

Reduction of blood loss after total knee arthroplasty by tranexamic acid

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Abstract

Background: Total knee arthroplasty is associated with significant perioperative blood loss. Various studies have shown that the use of tranexamic acid reduces post-operative blood loss and need for allogeneic blood transfusion in total knee arthroplasty.

Objectives: To assess the effect of tranexamic acid in the reduction of the postoperative blood loss in total knee arthroplasty.

Methodology: An analytical cross-sectional study was carried out in 14 patients who underwent primary total knee arthroplasty during the study period of September 2017 to September 2018 at Kathmandu Medical College. Seven patients were allocated to the case group and received one gram of tranexamic acid 30 minutes prior to the incision and five hundred milligram orally three times a day till the drain was removed. Tranexamic acid was not given to the seven patients in control group. The haemoglobin of the patient was recorded on the day of surgery and the total amount of drain output was recorded on postoperative period until the drain was removed.

Results: Out of 14 patients operated, it was found that the average amount of drain in the patients in case group was 628 ± 234 millilitre (ml) which was significantly lower than the control group 1028 ± 183 ml ($p < 0.05$). Though there was difference in the amount of drain output, there was no significant change in the postoperative haemoglobin level in both the groups ($p = 0.381$).

Conclusion: Tranexamic acid, an antifibrinolytic agent, can be effective to reduce blood loss in patients who undergo major surgeries like total knee arthroplasty.

Key words: Blood loss; Knee arthroplasty; Tranexamic acid.

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INTRODUCTION

Total knee arthroplasty (TKA) is associated with significant intraoperative and postoperative (postop) blood loss. Various researches have concluded an average loss of about 1400-1700 millilitre (ml) of blood following this surgery^{1,2}. It is estimated that 20-70% of these patients need one to three units (around 300 to 1000 ml) of blood transfusion¹⁻⁴. Various techniques have been employed to reduce this blood loss during the perioperative period like the use of cemented prosthesis⁵, and pneumatic tourniquet⁶. Though these methods reduce the perioperative blood loss, the activation of coagulation cascade and local fibrinolysis following the tourniquet release is responsible for a significant postoperative blood loss^{7,8}.

Tranexamic acid is a competitive inhibitor of plasminogen activation thus preventing the conversion of plasminogen into plasmin. Various studies have

shown that the use of tranexamic acid reduces the postoperative blood loss and need for allogeneic blood transfusion in TKA⁹⁻¹¹.

The effectiveness of tranexamic acid in significantly reducing the postoperative blood loss has not been studied in Nepalese population undergoing TKA. As the number of total knee arthroplasty has been increasing worldwide the number of surgery among the Nepalese patients are also expected to rise. Hence, a good knowledge of the use of tranexamic acid and its relation to the postoperative blood loss seems justified. Thus, the aim of this research was to study the effect of tranexamic acid in postoperative blood loss reduction in a sample of Nepalese patients undergoing TKA at the hospital.

METHODOLOGY

An analytical cross-sectional study was conducted for a period of 12 months from September 2017 to September 2018 among the patients undergoing total knee arthroplasty in Kathmandu Medical College Teaching Hospital (KMCTH), Sinamangal, Kathmandu, Nepal. The study was performed after obtaining informed written consent from the patient and approval from the Institutional Review Committee of the college (Ref. 2812201807). All patients undergoing primary TKA were requested to participate in the study. Patients undergoing simultaneous bilateral TKA, raised Prothrombin time/INR, history of thromboembolic phenomenon, renal or hepatic dysfunction, and cardiovascular disorders were excluded from the study. The collected data was entered in Microsoft Excel sheet 2013. IBM Statistical Package for Social Science (SPSS), version 20 (IBM Corp., Armonk, N.Y., USA) was used for the analysis of data. Post-operative blood loss in terms of drain output and post-operative haemoglobin level were compared between the two groups by using independent sample t-test.

A total of 14 patients were included in the study out of which seven patients were assigned to the case group (patients who received tranexamic acid) and seven patients to control group (patient who did not receive tranexamic acid). Haemoglobin of the patients

were recorded 24 hours prior to the surgery. No thromboprophylaxis was given to the patients prior to the surgery.

In the operation theatre the patients allocated to the case group received 1 gm of tranexamic acid intravenously 30 minutes prior to the incision. All the surgeries were done under spinal and epidural anaesthesia with pneumatic tourniquet. The author performed all the surgeries. Cemented prosthesis was used in all the patients and the skin incision was finally closed over a vacuum sealed drain. The pneumatic tourniquet was released after the wound closure. The duration of operation and duration of tourniquet application were recorded. During the post-operative period haemoglobin was measured at the evening of the surgery and drop in the haemoglobin was recorded. The collection in the drain was recorded in the subsequent days. The patient received 500 mg of oral tranexamic acid three times a day for three days or until the drain was removed which ever was earlier.

RESULTS

There was no significant difference in the distribution of age, sex, preoperative platelets count, Prothrombin time/INR and haemoglobin among the patients (Table 1).

The average amount of drain in the patient who were given tranexamic acid was 628 ± 234 ml which was significantly lower than the patient who were not given tranexamic acid $1028 \text{ ml} \pm 183. \text{ml}$ ($p < 0.05$). The time to drain removal (2.8 days in test group and 3.8 days in the control group) was also significantly lower in the test group ($p < 0.05$) as shown in Table 2. The decrease in the haemoglobin level after the operation (1.41 in test and 1.92 in control group; $p > 0.05$) was not significantly different.

None of the patient required blood transfusion in the postoperative period. Two patients, one in each group, developed superficial surgical site infection for which debridement and lavage was done and oral antibiotic administered. None of the patient developed deep vein thrombosis and other thromboembolic events.

Table 1: Demographic variables between two groups

Variables	Tranexamic acid (n=7)	Control group (n=7)
Age (in years)	64.5±9.0	61.8±8.6
Sex (Male/Female)	3/4	2/5
Preoperative platelets	280500±74497/mm ³	235285.71±52860/mm ³
Preoperative PT (seconds)	13.33	15.57
Preoperative haemoglobin (gm/dl)	12.83	12.45

Table 2: Comparison of postoperative blood loss in terms of drain output and post-operative haemoglobin between two groups

	Tranexamic acid (n=7)	Control group (n=7)	p-value
Drain output (in ml)	628.33 ± 234.982	1028.57 ± 183.79	p < 0.05
No. of days of drain	2.83 ± 0.9	3.86 ± 0.69	p < 0.05
Decrease in postop haemoglobin (gm/dl)	1.41 ± 0.57	1.92 ± 1.25	p > 0.05

Table 3: Comparison of result of our study with various other study

Authors	No. of patients	Drain output control	Drain output in tranexamic acid
Current study	14	1028.57ml ± 183.79	628.33 ± 234.982 ml
Seol et al. (2016) ¹⁵	100	886.0±375.5 ml	580.6±355.0 mL
Krishnan et al. (2017) ¹⁶	100	465 ±298 ml	296.7 ±195.6 ml
Molloy et al. (2006) ¹⁷	100	1415 ± 416 ml	1225 ± 499 ml
Benoni et al. (1996) ⁴	86	1410 ± 480 ml	730 ± 280 ml
Sreehari et al. (2014) ¹⁸	105	1828 ml	826 ml
Hiippala et al. (1995) ¹	29	1549 ±574 ml	847±356 ml
Good et al. (2003) ²	55	845 (523±990)ml	385 (331±586) ml
Shinde et al. (2015) ¹⁹	56	482±186 ml	295±218 ml

DISCUSSION

Tranexamic acid (1, 4-aminomethylcyclohexane carboxylic acid) is an antifibrinolytic agent which prevents the conversion of plasminogen into plasmin. It prevents the interaction of the plasmin and fibrin, eventually preventing the degradation of fibrin¹². Tranexamic acid has been found to be 6-10 times more potent in binding with plasminogen/plasmin than other synthetic antifibrinolytic agents¹³. Fibrin along with platelets are responsible for forming the hemostatic plug which prevents the bleeding from the site of trauma. This property of tranexamic acid to promote hemostasis has been used in various surgeries (cardiopulmonary bypass surgery, oral surgery, liver transplant surgery, transurethral prostatic surgery), acute upper GI bleeding and gynaecological and obstetric conditions (postpartum hemorrhage, placental abruption, and menorrhagia) and its benefit has been well documented¹⁴.

In Orthopaedic surgical procedures like total knee arthroplasty the loss of blood is significant and often demand blood transfusion. Most of the patients undergoing TKA are of older age group thus the adverse effects of decreased blood volume after surgery in body is significant (anaemia and postoperative cardiopulmonary compromise). Blood transfusion is further associated with its own side effects and risks.

The study of the use of tranexamic acid in total knee arthroplasty was first done by Hippala et al. (1997) and

Benon et al. (1996)¹⁴. In both the studies the patients receiving tranexamic acid had a significant reduction in postoperative blood loss in comparison to the patients who were operated without tranexamic acid (1549 ±574 ml/ 847±356 ml and 1410 ± 480 ml/ 730 ± 280 ml, respectively). The average amount of blood loss in the drain has been found to vary with different authors with the highest reported by Sreehari et al. (1828 ml/ 826 ml) and lowest reported by Krishnan et al. (465 ±298 ml/296.7 ±195.6 ml)^{16,18}. Though there is variation among the research in terms of the amount of the drain output there is a significant decrease of the post-operative blood loss in the patient with tranexamic acid¹⁴.

In this study it was found that there is significant reduction in the amount of drain output in patients who have been given tranexamic acid prior to the surgery. This study result matches the result of study done by various authors which have been summarized in Table 3. Though there was significant reduction in the drain output in the patients who were given tranexamic acid the decrease in immediate postoperative haemoglobin in the control group was not significantly different from that of the case group which contradicts with the findings by various other authors. We believe that this difference in the drop in haemoglobin level after surgery in our study and other literatures is because of the fact that postoperative haemoglobin was only measured once at the evening of surgery in our study and that amount of time does not properly reflect the accurate drop in

haemoglobin following surgery. In addition, because of the limited sample size of our study, the slight difference that was observed was not significant.

As tranexamic acid affects the fibrinolytic system, it theoretically has the potential to increase the risk of thrombolysis. Despite the increase in the risk of thrombolysis, none of the patients in the case group and the control group developed such thromboembolic complications (DVT, Pulmonary embolism). This finding in our study is also consistent with the findings in the above mentioned literatures. The incidence of superficial surgical site infection cannot be attributed to the use of tranexamic acid in our study as the incidence was similar in both the case and control group and the significance of it could not be accurately assessed due to the limited number of total cases in our study.

No research has been done in the Nepalese patients regarding the efficacy of tranexamic acid in reducing the blood loss after total knee arthroplasty till date. We hope that this research acts as a pilot project for further research in this topic among Nepalese population. The limitation of this study is that it includes a very few cases and the researchers were not blinded.

CONCLUSION

Tranexamic acid is an effective method of reducing the blood loss in the postoperative period after total knee arthroplasty. No systemic side effects of the use of tranexamic acid were seen in this study. The authors recommend that tranexamic acid should be routinely used in patient undergoing TKA.

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