Research Paper

Volume : 4 | Issue : 8 | Aug 2015 • ISSN No 2277 - 8179

Effect of Single Dose Tranexamic Acid on Blood Loss in Total Hip Arthroplasty in Indian Population

Medical Science

KEYWORDS : Total hip arthroplasty, blood loss, tranexamic acid

Dr. Taufiq R. Panjwani	Senior Registrar, Dept. of Orthopaedics, 6th floor, Multistorey building, Seth G.S. Medical College & K.E.M. Hospital, Mumbai.
Dr. Rishi A. Aggarwal	Senior Registrar, Dept. of Orthopaedics, Seth G.S. Medical College & K.E.M. Hospital, Mumbai.
Dr. Zainab S. Nayani	Registrar, Dept. of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences, Karad.
Dr. Kapil A. Pawar	Assistant Professor, Dept. of Orthopaedics, Seth G.S. Medical College & K.E.M. Hospital, Mumbai.

ABSTRACT

Introduction: *Total hip arthroplasty (THA) has become one of the most successful and cost-effective procedures in modern medicine. Peri-operatively, there can be considerable blood loss sometimes requiring allogenic blood transfusion which carries significant risks of immunological reactions, transmission of disease, intravascular haemolysis, transfusion induced coagulopathy, renal failure, admission to intensive care and even death. Tranexamic acid is an inexpensive synthetic antifibrinolytic agent. Tranexamic acid prevents the degradation of fibrin and delays the breakdown of haemostasis clots.We studied the effect of single dose of intravenous preoperative tranexamic acid on perioperative blood loss in patients undergoing total hip arthroplasty and also its effect on reducing postoperative allogenic blood transfusions.*

Materials and methods: *We included 40 patients with undergoing primary total hip arthroplasty for osteonecrosis in our study. Patients with proven rheumatoid arthritis, hipjoint infection, malignancy, coagulopathies and known allergy to tranexamic acid were excluded from the study.The participants were randomly allocated to the study and control group receiving single dosetranexamic acid and placebo, respectively. We collected preoperative and day 2 postoperative hemoglobin, total blood loss and need for blood transfusion, if any, and compared the two groups by statistical analysis.*

Results: *There was significant difference in blood loss and need for blood transfusion between the two groups. Study group had a significantly lower decrease in post-operative hemoglobin as compared to the control group. The mean age, weight, height and body-mass index comparison between the study and control groups were not statistically significant.*

Conclusion: *Our study demonstrates that single preoperative dose of tranexamic acid significantly reduces intraoperative blood loss, postoperative blood loss, total blood loss and the need for blood transfusion in primary total hip arthroplasty in Indian population.*

INTRODUCTION:

Total hip arthroplasty (THA) is one of the most widely performed procedures in orthopedic practice. It has become one of the most successful and cost-effective procedures in modern medicine since its introduction and advancement in the 1960s by the British orthopaedic surgeon Sir John Charnley. Peri-operatively, there can be considerable blood loss sometimes requiring allogenic blood transfusion. This carries significant risks of immunological reactions, transmission of disease, intravascular haemolysis, transfusion induced coagulopathy, renal failure, admission to intensive care and even death.

The incidence of major bleeding events (requiring more than two red-blood-cell [RBC] packs or reoperation or causing death) is 1.4%. Overall, the mean mortality rate in orthopaedic surgery is less than 1%. Importantly, mortality is increased 5-fold in patients with anaemia. Half the deaths ascribable entirely or in part to inadequate blood management during anaesthesia occur in orthopaedic surgery.

A variety of blood-conserving techniques have been developed to reduce blood loss and post-operative transfusion rates, including controlled hypotension, regional anaesthesia, autologous blood transfusion, intra-operative blood salvage, and the use of erythropoietin and antifibrinolytic agents.

The antifibrinolytics include tranexamic acid (TXA), aprotinin and ε-aminocaproic acid (EACA), which have different mechanisms to inhibit the dissolution of blood clots. They have been used successfully to stop bleeding after dental extraction, tonsillectomy, prostate surgery, heavy menstrual bleeding, cardiac surgery, and in patients with haemophilia.

Tranexamic acid is an inexpensive synthetic antifibrinolytic agent. Tranexamic acid prevents the degradation of fibrin and delays the breakdown of haemostasis clots. A 30% reduction in blood transfusion requirements due to a decrease by one-third in blood losses has been demonstrated with TXA in orthopaedic surgery. However, tranexamic acid is used in only 17% of patients meeting theoretical criteria for this treatment, due to the wide variability in administration regimens (dose, duration, and route). Furthermore, the potential prothrombotic effect of tranexamic acid is a source of concern among orthopaedic surgeons and has not been investigated in specifically designed studies providing a high-level of evidence.

We studied the effect of single dose of intravenous preoperative tranexamic acid on perioperative blood loss in patients undergoing total hip arthroplasty and also its effect on reducing postoperative allogenic blood transfusions.

MATERIALS AND METHODS:

The size of the study population was decided on the basis of calculation from a pilot study of 10 patients, participating in a pharmacokinetic study on tranexamic acid in total hip replacements by Benoni et al in 1995. We calculated the number of participants required for the study at 90% power and at 5% significance level to be 36. Thus, we included 40 participants in our present study.

Patients undergoing unilateral, primary total hip arthroplasty for osteonecrosis or primary arthrosis of hip joint operated by senior orthopedic surgeons at our institute, were included in the study. Patients with proven rheumatoid arthritis, hip joint infection, malignancy, coagulopathies and known allergy to tranexamic acid were excluded from the study.

All patients gave their informed consent to participation. The study was approved by the institutional ethics committee.

We included 40 participants and divided them into study and control group based on a validated web-based random allocator. Preoperative hemoglobin levels which are routinely done for anaesthesia fitness were noted. Patients vital information such as age, weight and height were also note routinely for all patients.

All patients were operated in lateral position and total hip arthroplasty was done by posterior approach with both components uncemented. All patients will be given spinal plus epidural anaesthesia with post-operative epidural top-ups every 12 hours for pain relief upto 48 hours post-operatively.

The participants allocated to the study and control group received tranexamic acid and placebo respectively as follows:

1. 15mg/kg of single dose tranexamic acid as a slow infusion in 100 ml normal saline about 15 minutes before surgery in the study group.
2. 100 ml normal saline was given as a placebo 15 minutes before surgery in the control group.

Inj. Cefuroxime (25mg/kg) was given routinely as antibiotic prophylaxis to all the patients undergoing surgery.

We determined the blood loss during the operation by measuring the volumes in the suction apparatus and estimating the swab and mop contents. One subfascial drain (Romovac No. 14) was routinely used and the volumes in the drain was recorded at 24 hours and 48 hours.

Blood transfusion was decided in a standardised way as per hospital protocol. Hemoglobin was measured on admission and second postoperative days. Patients who were having second postoperative hemoglobin level less than 8.5 g/dl or had clinical symptoms, a blood transfusion was given. Blood transfusions given upto third postoperative day were noted.

All patients were given post-operative mechanical deep vein thrombosis prophylaxis as per hospital protocol in the form of ankle pump, static and dynamic quadriceps exercises.

All the collected data was entered in Microsoft Excel Sheet. It was then transferred to SPSS version 17 software for statistical analysis. Quantitative data was presented as mean and standard deviationand compared using student's t-test. Qualitative data was presented as frequency and percentage and analysed using Chi-squared test. P-value of <0.05 was considered as significant.

RESULTS:

The preoperative mean hemoglobin level between the study group (11.8 ± 1.1 g/dl) and control group (11.7 ± 1.3 g/dl) was comparable (p value = 0.70) but second day postoperative hemoglobin level was significantly higher in the study group (10.7 ± 1.1 g/dl) as compared to control group (9.9 ± 1.4 g/dl). (P value < 0.05).

Table 1: Hemoglobin levels comparison

Hemoglobin (gm%)	Group	N	Mean	SD	p-value
Pre-op	Study	20	11.8	1.1	0.70
	Control	20	11.7	1.3	
Post-op	Study	20	10.7	1.1	< 0.05
	Control	20	9.9	1.4	

The mean intraoperative blood loss in the study group (415 ± 109.6 ml) was significantly higher (p value < 0.05) than control group (525.5 ± 109.3 ml).

Table 2: Mean intraoperative blood loss

Blood Loss (ml)	Group	N	Mean	SD	p-value
Intra-op	Study	20	415.0	109.6	< 0.05
	Control	20	525.5	109.3	

The mean postoperative blood loss in the study group (332.7 ± 100.2 ml) was found to be significantly lower (p < 0.05) as compared to the control group.

Table 2: Mean Post-operative blood loss

Blood Loss (ml)	Group	N	Mean	SD	p-value
Post-op	Study	20	332.7	100.2	< 0.05
	Control	20	502.6	96.7	

The total blood loss was also significantly higher (p<0.05) in the control group (1028 ± 180 ml) as compared to study group (747.7 ± 178 ml).

Table 3: Mean total blood loss comparison

Total Blood Loss	N	Mean	SD	p-value
Study	20	747.7	177.8	< 0.05
Control	20	1028.1	180.1	

The total number of patients requiring postoperative blood transfusion was 10 (study group = 2; control group = 8) which is statistically significant (p<0.05).

The mean age, weight, height and body-mass index comparison between the study and control groups were not statistically significant.

DISCUSSION:

Tranexamic acid has a therapeutic blood concentration of 5–10 mg/L and thus, theoretically, should reach this antifibrinolytic level during surgery, when given intravenously in doses of 15 mg/kg just before the incision, resulting in less intraoperative bleeding. However, only one previous study has shown that tranexamic acid significantly reduced intraoperative bleeding (Ekbäck et al. 2000).

We found that it reduced the intraoperative blood loss by 21% which was clinically significant (p < 0.05). Our study showed that the intraoperative blood loss was not influenced by the administration of 15mg/kg of tranexamic acid, which is consistent with the results of other studies using this dose. We found that early blood loss and total blood loss were significantly reduced in the tranexamic acid group while the late blood loss was not. Again, this was consistent with the findings of previous studies

and supported the hypothesis that tranexamic acid induces inhibition of early fibrinolysis before the body's usual response after 24 hours.

We found a significant reduction of 36% in the mean postoperative blood loss, which is a rather dramatic clinical effect and in accordance with the 4 studies published so far, which all used a bolus of tranexamic acid of 15 mg/kg or more before incision.

We made no attempt to evaluate postoperative hematomas, since one of the previous studies had noted no significant difference in the amounts of the hematomas between patients treated with tranexamic acid or placebo (Benoni et al. 2001).

The significant reduction of 28% in total blood loss in our study also accords with the 2 studies, which investigated this matter (Ekbäck et al. 2000, Benoni et al. 2001).

Our study suggest that the use of tranexamic acid reduces the requirement of the number of blood transfusions by 30% and the difference in the study and control groups was statistically significant.

In previous studies, apart from that by Ekback et al. (2000), tranexamic acid has only reduced the postoperative, but not the peroperative, blood loss (Hedlund 1969, Hiippala et al. 1995, 1997, Benoni and Fredin 1996).The reason for this difference between our present and our previous studies may be a biochemically more accurate timing for the administration of tranexamic acid in the present study.

Tranexamic acid inhibits fibrinolysis mainly by blocking the lysine binding sites of plasminogen (Nilsson 1980), the same sites which plasminogen uses for its binding to fibrin. On the fibrin surface, plasminogen is activated to plasmin and starts to degrade the fibrin molecules. To be effective, tranexamic acid probably has to interact with the plasminogen binding site before binding to fibrin occurs. In hip arthroplasty, fibrin plug formation occurs during the operation while blood vessels are severed, leaving ample time for plasminogen binding if tranexamic acid is not present initially. If tranexamic acid is given later, the drug is probably much less likely to affect the fibrinolytic process, since the plasminogen is already bound to fibrin.

In an in vitro study, Krishnamurti et al. (1994) found that tranexamic acid inhibited clot lysis more efficiently when it was added before clot formation than after it.

Concern is often expressed that the perioperative use of tranexamic acid may increase the risk of postoperative deep venous thrombosis (DVT) (Howes et al. 1996). This has no support in the literature (Dunn and Goa 1999). Studies have failed to show any statistically significant increase in the risk of DVT after various types of surgery or in pregnancy, even after prolonged use of the drug.

The study did not include long term follow up postoperatively to look for complications which may include deep vein thrombosis. Also, the cost benefit, if any, by using tranexamic acid was not evaluated.

CONCLUSION:

In conclusion, our study demonstrates that single preoperative dose of tranexamic acid significantly reduces intraoperative blood loss, postoperative blood loss, total blood loss and the need for blood transfusion in primary total hip arthroplasty in Indian population. This is in line with the results drawn from previous studies.

This dose seems to be an adequate compromise between fibrinolytic inhibition by tranexamic acid in the early hyperfibrinolytic stage and the postoperative period of fibrinolytic shutdown.

REFERENCE

1. Salido JA, Marin LA, Gomez LA, Zorrilla P, Martinez C.(2002) Postoperative haemoglobin levels and the need for transfusion after prosthetic hip and knee surgery: analysis of predictive factors. J Bone Joint Surg [Am];84-A:216-20. | | 2.Ekback G, Axelsson K, Ryttberg L, et al.(2000)Tranexamic acid reduces blood loss in total hip replacement surgery. AnesthAnalg91:1124-30. | | 3. Benoni G, Fredin H, Knebel R, Nilsson P.(2001) Blood conservation with tranexamic acid in total hip arthroplasty: a randomized double-blind study in 40 primary operations. ActaOrthop Scand;72:442-8. | | 4.Benoni G, Lethagen S, Nilsson P, Fredin H.(2000)Tranexamic acid, given at the end of the operation, does not reduce postoperative blood loss in hip arthroplasty. ActaOrthop Scand;71:250-4. | | 5.Hynes MC, Calder P, Rosenfeld P, Scott G.(2005) The use of tranexamic acid to reduce blood loss during total hip arthroplasty: an observational study. Ann R CollSurg Engl;87:99-101. | | 6.Claeys MA, Vermeersch N, Haentjens P.(2007) Reduction of blood loss with tranexamic acid in primary total hip replacement surgery. ActaChir Belg;107:397-401. | | 7.Duquenne P, Hoest L, Henkes W, De Sart F.(1999)Tranexamic acid reduces postoperative blood losses associated with elective total hip replacement. J Bone Joint Surg [Br];81-B(Suppl II):233-4. | | 8. Johansson T, Pettersson L-G, Lisander B.(2005)Tranexamic acid in total hip arthroplasty saves blood and money: a randomized, double-blind study in 100 patients. Acta Orthopaedica;76:314-19. | | 9. Krishnamurti C, Vukelja S.(2004) Inhibitory effects of lysine analogues on t-PA induced whole clot lysis. Thromb Res;73:419-30. | | 10. Eriksson B, Hultman E, Martinell S, et al.(1991)S Regional fibrinolysis following total hip replacement. Thromb Res;62:441-7.