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## **A comparative study of reduction of blood loss after use of tranexamic acid intravenous versus topical in unilateral total hip replacement: A prospective study**

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### **Abstract**

Total hip Replacement (THR) is one of the most widely performed elective orthopaedic surgery. THR is a successful procedure but it has its own complications. Some complications that have been seen in THR are blood loss, infection, dislocation, thromboembolism, neurovascular injuries, limb length discrepancy & implant failure. Current research in THR is targeted at reducing post-operative complications including blood loss and improving the design to improvise patient function. Many interventions have been developed to reduce intraoperative and post-operative blood loss. The use of tranexamic acid in primary THR is widely accepted today and several studies have confirmed its efficacy for decreasing blood loss without any significant increase in complications. The efficacy and safety of topical versus IV tranexamic acid often differs and more studies are required to validate the results. Our study aimed to compare reduction of blood loss after use of tranexamic acid intravenous versus topical in unilateral total hip replacement.

**Materials & Methods:** The study comprised of 82 patients scheduled for primary THR. Tranexamic acid was given locally in 41 patients and intravenously in another 41 patients. Blood samples were collected from all the subjects on post-operative day 1 & 3. Blood loss was calculated using standard parameters & Good *et al* 2003 equation.

**Results:** In our study, the amount of blood loss was found to be lower in IV group as compared to the local group. In group A (topical), amount of the blood loss ranged from 224.4 - 1834.5 ml amongst the subjects, with a mean ( $\pm$  SD) of  $828 \pm 406.6$  ml. Whereas, in group B (intravenous) the amount of blood loss varied from 172.3 - 937.2 ml with a mean ( $\pm$  SD) of  $598.3 \pm 207.5$  ml. When analyzed, there was a statistically significant difference between the groups ( $p = 0.001$ ).

**Conclusion:** Our study concluded that the amount of blood loss in THR to be lower in IV group as compared to the local group.

**Keywords:** THR, blood loss, tranexamic acid, intravenous, topical

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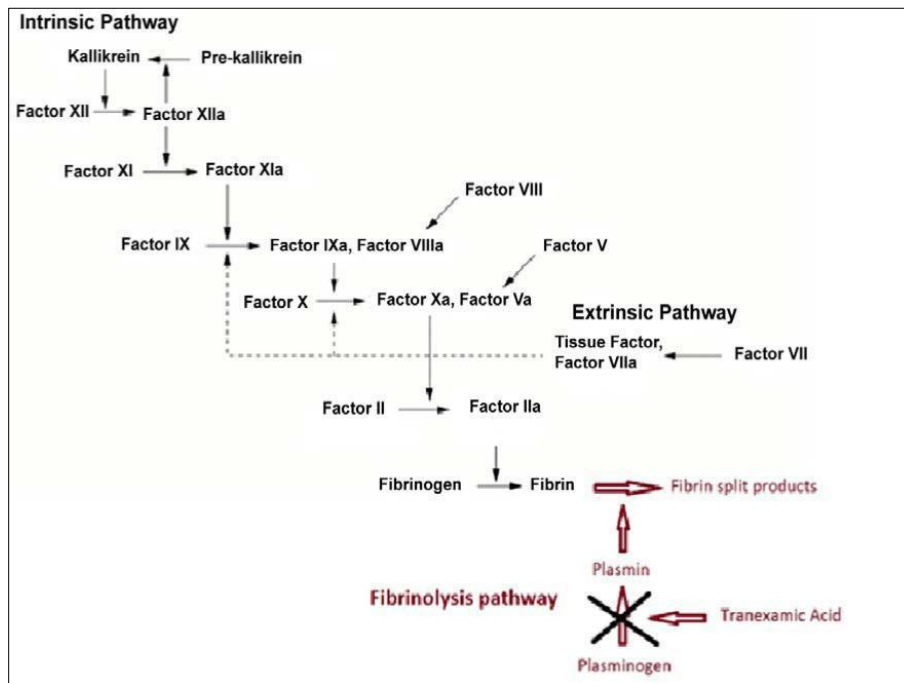
### **Introduction**

Total hip Replacement (THR) is one of the most successful and widely performed elective orthopaedic surgery. The burden of hip arthritis is on the rise and it is estimated that more than 9,50,000 primary and revision THAs were performed globally in 2010 [1]. THR is a successful procedure but it has its own complications. Some complications that have been seen in THR are blood loss, infection, dislocation, thromboembolism, neurovascular injuries, limb length discrepancy, loosening of implant, implant failure and mortality. Current research in THR is targeted at reducing post-operative complications including blood loss and improving patient function. Around 700 to 2000 ml blood can be lost during perioperative period after THR and allogenic blood transfusion is required in 16% to 37% of patients [2]. This can result in increased medical expenditure and transfusion related complications, such as fluid overload,

cardiopulmonary events, graft versus host diseases and transfusion transmitted diseases like HIV, Hepatitis B, Hepatitis C etc. Fibrinolysis is considered as the major cause of postoperative bleeding in THR.

Many interventions have been developed to reduce intraoperative and post-operative blood loss, including controlled hypotensive anesthesia, electrocautery, autologous blood transfusion, post op drains, anti fibrinolytics and various other blood salvage techniques such as, maintaining normal body temperature reduces blood loss [3].

Several agents have been used which act on the coagulation pathway to reduce blood loss in patients with THR. In recent years, use of antifibrinolytics such as Aprotin, Amino caproic acid (EACA) and Tranexamic acid has increased. Tranexamic acid is a synthetic amino acid, which competitively inhibits the degradation of plasminogen, thus decreases fibrinolysis [4].



**Fig 1:** Shows coagulation pathway with site of action of Tranexamic acid

The first study to examine efficacy of tranexamic acid in reducing blood loss after total joint arthroplasty was done in 1997<sup>[5]</sup> whose findings suggested that tranexamic acid was associated with a significant reduction of blood loss with no increase in venous thromboembolic events following total knee arthroplasty. The first study demonstrating the efficacy of tranexamic acid when used during total hip arthroplasty was published in 2000<sup>[6]</sup>. The use of tranexamic acid in primary THR is widely accepted today and several studies and meta-analysis have confirmed its efficacy for decreasing blood loss without any significant increase in complications. It is reported that 65% of blood loss occurs within 8 hours after THR and tranexamic acid as an antifibrinolytic drug would last for 8 hours<sup>[7]</sup>.

Topical tranexamic acid is thought to have an advantage over IV tranexamic acid as it provides a higher concentration of drug at surgical site and is associated with little systemic absorption<sup>[8,9]</sup>. Blood transfusion in itself carries significant risk of infections. The rate of seropositivity in the blood donor population has been shown to be approximately 0.76 for HBV, 2.0 for HCV; 28 for HIV and 0.34 for HTLV per 10,000 blood donations<sup>[10]</sup>.

Our study aimed to compare reduction of blood loss after use of tranexamic acid intravenous versus topical in unilateral total hip replacement. The primary purpose of this study is to estimate blood loss in both the groups. We also assessed the need of blood transfusion & functional outcome using WOMAC score in both these groups.

### Materials and Methods

This was a case control study conducted in the Department of Orthopaedics, ESIC Hospital, Okhla, New Delhi from November 2018 to November 2019. A total of 82 patients were recruited who were scheduled for primary total hip arthroplasty. Patients who got admitted for unilateral total hip replacement were randomly divided into group A (local) and group B (intra-

venous). There were 41 patients in group A who received local tranexamic acid and 41 patients in group B who received intravenous tranexamic acid through drain. All the patients were between 30-80 years of age, mentally competent, alert and fit for surgery. Patients excluded from the study were those with history of cerebrovascular accident (stroke), deep venous thrombosis, pulmonary embolism, myocardial infarction, patients with stent in situ, creatinine level more than 1.5mg/dl, history of coagulopathic disorders, preoperative Hb less than 8.5 gm /dl, bilateral THR, complex or Revision THR & patient not willing to be a part of the study.

Similar type of anesthesia i.e. combined spinal and epidural were given to all the patients. All surgeries were done through the same lateral approach to hip. Tranexamic acid was used in a dose of 10- 15 mg /kg intravenous before surgery & in a dose of 2 gm topical dose per-operatively in unilateral total hip replacement cases. In the immediate post-operative period, blood loss, general condition and vitals were assessed. If blood transfusion was required after this assessment, then packed red blood cell (PRBC) were transfused. Symptoms of deep vein thrombosis and pulmonary embolism were monitored throughout the post-operative period and prophylactic low molecular weight heparin was given in both the study groups. Suction drain was removed 24 hours after surgery. In next subsequent post-operative day, hemoglobin and other vitals were monitored. On 3rd post-operative day hemoglobin level was measured in both groups.

The amount of blood loss was calculated using Good *et al.*<sup>[10]</sup> equation.  $Hb\ loss = BV \times (Hbi - Hbe) \times 0.001 + Hbt$ . Note: *Hbi* – Hb concentration before surgery; *Hbe* – Hb concentration on the third day after surgery; *Hbt* – total amount of allogenic Hb transfused; *BV* – blood volume taken as 7% of total body weight of the patient. A unit of banked blood was considered to contain 52 g Hb. The blood loss (ml) was related to the patients' preoperative Hb value (g/l) (blood loss = 1000 × Hb loss/Hbi).

Short term functional assessment of patient was done using WOMAC scoring pre operatively, on 2-week post-operative and 6-week post-operative period.

This was a prospective study, and prior approval was obtained from the Institutional Review Committee. Results were analyzed using student's t test.

## Results

In this study, the mean age ( $\pm$ SD) was  $52.9 \pm 16.2$  years in patients of group A (topical) and  $51.1 \pm 16.6$  years in group B (intravenous). There were 24 (58.5%) males and 17 (41.5%) females in group A (topical) while there were 23 (56.1%) males and 18 (43.9%) females in group B (intravenous).

The mean ( $\pm$  SD) pre-operative WOMAC score in patients of group A(topical) was  $55.88 \pm 6.9$ , with a range of 43 - 69. Whereas in group B(intravenous) patients, mean ( $\pm$  SD) WOMAC score was  $55.59 \pm 8.4$ , ranging from 40 – 70. No significant difference was found ( $p = 0.86$ ) and the results in both the groups were comparable.

The mean blood volume ( $\pm$ SD) was  $5.3 \pm 0.80$  lt in patients of group A(topical) &  $5.2 \pm 0.80$  lt in group B (IV). In group A (Topical), mean ( $\pm$  SD) value of blood loss was  $828 \pm 406.6$  ml, whereas in group B (IV) it was  $598.3 \pm 207.5$  ml. There was a significant difference across the two groups ( $p = 0.001$ ). Table 1.

**Table 1:** Distribution of blood loss in both groups

	Min (ml)	Max (ml)	Mean $\pm$ SD	p value
Group A	224.4	1834.5	$828 \pm 406.6$	0.001
Group B	172.3	937.27	$598.3 \pm 207.5$	

In group A (Topical), mean ( $\pm$  SD) value of hemoglobin loss was  $109.4 \pm 56.8$  gm/dl whereas in group B(IV) it was  $74 \pm 27.6$  gm/dl. There was a statistically significant reduction in intravenous group compared to topical group ( $p=0.009$ ). Table 2.

**Table 2:** Distribution of hemoglobin loss in both groups

	Min (gm/dl)	Max (gm/dl)	Mean $\pm$ SD	p value
Group A	26.3	242.1	$109.4 \pm 56.8$	0.0009
Group B	22.4	124.7	$74 \pm 27.6$	

Total no. of unit of blood transfusion in group A was 6 units and 4 units in group B. The blood transfusion in entire group A is similar to that in Group B. Regular DVT screening was done up to 4th post-operative day. No patient in the study had DVT.

Patient in group A (topical) had a mean 2-week post-op WOMAC score  $22.7 \pm 1.9$  while in group B it was  $21.8 \pm 1.5$  ( $p$  value = 0.02). At 6 weeks WOMAC score in group A(topical) was  $10.10 \pm 3.1$  while in group B(intravenous) it was  $9.61 \pm 3.1$ . No significant difference was found ( $p = 0.482$ ) and the results in both the groups were comparable.

## Discussion

Large clinical studies and several meta-analyses have confirmed that intravenous administration of tranexamic acid could effectively reduce blood loss and transfusions rate (UPTO 50%) in THR. However, concerns remain over the risk of thromboembolic complications after systemic administration. Therefore, many studies have focused on topical administration

of tranexamic acid as a potential alternative to intravenous [6, 11]. Nevertheless the efficacy and safety of topical versus IV tranexamic acid often differs between cases and more studies are required to validate the results.

Our study aimed to assess the difference in blood loss in patients undergoing total hip replacement after application of tranexamic acid by two techniques i.e. topical versus intravenous.

This case control study comprised of 82 subjects who underwent total hip arthroplasty. Out of these, 41 patients were given tranexamic acid locally (group A) and another 41 patients were given tranexamic acid intravenously (group B). Mean age ( $\pm$ SD) of subjects was  $52.9 \pm 16.2$  years in group A and  $51.1 \pm 16.6$  years in group B. All subjects were between 30-80 years of age. There were 24 (58.5%) males and 17 (41.5%) females in group A while there were 23 (56.1%) males and 18 (43.9%) females in group B. Proportion of males undergoing THR were slightly higher than the females with M: F ratio of around 1.3:1 in both the groups. The mean age of patients is reported to vary across various studies.

The mean height ( $\pm$ SD) was  $165.7 \pm 7.8$  cm in patients of group A and  $165.1 \pm 8.3$  cm in group B. This was in the range of average Indian population and was comparable to the average height of subjects in a study done by Wei *et al* (2014) [12]. The mean weight ( $\pm$ SD) was  $75.8 \pm 11.5$  kg in group A patients and  $74.2 \pm 12.1$  kg in group B. This was comparable to the average weight of subjects in a study done by Ekback G (2000) [6].

In the present study, causes behind the development of osteoarthritis (OA) were found to be either idiopathic, rheumatic or infective. The etiological distribution of subjects in group A were as, 87.8% of the patients had idiopathic OA, 9.8% had rheumatoid arthritis and 2.4% of the patients had shown infective etiology. Whereas in group B, idiopathic OA was seen in 95.1% patients, 2.4% patients had rheumatoid arthritis and another 2.4% showed infective cause.

Patients in group A had a mean pre op hemoglobin value of  $12.9 \pm 1.5$  gm/dl ranging from 10.0 to 16.3 gm/dl. And in group B, mean pre op hemoglobin value was  $12.3 \pm 0.9$  gm/dl ranging from 10.0 to 14.1 gm/dl.

Total blood volume in the body was calculated for each subject. In group A, the mean ( $\pm$  SD) value of blood volume was  $5.3 \pm 0.8$  lt, falling in the range of 3.9 - 7.1 lt. Whereas in group B patients, mean ( $\pm$  SD) value of blood volume was  $5.2 \pm 0.8$  lt, falling in the range of 3.9 – 7.8 lt. No significant difference was observed ( $p= 0.57$ ).

Post-operative hemoglobin was estimated to observe the effect of blood loss. The mean ( $\pm$  SD) value of post op hemoglobin was  $11.1 \pm 1.1$  gm/dl, ranging from 8.8 - 13.3 gm/dl in group A subjects. In group B, mean ( $\pm$  SD) value of post op hemoglobin was  $11 \pm 0.71$  gm/dl, ranging from 10 - 12.5 mg/dl.

Total loss in hemoglobin value between the groups was observed. In group A, the average loss was 109.4 gm/dl with wide variation from 26.3 to 242.1 gm/dl. Whereas in group B, mean Hb loss was 74 gm/dl with a range of 22.4 - 124.7 gm/dl. The loss was higher in the local group as compared to the i.v group. This finding of our study was found to be similar to the study carried out by North WT *et al*. (2016) [4]. In contrast, the meta-analysis done by Jian L *et al*. (2016) [13] showed no significant difference in the Hb loss between i.v and local group.

In our study, the amount of blood loss was found to be lower in

IV group as compared to the local group. In group A(topical), amount of the blood loss ranged from 224.4 - 1834.5 ml amongst the subjects, with a mean ( $\pm$  SD) of  $828 \pm 406.6$  ml. Whereas, in group B(IV) the amount of blood loss varied from 172.3 - 937.2 ml with a mean ( $\pm$  SD) of  $598.3 \pm 207.5$  ml. When analyzed, there was a statistically significant difference between the groups ( $p < 0.05$ ). This result was comparable to the study conducted by North WT *et al* (2016) <sup>[4]</sup>, who observed lower Hb loss in IV compared to local route. In contrast, study done by Jian L *et al* (2016) <sup>[13]</sup> showed no significant difference between the two study groups.

The present study observed no difference in the transfusion rate across IV and local group. Units of blood transfused in entire group A(topical) was 6 and in group B(IV) was 4. However, in a study conducted by T. Wind *et al* (2014) <sup>[11]</sup>, IV infusion of tranexamic acid produced a statistically significant difference in transfusion rate ( $p < 0.001$ ) compared to topical tranexamic acid. The transfusion rate without tranexamic acid was 19.86%, with tranexamic acid infusion was 4.39% and with topical 12.86%.

Screening for DVT was done daily up to 4th post-operative day. No patient in both the study groups was found to have any sign and symptom of DVT. This proves that tranexamic acid did not increase the incidence of DVT by either route. The prophylaxis for prevention of DVT was given to both the groups with sequential mechanical compression and low molecular weight heparin. This observation was similar to the findings of Wei Z *et al* (2015)<sup>[4]</sup> who suggested that the administration of tranexamic acid significantly reduced the blood loss and need for allogeneic blood transfusion, without apparent increased risk of DVT or thromboembolic complications.

Our study showed no difference in the functional outcome i.e the WOMAC score either after 2nd or 6th week post-operatively in both local and i.v group.

### Conclusion

Our study shows that intravenous tranexamic acid is more efficacious than topical tranexamic acid in reducing the hemoglobin loss and blood loss. Also, there were no adverse complications associated with the use of tranexamic acid by either route. However, no change in the requirement for blood transfusion was noted. There was no difference in the functional outcome i.e the WOMAC score either after 2nd or 6th week post-operatively in both local and i.v group. Therefore, our study recommends the use of tranexamic acid by i.v. route during peri- and post-operative period in patients undergoing Total hip replacement.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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