



COMPARISON OF EFFECTIVENESS OF INTRAARTICULAR TRANEXAMIC ACID AND INTRAVENOUS TRANEXAMIC ACID IN PREVENTION OF BLOOD LOSS IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY.

Anaesthesiology

**Dr. Koramutla
Pradeep Kumar**

**Dr. Pothala
Kishore Kumar**

ABSTRACT

Background & Purpose: This study was aimed to evaluate the effectiveness of administration of intraarticular vs intravenous tranexamic acid in reducing blood loss in total knee replacement surgery. Total knee replacement often requires blood transfusion. Allogenic blood transfusion in elective orthopaedic surgery is best avoided owing to its associated risks and many strategies are currently being employed to reduce peri-operative Blood loss and its transfusions. Anti-fibrinolytic compounds such as aminocaproic acid and tranexamic acid have been used systemically in perioperative settings with promising results. **Material And Methods:** One hundred and thirty four adult patients with ASA 1 to ASA3 were randomly allocated to 1 of 2 groups using a computer-generated random number table with 67 patients in each group. Group IA (Intraarticular) patients received tranexamic acid in a dose of 1.5 gram intraarticularly and Group IV patients received Tranexamic acid 1.5grams intravenously. **Results:** The average blood loss assessed by means of the haemoglobin in the group IA was significantly lower than the group IV. The requirement of blood transfusion in the group IV was significantly higher when compared to the group IA receiving Tranexamic acid (1.1 units in TAS group vs 2.2 units in group 2). The mean drop in the post-operative haemoglobin concentration in Group-IV for unilateral was 2.21 gm/dl. In comparison, the mean drop in the post-op haemoglobin in Group-IA was 0.5 gm/dl (unilateral) with a (p-value < 0.001). **Conclusion:** Intraarticular Tranexamic acid injection is more effective in reducing blood loss and thereby reducing post-operative blood transfusion after knee replacement.

KEYWORDS

Tranexamic acid; blood loss; Total knee replacement; intraarticular.

INTRODUCTION

Total knee replacement (TKR) is a commonly performed surgical procedure performed with an aim to relieve pain and improve the functional recovery especially in patients suffering from advanced degenerative arthritis or rheumatoid arthritis.¹ Total knee replacement is a frequently done procedure in modern day practice of any Orthopaedics unit. Limiting blood loss both intraoperatively and post operatively presents a challenge to the Anesthesiologist². In the postoperative period Blood continues to ooze from the cut ends of bone, the open intra-medullary canal and the raw, dissected soft tissues. This can amount to significant bleeding with loss ranging from 600 - 1500 ml³. As this procedure is performed under tourniquet control, there is an associated increase in localized fibrinolysis⁴. Allogenic blood transfusion may be needed on the basis of amount of blood lost during the procedure. Moreover, high post-operative infections are also associated with this procedure, measures which can reduce operative loss of blood and subsequent necessitating blood transfusion have always been adored and a hot focus of medical research. Hence the aim should be to minimize blood loss and avoid transfusion. Various modalities have been tried to decrease blood loss including use of epoetin injections, platelet rich plasmapheresis, fibrin sealing and anti-fibrinolytic drugs and use of hypotensive epidural anaesthesia have been tried with varying success.⁵ Tranexamic acid (TXA), a synthetic antifibrinolytic agent inhibits the activation of plasminogen to plasmin. Tranexamic acid is an antifibrinolytic agent, which effectively blocks this fibrinolytic activity, thus causing a marked reduction in post-operative bleeding.⁶ It works by blocking the lysine binding sites of plasminogen and prevents the degradation of fibrin. Tranexamic acid has been used topically, administered intra-articularly and intravenously in TKA and has been shown to be effective in reducing blood loss and transfusion.⁷⁻⁹ Tranexamic acid can be used intravenously, topically, or orally. Though, in total knee arthroplasty majority, of the studies have focused on the intravenous route, topical spraying of TXA has been proved to be equally efficacious while being safer as far as post-operative problems like DVT are concerned.¹⁰ The existing evidence on the efficacy of this topical application contained controversy where some studies claimed no difference between IV and IA routes in terms of blood loss, other showed significant difference and advocated intra-articular application while still others reported intravenous route to be better and associated with significantly lower operative blood loss.

MATERIALS AND METHODS

Each group was comprised of 100 cases in this study having 200 cases sample size calculated with 95% significance level and 80% power of

test considering expected mean post-operative hemoglobin to be 11.0 ± 0.67 g/dL in patients with intravenous and 10.6 ± 1.26 g/dL in patients with intra-articular tranexamic acid¹¹. In this study, patients had age between 40 and 80 years belonging to both the genders suffering from advanced degenerative disease of knee planned for unilateral total knee replacement (TKR). However, patients with complex and revision complex knee arthroplasty, single stage bilateral total knee replacement, and unicompartmental knee arthroplasty were excluded from the study. By random allocation of these patients, two equal-sized treatment groups were made. Patients in IA group received 2 g of TXA in 20 mL solution injected by syringe into the joint after the prosthesis was inserted and cemented and the entire operative field was thoroughly rinsed and dried, no drain was placed and wound closed in layers before skin closure. Patients in IV group received intravenous dose of 1 g TXA administered 5–10 min before the pneumatic tourniquet was inflated. under a high thigh tourniquet, The procedures were performed under spinal anesthesia combined with an epidural. Before the closure of the wound, the tourniquet was deflated and hemostasis secured. No drain was placed in both groups. After layered closure and intra-articular injection in IA group, a compression bandage with the knee in extension was given, which stayed for about six hours post-operatively. Outcome variables were mean post-operative hemoglobin, mean fall in hemoglobin measured 24 h after surgery. Numerical variables like age, pre-operative and post-operative hemoglobin, and fall in hemoglobin have been described as mean $\pm$ SD. By taking p-value ≤ 0.05 as statistically significant, for comparing mean of these various variables in the study group, independent sample t-test was applied. Categorical variable like gender has been described as frequency and percentage. In order to minimize biasness, standard operative technique was used and a single surgeon performed all these procedures. Thromboprophylaxis in the form of subcutaneous low molecular weight heparin was given to all patients starting from day 1 and continued till the time of discharge. Additional care in the form of postoperative use of DVT stockings, ankle pumps, and early mobilization was also ensured as a part of thromboprophylaxis which is practiced for all patients routinely.

Statistical Analysis : Data is expressed as mean $\pm$ standard deviation for continuous variables and as frequency (number [%]) for categorical variables. Independent samples T test was used to assess the difference in markers between the two groups. All statistical analysis were performed using Microsoft excel spreadsheets (Microsoft, Redmond, WA USA) and Statistical package for social sciences for windows version 16.0 (SPSS Inc., Chicago IL, USA). A 'p' value <0.05 was considered as statistically significant.

RESULTS

As shown in table 1, the groups were matching in terms of age and the male female ratio. The mean age was 60.9 years and 59.3 years in the TX IV and TX IA groups respectively. There were 30 males in the TAS group and 37 males in the TAD group. The baseline haemoglobin levels were similar in both the groups ($p=0.631$). However, a significantly lower haemoglobin was found in the TX IA group postoperatively compared to the TX IV group ($p=0.006$).

As shown in Table 1, the average blood loss assessed by means of the post operative hemoglobin level. The requirement of blood transfusion in the TXIA group was significantly lower compared to the group receiving TXIV (3.7 units in vs 2.7 units). Majority of the patients had osteoarthritis while remaining 9 (4.5%) patients had rheumatoid arthritis. The two study groups were homogenous in terms of mean age ($p\text{-value} = 0.979$), mean pre-operative hemoglobin ($p\text{-value} = 0.606$), mean pre-operative hematocrit ($p\text{-value} = 0.953$) and gender ($p\text{-value} = 0.863$) and etiologic ($p\text{-value} = 0.733$) groups distribution (Table 1).

DISCUSSION

Different measures to reduce operative blood loss have been employed in orthopaedic surgery to reduce the need for transfusion and hasten the patient's recovery in the post-operative period. The common method for control of the perioperative blood loss is the application of anti-fibrinolytic agents including aprotinin, epsilon-aminocaproic acid, and tranexamic acid (TXA) [12]. Among them, TXA has gained the maximum attention which can be given intravenous or intra-articular during the surgery. The available evidence on the selection of more appropriate route of administration of TXA bears controversy. In the present study, we observed that the mean age of patients was 60.9 years and 59.3 years. Khan et al. [13] reported similar mean age of 64 ± 6.3 years in patients undergoing total knee replacement at Ghurki Trust Teaching Hospital Lahore while Obaid-ur-Rahman et al. [14] reported it to be 64 ± 8.4 years in such patients at Combined Military Hospital, Rawalpindi. A similar mean age of 67 ± 7.96 years has been reported by Maniar et al. [15] in Indian such patients while Pinsornsak et al. [16] reported it to be 67.63 ± 7.96 years in Thailand. Keyhani et al. [17] and Sarzaem et al. [18] reported comparable mean age of 67 ± 11.9 years and 67.5 ± 7.6 years in Iran while Seo et al. [19] reported it to be 67.5 ± 6.6 years in Korea. We observed a female predominance in patients undergoing TKR with a male-to-female ratio of 1:3.7. In the present study, we observed insignificant difference between intravenous and intraarticular tranexamic acid in terms of mean post-operative hemoglobin fall. Similar results have also been published by Soni et al. [20] (2.21 ± 0.64 vs. 2.42 ± 0.86 g/dL; $p\text{-value} = 0.38$), Tzatzairis et al. [21] (2.95 ± 1.33 vs. 3.2 ± 1.29 g/dL; $p\text{-value} = 0.551$), Seo et al. [22] (1.8 ± 0.8 vs. 1.6 ± 0.8 g/dL; $p\text{-value} > 0.05$), Pinsornsak et al. [16] (1.85 ± 0.95 vs. 1.87 ± 1.37 g/dL; $p\text{-value} = 0.840$) and Sarzaem et al. [23] (3.9 ± 1.1 vs. 2.6 ± 0.9 g/dL; $p\text{-value} > 0.05$). No significant difference in terms of mean post-operative hematocrit with IA and IV TXA in patients undergoing TKR has also been reported by Tzatzairis et al. [21] (32.44 ± 3.33 vs. 30.92 ± 3.11 ; $p\text{-value} = 0.112$), Drosos et al. [24] (33.19 ± 2.97 vs. 32.41 ± 5.20 ; $p\text{-value} = 0.197$) and Pinsornsak et al. [16] (31.0 ± 2.7 vs. 31.8 ± 3.4 ; $p\text{-value} = 0.352$). This is the first single centre clinical research study conducted in the exclusive tertiary orthopedic hospital. Main strength of this study is being the larger sample size of 100 cases and randomization to prevent Bias was which makes the results more reliable. From evidence, Both intra-articular tranexamic acid and intravenous administration has great decrease in the post operative blood loss, but preference of Intraarticular over intravenous route will avoid the inconvenience of IV administration and possibly avoids the complication of intravenous administration of TXA like deep vein thrombosis, myocardial infarction, pulmonary embolism, and cerebrovascular events [25]. We had not compared the coagulation profile which is the limitation for the study.

CONCLUSION

In primary total knee arthroplasty, to reduce blood loss, intra-articular administration of tranexamic acid was found to be as effective and safe as intra-venous administration. Due to convenience, the use of intra-articular administration of tranexamic acid after primary TKA may be considered in future practice.

Variables	TX IV group (Mean $\pm$ S.D)	TX IA group (Mean $\pm$ S.D)	P value
Age (years)	60.9 ± 8.7	59.3 ± 9.8	0.348
Sex ratio (male:female)	0.8 30 males	1.2 7 males	0.300

Baseline haemoglobin (g/dL)	13.3 ± 1.4	13.4 ± 1.2	0.631
Postoperative Hb (g/dL)	9.93 ± 1.16	9.87 ± 1.28	0.748

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