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**Dr. Varsha S Kurhade**
MBBS, DA, DNB Department of Anesthesiology, Pain Consultant Ruby Hall Clinic Pune, Maharashtra, India

**Dr. Jaspreet Kaur Nagpal**
MBBS, DADNB,
Assistant Professor,
Department of Anaesthesia,
Dr. DY Patil Medical College Pimpri, Pune, Maharashtra, India

**Dr. Varun O Agrawal**
Consultant Orthopedic Surgeon, Joint Replacement and Trauma Department,
Lokmanya Hospital,
Pune, Maharashtra, India

**Corresponding Author:**
**Dr. Jaspreet Kaur Nagpal**
MBBS, DADNB,
Assistant Professor,
Department of Anaesthesia,
Dr. DY Patil Medical College Pimpri, Pune, Maharashtra, India

# Effect of tranexamic acid use on blood loss in hip surgeries: A prospective randomized controlled study

**Dr. Varsha S Kurhade, Dr. Jaspreet Kaur Nagpal and Dr. Varun O Agrawal**

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**Abstract**
Major orthopedic surgeries are usually associated with high blood loss and the need for blood transfusions. Blood transfusion has got its disadvantages so also the various blood conservation techniques described so far. A prospective, randomized, double-blind, comparative study was done to study the role of tranexamic acid in 60 adults undergoing elective hip surgeries, *viz*. total hip replacement, hemiarthroplasty hip, intertrochanteric fracture fixation. The patients were grouped into group 'T' (Tranexamic acid group) and group 'S' (Normal Saline group). Bolus preoperative dose followed by continuous intraoperative infusion was given. The mean blood loss was 412 ± 129.49 ml among 'T' group which was less than 528± 117.16 ml in 'S' group. The total number of patients who required blood transfusion was higher (26.7%) in 'S' group than those in 'T' group (16.07%). Thus, preoperative tranexamic acid is effective in reducing intraoperative blood loss and blood transfusion requirements in elective hip surgeries.

**Keywords:** Tranexamic acid, hip surgeries, total hip replacement, blood loss, blood transfusion, antifibrinolytics.

## 1. Introduction
All major surgical procedures especially orthopedic surgeries are associated with high intraoperative and postoperative blood loss, which may result in need for whole blood transfusions in majority of patients. Blood transfusion also has some disadvantages. Number of ways have been recommended as useful means to decrease the need for allogenic transfusions [1]. However, these techniques have got several disadvantages.
The patients who have low preoperative hemoglobin value, those subjected to bilateral Total Hip Replacement (THR) & Jehovahs witnesses who are unable to receive allogenic blood transfusion [2] need special care and efforts to reduce the blood loss.
In total hip replacement, fibrinolysis, induced by surgical trauma [3], increases the blood loss. This justifies the use of antifibrinolytic agents in such surgeries.
Currently, there is sufficient literature evidence concerning the efficacy of antifibrinolytic agents in reducing blood loss and transfusion requirements in orthopedic and other surgeries [4-12].
This prospective randomized study evaluates the efficacy of tranexamic acid to decrease blood losses and blood transfusions in patient undergoing elective hip surgery.

## 2. Materials and Methods
A prospective randomized double-blind controlled study was done.
Preoperative general and systemic examination was done in all 60 patients. Baseline investigations such as Hemogram, Urine routine –microscopy, Bleeding Time, Clotting time, Prothrombin time-INR, Blood urea, Serum creatinine, X ray chest, Electrocardiography and any special investigation as per requirement were done.
The patients were randomly allocated into group 'T' and group 'S', by picking up lots after shifting to operating room. 30 patients in each group were considered for the study.

**Group 'T':** These patients received tranexamic acid 10 mg/kg intravenously, as a bolus slowly, 30 minutes prior to skin incision and then 1 mg/kg/hr intravenous infusion till the closure of skin incision.

**Group 'S':** These patients formed control group and received normal saline 0.1ml/kg intravenously, as a bolus slowly, 30 minutes prior to skin incision and then 0. 1ml/kg/hr intravenous infusion till the closure of skinincision.

Intraoperatively, routine monitoring was done with, electrocardiography (leads II & $V_5$), pulse oximetry and non-invasive blood pressure. Baseline parameters like pulse rate, blood pressure and oxygen saturation were noted.

All patients received spinal – epidural anesthesia and the level of sensory block was maintained at $T_{10}$ dermatomal level. All the surgeries in both groups were performed by single experienced orthopedic surgeon.

Prefilled syringes with 10 ml and 50 ml volume were given by the investigator to the other anesthesiologist who was blinded for the study group. In 10 ml syringe tranexamic acid (500 mg in 5 ml ampoule) was loaded as 100 mg/ml (1000 mg/10 ml) and bolus was given (4.5 – 8 ml), as per calculated by weight for study group. Similarly, for control group, saline was given from 10 ml syringe as per weight (0.1ml/kg).

For continuous infusion, tranexamic acid 5 ml (500 mg) was mixed with 45 ml of distilled water to make total volume up to 50 ml (10 mg/ml concentration) and given by infusion pump at the rate calculated as per weight (1mg/kg/hr). Similarly, 50 ml normal saline was loaded for control group and given as 0.1ml/kg/hr, so the volumes are matched in both the groups and the blinded anesthesiologist was not biased.

Intraoperative blood loss was assessed by weighing mops and drapes before and after soakage (gravimetric method) [7, 13, 14, 15]. The dry weight was deducted from the weight obtained after soakage. Blood loss was obtained by converting 1 g to 1 ml. Also, blood collected in suction drain was calculated. Total blood loss was calculated and values were rounded up.

Blood transfusion trigger for these patients was established as estimated blood loss being equal to their allowable blood loss [7, 13, 14, 15, 16].

Allowable blood loss = (patient Hb –trigger Hb) x (blood volume) / (average Hb) (Trigger Hb was set as 9 gm %).

Measured blood loss was replaced with crystalloids (Ringer's Lactate) in a 3:1 ratio till blood loss reached half that of allowable blood loss and thereafter with colloid (Voluven 6%) in 1:1 ratio until trigger for blood transfusion is reached. Once the trigger point was reached, they received blood. If the patient's blood pressure falls by more than 20% of preoperative BP and blood loss does not exceed the limits of transfusion trigger, then vasopressor - ephedrine was to be given to the patient to maintain the BP within 20% of preoperative value.

Factors noted during operation – type of surgery, position of patient, length of surgery, number of units of colloid, crystalloid and blood transfused. Postoperative Hb was recorded in postoperative ward 4 hours after surgical closure.

If any rise or fall in blood pressure 20% more than baseline occurred for more than 30 minutes, in spite of adequate volume resuscitation and treatment with vasopressor, then such patient was excluded from study.

With the above information group 'T' and group 'S' were compared and evaluated for blood loss, units of whole blood transfused and results were drawn from statistical analysis.

| Inclusion *Criteria* | Exclusion *Criteria* |
|---|---|
| ASA grade I –II, patients undergoing elective hip surgery | ASA grade III - V patients |
| Hb > 10 gm% | History of previous hip surgery |
| Age group of 30 – 90 years of either sex | Surgeries involving tourniquet |
| Normal coagulation study report. | Hb <10 gm% |
| | Inherited / acquired hemostatic diseases |
| | Abnormal coagulation screening tests |
| | Ingestion of aspirin /NSAID up to days prior to surgery |
| | Serum creatinine >1.5 mg% |
| | Pregnancy |
| | History of Deep Vein Thrombosis (DVT) |
| | Hepatic insufficiencies |
| | Allergy to tranexamic acid. |

## 3. Results and Observations

This was a prospective, randomized, comparative study of 60 healthy adults of ASA physical status I and II, admitted for elective hip surgeries. This study was conducted to examine the effect of pre and intraoperative use of tranexamic acid on blood losses and blood transfusion requirement in patients undergoing elective hip surgeries, *viz*. total hip replacement, bipolar prosthesis placement, fixation of intertrochanteric fracture, where tourniquet is not used.

The two groups were comparable for age, sex, weight, length of surgery and preoperative coagulation test results. Pre- and intraoperative hemodynamic parameters were stable and comparable. Mean requirement of crystalloid and colloid was also similar in both the groups.

In our study, mean blood loss was 412 ± 129.49 ml among 'T' group which was less as compared to 528± 117.16 ml in 'S' group and the difference was statistically significant ($p$= 0.0006). The mean Hb in both the group was comparable in pre- and intraoperative period.

Total number of patients who required blood transfusion was higher 26.7% among those without treatment as compared to 16.07% in those treated with tranexamic acid, but the difference was not statistically significant.

There were no thromboembolic complications detected in our study.

**Table 1:** Profile of Surgeries in both the groups

| Type of Surgeries | Group 'T' (n = 30) | | Group 'S' (n = 30) | |
|---|---|---|---|---|
| | Number | % | Number | % |
| Total Hip Replacement | 10 | 33.3 | 10 | 33.3 |
| Bipolar Prosthesis | 10 | 33.3 | 10 | 33.3 |
| Inter-trochanteric Fixation | 10 | 33.3 | 10 | 33.3 |

**The two groups were comparable for type of surgery.**

**Table 2:** Comparison of Mean Blood Loss between two groups

| Groups | Mean Blood Loss(ml) Mean ± SD | *p* value |
|---|---|---|
| Group 'T' | 412 ± 129.49 | 0.0006 Significant |
| Group 'S' | 528± 117.16 | |

Unpaired Student's 't' test was used for statistical analysis of blood loss.

There was significant difference in mean intraoperative blood loss amongst both the groups. ($p$ – 0.0006)

**Table 3:** Comparison of Number of Blood Units Transfused in both groups

| Number of Blood Transfusion Units | Group 'T' (n = 30) | | Group 'S' (n = 30) | | *p* value |
|---|---|---|---|---|---|
| | Number | % | Number | % | |
| 1 | 03 | 16.67 | 05 | 27.77 | 0.5957 NS |
| 2 | 02 | 11.11 | 03 | 16.67 | |
| Total Units | 07 | 38.89 | 11 | 61.11 | |

There was no statistically significant difference.

**Table 4:** Comparison of Number of Patients with Blood Transfusion in both the groups

| Blood Transfusion received | Group 'T' (n=30) | | Group 'S' (n=30) | | *p* value |
|---|---|---|---|---|---|
| | Number | % | Number | % | |
| Yes | 05 | 16.67 | 08 | 26.67 | 0.53 NS |
| No | 25 | 83.33 | 22 | 73.33 | |

In Group 'T', 5 patients needed blood transfusion whereas in Group 'S', 8 patients were transfused with blood, the difference is not statistically significant.

## 6. Discussion

Surgical procedures are inevitably associated with bleeding. Moderate to massive blood loss during any surgery is associated with coagulopathy secondary to tissue injury, hypoperfusion, dilution and consumption of clotting factors and platelets, and coagulopathy, together with hypothermia and acidosis, forms a 'lethal' triad. To prevent this vicious cycle, efforts should be taken to limit the blood loss to the minimum.

Hip surgeries may result in need for whole blood transfusions in up to 97% of the patients in the absence of blood conservation strategies.[13] Practice of blood transfusion also has some disadvantages like blood-borne infections, immune reactions, volume overload, electrolyte disturbances, coagulation abnormalities and finally, adding to the cost of health care.

To avoid allogenic blood transfusion, different techniques have been employed *viz*. preoperative autologous blood donation with or without erythropoietin, acute normovolemic hemodilution, intraoperative blood salvage etc., but these techniques are either time consuming, need expensive devices, or increase the risk of poor blood quality, especially if using postoperatively salvaged but untreated blood. This is not encountered while using pharmacological therapies.

Various studies done by Benoni G *et al*., [17] Ekback G *et al*., [18] Lemay E *et al*., [7] Claeys MA *et al*., [14] Hynes Mc *et al*. [8] have proved the role of tranexamic acid in reducing blood loss in patients undergoing THR. Phillips *et al*. [19] showed that a significant reduction in blood transfusion can be made using combined cell salvage and tranexamic acid in revision THR. However, the role of tranexamic acid in decreasing blood loss in other surgeries of hip, *viz*. bipolar prosthesis placement and intertrochanteric fracture fixation, has not been studied so far.

Amongst all fibrinolytics, tranexamic acid has been shown to be superior over aprotinin and epsilon-amino-caproic acid, for effectively reducing blood loss, having less incidence of allergic reactions and less cost of treatment [20, 21].

Previous studies done by Duquenne *et al*., [22] Benoni G *et al*. [17] and Rajesparan K *et al*. [23] have shown tendency towards decrease in blood loss in women as compared to men which led to ascribe it to short stature of most of the women. The similar distribution of men and women in this study does not affect our results.

Similar to Claeys MA *et al*. [14], this study included patients with ASA grade I-II.

From the previous reports, it is seen that type of anesthesia, body temperature and mean intraoperative blood pressure could influence blood loss in patients undergoing orthopedic surgeries. Regional anesthesia is preferred in properly selected patients due to its advantages. Epidural anesthesia has been used in the studies done by Sharrock NE *et al*., [24] Williams-Russo *et al*., [25] and Kazemi SM *et al*. [26] in patients undergoing total hip arthroplasty and found it to be effective in reducing perioperative blood losses and blood requirement. Regional (i.e. spinal-epidural) anesthesia was used in this study. Body temperature was not recorded intraoperatively, but methods to maintain euthermia such as restricting operation theater temperature, use of heating mattress, use of warm infusions were implemented.

Transfusion trigger was set to 9 gm % considering older population, which was comparable to that of study done by Zufferey PJ *et al*. [16] with Hb trigger of 9 gm %, Claeys MA *et al*. [14] with trigger 8.5 gm %, Niskanen *et al*. [15] with 0.28–0.30 level of hematocrit, Lemay E *et al*. [7] with trigger as 9 gm % for high risk patients & 7 gm % for others. In the study done by Mc Swiney MM *et al*., [13] he set the transfusion protocol by calculating maximum allowable blood loss to avoid side effects of over-transfusion. Similar method was followed in this study.

Various dosages of tranexamic acid have been studied with respect to decrease blood loss in hip surgeries. Malhotra *et al*. [27] showed decreased blood loss when patients were given 15 mg/kg of tranexamic acid as a single bolus prior to skin incision. Yamasaki S *et al*. [28] used higher dose of 20 mg/kg of tranexamic acid as a single bolus dose. Benoni G, Lethagen S *et al*. [29] administered tranexamic acid after the operation and 3 hours later, but failed to show any significant reduction in postoperative blood loss. Ekback *et al*., [18] Lemay E *et al*. [7] and Husted H *et al*., [30] showed that the total blood loss was less when 10 mg/kg of tranexamic acid was given prior to skin incision, followed by infusion of tranexamic acid at the rate of 1mg/ kg/hr till the closure of skin incision. Comparing all above studies, as shown by Ekback *et al*., [18] Lemay E *et al*. [7] and Husted H *et al*., [30] bolus dose of tranexamic acid followed by continuous infusion is more effective in reducing blood loss than bolus dose alone. Similarly Horrow JC *et al*. [31] has shown that larger doses don't have additional hemostatic benefits. Similar protocol was also followed in this study.

No patient in either group had long duration of surgery to produce more blood loss or third space loss. Administration of dextran has been shown to decrease fibrinolytic inhibition postoperatively, a finding which has potential influence on this study. So, hydroxyethyl starch (Voluven 6%) was used for volume expansion.

Amongst studies done for assessing blood loss in cases receiving tranexamic acid, majority have proved its beneficial effect in reducing perioperative blood loss and transfusion requirements. Study by Niskanen *et al*. [15] showed reduced blood loss by 27.27% and reduced

incidence of red cell transfusion by 44.45 % in tranexamic acid group. In the study done by Ekback *et al*., [18] there was 35% decrease in measured blood losses. In these studies, the total blood loss was estimated by intraoperative blood loss and blood collected in the drain in 24 hours postoperatively. In order not to increase postoperative prosthesis infection, drains are either rapidly removed or even avoided in our institution. Therefore, this study has estimated only intraoperative blood losses. Total reduction in blood loss of 21.97% has high clinical significance, which is similar to studies by Benoni G *et al*., [17] Niskansen *et al*. [15] and Ekback *et al*. [18]

There was no significant difference in mean Hb level in both the groups, which was similar to that shown by Lemay E *et al*. [7] Less fall in mean Hb level in spite of greater blood loss in Group 'S' can be attributed to higher number of blood transfusions in this group.

Total number of patients who required blood transfusion was higher 26.7% among those without treatment as compared to 16.07% in those treated with tranexamic acid, but the difference was not statistically significant though it is clinically significant. The blood transfusion requirement was reduced by 36.36%. These results are comparable with those shown by Niskanen *et al*. [15] (where blood transfusion requirement was reduced by 44.45% in tranexamic acid group), Benoni G, Fredin H *et al*. (61.5%) [17] and Zufferey PJ *et al*. (18%) [16].

In various studies done before, it is observed that the rate of thromboembolic events is not more in tranexamic acid group compared to control [15, 20, 30]. There were no thromboembolic complications detected in this study.

In conclusion, there was significant difference in blood loss in either group. Though tranexamic acid decreased number of patients who required blood transfusion and the number of units of blood transfused per patient, the difference was not statistically significant.

## 7. Conclusion

In patients undergoing elective hip surgeries, preoperative administration of tranexamic acid is effective in reducing intraoperative blood loss and blood transfusion requirement.

## 8. Abbreviations

TA- Tranexamic Acid, THR- Total Hip Replacement, ASA- American Society of Anesthesiologists, DVT- Deep Vein Thrombosis, INR- International Normalized Ratio.

## 9. Ethical committee approval

This study was conducted after obtaining approval from the institutional ethics committee. Informed consent was obtained from all the patients.

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