

Does tranexamic acid reduce blood transfusion following surgery for inter-trochanteric fracture? A randomized control trial

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Abstract

Objective: To compare the frequency of blood transfusion after surgery for fixation of inter-trochanteric fractures in patients given tranexamic acid versus placebo.

Methods: The randomised control trial was conducted at the Aga Khan university hospital from May 1 to October 31, 2014, and comprised patients diagnosed with Inter-trochanteric fracture based on X-ray imaging. The patients were randomised into two equal groups based on a computer-generated random number table. The Intervention group received two doses of 10mg/kg body weight of tranexamic acid just before surgery and three hours later intravenously. The Control group received two doses of 10mg/kg body weight of normal saline at similar intervals. Numbers of blood transfusions required postoperatively were noted based on the postoperative haemoglobin readings.

Results: There were 100 patients who were divided into groups of 50(50%) each. Mean post-op haemoglobin for the intervention group was 10.2 ± 2.4 g/dl and for the control group it was 8.9 ± 2.4 g/dl ($p=0.007$). Nine (18%) patients in intervention group required blood transfusion compared to 21(42%) in control group ($p=0.009$).

Conclusion: Administering tranexamic acid was a useful and safe option for reducing requirement of blood transfusion postoperatively after inter-trochanteric hip fractures.

Keywords: Hip fractures, Tranexamic acid, Blood transfusion. (JPMA 65: S-17 (Suppl. 3); 2015)

Introduction

Hip fracture surgery accounts for a major load of any orthopaedic surgery. Most of the patients are elderly with multiple comorbidities and the estimated one-year mortality is about 25%.¹ Major muscles insert are involved around the proximal femur and hence these surgeries are associated with significant intraoperative bleeding, leading to postoperative anaemia. This in turn may lead to reduced functional recovery, resulting in decreased long-term mortality.² About one half of all patients undergoing hip fracture surgery require at least 1100ml of red blood cell (RBC) transfusion.³

Blood transfusion itself is not free from adverse events. It can be a source of transmission of various blood-borne infections and can also cause severe immunological reactions.⁴ With recent advances, various methods have been designed to prevent intraoperative blood loss, like permissive hypotension, topical freezing saline, thromboplastic agent and intraoperative administration of anti-fibrinolytic agent like tranexamic acid (TXA).⁵ All these modalities are effective in reducing intraoperative blood loss, but their role is still unclear.

TXA is an inexpensive pharmacological agent and is a

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derivative of amino acid lysine. It occupies lysine sites on the plasminogen molecules and therefore causes reduced formation of activated plasmin which is responsible for the dissolution of clot. This in turn results in stabilisation of clot and decreased blood loss. Use of TXA has been extensively studied in cardiac, spine, maxillofacial and other surgeries and has been proved to be an important factor in decreasing operative blood loss and, hence, the need for postoperative blood transfusion.⁶⁻⁸

With limited literature for TA use in hip fracture surgery, the current study was planned to compare the frequency of blood transfusion after surgery for fixation of inter-trochanteric fractures in patients given TXA versus placebo.

Patients and Methods

The prospective double blind, randomised control trial was performed during at the Aga Khan University hospital from May 1 to October 31, 2014, and comprised patients between the ages 50 and 90 years diagnosed with Inter-trochanteric fracture on X-ray imaging. Patients having multiple fractures on X-ray were excluded and so were those with rheumatoid arthritis, ischemic heart disease, pregnant or lactating women, those with known coagulation disturbances, use of warfarin or other anticoagulants and allergy to TXA. Written informed consent was obtained from all participants and the study

was approved by the institutional ethics review committee.

The patients were randomly allocated into two equal groups using a computer-generated random number table which was prepared using the help of a senior statistician. Patients in intervention TXA group received two doses of 15mg/kg body weight of TXA, while those in the control group received two doses of 15mg/kg body weight of placebo which was normal saline, intravenously. In both groups the first dose was administered just before surgery and the second was given 3 hours later. An orthopaedic Resident not part of the primary surgical team was responsible for administration of the placebo or TXA while keeping the investigator and primary surgery team blinded. Neither the patient nor the investigator knew of the group allocation.

Haemoglobin (Hb) was measured preoperatively (pre-op Hb) and at 24 hours postoperatively (post-op Hb). All patients were given routine prophylaxis for DVT with injection Enoxaparin 40mg subcutaneously once a day. To minimise bias, all patients were operated upon by a senior orthopaedic surgeon with minimum 5 years of experience. Patients who were required to receive blood transfusion were noted. Blood was transfused if the post-op Hb was <7g/dl.

Data was analysed using SPSS 20. Continuous variables were expressed as mean \pm standard deviation (SD) and categorical variables were expressed as frequencies and percentages. For comparison of means, Independent sample t-test was used and Chi-square test was used for comparison of categorical variables. $P < 0.05$ was considered significant.

Results

There were 100 patients who were divided into groups of 50(50%) each. There were no significant differences between the groups in terms of age, gender, site, pre-op

Table-1: Baseline Characteristics.

Characteristics	Intervention group (n=50)	Control group (n=50)	P-value
Age (years)	69.0 \pm 10.0	70 \pm 9.4	0.6
Gender			
Male	21	24	0.5
Female	29	26	
Site			
Right	27	31	0.4
Left	23	19	
Pre-op Haemoglobin (g/dl)	11.5 \pm 1.8	11.3 \pm 1.7	0.7
Duration of surgery (mins)	112.9 \pm 46.7	112.3 \pm 47.7	0.9

Table-2: Comparison of blood transfusion between intervention and control groups.

	Blood Transfusion		P-value	Relative Risk
	Yes (n=50)	No (n=50)		
TXA group	9 (18%)	41 (82%)	0.009	0.51 (0.29-0.92)
Control group	21 (42%)	29 (58%)		

TXA: Tranexamic acid.

Hb and duration of surgery ($p > 0.05$ each) (Table-1).

The mean post-op Hb 24 hours after surgery was 10.2 \pm 2.4 g/dl for the intervention group, while it was 8.9 \pm 2.4 g/dl for the control group ($p = 0.007$).

There was a significant difference in the requirement of blood transfusion between the groups ($p = 0.009$) (Table-2). The relative risk (RR) for transfusion was 0.51 when TXA was administered compared to when placebo was administered.

Discussion

The role of TXA in reducing surgery-related blood loss, and, hence, the need for blood transfusion, has been researched a lot in different surgical fields, including orthopaedics. A randomised control trial (RCT) performed in 2001 showed that there was significantly less intraoperative blood loss and need for blood transfusion in patients receiving TXA for scoliosis surgery.⁷ A meta-analysis of 129 RCTs, carried out in 2012 also concluded that the probability of receiving transfusion after surgery was reduced by one-third after administering TXA.⁹ Benoni G et al. conducted a study to assess the role of TXA in total knee replacement (TKR). Two doses of 10mg/kg body weight of TXA were administered; one before release of tourniquet and the second three hours later. Giving TXA significantly reduced the amount of blood loss and the need for blood transfusion.¹⁰ Similarly, other trials and meta-analyses have also shown similar results after total hip and knee replacement procedures.¹¹⁻¹³

Despite having many studies to evaluate the role of TXA in surgeries, limited literature is available on its role in hip fracture surgeries. In an RCT, TXA was administered as an initial bolus dose of 500mg before surgery followed by continuous infusion at 1mg/kg/h for the duration of surgery. Results showed that the differences in mean reduction in Hb and mean volume of blood loss postoperatively between TXA and placebo groups were significant. In addition, only 7 out of 45 patients in TXA group required blood transfusion compared to 18 out of 45 in placebo group and the difference was again significant.⁵ On the contrary, another RCT in 2010 concluded that there was no significant difference in

blood transfusion rates between TXA and placebo groups after surgery for hip fracture.³ Therefore, although effectiveness of TXA in reducing post-surgical blood loss and transfusion requirements have been shown by multiple studies, but its effectiveness, specifically in hip fracture surgeries, is yet to be established.

Blood loss in hip fracture surgeries is different from those in elective procedures of hip and knee joint because in hip fractures, the fibrinolytic system gets activated at the time of trauma and continues to increase during surgery.⁵ As a result, these surgeries are associated with increased blood loss and increased requirement of blood transfusions. Therefore, it is important to assess the role of TXA in hip fracture surgeries separately. The current study showed that in hip fracture surgery, the need for blood transfusion was significantly reduced in patients receiving TA, as 18% patients in intervention group versus 42% in control group required blood transfusion. This is comparable to a trial in which 15.5% patients in TXA group and 40% in control group required transfusion after hip fracture surgery.⁵ These results substantiate the findings of previously mentioned studies regarding the importance of TXA in surgical procedures.

The pre-op and post-op Hb was also comparable to another study conducted in Iran in 2007 in which a bolus dose of 15mg/kg body weight of TXA was administered at the time of induction of anaesthesia. The pre-op Hb for TXA and control group was 11.1±2.2 and 11.4±1.3 g/dl respectively and post-op Hb was 10.1±1.4 and 8.9±2.1 g/dl respectively. This study also showed that TXA is associated with reduced post-surgical blood transfusions.¹⁴

A few surgeons also believe that TXA increases the risk of thromboembolic events, including DVT and pulmonary embolism (PE).¹⁵ But during our study, no such complication was noted in the intervention group. This is also supported by a meta-analysis conducted in 2003 which concluded that TXA is not associated with an increased risk of thromboembolic accidents.¹⁶ Administering TXA is also more cost-effective compared to transfusing blood, and therefore increasing its use in reducing the requirement for transfusion will result in decreased economic burden on health system, which is a bonus, especially in developing countries like Pakistan.^{17,18}

Although this study successfully proves the effectiveness of TXA, but some of the confounding factors which could have affected the results include body mass index (BMI) of the patients, American Society of Anaesthesiologists (ASA) status and use of any anti-coagulants prior to the

surgery by the patients. The study also takes into account only the post-op Hb measured 24 hours after surgery. To further substantiate the results, volume of blood loss intraoperatively and postoperatively can also be measured. Hb levels can also be measured daily for a week after surgery to evaluate the long-term effect of TXA. Further studies can also be carried out to test the effectiveness of TA in different types of orthopaedic fractures.

Conclusion

Administering TXA was a safe and useful option for reducing the need for blood transfusion after surgery for inter-trochanteric hip fractures.

References

- Davidson C, Merrilees MJ, Wilkinson TJ, McKie JS, Gilchrist N. Hip fracture mortality and morbidity - can we do better? *N Z Med J* 2001; 114: 329-32.
- Lawrence VA, Silverstein JH, Cornell JE, Pederson T, Noveck H, Carson JL. Higher Hb level is associated with better early functional recovery after hip fracture repair. *Transfusion* 2003; 43: 1717-22.
- Zufferey PJ, Miquet M, Quenet S, Martin P, Adam P, Albaladejo P, et al. Tranexamic acid in hip fracture surgery: a randomized controlled trial. *Br J Anaesth* 2010; 104: 23-30.
- Marcucci C, Madjdpour C, Spahn DR. Allogeneic blood transfusions: benefit, risks and clinical indications in countries with a low or high human development index. *Br Med Bull* 2004; 70: 15-28.
- 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 J Anaesth* 2013; 7: 29-32.
- Zabeeda D, Medalion B, Sverdlöv M, Ezra S, Schachner A, Ezri T, et al. Tranexamic acid reduces bleeding and the need for blood transfusion in primary myocardial revascularization. *Ann Thorac Surg* 2002; 74: 733-8.
- Neilipovitz DT, Murto K, Hall L, Barrowman NJ, Splinter WM. A randomized trial of tranexamic acid to reduce blood transfusion for scoliosis surgery. *Anesth Analg* 2001; 93: 82-7.
- Weber BJ, Kjelland CB. The use of tranexamic acid for trauma patients? *CJEM* 2012; 14: 53-6.
- 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. doi: 10.1136/bmj.e3054.
- 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.
- Johansson T, Pettersson LG, Lisander B. Tranexamic acid in total hip arthroplasty saves blood and money: a randomized, double-blind study in 100 patients. *Acta Orthop* 2005; 76: 314-9.
- Yang Z-G, Chen W-P, Wu L-D. 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.
- Hiippala ST, Strid LJ, Wennerstrand MI, Arvela JV, Niemelä HM, Mäntylä SK, et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesth Analg* 1997; 84: 839-44.
- Sadeghi M, Mehr-Aein A. Does a single bolus dose of tranexamic acid reduce blood loss and transfusion requirements during hip

- fracture surgery? A prospective randomized double-blind study in 67 patients. *Acta Medica Iranica* 2007; 45: 437-42.
15. 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. *Clin Orthop Relat Res* 2013; 471: 150-4.
 16. Ho K, 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.
 17. Sepah YJ, Umer M, Ahmad T, Nasim F, Chaudhry MU, Umar M. Use of tranexamic acid is a cost effective method in preventing blood loss during and after total knee replacement. *J Orthop Surg Res* 2011; 6: 22. doi: 10.1186/1749-799X-6-22.
 18. Rajesparan K, Biant L, Ahmad M, Field R. The effect of an intravenous bolus of tranexamic acid on blood loss in total hip replacement. *J Bone Joint Surg Br* 2009; 91: 776-83.
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