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Original research article

Intravenous vs. oral tranexamic acid in unilateral total knee replacement: A correlational research

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Abstract

Background and objectives: To determine whether or not tranexamic acid administered orally or intravenously is more effective in reducing the amount of blood lost during complete knee arthroplasty. To determine which method, oral or intravenous tranexamic acid, is more effective at preserving blood volume.

Methods: A randomised control prospective interventional research was carried out at Department of Orthopaedics, Kamineni Institute of Medical Sciences, Narketpally, Telangana State, during November 2019 to September 2021. This research consisted 24 individuals with knee osteoarthritis who underwent total knee replacement. Where Group A-12 received oral tranexamic acid. Intravenous tranexamic acid was given to 12 patients in Group B. Pre- and post-op Hb were observed. All participant's blood transfusions were reported.

Results: Both groups' ages were similar. Group A had 4, 60-70-year-olds and B had 6. Neither oral nor IV tranexamic acid influenced surgical blood loss (p-value 0.765). After surgery, group A lost 650 millilitres of blood, while group B lost 608.3 millilitres, which was not noteworthy. Groups didn't accumulate more drains (p-value of 0.838). Blood loss and transfusions are similar in both groups. Group A's 911.6 ml and group B's 849.2 ml total blood loss were statistically identical. Group A needed 0.92 blood transfusions, while group B needed 0.75.

Conclusion: Taking tranexamic acid orally is just as beneficial as taking it intravenously. Also, it limits blood loss during total knee replacement.

Keywords: Tranexamic Acid, Total knee replacement, preoperative Hb, Intraoperative blood loss

Introduction

The degenerative disorder known as osteoarthritis of the knee (OA) is the leading cause of knee pain and physical disability. Symptoms of knee osteoarthritis (OA) affect approximately 11 percent of all women over the age of 60.

For patients who have reached the end stage of knee osteoarthritis, total knee arthroplasty, often known as TKA, is considered to be an effective treatment option. The TKA has been shown to significantly reduce patients' levels of pain and enhance their quality of life. Because of the considerable soft tissue release and bone incisions involved in TKA surgery, severe blood loss is almost always a side effect. The operation comes with an inherent and unavoidable risk of bleeding, which may result in the necessity of receiving a blood transfusion [1, 2, 3].

It has been documented that blood transfusions can result in a wide variety of problems. These comprised a rise in price, febrile and allergic reactions, haemolysis, blood-borne infectious diseases, circulatory overburden, electrolyte imbalance, periprosthetic diseases, abnormalities of acid-base balance, transfusion-associated acute lung problems, and even fatality. Additionally, there is a possibility that transfusions can cause periprosthetic infectious diseases.

Between 800-1700ml of blood is lost during TKA, and about half of the individuals will need a transfusions as a result. TXA, which acts as an inhibitor of fibrinolysis, is a lysine analogue. It does this by inhibiting the binding of lysine to plasminogen, which in turn stops the development of the complexes that involves plasminogen, fibrin, and tissue plasminogen activator [3, 4, 5].

There's been a number of research studies conducted on the usefulness of intravenous tranexamic acid for minimising post-operative and intraoperative bleeding in people treated for total knee arthroplasty. On the other hand, the efficiency of oral tranexamic acid hasn't been examined very thoroughly [5, 6]. Therefore, the purpose of this research was to investigate the efficacy of oral tranexamic acid in limiting bleeding in TKA and to comparing it to the efficiency of intravenous tranexamic acid in doing so.

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Material and Methods

From November 2019 to September 2021, the Department of Orthopaedics at the Kamineni Institute of Medical Sciences, Narketpally, Telangana State, undertook this randomised control prospective interventional investigation. 24 participants with osteoarthritis of their knees who met the eligibility criteria and underwent surgical total knee replacement were part of the research.

In accordance with rules of the ethics committee, department authorization was acquired from the institution. The research was carried out after receiving the participants' written consent in advance. In addition to other pertinent information, personal information including name, age, sex, occupation, address, and a thorough clinical history were collected. The sufferers were placed into two categories at randomization. Twelve individuals in Group A received oral tranexamic acid treatment. A 2 g tablet of tranexamic acid was administered 3 hours before induction of anaesthesia and again 3 hours after the procedure. Tranexamic acid was administered intravenously to the 12 individuals in Group B. 1g of intravenous tranexamic acid was administered 10 minutes prior to the surgical incision and again 3 hours following the procedure. Bleeding during surgery and blood that accumulated in drains for two days were assessed in both categories. Additionally noticed was pre- and post-operative haemoglobin levels. Every participant's total number of blood transfusions was recorded as well.

Inclusion criteria

1. Patients receiving total knee arthroplasty surgery who have primary osteoarthritis of the knee

Exclusion criteria

1. Total knee replacement surgery to treat secondary osteoarthritis
2. Individuals who have already experienced thromboembolic events.
3. Revision total knee replacement
4. Previously, a high tibial osteotomy was performed.
5. Individuals with greater than 30 degree varus deformity.

Result

Table 1: Age distribution (n=24)

Age group (years)	Group A	Group B	Chi-square	P - value
60 to 70	4(33.3%)	6(50.0%)	0.686	0.408
70 to 80	8(66.7%)	6(50.0%)		
Total	12 (100)	12 (100)		

There was not a significant difference between the two groups in terms of the age distribution of the patients. For example, there were four patients in group A and six patients in group B who were between the ages of 60 and 70. Age range between 70 and 80 years was represented by 8 patients in group A and 6 patients in group B.

Table 2: Gender Distribution (n=24)

Gender	Group A	Group B	Chi-square	P - value
Men	5 (41.7)	6 (50.0)	0.168	0.682
Women	7 (58.3)	6 (50.0)		
Total	12 (100)	12 (100)		

In the current investigation, the number of male and female participants was very close to being equivalent. Female patients made up 58.3% of patients in group A and 50% of patients in group B, respectively, whereas male patients made up 41.7% of patients in group A and 50% of patients in group B.

Table 3: Operated side distribution (n=24)

Operated side	Group A	Group B	Chi-square	P - value
Right	4 (33.3)	7 (58.3)	1.51	0.219
Left	8 (66.7)	5 (41.7)		
Total	12 (100)	12 (100)		

There was no statistically significant difference seen between the oral and intravenous tranexamic acid groups for the operated side.

Table 4: Group A and Group B preoperative hemoglobin (n=24)

S.no	Hemoglobin in group A (g/dl)	Hemoglobin in group B (g/dl)
1.	12.1	11.7

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2.	11.5	11.3
3.	10.2	10.8
4.	12.8	11.1
5.	11.8	10.6
6.	11.5	11.6
7.	11.8	12
8.	10.8	11.2
9.	13.4	11.6
10.	10.6	10.8
11.	11.6	11
12.	10.1	11.9

Table 5: Pre-operative Hb comparison in both groups in g/dl (n=24)

Group A	Group B	T value	P value
11.5 ± 1.0	11.3 ± 0.5	0.687	0.499

Because the p-value came out to be 0.499, the researchers concluded that there was no statistically significant difference between the two groups in terms of the average pre-operative haemoglobin readings. It was determined that there was no statistically significant difference between the two groups' average pre-operative haemoglobin readings, which were 11.5g/dL in group A and 11.3g/dL in group B respectively.

Table 6: Group A and Group B postoperative Hb (n=24)

S.no	Hemoglobin in group A (g/dl)	Hemoglobin in group B (g/dl)
1.	9.8	9.7
2.	8.1	10
3.	10.6	9.3
4.	10.5	10
5.	10.8	9.5
6.	8	9.4
7.	10.4	10.8
8.	8.5	10.3
9.	10.8	9.7
10.	8.4	9.4
11.	10.1	8.9
12.	8.3	10.6

Table 7: Post-operative Hb comparison in both groups' g/dl (n=24)

Group A	Group B	T value	P value
9.5 ± 1.2	9.8 ± 0.6	0.741	0.466

The p-value for the difference in post-operative haemoglobin levels between groups A and B is 0.466, which indicates that the difference is not statistically significant. In group A, the postoperative haemoglobin level averages out to 9.5 g/dL, whereas in group B, it is 9.8 g/dL.

Table 8: Blood loss in group A (oral tranexamic acid) (n=12)

S. No	Intraoperative blood loss	Drain collection	Total blood loss	Number of transfusions given
1.	400 ml	300 ml	700 ml	1
2.	750 ml	500 ml	1250 ml	2
3.	250 ml	300 ml	550 ml	0
4.	500 ml	660 ml	1160 ml	0
5.	700 ml	500 ml	1200 ml	0
6.	2000 ml	100 ml	2100 ml	2
7.	400 ml	180 ml	580 ml	0
8.	600 ml	140 ml	740 ml	2
9.	700 ml	80 ml	780 ml	0
10.	500 ml	150 ml	650 ml	2
11.	600 ml	120 ml	720 ml	0
12.	400 ml	110 ml	510 ml	2

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Table 9: Blood loss in group B (intravenous tranexamic acid) (n=12)

S.no	Intra-operative Blood loss	Drain collection	Total blood loss	Number of transfusions given
1.	800 ml	400 ml	1200 ml	1
2.	500 ml	200 ml	700 ml	0
3.	400 ml	300 ml	700 ml	1
4.	650 ml	200 ml	850 ml	0
5.	450 ml	200 ml	650 ml	1
6.	600 ml	300 ml	800 ml	2
7.	550 ml	150 ml	700 ml	0
8.	450 ml	350 ml	800 ml	0
9.	700 ml	300 ml	1000 ml	1
10.	750 ml	180 ml	930 ml	1
11.	900 ml	160 ml	1060 ml	2
12.	550 ml	250 ml	800 ml	0

Table 10: Comparison of intraoperative blood loss (in ml) in both groups (n=24)

Group A	Group B	T value	P value
650.0 ± 450.8	608.3 ± 155.0	0.303	0.765

There was no significant difference in the amount of blood loss that occurred during the operation between the patients who had oral and intravenous tranexamic acid (p-value 0.765). In group A, the average amount of blood lost during the operation was 650 millilitres, whereas in group B, the amount of blood lost was 608.3 millilitres, which was not statistically significant.

Table 11: Drain collection (in ml) comparison in both groups (n=24)

Group A	Group B	T value	P value
261.7 ± 193.4	249.2 ± 80.1	0.207	0.838

There was no apparent difference in the amount of drain collection performed by any group (p-value of 0.838). The statistical significance of the difference in the mean value of drain collection between group A, where it was 261.7 ml, and group B, where it was 249.2 ml, was not determined.

Table 12: Total blood loss and blood transfusions needed comparison in both groups (n=24)

Groups	Group A	Group B	T value	P value
Total blood loss (ml)	911.6 ± 193.4	849.2 ± 168.0	0.447	0.659
Transfusions needed (units)	0.92 ± 1.0	0.75 ± 0.75	0.462	0.649

There is not a statistically significant difference between the two groups in terms of the total amount of blood lost or the number of transfusions that were required. The statistically insignificant difference between group A's mean total blood loss of 911.6 ml and group B's total blood loss of 849.2 ml was not significant. It was determined that there was no significant difference between the two groups when comparing the average number of units of blood transfusions required, which was 0.92 unit in group A and 0.75 unit in group B.

Discussion

Most major orthopaedic procedures cause considerable blood loss that increases morbidity and mortality, particularly in low-hemoglobin individuals. Transfusion rates for elective orthopaedic procedures range from 11% to 65%. Total Knee Replacement is prevalent in grade III/IV knee osteoarthritis patients. Massive surgeries reveal vast volumes of tissue, releasing enzymes. TPA stimulates fibrinolytic system.

An estimated 870 to 170 millilitres of blood are lost during TKA, and 50% of patients need blood transfusions. Blood transfusions for haemorrhage instances may save lives, but they are expensive in underdeveloped countries like India and might occasionally come with a number of risks. Even when transfusions are compatible, there is still a chance of febrile reactions, allergic reactions, blood-borne infections, circulatory overload, acid-base imbalance, electrolyte abnormalities, acute lung injury related to transfusion, delayed functional recovery, prolonged hospital stay, and death. Hypothermia and coagulopathy could be brought on by the packed red blood cells. As a result of their moral or religious convictions, some people reject blood transfusions. Therefore, it is best to limit blood transfusions and to only use them in emergency situations [6, 7, 8].

For total knee arthroplasty to be successful, effective intraoperative hemostasis is also necessary to stop the development of hematomas and minimise blood loss through suction drains. Adequate hemostasis is also required for the achievement of post-operative range of motion. After surgery, persistent bleeding can result in discomfort, wound hematomas, seroma formation, and arthrofibrosis, all of which can reduce the procedure's effectiveness. Therefore, it's crucial to limit blood loss during knee arthroplasty.

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To accomplish this, a variety of therapies, including controlled hypotensive anaesthesia and different blood salvage methods, have been developed over the past few decades. Methods for surgical biological hemostasis have been developed [8, 9, 10]. Several medical strategies have become more popular recently. Tourniquets, hemodilution, tissue-binding fibrin, intraoperative and postoperative autotransfusion, erythropoietin (EPO), iron therapy before surgery, flexibility of the operated knee joint in the early postoperative hours, and temporary drain closure are a few of these. But no established standard approach was discovered. EPO is expensive in developing nations like India, and patients find it difficult to adjust to iron supplements because of their severe gastrointestinal side effects. In patients with ischemic heart disease and cardiac insufficiency, hemodialysis, hypotensive anaesthesia, and the use of autologous blood transfusion are not permitted. Due to scarcity, high cost, and unfavourable side effects, some drugs have a finite number of applications. According to reports, a femoral plug application, maintaining knee flexion, and momentarily shutting the drain did not significantly reduce blood loss. Particularly in large surgeries like orthopaedic surgery, tranexamic acid is currently being explored as a potential treatment for achieving hemostasis [10, 11, 12].

The most effective method of administering TXA has been discussed. Studies on the effectiveness of intravenous tranexamic acid for minimising intraoperative and postoperative bleeding in patients undergoing total knee arthroplasty have been conducted in great numbers, but not enough has been done on the effectiveness of oral tranexamic acid. This study compared and contrasted two different tranexamic acid delivery techniques. A randomised controlled trial involving 12 TKA patients who received oral tranexamic acid and 12 TKA patients who received intravenous tranexamic acid was conducted to meet the objectives of the study. Both groups' intraoperative blood loss and blood that accumulated in the drain for two days were measured. Prior to and following surgery, the haemoglobin levels were assessed. Each patient's need for blood transfusions was recorded [12, 13, 14].

Because the average pre-operative haemoglobin in the oral tranexamic acid group was 11.5 +/-1.0 g/dl and the average pre-operative haemoglobin in the intravenous tranexamic acid group was 11.3+/- 0.5 g/dl, the correlation between the two groups was negligible (p-value 0.499). The requirement for blood transfusions is supported by the lower haemoglobin before surgery and in view of intraoperative blood loss.

Patients in the oral and intravenous tranexamic acid group experienced post-operative haemoglobin levels that were typically 9.5 g/dl and 9.8 g/dl, respectively; the correlation between the two groups (p-value 0.466) was not statistically significant. Haemoglobin levels fall following surgery because of blood loss during the procedure. The difference in the haemoglobin decline, which was 2 g/dl in one group and 1.5 g/dl in the other, was not very significant. A study by Surannavar *et al*. reported decrease of less than 1 mg/dl of hemoglobin in the tranexamic acid group in 12 out of 15 patients and in control group 13 of 15 patients had preoperative and postoperative Hb difference of more than 1 mg/dl. In a different non-randomized trial, Gupta *et al*. found that the tranexamic acid group experienced a mean haemoglobin drop of 2 mg/dl following surgery. Haemoglobin levels in the tranexamic acid group and the control group in a study by Guerreiro *et al*. were substantially different after 24 and 48 hours (24 Hour: $p > 0.05$ & 48 Hours: $p<0.05$) [14, 15, 16].

The average Hb decline in the IV TXA group, according to Chen *et al*'s findings, was 2.81 g/dL on average, which is similar with previous studies and shows how effective IV TXA is at preventing blood loss in TKA and THA. The effects of oral TXA in total joint arthroplasty have only been studied in a small number of trials, in addition to the IV TXA group. The mean Hb drop of 2.85 g/dL during the experiment demonstrated that oral TXA had beneficial blood-sparing effects. More than our group, the oral TXA group in Luo *et al*. RCT decreased. Hb by 3.48 g/dL. The oral TXA group likewise showed a 3.0 g/dL Hb drop in a study by Lee *et al*. The fact that their study only included individuals undergoing THA, which typically results in greater blood loss than TKA, may be the cause of this discrepancy. Additionally, we found that oral and intravenous TXA had the same effect on Hb decline, demonstrating that both therapies were equally effective at lowering TKA blood loss. In the studies by Sun *et al*., there were no differences in Hb decrease or overall blood loss between oral and IV TXA (p=0.64). The effects of oral and intravenous TXA on TKA and THA were comparable across numerous RCTs [16, 17, 18].

For Intraoperative bleeding during surgery study showed the average intraoperative blood loss was 608.3 ml in the intravenous tranexamic acid group and 650 ml in the oral tranexamic acid group. The average intraoperative blood loss following the administration of tranexamic acid was 433 ml, according a study by Gupta *et al*. According to a study by Surannavar *et al*., only 2 patients in the tranexemic acid group lost more blood than 600 ml as opposed to 8 patients in the control group.

In this experiment, the drain collections were 249.2 ml for the intravenous tranexamic acid group and 261.7 ml for the oral tranexamic acid group. In a study by Kerakkanavar *et al*., the tranexamic acid group's drain collection dramatically decreased (p0.001). The average drain collection in the pneumatic compression group was 446 ml compared to 293 ml in the tranexemic acid group. In research by Surannavar *et al*., 13 out of 15 had drain collections larger than 100 ml on the first postoperative day and 8 out of 15 in tranexmic acid group had drain collected less than 100ml. This present study also shown that the volume of drain collected did not differ statistically significantly, demonstrating that tranexemic

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acid administered orally and intravenously had the same effectiveness for reducing postoperative blood loss [19, 20].

560 patients receiving primary unilateral TKA were divided into 4 groups by Yuan *et al*. a control group, a topical group, an intravenous group, and an oral group. They discovered that when compared to the control group, each of the three TXA delivery techniques dramatically lowered drain output. Regarding drain blood loss, there was no discernible difference between oral TXA and IV TXA, which is consistent with our findings (p 0.05).

In our study, the total blood loss was 849.2 ml in the intravenous tranexamic acid group and 911.6 ml in the oral tranexamic acid group. Despite the fact that the intravenous group experienced less overall blood loss than the control group, this distinction was not statistically significant (p=0.447, NS). It reveals that tranexemic acid may often halt bleeding when administered orally equally as effectively as when administered intravenously. According to Gupta *et al*. study's the average blood loss was 433 ml.

Patients receiving oral tranexamic acid required an average of 0.92+/-1 transfusion units, while those getting intravenous tranexamic acid required an average of 0.75+/-0.75 units. With a p-value of 0.649, it was found that there was no difference between the two. This proves that whether tranexamic acid was given orally or intravenously, the number of blood transfusions required was the same. 6 blood transfusions in the tranexamic acid group and 17 in the pneumatic compression group in a study by Kerakkanavar *et al*. were statistically significant (p=0.003) [20, 21].

The study by Chen *et al*. indicates that both oral and intravenous TXA may considerably lower the risk of transfusions when compared to the control group. Additionally, there was no discernible difference in the transfusion rates between the oral and IV TXA groups, indicating that these two delivery strategies may be effective enough in TKA for blood sparing.

Conclusion

The effectiveness of oral tranexamic acid is comparable to that of intravenous tranexamic acid. In the process of minimising the amount of blood that is lost during total knee arthroplasty.

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Conflict of interest

None

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