

RESEARCH ARTICLE

Intraarticular Administration of Tranexamic Acid Following Total Knee Arthroplasty: A Case-control Study

Mohammad N Tahmasebi, MD; Kaveh Bashti, MD; Gholamreza Ghorbani, MD; Mohammad R Sobhan, MD

Research performed at Tehran University of Medical sciences, Tehran, Iran

Received: 17 August 2014

Accepted: 3 September 2014

Abstract

Background: Tranexamic acid (TXA) has received extensive attention in management of blood loss in orthopedic surgeries. However, the ideal method of TXA administration is still controversial.

This study aims to determine whether intraarticular injection of TXA reduces blood loss after total knee arthroplasty (TKA).

Methods: Through a retrospective case-control study consecutive TKA patients receiving intraarticular TXA (Case group) were compared with similar patients undergoing TKA using traditional blood management strategy (Control group). Hemoglobin levels (Hb) before and after the surgery, need for transfusion, and reoperation due to massive blood loss were compared between the two groups.

Results: Fifty TXA patients were compared with 50 patients of the control group. There was no significant difference between the two groups in terms of age, gender, and preoperative Hb. Postoperative blood loss and transfusion rate were significantly reduced in TXA patients compared to the control group ($P < 0.05$).

Conclusions: Our study revealed that intraarticular administration of TXA reduces postoperative blood loss as well as need for blood transfusion in patients undergoing TKA.

Key words: Blood Loss, Hemostasis, Intraarticular Injection, Total Knee Arthroplasty, Tranexamic Acid, Transfusion

Introduction

Total knee arthroplasty (TKA) is among the most popular procedures in orthopedic surgery and the ideal treatment for painful arthritic knee (1). However, there is still way to go to achieve the best results from the procedure and obtain the highest level of patient satisfaction (2). Leg swelling, postoperative pain and blood loss are some of frequent complications following TKA which may compromise the rehabilitation process (3-6).

Due to hemodynamic instability, heart failure, and wound infection, blood loss after TKA can be threatening (7-10). The problem is more serious when the patient has very low tolerability to acute anemia and requires

transfusion which in turn results in serious complications such as viral infections and graft-versus-host disease (10-12). Moreover, blood loss requiring transfusion increases associated costs with TKA due to expensive blood products imposing a heavy burden on health care resources (13).

Given the challenges of perioperative and adverse consequences of inadequate blood management in TKA patients, blood sparing strategies have gained increasing popularity during the last years (7, 14). Tranexamic acid (TXA) is an antifibrinolytic agent and also acts as an activator of plasminogen (13-16). As an inexpensive and easily available synthetic product, TXA has been shown to reduce blood loss in TKA patients (5, 13, 15-16).

Corresponding Author: Kaveh Bashti, Department of Orthopedic Surgery, Division of Knee Surgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Email: bashtikaveh@yahoo.com



THE ONLINE VERSION OF THIS ARTICLE
ABJS.MUMS.AC.IR

Table1. Comparison of baseline characteristics between TXA and control groups

	TXA Group (N=50)	Control Group (n=50)	P
Age(yrs)	65.1±6.9	63.5±7.1	0.25
Sex (n, %)			
Male	23 (46%)	25 (50%)	0.69
Female	27 (54%)	25 (50%)	
Side of Operation (n, %)			
Right	26 (52%)	26 (52%)	1.00
Left	24 (48%)	24 (48%)	

Nevertheless, the ideal method of administration is a matter of debate despite the large number of reports on TXA (5). On the other hands, orthopedic surgeons have avoided wide application of TXA as a preventive product for blood loss in knee surgeries. One reason may be due to its fearsome prothrombotic effect while another reason to be variability of the proposed administration regimen and route (5, 17-19).

TXA has been repeatedly used intravenously in single or repeated doses (19-20). However, it has been criticized that only small fraction of injected drugs may reach the target location and hence diminishes its ultimate efficacy (5). For this reason, intraarticular administration of TKA has been suggested by few studies as an alternative strategy which may improve its efficacy (5, 21-22). The aim of the present study was to investigate the benefits of intraarticular injection of TXA in TKA-related blood loss management.

Materials and Methods

Study Design

A retrospective case-control study was conducted in Orthopedics ward of a University and a Private Hospital in Tehran, Iran reviewing prospectively collected data of patients undergoing TKA from March 2013 to March 2014. TKA Patients who received TXA (Case group) were compared with those with traditional blood management approach (Control group). Our internal review committee of orthopedic research approved the study protocol as an observational human project.

Participant

Fifty consecutive adult patients undergoing TKA and subsequent intraarticular injection of TXA were included in this study. Patients with placement of drainage tube and previous coagulopathy were excluded from analysis. All study data and collected information from patients profile were remained confidential and the statements of Helsinki were adhered during the study.

Operation and Blood Management

All TKA were performed by a single team of

Table2. Comparison of study outcomes between TXA and control groups

	TXA Group (N=50)	Control Group (n=50)	P
Preoperative Hb(g/dl)	13.2±1.4	13.4±1.3	0.37
Postoperative Hb(g/dl)	11.8±1.9	11.2±1.4	0.02
Hb Change(g/dl)	1.3±0.5	2.3±0.6	<0.001
Need to Transfusion(n, %)	0	4 (8%)	0.04
Reoperation(n, %)	0	0	NA
Hemarthrosis(n, %)	0	0	NA

orthopedic surgery and under similar anesthetic and surgical protocols. In the case group, TXA (1500 mg diluted in 50 cc of normal saline) was administered intraarticularly after tight closure of retinaculum with no placed draining tube. The traditional approach of blood management was considered for the control group. Tourniquet was used in all surgeries at the beginning of TKA and removed after injection of TXA and dressing.

Outcome Measure

As the main study outcome, hemoglobin (Hb) was measured preoperatively and 48 hours postoperatively. Need to transfusion, reoperation due to blood loss, and occurrence of hemarthrosis were the secondary outcomes.

Statistical Analysis

Data were analyzed using SPSS for windows (Version 18, Chicago, Inc, US). Student t-test and Chi square test were used for quantitative and qualitative variables, respectively. Data are presented as mean ± SD and number (%) and a statistical difference considered significant when $P < 0.05$.

Results

Overall Demographics and Baseline Characteristics of Study patients

A total of 100 consecutive patients with an average age of 64.3 ± 6.9 years were included in our analysis constituting of 48 males (48%) and 52 females (52%). Fifty two percent of surgeries were on the right side and 48% on the left side. Mean ± SD Hb levels were 13.3 ± 1.30 g/dl and 11.5 ± 1.4 g/dl before and after the surgery, respectively with an average Hb change of 1.8 ± 0.7 g/dl (range from 0.2 g/dl to 3.5 g/dl). There was need to transfusion in 4 cases (4%) but no reoperation or hemarthrosis occurred.

Comparison of Primary Characteristics between Study Groups

Table 1 compares primary characteristics of TXA and control groups. As from the table, there is no significant difference between the two groups for age, sex distribution and side of operation ($P > 0.05$).

Comparison of Primary Characteristics between TXA and Control Groups

Study outcomes are compared between the two groups in Table 2. While there was no significant difference in terms of preoperative Hb, postoperative Hb was significantly lower in control patients (11.2 ± 1.4 g/dl) than TXA group (11.8 ± 1.9 g/dl) ($P=0.02$). Moreover, Hb change/decrease was more significant in the control group than in the TXA group (2.3 ± 0.6 g/dl vs. 1.3 ± 0.5 g/dl, $P<0.001$). On the other hands, 4 patients (8%) in the control group required blood transfusion which revealed a statistically significant difference compared to the TXA patients with no need to transfusion ($P=0.04$).

Discussion

Our study showed that intraarticular injection of TXA after TKA can effectively diminish Hb drop, blood loss, and need for transfusion up to 48 hours postoperatively which are consistent with other studies in the literature. In a randomized controlled trial of 100 TKA patients equally receiving TXA or normal saline through a closed suction drain, Ishida et al. showed that administration of TXA significantly reduced blood loss as well as knee joint swelling after TKA (5). Despite strong evidence supporting TXA effectiveness in diminishing blood loss and requirement of blood transfusion in TKA patients regardless the total dose of TEA given, there are minor controversies existing for the ideal administration route and a suitably scheduled dosage (23). Good et al. in a small cohort compared blood controlling effect of TXA 10 mg/Kg with placebo in TKA patients under spinal anesthesia (19). While they have criticized TXA by hidden blood loss and concluded that concealed loss was not substantially reduced by TXA, they did not report Hb changes after TKA which is a better marker of total blood loss. On the other hands, Rally et al. retrospectively compared 259 patients of hip and knee arthroplasty receiving TXA 20 mg/Kg with 234 similar patients undergoing arthroplasty before establishing TXA protocol (20). Their study showed that one 20-mg/kg dose of TXA administered intraoperatively reduced perioperative Hb drop and need to transfusion. While these authors have commented in their study that the effective administration protocol of TXA reported in the literature is composed of two 10 mg/Kg doses in 3-hours interval, we did not employ such a multi-dose protocol for TXA injection. Besides, while our total 1500 mg TXA is a medium dosage, it was given in a relatively larger volume (50cc) compared to other studies which injected the agent through a draining tube (5, 19-20).

Perioperative bleeding in TKA patients is very common and probably results from patient hematological characteristics (coagulopathies, medical conditions, and medications) and surgical techniques (bone cuts, dissection of soft tissue, and damage to the vasculatures) (9). Blood loss can cause a mismatch between oxygen supply and demand increasing the risk of myocardial infarct (8, 10). Additionally, despite numerous blood controlling strategies such as pneumatic tourniquet and low pressure anesthesia, blood transfusion remains the only true treatment for acute anemia in low tolerability

patients (10, 13). While the risks of non-transfusion outweighs those of transfusion-related complications, associated costs, shortage of matched and blood born-screened packed red cells, and adverse events due to cross-reaction justify investigating efforts to find new blood preserving methods (11, 24). Although TXA has been available for over 20 years in surgery, orthopedist have hesitated the routine use of this agent due to insufficient evidence regarding its effectiveness versus unresolved issue of thromboembolic events (14, 15, 17-18). On the other hands, among those studies with satisfactory results, administration route and dosage are varying (5, 7, 12, 14, 19, 23, 25). The present study settles in the middle of other reports in terms of TXA dosage and administration protocol. We injected TXA intraarticularly after tight closure of retinaculum, with additional suture to strengthen its resistance to water, once the TKA was completed. Moreover, unlike other studies we did not place drainage to allow absorption of the blood in the surgical site (5, 19-20). Fortunately, this approach did not result in hemarthrosis and no patients required reoperation due to massive bleeding nor there was any complicated rehabilitation case.

We acknowledge that our retrospective review poses some limitations including a relatively small sample size, lack of another arm for comparison of other TXA administration methods, and considering other endpoints such as postoperative pain, length of hospital stays, and time of full recovery to return to work. Moreover, longitudinal follow-up of TKA patients and serial measurement of Hb until the first postoperative week would permit a more realistic knowledge of blood loss and the possibility of assessing patient satisfaction and final outcomes of TKA with this new blood management strategy.

Because literature reviews has revealed no significant risk of thrombosis in relation to TXA, its wide application as a prophylactic agent for controlling blood loss may be recommended with fewer hesitations (25). We had no cases of Thromboembolic complication among our patients nor any other complications related to TXA. However, due to lack of objective assessment of deep vein thrombosis i.e. sonographic examination in our study, future studies are expected to investigate the risk of TKA-related thrombosis through high power randomized trials.

Intrarticular injection of TXA reduces postoperative blood loss, Hb drop and transfusion rate in patients undergoing TKA.

Mohammad N Tahmasebi MD

Kaveh Bashti MD

Gholamreza Ghorbani MD

Department of Orthopedic Surgery, Division of Knee Surgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

Mohammad R Sobhan MD

Department of Orthopedic Surgery, Division of Knee Surgery, Yazd University of Medical Sciences, Yazd, Iran

References

1. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am.* 2007; 89(4):780-5.
2. Noble PC, Conditt MA, Cook KF, Mathis KB. The John Insall Award: Patient expectations affect satisfaction with total knee arthroplasty. *Clin Orthop Relat Res.* 2006; 452:35-43.
3. Giesinger K, Hamilton DF, Jost B, Holzner B, Giesinger JM. Comparative responsiveness of outcome measures for total knee arthroplasty. *Osteoarthritis Cartilage.* 2014; 22(2):184-9.
4. Sasaki E, Tsuda E, Yamamoto Y, Meada S, Otsuka H, Ishibashi Y. Relationship between patient-based outcome score and conventional objective outcome scales in post-operative total knee arthroplasty patients. *Int Orthop.* 2014; 38(2):373-8.
5. 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 Orthop.* 2011; 35(11):1639-45.
6. Kim J, Nelson CL, Lotke PA. Stiffness after total knee arthroplasty. Prevalence of the complication and outcomes of revision. *J Bone Joint Surg Am.* 2004; 86(7):1479-84.
7. 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(12):1577-85.
8. Mantilla CB, Wass CT, Goodrich KA, Johanns CJ, Kool ML, Zhu X, et al. Risk for perioperative myocardial infarction and mortality in patients undergoing hip or knee arthroplasty: the role of anemia. *Transfusion.* 2011; 51(1):82-91.
9. Prasad N, Padmanabhan V, Mullaji A. Blood loss in total knee arthroplasty: an analysis of risk factors. *Int Orthop.* 2007; 31(1):39-44.
10. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. *Anesthesiology.* 2010; 113(2):482-95.
11. Bolton-Maggs PH, Cohen H. Serious Hazards of Transfusion (SHOT) haemovigilance and progress is improving transfusion safety. *Br J Haematol.* 2013; 163(3):303-14.
12. Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev.* 2011; 1:CD001886.
13. Banerjee S, Issa K, Kapadia BH, Khanuja HS, Harwin SF, McInerney VK, et al. Intraoperative nonpharmacotherapeutic blood management strategies in total knee arthroplasty. *J Knee Surg.* 2013; 26(6):387-93.
14. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. *Drugs.* 1999; 57(6):1005-32.
15. Panteli M, Papakostidis C, Dahabreh Z, Giannoudis PV. Topical tranexamic acid in total knee replacement: a systematic review and meta-analysis. *Knee.* 2013; 20(5):300-9.
16. Zhang H, Chen J, Chen F, Que W. The effect of tranexamic acid on blood loss and use of blood products in total knee arthroplasty: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc.* 2012; 20(9):1742-52.
17. Krivokuca I, Lammers JW. Recurrent pulmonary embolism associated with a hemostatic drug: tranexamic acid. *Clin Appl Thromb Hemost.* 2011; 17(1):106-7.
18. Taparia M, Cordingley FT, Leahy MF. Pulmonary embolism associated with tranexamic acid in severe acquired haemophilia. *Eur J Haematol.* 2002; 68(5):307-9.
19. Good L, Peterson E, Lisander B. Tranexamic acid decreases external blood loss but not hidden blood loss in total knee replacement. *Br J Anaesth.* 2003; 90(5):596-9.
20. Ralley FE, Berta D, Binns V, Howard J, Naudie DD. One intraoperative dose of tranexamic Acid for patients having primary hip or knee arthroplasty. *Clin Orthop Relat Res.* 2010; 468(7):1905-11.
21. Hegde C, Wasnik S, Kulkarni S, Pradhan S, Shetty V. Simultaneous bilateral computer assisted total knee arthroplasty: the effect of intravenous or intraarticular tranexamic acid. *J Arthroplasty.* 2013; 28(10):1888-91.
22. MacGillivray RG, Tarabichi SB, Hawari MF, Raouf NT. Tranexamic acid to reduce blood loss after bilateral total knee arthroplasty: a prospective, randomized double blind study. *J Arthroplasty.* 2011; 26(1):24-8.
23. 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(8):1302-7.
24. Rosencher N, Bellamy L, Chabbouh T, Arnaout L, Ozier Y. Blood conservation approaches in orthopedic surgery. *Transfus Clin Biol*. 2008; 15(5):294-302.
25. Kagoma YK, Crowther MA, Douketis J, Bhandari M, Eikelboom J, Lim W. Use of antifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: a systematic review of randomized trials. *Thromb Res*. 2009; 123(5):687-96.