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Single Dose Intravenous Tranexamic Acid Efficacy in Reducing Blood Loss in Total Hip Replacement

Muhammad Badar Ud Din Zafir[1*], Rana Shahid Waseem Ronaq[1], Mazhar Ali[1], Mukhtar Ahmad Tariq[2] and Israr Ahmad[3]

[1]Department of Orthopedic Surgery, Nishtar Medical University Hospital, Multan, Pakistan
[2]Department of Orthopedic Surgery, Tertiary Care Hospital, Nishtar II, Multan, Pakistan
[3]Department of Orthopedic Surgery, Multan Medical and Dental College, Multan, Pakistan

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***Corresponding Author:**
Muhammad Badar Ud Din Zafir
Department of Orthopedic Surgery, Nishtar Medical University Hospital, Multan, Pakistan
drzafir77@yahoo.com

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ABSTRACT

Total Hip Replacement is a commonly performed procedure for Hip joint degeneration. Despite its hazards, blood transfusion has to be performed due to significant perioperative blood loss. The effects of pre-operative intravenous single-dose tranexamic acid in our population have been presented in this study. **Objectives:** To compare the mean blood loss during and after total hip replacement for hip osteoarthritis with or without a single dose of tranexamic acid. **Methods:** This quasi-experimental study was performed in the Orthopedic Surgery Department Unit II, Nishtar Medical University Hospital, Multan, from October 2022 to March 2024. In the experimental group, tranexamic acid (20mg/kg) was administered intravenously ten minutes before skin incision, while in the control group, no such drug was given.Preoperative and postoperative Hematocrit data were collected. THA was done as per standard protocol.The operative blood loss and blood transfusions were recorded and compared with the controls. **Results:** Among 60 patients, the mean age was 54.85 ± 12.23 years. Male were 19 (31.7%) and female were 41 (68.3%). BMI was 26.04 ± 3.48 Kg/m2. Mean age (p=0.746), mean BMI (p=0.633), age (p=0.417), gender (p=0.781) and BMI (p=0.749) were comparable in both groups. The estimated total loss of blood was significantly less in patients receiving intravenous tranexamic acid (1169.10 ± 191.92ml vs. 1730.07 ± 203.62ml; p<0.001) as compared to the control group. **Conclusions:** It was concluded that a pre-operative intravenous single dose of tranexamic acid decreased blood loss during surgery significantly in patients having total hip arthroplasty regardless of gender, age and BMI.

INTRODUCTION

Osteoarthritis affects life quality and is the major cause of morbidity in patients with advancing age [1]. Surgery is a choice for patients who have failure of conservative management [2]. Heavy intraoperative bleeding is a critical issue during total hip arthroplasty that usually has high mortality and morbidity [3]. Such bleeding may need transfusion of blood that is usually allogenic. Blood transfusion has risks and bears costs as well, along with issues in arranging sufficient blood products. So interest has been generated in blood-sparing protocols. These include red cell salvage (intraoperative), hypotensive anesthesia, local anesthesia, re-transfusion of autologous blood and the antifibrinolytic drugs [4]. Antifibrinolytic medicines are easily accessible and promote hemostasis and decrease bleeding, resulting in a decrease in the need for blood transfusion [5]. The efficacy of such medicines has been assessed in hepatic, cardiovascular, orthopedics and other surgeries. Two such drugs are tranexamic acid and aprotinin, whose efficacy is proven in many surgeries [6]. When primary fibrinolysis is the main cause of bleeding, tranexamic acid effectively inhibits fibrinolysis and so promotes hemostasis without the risk of complications like thrombosis or embolism. The possible prothrombotic effects of tranexamic acid are also a matter

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of concern among many orthopedic surgeons, which has yet to be investigated in further studies providing evidence of a high level [7]. Even with these good results, valid data is lacking regarding its safety. Thus, the use of tranexamic acid in routine remains a concern. Data on perioperative outcomes are rare. Further, population-based data is not available, with limited randomized trials including selected patients. It can be seen that there is wide variation not only in the conduct of studies with some retrospective, dose, as well as mode of administration, but also in the results. It was thus necessary to conduct another study to increase the evidence of effectiveness and safety of tranexamic acid from a developing country to reduce the costs associated with the procedure and complications in the peri-operative period with this promising intervention, which is still not being used frequently locally. There is no local study according to our knowledge.

Although tranexamic acid has demonstrated effectiveness in reducing blood loss during various surgical procedures, its routine use in total hip arthroplasty remains limited due to concerns regarding safety and inconsistent evidence related to dosage, administration routes, and perioperative outcomes. Moreover, there is a lack of local, population-based data from developing countries like Pakistan to support its widespread adoption. This study aims to compare mean blood loss with or without tranexamic acid, during and after total hip arthroplasty for hip osteoarthritis.

METHODS

This quasi-experimental study was done at the Orthopedic Surgery Department, Unit II, Nishtar Medical University (NMU) Hospital, Multan, from October 2022 to March 2024 after approval from the institutional ethical review board of NMU vide NO. 13321/NMU. The sample size was 60 patients, calculated with 80% test power and 95% CI., predicted mean blood loss for the tranexamic group was 1107 ± 508 ml, while the non-tranexamic acid group was 1729 ± 552 ml [8]. Non-probability consecutive sampling was used for the inclusion of the patients. Patients of both genders, having an age between 40-80 years, having pain in the hip joint for the last 3 months with evidence of grossly decreased space of the joint with osteophytes and deformity of the head of the femur and acetabulum on Antero Posterior as well as Lateral view were includedS. The patients were selected for Total Hip Arthroplasty and were included in the study after proper consent. Patients with medical contraindication to tranexamic acid, which include previous attacks of seizures, severe kidney failure with creatinine clearance less than 30 mL/min or having bleeding disorders, thromboembolic disorders like thrombosis in deep veins, pulmonary emboli, ischemic heart disease, acute lower-limb ischemia and stroke, were excluded from the study. Detailed assessment comprising history (age, gender, etc.), examination and relevant laboratory investigations (hematocrit) was carried out. Patients were randomly divided into the two groups by the lottery method: the tranexamic group and the control group. In the tranexamic group, ten minutes before incision, an intravenous tranexamic acid (20 mg per kg) was administered as a single dose. Patient's detailed assessment was done again, and a daily hematocrit level postoperatively was collected. All blood transfusions were recorded. The standard blood management protocol was adhered to, which calls for a stringent transfusion Hb trigger of 8.0 and the infusion of 500 mL of plasma expander volume expansion before considering a transfusion in the event of postoperative hypotension, lightheadedness, or dizziness. Total hip arthroplasty was done as per standard protocol. All the patients were monitored regularly for cardiac or brain ischemia signs, along with deep vein thrombosis. Using the Gross formula, total blood loss (TBL) was computed from hematocrit levels: TBL = Predicted Blood Volume × (Preoperative Hematocrit – Postoperative Hematocrit) / Average Hematocrit [9]. The difference between hematocrit values before surgery and hematocrit values on the 8th day after surgery was considered the hematocrit reduction. Blood volume (BV) (ml) = 70 x weight (kg). SPSS (version 24.0) was used to enter all of the data for statistical analysis. Numerical variables, i.e. age, BMI and total blood loss, are presented by mean ± SD. The frequency and proportion of categorical variables, such as gender, have been displayed. To compare the mean blood loss between two study groups (i.e. tranexamic acid and controls) independent sample t-test was applied at 95 % CI with p-value equal to or less than 0.05. Data were also stratified by gender, age and BMI, and post-stratification independent sample t-test was reapplied, with a p-value≤0.05 being considered significant, while the Mann-Whitney U test was applied for data that was not normally distributed. To calculate the effect size, Cohen's d was used.

RESULTS

The mean age of the patients was 54.85 ± 12.23 years, with a range of 40 to 80 years.The patients' BMIs ranged from 20.3 to 33.2 kg/m^2, with a mean of 26.04 ± 3.48 kg/m^2 (Table 1).

Table 1: Baseline Features (n=60)

Characteristics	Participants (n=60)
Age	
Overall Years	54.85 ± 12.23
40-59 Years	39 (65.0%)
60-80 Years	21 (35.0%)
Gender	
Male	19 (31.7%)
Female	41 (68.3%)
BMI	
Overall	26.04 ± 3.48
20-25 Kg/m^2	25 (41.7%)
25-30 Kg/m^2	27 (45.0%)
≥30 Kg/m^2	8 (13.3%)

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The distribution of the two groups in this study was similar in terms of mean age (p=0.746), mean BMI (p=0.633), age (p=0.417), gender(p=0.781), and BMI(p=0.749)(Table 2).

Table 2: Baseline Characteristics of Study Groups(n=60)

Characteristics	Tranexamic Acid (n=30)	Controls (n=30)	p-Value
Age			
Overall Years	55.37 ± 13.49	54.33 ± 11.02	0.746
40-59 Years	18 (60.0%)	21 (70.0%)	0.417
60-80 Years	12 (40.0%)	9 (30.0%)	
Gender			
Male	10 (33.3%)	9 (30.0%)	0.781
Female	20 (66.7%)	21 (70.0%)	
BMI			
Overall	25.82 ± 3.21	26.26 ± 3.77	0.633
20-25 Kg/m^2	13 (43.3%)	12 (40.0%)	0.749
25-30 Kg/m^2	14 (46.7%)	13 (43.3%)	
≥30 Kg/m^2	3 (10.0%)	5 (16.7%)	

According to the independent sample t-test and chi-square test, the observed difference was statistically insignificant

Compared to the controls, patients who received intravenous tranexamic acid experienced a considerably lower estimated total blood loss (1169.10 ± 191.92ml vs. 1730.07 ± 203.62ml; p<0.001).There were also highly significant differences across different age, gender, and BMI categories, and it is evident from the findings that these changes in blood loss are consistent across various subgroups(Table 3).

Table 3: Comparison of Total Blood Loss(ml)Between the Study Groups(n=60)

Characteristics	Tranexamic Acid (Mean ± SD)	Controls (Mean ± SD)	p-Value	Cohen's d
Age				
Overall	1169.10 ± 191.92	1730.07 ± 203.62	<0.001*	2.84
40–59 Years	1171.28 ± 199.88	1734.29 ± 212.17	<0.001*	2.78
60–80 Years	1165.83 ± 188.00	1720.22 ± 193.90	<0.001*	2.90
Gender				
Male	1152.70 ± 204.46	1742.89 ± 209.70	<0.001*	2.86
Female	1177.30 ± 190.28	1724.57 ± 205.97	<0.001*	2.76
BMI				
20–25	1162.00 ± 218.12	1751.67 ± 221.17	<0.001*	2.69
25–30	1172.29 ± 190.60	1709.15 ± 196.26	<0.001*	2.78
≥30	1185.00 ± 108.30	1732.60 ± 218.39	0.007*	2.98

*The observed difference was statistically significant. Independent sample t-test

DISCUSSION

Total hip replacement is the best treatment for patients with failure of conservative management for osteoarthritis hip [10]. The antifibrinolytic medication tranexamic acid, which increases haemostasis, has a well-established track record in general surgery to decrease the bleeding volume and ultimately decrease the requirement of the allogenic transfusion [11]. Nonetheless, there was debate surrounding the available data about tranexamic acid's ability to lower surgical blood loss during and following total hip replacement. The male-to-female ratio in the current study group was 1:2.2, where 19 (31.7%) were males and 41 (68.3%) were female. The patients in our study had a mean BMI of 26.04 ± 3.48 kg/m2. Regardless of the patient's age, gender, or BMI, we discovered that the estimated total blood loss was considerably lower in patients receiving intravenous tranexamic acid (1169.10 ± 191.92ml vs. 1730.07 ± 203.62ml; p<0.001) than in controls. Haratian *et al.*, also observed a reduction in blood transfusion volume in patients receiving tranexamic acid and thus minimizing perioperative loss of blood [12]. Many studies have revealed that tranexamic acid in total hip arthroplasty is a successful way of decreasing blood loss; therefore, it is an effective way to achieve hemostasis in clinical situations. Likewise, researcher found similar findings in trauma and significant hemorrhage, showing broader applicability of tranexamic acid [13]. In a retrospective study, Akti *et al.*, evaluated the role of tranexamic acid(TXA)on the blood losses in patients of total hip arthroplasty. They studied 120 patients, among whom 45 were male and 75 were female, having 57.2 ± 4.9 years of age with a range of 45 to 67 years.Their patients had primary osteoarthritis.Sixty-seven patients underwent THA without the use of TXA, and 53 patients received TXA. They found a significant difference (p<0.05) between their groups regarding intraoperative blood loss, blood in the drain, total blood loss and the blood transfusion.They recommended routine use of tranexamic acid if not contraindicated [14].Magill *et al.*, examined 534 patients in a randomized control trial, having 233 in group 1 (1 g IV TXA intraoperative + 24 hrs.postoperatively), 235 in group 2 (1g IV TXA intraoperative only) and 66 in group 3 (no TXA at all). There was no significant difference in the mean intraoperative Blood Loss between the two experimental groups, 848.4 ml ± SD 463.8 in group 1 and 843.7 ml± 478.7 in group 2; the mean difference was -4.7 ml (95% confidence

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interval was -82.9 to 92.3); p=0.916)[15]. Their study results also support the intraoperative use of TXA, as per our study results. Vles *et al.*, reported the results of their randomized controlled trial, in which 60 patients received intravenous administration of 1.5 g of tranexamic acid was administered just before wound closure, and in other 60 patients' topical application of 3.0 g of tranexamic acid was given by a subfascial drain at the end of the procedure.Post-operative blood loss was calculated. They found no significant difference statistically as far as the post-operative blood loss is concerned. This study also provides evidence that tranexamic acid is an effective tool for blood loss prevention in hip arthroplasty [16]. Zheng *et al.*, reported similar results. They assessed 56 RCTs having different regimens. They found that all high doses of tranexamic acid were effective for decreasing total blood loss, without the risk of pulmonary embolism or deep vein thrombosis when compared with placebo.They recommended a medium dose of 20-40 mg/kg or 1.5–3.0 g of combined Intravenous/Intra-Articular tranexamic acid to control the bleeding in total hip arthroplasty patients [17]. Zha and his colleagues retrospectively analyzed prospectively collected data of seventy patients who underwent total hip arthroplasty. They studied two groups: the tranexamic acid group of 39 patients who received 1.5 g intravenous tranexamic acid and the control group of 31 patients who did not receive tranexamic acid.Total blood loss as well as postoperative hemoglobin drop in the tranexamic acid group was significantly lower as compared to the control group, with a p value of <0.050 [18]. Avcı *et al.*, retrospectively studied the effect of two doses of TXA intravenously before and after surgery in THA patients on total blood loss and blood transfusion need. In this study, total mean blood loss, decrease in hemoglobin levels and amount of blood transfusion were lower in the TXA group compared to the control group (p=0.001; p=0.001; p=0.001, respectively). They concluded that TXA is an effective and reliable way in THA for significantly reducing blood loss and the need for blood transfusion without causing an increase in thromboembolic complications [19]. Khanna *et al.*, investigated 60 patients who were undergoing Total hip arthroplasty. The TXA group received IV tranexamic acid at a dose of 15mg/kg, and the other group received no drug. They noted less direct blood loss (p value=<0.001) in the tranexamic group as compared to a control group, which is 988 vs 1295 ml. They found tranexamic acid, given before incision, to be efficient in reducing Direct and Indirect blood loss in the Total hip arthroplasty procedure [20]. Khorram *et al.*, searched PubMed, Web of Science, Scopus, Embase, and the Cochrane Library and selected 14 studies having 1358 patients for inclusion in their meta-analysis. They reported the TXA role in decreasing total blood loss in all approaches. They further noticed that the lateral approach (LA) maintains the postoperative Hb level more effectively (WMD=1.081, 95 % CI: 0.620–1.541), while the posterolateral approach has significantly less Intraoperative blood loss (PLA; WMD = –70.578, 95 % CI: [-130.389] – [-10.766]) and the posterior approach (PA) was associated with a reduction in total blood loss (WMD = –392, 95 % CI: [-474.439] – [-310.231], p-value <0.001) [21]. Current study is the first of its kind in our population and has found that pre-operative Intravenous tranexamic acid bolus reduced blood loss during surgery significantly in contrast to controls in patients who are having a complete hip replacement or arthroplasty for grade IV osteoarthritis without regard to patients' age, gender and BMI. Based on this evidence, it can be recommended that in future practice, patients undergoing total hip arthroplasty for osteoarthritis hip should receive an intravenous bolus of TXA to reduce loss of blood and subsequent requirement for post-operative transfusion with its associated complications.

The relatively small sample size and single-center design may limit the generalizability of the findings to broader populations. Additionally, variations in surgical technique and perioperative management were not fully controlled, which could influence blood loss outcomes. Future large-scale, multicenter randomized trials are recommended to further validate the optimal dosing and administration protocols of tranexamic acid in total hip arthroplasty.

CONCLUSIONS

It was concluded that a pre-operative intravenous tranexamic acid as a single dose reduced operative blood loss significantly as compared to controls in patients having total hip arthroplasty for grade IV osteoarthritis, regardless of patient's gender, age and BMI.

Authors' Contribution

Conceptualization: RSWR
Methodology: MBUDZ, RSWR, MA
Formal analysis: MAT, IS
Writing and Drafting: MBUDZ
Review and Editing: MBUDZ, RSWR, MA, MAT, IA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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