

Application of Tranexamic Acid in Total Knee Replacement Surgeries

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Abstract: Total knee replacement surgeries are associated with perioperative blood cell transfusions and a higher rate of postoperative morbidity and mortality. Perioperative antifibrinolytic therapy is recommended to reduce blood loss. This study was conducted on a total of 30 subjects randomly divided into two groups of 15 patients each. The first group (Group T) received Tranexamic acid (15 mg/kg of body weight mixed in 100 ml normal saline). The second group (Group P) received a bolus of an equivalent volume of placebo (normal saline), 10 minutes before the deflation of the pneumatic tourniquet respectively. Our study showed that Group P lost almost five times more blood during the recovery phase and twice the volume of Group T in the surgical ward. Based on the results of the present study, we concluded that use of Tranexamic Acid significantly reduces blood loss caused by TKR performed with a tourniquet.

Keywords: Tranexamic acid, blood loss, anemia, coagulation

1. Introduction

Tranexamic acid (TXA), a synthetic derivative of the amino acid lysine, is an effective antifibrinolytic agent^(1, 2). It acts by competitively inhibiting the activation of plasminogen to plasmin^(1, 2). The binding of plasmin to fibrin is also almost completely blocked which results in retardation of fibrinolysis. It therefore reduces blood loss by clot stabilisation rather than promotion of clot formation^(2, 3). At higher concentrations, tranexamic acid also acts as a non-competitive inhibitor of plasmin^(1, 3).

Primary total knee replacement is a procedure associated with significant amount of bleeding that can reach up to 20% of blood volume in patients with significant comorbidities related to cardiovascular, cerebrovascular and metabolic systems⁽³⁾. In these patients, blood loss leading to perioperative anemia promotes high morbidity and mortality^(3, 4). Patients with perioperative anemia have a longer hospital stay associated with a greater need for the use of resources, including transfusion of blood and blood products and admission to the intensive care unit⁽⁵⁾. Strategies for minimising bleeding have been used to reduce the need for transfusion of blood and its products in view of transfusion associated complications. In this study we propose to evaluate the use of Tranexamic acid in reducing bleeding and the need for transfusion of blood and blood products in primary total knee replacement.

2. Objective

- To assess the effect of Tranexamic acid on perioperative blood loss in primary Total Knee Replacement surgeries (TKR).
- To compare the perioperative blood loss in Total knee replacement surgeries with Tranexamic acid and without Tranexamic acid.
- To study the adverse effects of Tranexamic acid

3. Materials and Methods

This is a prospective, randomised, case control study on the patients admitted to the orthopaedic department of FMMC Mangalore for elective Unilateral Primary total knee replacement between July 2017- July 2018. The Institution's ethical committee has approved the study. A written informed consent was taken from 30 patients due to undergo unilateral total knee replacement.

Inclusion criteria: ASA I-III Patients posted for a total knee replacement were considered eligible for the trial.

Exclusion criteria: History of thromboembolic disease, cerebrovascular disease, recent history of myocardial infarction or unstable angina, coagulation defects, those detected allergic to Tranexamic acid, patient refusal to participate in the study.

Routine Pre Anesthetic evaluation was carried out, Complete haemogram, Coagulation Profile, Renal/Liver/Cardiac function were investigated prior to surgery. Patients were asked to discontinue non-steroidal anti-inflammatory medications at least 1 week prior to surgery, in accordance with existing practice. All patients were premedicated with Tab. Diazepam 5 mg and Tab. Ranitidine 150mg orally at 10 PM on the night before the surgery. Patients were randomly allotted into two groups using sealed envelope technique.

Group T received TXA (15 mg/kg of body weight mixed in 100 ml normal saline).

Group P received a bolus of an equivalent volume of placebo (normal saline), 10 minutes before the deflation of the pneumatic tourniquet respectively.

On arriving at the operation theatre baseline vitals were recorded, an 18 gauge intravenous cannula was inserted and lactated ringers solution of 15ml/kg was infused for preloading over 15 minutes. The patient was placed in the lateral decubitus position and under strict aseptic precautions a lumbar puncture was performed through a midline approach using a 25 gauge spinal needle at the L3-L4 inter vertebral space after local infiltration with 2% lignocaine,

Once a free flow of cerebrospinal fluid was obtained, 3ml of 0.5% of Bupivacaine was injected at a rate of 0.2ml/s following negative aspiration for blood. After the spinal injection the patient was returned to supine position and retained in that position for at least 10 minutes. An epidural catheter was also inserted but was activated only after the surgical procedure for post operative analgesia. Following anesthesia the limb was elevated, a pneumatic tourniquet was inflated to 300mmHg and the time of inflation was noted. The study drug was administered at a dose of 15mg/kg body wt. Non invasive arterial pressure and heart rate was monitored every 5 minutes for the first half an hour followed by every 10 minutes till the end of the procedure. Intraoperative monitoring included ECG, noninvasive blood pressure (NIBP), pulse oximetry, temperature, and urine output. Total blood loss was calculated as the sum of blood soaked swabs, blood in suction bottles, and blood in the surgical drainage system installed by the surgeon in the surgical wound, and recorded 24hrs after surgery. Hemoglobin concentration was determined preoperatively, immediately after arrival in the recovery room and before discharge to surgical ward in the evening of surgery, and on first three postoperative days. The need for blood transfusion was observed in both the groups at 24hrs following surgery. The criteria for transfusion was established according to the protocol used by the surgeon: bleeding greater than 20% of blood volume or post operative haemoglobin less than 8g/dl or Packed Cell Volume less than 24 %.

Sample size

Sample size was collected from a previous study

- $n = \frac{2(Z\alpha + Z\beta)\sigma^2}{(X_1 - X_2)^2}$
- $Z\alpha = 1.96$ at 95% C.I
- $Z\beta = 0.841$ at 80% Power
- $Z\beta = 1.281$ at 90% Power
- $n = 15$ in each group, Total = 30

The continuous variables of the Group T and Group P were compared with two-tailed Student's t-test and the nominal data and frequencies were analyzed with two-tailed Fisher's exact test. Probability less than 0.05 was considered significant.

Table 1: Demographic and Preoperative Hemostatic Data

	Group T (n = 15)	Group P (n = 15)
Age (years)	70 ± 7	69 ± 5
Weight (kg)	74 ± 13	78 ± 12
Height (cm)	162 ± 7	164 ± 7
Sex (M/F)	4/11	8/7
Hemoglobin (g / dL)	13.6 ± 1.1	13.6 ± 1.4
Platelet concentration	279 ± 72	307 ± 96
Bleeding time (s)	317 ± 94	334 ± 103
aPTT (s)	34 ± 3	34 ± 4
Prothrombin time (%)	106 ± 19	107 ± 20

Values are mean ± SD.

Prothrombin time is expressed as percent of reference plasma activity

aPTT = activated partial thromboplastin time

Table 2: Time Factors and Technical Data Associated with Total Knee Replacement

	Group T (n = 15)	Group P (n=15)
Duration of operation (min)	101 ± 21	96 ± 18
Duration of tourniquet	73 ± 18	67 ± 14
Inflation (min)		
Cemented tibial component (n)	7	10
Cemented femoral component (n)	8	5

Values are mean ± SD

Table 3: Replacement Solutions Used by the End of First Postoperative Day and the Number of Red Cell (RC) Units Transfused During the Hospital Stay

	Group T (n = 15)	Group P (n = 15)
Patients		
Crystalloids (mL)	3295 ± 425	3842 ± 669*
HES (mL)	205 ± 297	605 ± 371
RC units	± 1	2.1 ± 1

HES = hydroxyethyl starch, TA = tranexamic acid, NS = normal saline

* P < 0.0001.

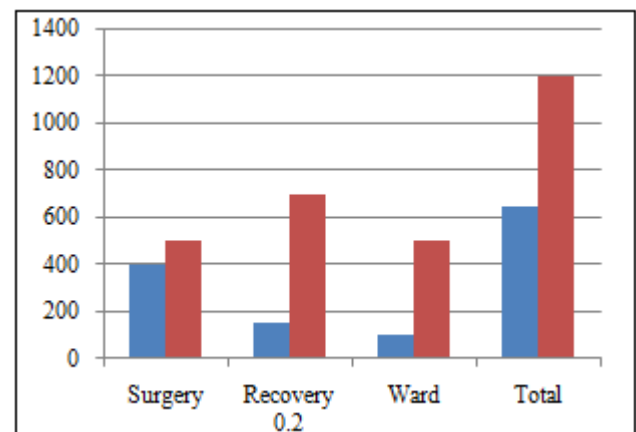


Figure 1: Perioperative blood loss (mean ± SD). The tranexamic acid group is shown in blue and the placebo group in brown. * P < 0.0001.

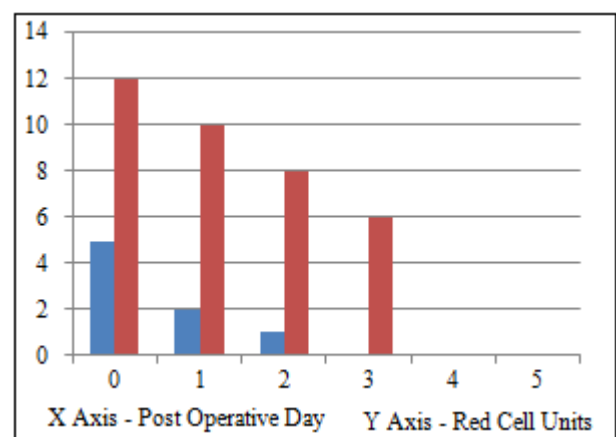


Figure 2: The number of daily transfused red cell units. The tranexamic acid group is shown in blue and the placebo group in brown

4. Results

The demographic factors and the preoperative hemostatic status were comparable in both groups (Table1). Also the

factors describing time factors and technical aspects of the surgical procedure were similar (Table 2). There was no significant difference in blood loss between the Group P and Group T during surgery (320 ± 80 ml versus 253 ± 60 ml) (Fig. 1). However, Group P lost three times the blood when compared to Group T during the recovery phase (280 ± 49 ml versus 80 ± 20 ml, $P < 0.0001$).

The total blood loss in the Group P was almost two times greater compared to Group T (600 ± 129 mL versus 330 ± 80 mL, $P < 0.0001$).

In Group P more blood, colloid, and crystalloid solution was used to replace blood loss (Table 3). The number of transfused RC units was 2.1 ± 1 in Group P ± 1 in Group T ($P < 0.001$).

Despite the more numerous transfusions, hemoglobin concentration was constantly 0.6-0.8 g/dl lower in the Group P compared to Group T after the recovery phase (Fig. 2). In the TXA group 12 patients were treated without transfusions compared to only 4 in Group P ($P < 0.00003$). All patients eventually recovered and were discharged. Due to technical problems, the postoperative epidural analgesia failed in three cases and had to be substituted with a conventional (two cases, Group T) (one case, Group P) opioid analgesia.

5. Discussion

The reported blood loss associated with unilateral TKR ranges from 600 ml to 1250 ml depending on the clinical setting and study design. The different methods used to define and determine perioperative blood loss are probably the main reason for this great variation. At best, the carefully performed measurements are acceptable estimates of the true blood loss. However, the figures represented in many investigations are based on the estimates retrieved from patient records retrospectively. Despite the possible differences in transfusion policies, the volume of transfused red cells, usually equivalent of two to three units, gives a more coherent and probably also a more objective picture of the total perioperative blood loss. Several studies have evaluated the effects of various operative techniques and treatments on TKR associated blood loss, but until recently only one clinically relevant factor has been identified.

6. Conclusion

Based on the results of the present study, we conclude that the use of Tranexamic Acid significantly reduces blood loss caused by TKR performed with a tourniquet. No adverse effects were seen with the use of Tranexamic acid.

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