazemian G, et al. Comparing efficacy of three methods of tranexamic acid administration in reducing hemoglobin drop following total knee arthroplasty. J Arthroplasty 2014; 29(8): 1521–1524.
12. Alshryda S, Sukeik M, Sarda P, Blenkinsopp J, Haddad FS, Mason JM. A systematic review and meta-analysis of topical administration of tranexamic acid in total hip and knee replacement.Bone JointJ.2014;96-B(8):1005-15.
13. 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;45:1302-7.[PubMed]

14. Ho KM, Ismail H.. Use of intravenous tranexamic acid to reduce allogeneic blood transfusion in total hip and knee arthroplasty: a meta-analysis. Anaesth Intensive Care 2003;31:529-37. [PubMed]
15. Kagoma YK, Crowther MA, Douketis J, et al. Use of antifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: a systematic review of randomized trials. Thromb Res2009;123:687-96. [PubMed]
16. Yang ZG, Chen WP, Wu LD.. Effectiveness and safety of tranexamic acid in reducing blood loss in total knee arthroplasty: a meta-analysis. J Bone Joint Surg Am 2012;94:11539. [PubMed]
17. Wind TC, Barfield WR and Moskal JT. The effect of tranexamic acid on blood loss and transfusion rate in primary total knee arthroplasty. J Arthroplasty 2013; 28(7): 1080–1083.
18. McCormack PL.. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. Drugs2012;72:585-617.
19. Seo JG, Moon YW, Park SH, et al. The comparative efficacies of intra-articular and IV tranexamic acid for reducing blood loss during total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc 2013; 21(8): 1869–1874.
20. Soni A, Saini R, Gulati A, et al. Comparison between intravenous and intra-articular regimens of tranexamic acid in reducing blood loss during total knee arthroplasty. J Arthroplasty 2014; 29(8): 1525–1527.
21. Gomez-Barrena E, Ortega-Andreu M, Padilla-Eguiluz NG, et al. Topical intraarticular compared with intravenous tranexamic acid to reduce blood loss in primary total knee replacement: a double-blind, randomized, controlled, noninferiorityclinical trial. J Bone Joint Surg Am 2014;96(23):1937.
22. Wang H, Shen B, Zeng Y. Comparison of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled and prospective cohort trials. Knee. 2014; 21(6):987-93.
23. Hamlin BR, DiGioia AM, Plakseychuk AY, Levison TJ. Topical versus intravenous tranexamic acid in total knee arthroplasty. J Arthroplasty. 2015; 30(3):384-6.
24. Ishida K, Tsumura N, Kitagawa A, et al. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee arthroplasty. Int Orthop 2011; 35(11): 1639–1045.