DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20240418

Original Research Article

Assessment of the safety and efficacy of intravenous versus topical tranexamic acid in patients undergoing primary total hip and knee arthroplasty surgeries with respect to decreasing peri-operative blood loss and blood transfusion rates: a prospective and comparative study

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Received: 12 January 2024
Accepted: 13 February 2024

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ABSTRACT

Background: Synthetic antifibrinolytic agent like tranexamic acid has been increasingly used in Arthroplasty surgeries to decrease the peri-operative blood loss. The current study was undertaken to compare the efficacy between the intravenous and Topical route of TXA in deceasing the blood loss and transfusion rate in patients undergoing primary total hip and knee arthroplasty (THR and TKR) surgeries.
Methods: A total of 120 patients were enrolled in the study with 60 each undergoing THR and TKR surgeries with 30 each given TXA in IV and Topical routes. Outcomes were assessed in terms of mean 24 hours drain output, mean blood loss, mean drop in hemoglobin blood transfusion rate.
Results: The mean drain output was more in the IV group in both THR and TKR patients ($p>0.05$). The mean blood loss was more in the Topical group in both THR and TKR patients ($p>0.05$). The mean drop in hemoglobin was more in the Topical group, with the difference being significant in the THR patients ($p<0.05$) and being insignificant in TKR patients ($p>0.05$). In IV group 9 patients (15%) and in Topical group 25 patients (41.67%) needed blood transfusions, the difference being statistically significant.
Conclusions: Both IV and Topical routes of TXA are equally effective in decreasing the peri-operative blood loss and transfusion rates in patients undergoing primary arthroplasty surgeries, with IV route having slightly upper hand as compared to the Topical route.

Keywords: Tranexamic acid, Arthroplasty, Intravenous, Topical, THR, TKR, Hemoglobin, Blood transfusion

INTRODUCTION

Arthroplasty, a prominent surgical procedure in the realm of orthopedics today, presents a critical concern regarding peri-operative blood loss leading to potential anemia, as well as the associated risks related to transfusions, including hemolysis and immunosuppression. In addressing these challenges, the use of alternative approaches, such as the application of a synthetic antifibrinolytic agent known as tranexamic acid (TXA), has gained attention.[1-4]. Despite the widespread use of TXA, there remains an unresolved query concerning the optimal and safest route of administration. Hence, the present study was undertaken to conduct a comparative analysis between the efficacy of topically applied TXA and intravenously administered (IV) TXA. The primary

objective was to assess their respective abilities in mitigating blood loss and diminishing transfusion rates in individuals undergoing arthroplasty procedures. By examining the outcomes and effects of both topical and IV TXA administration, this study aims to provide comprehensive insights into the comparative effectiveness of these modes of application, aiding clinicians in making informed decisions about the most efficacious and safe method to manage blood loss and minimize transfusion-related risks in arthroplasty surgeries.

METHODS

The present study was a prospective and comparative study conducted in the Department of Orthopaedics at Bharat Ratna Doctor Babasaheb Ambedkar Municipal Hospital, Mumbai from July 2021 to December 2023, with prior approval taken from the institutional ethical committee. The study population consisted of 120 patients undergoing either Primary Total Hip Replacement (THR, N=60), or Primary Total Knee Replacement (TKR, N=60) surgeries for hip/knee arthritis respectively; after taking prior written informed consent.

Inclusion and exclusion criteria

All patients undergoing Primary THR or TKR were included in the study. Patients with history of allergy to TXA; pre-operative hepatic or renal dysfunction; cardio-respiratory compromise to undergo major surgeries; pre-operative Hb <10gm%; age >80 years or <40 years; previous history of thrombo-embolic events; any history of bleeding disorders, were excluded from the study.

All the patients were divided into 2 groups: Group A with those receiving TXA in intravenous route, who were further subdivided into Group AH (IV TXA in THR patients) and Group AK (IV TXA in TKR patients); and Group B with receiving TXA in topical route, who were further subdivided into Group BH (Topical TXA in THR patients) and Group BK (Topical TXA in TKR patients). In Group A, patients received intravenous (IV) TXA in two 1 gm doses. The initial IV dose was administered before the incision, while the second dose was given three hours after the first dose for both THR and TKR procedures. In Group BH (Topical TXA in THR), the standard posterior approach was employed. Surgical measures included standard cauterization of major bleeding points. During the procedure, the acetabulum was treated with a 20 ml solution containing 3 grams of tranexamic acid (TXA) per 100 ml of saline for 3-5 minutes before impacting the uncemented acetabular component. Subsequently, after the femoral canal preparation, a 20 ml TXA solution was introduced via a drain tube for 3-5 minutes before impacting the uncemented femoral stem. Post-implantation, routine repair of the external rotator and capsule was conducted. Closure involved typical procedures with the deep fascia, subcutaneous layers, and skin, utilizing a drain. An additional 60 ml of TXA solution was injected through the drain tube and left clamped for an hour before release, and the drain was removed the day after the surgery. In Group BK (Topical TXA in TKR), a standard medial parapatellar approach was utilized under tourniquet control. Post cementation and final placement of components, hemostasis was achieved upon tourniquet release. Subsequently, a deep drain was positioned, followed by closure of the arthrotomy and parapatellar incision. Following closure, a 3 gm TXA solution in 100 ml of normal saline was injected into the knee via the drain tube. The drain was clamped for an hour before release, and all drains were removed the day after the surgery.

The study's outcome measurements involved comprehensive assessments across multiple parameters. Firstly, the drainage output at the 24-hour mark was quantified using a beaker. Additionally, the number of patients necessitating transfusions due to a drop in Hemoglobin levels below 10 grams per deciliter (%Hb) was recorded. The analysis also included evaluating the decline in Hemoglobin levels post-surgery, calculated by subtracting the lowest Hemoglobin level observed after 24 hours with the pre-operative values. Moreover, the study meticulously documented and scrutinized various complications occurring during the hospital stay, encompassing symptomatic Deep Vein Thrombosis (DVT), Cerebro-vascular accidents, and Arterio-occlusive events, such as Myocardial Infarction (MI). Lastly, to ascertain the extent of blood loss following the procedures, the mean calculated blood loss was determined using the Nadler et al formula[5]. These parameters collectively served as essential indicators in evaluating the efficacy and safety of the different approaches implemented in the study.

Statistical analysis

All the data was collected in a Microsoft Excel spreadsheet. The qualitative data was expressed as a number. The continuous (quantitative) data was expressed as mean, standard deviation, and range. Comparison for significance for the qualitative data was done by Chi-square test and Fischer's exact test where needed, and for the quantitative data was done by student t-test (paired for intra-group and unpaired for inter-group). A p value of <0.05 was considered statistically significant.

RESULTS

During the study period, a total of 120 cases were admitted under the Orthopedics Department. Within this cohort, 60 cases each (50%) underwent total hip replacement and total knee replacement. Predominantly, the study comprised male subjects, accounting for 85 cases (70.83%), whereas 35 cases (29.16%) involved female patients. The mean age across all patients undergoing these procedures was calculated at 56.17±16.71 years; with the most common age group to get operated being 50-60 years (56.67%) followed by 60-70 years age group (20.83%). Out of 60 cases each undergoing THR and TKR, 30 cases

(50%) each were treated using Intravenous Tranexamic Acid (IV TXA), and Topical Tranexamic Acid (topical TXA). The observed mean drain output in the Intravenous Tranexamic Acid (IV TXA) TKR group (Group AK) was 247.21±102.56 ml, whereas in the Topical Tranexamic Acid (topical TXA) TKR group (Group BK), it was recorded as 218.46±110.19 ml.

Table 1: Depicts the distribution of the study patients according to age groups.

Age group (years)	N	%
40-50	14	11.67
50-60	68	56.67
60-70	25	20.83
70-80	13	10.83

However, statistical analysis indicated that this difference was not statistically significant (p>0.05). Additionally, the observed mean drain output in the Intravenous Tranexamic Acid (IV TXA) THR group (Group AH) was 284.41±125.74 ml, whereas in the Topical Tranexamic Acid (topical TXA) THR group (Group BH), it was recorded as 245.81±131.91 ml. The difference was statistically not significant (p>0.05). In both the Total Hip Replacement and Total Knee Replacement groups, the mean blood loss was comparatively lower in cases where Intravenous Tranexamic Acid (IV TXA) was administered compared to cases where Topical Tranexamic Acid (topical TXA) was used. However, upon statistical analysis, the differences in mean calculated blood loss in both groups were found to be statistically insignificant (p>0.05). Following the topical administration of Tranexamic Acid in both the Total Hip Replacement and Total Knee Replacement, there was a greater mean drop in hemoglobin compared to cases where TXA was administered intravenously.

Table 2: Depicts the comparison between the two groups according to the mean drain output.

Mean drain output			
Parameters	**IV TXA (Group A)**	**Topical TXA (Group B)**	**P value**
THR	284.41±125.74 ml	245.81±131.91 ml	>0.05
TKR	247.21±102.56 ml	218.46±110.19 ml	>0.05

Table 3: Depicts the comparison between the two groups according to the mean blood loss.

Mean blood loss			
Parameters	**IV TXA (Group A)**	**Topical TXA (Group B)**	**P value**
THR	731.92±365.28 ml	846.65±289.31 ml	>0.05
TKR	423.36±184.54 ml	481.52±163.55 ml	>0.05

Table 4: Depicts the comparison between the two groups according to the mean drop in hemoglobin.

Mean drop in hemoglobin			
Parameters	**IV TXA (Group A)**	**Topical TXA (Group B)**	**P value**
THR	1.47±0.64	2.56±0.81	<0.05
TKR	1.36±0.71	1.54±0.69	>0.05

Table 5: Depicts the comparison between the two groups according to the patients needing blood transfusions.

Patients needing blood transfusions			
Parameters	**IV TXA (Group A)**	**Topical TXA (Group B)**	**P value**
THR	8	21	<0.05
TKR	1	4	>0.05
Total	9	25	<0.05

This difference was statistically significant when compared between Group AH and Group BH (IV in THR vs. Topical in THR), with Group BH recording significantly greater mean drop in hemoglobin levels. However, the difference of mean drop in hemoglobin levels when compared between Group AK and Group BK (IV in TKR vs. Topical in TKR), was found to be statistically insignificant. Specifically, in Group B (Topical group), 25 patients (41.67%) required blood transfusions. However, notably, in Group A (IV group) only 9 patients (15%) required a blood transfusion; the difference being statistically significant (p<0.05). Of these 25 patients in Group B, 21 underwent THR while 4 underwent TKR; while out of 9 patients in Group A who needed blood transfusions, 8 underwent THR while only 1 patient undergoing TKR needed blood transfusion. On group wise comparison for the patients undergoing THR, it was found that patients treated with IV TXA and needing

blood transfusions were significantly less as compared to the patients treated with Topical TXA. However, for the patients undergoing TKR, it was found that patients treated with IV TXA and needing blood transfusions were though less as compared to the patients treated with Topical TXA, but statistically insignificant.

DISCUSSION

Total knee replacement and total hip replacement surgeries often involve considerable peri-operative bleeding, potentially leading to hematomas and acute anemia necessitating blood transfusions[6]. This issue has prompted an increased utilization of Tranexamic Acid to mitigate blood loss during orthopedic procedures. However, the optimal dosage and method of administration of TXA remain debated, with rare but possible side effects like nausea, headache, and hypercoagulation.[7,8] Recent research, examining plasminogen levels in peripheral blood, indicates that TXA's effectiveness is more pronounced at the surgical wound site than in the peripheral blood.[9] Despite numerous studies and trials on TXA, a consensus is lacking regarding its most effective regimen, dosage, safety, and administration method in THA and TKA surgeries. Therefore, this present study aimed to compare the effectiveness of topical versus intravenous TXA in reducing blood loss and transfusion rates during THR and TKR procedures.

Current study observed a predominance of male participants, consistent with prior studies conducted by Gomez-Barrena et al and Keyhani et al.[10,11] The majority of patients fell within the 50-60 years age group (56.67%) and 60-70 years age group (20.83%), with a mean patient age of 56.17±16.71 years. This mean age is however on higher side when compared to the study conducted by Patel et al, where the mean patient age was 42 years.[12] Out of 60 cases each undergoing THR and TKR, 30 cases (50%) each were treated using Intravenous Tranexamic Acid (IV TXA), and Topical Tranexamic Acid (topical TXA). Notably, in study conducted by Bobin et al, 653 patients received Intra-articular (IA) TXA treatment, while 655 patients received IV TXA treatment. Additionally in study conducted by Wei et al, involved 32 patients each treated with Topical TXA and IV TXA.[13]

Analysis of drain output revealed a slightly higher amount in the IV TKR group (247.21±102.56 ml) as compared to the Topical TKR group (218±110.19 ml), although this variance was not statistically significant. These findings align well with results from other studies done by Bobin et al, Abdel et al, Chen et al and Fu et al.[13-17] Similarly, the observed mean drain output in the IV THR group (Group AH) was 284.41±125.74 ml, whereas in the Topical THR group (Group BH), it was recorded as 245.81±131.91 ml. The difference was statistically not significant.

In our investigation involving both Total Hip Replacement and Total Knee Replacement groups, we observed that the mean blood loss was marginally lower when Intravenous Tranexamic Acid (IV TXA) was administered in comparison to Topical TXA.[13-17] However, these differences in blood loss were not deemed clinically significant. These outcomes are consistent with previous research findings.[11,13,15-19] Specifically, after applying Topical TXA in the THR group, we noted a more considerable decline in mean hemoglobin levels compared to cases where TXA was intravenously administered. This disparity in hemoglobin decline was statistically significant. Similarly, within the TKR group, while the mean drop in hemoglobin was slightly less in cases where IV TXA was used compared to Topical administration, this distinction did not reach statistical significance. These findings align with earlier research investigations.[11,13,16,17,20]

Looking at the necessity for blood transfusions, in Group B (Topical group), 25 patients (41.67%) required blood transfusions. However, notably, in Group A (IV group) only 9 patients (15%) required a blood transfusion; the difference being statistically significant ($p<0.05$). Of these 25 patients in Group B, 21 underwent THR while 4 underwent TKR; while out of 9 patients in Group A who needed blood transfusions, 8 underwent THR while only 1 patients undergoing TKR needed blood transfusion. These outcomes are in line with studies conducted by Bobin et al, Abdel et al, and Zyla et al.[13,15,19] Importantly, we did not observe any major post-operative complications such as myocardial infarction, symptomatic deep venous thrombosis, or pulmonary embolism in any of the studied cases. The current study intentionally excluded high-risk patients, specifically individuals with a history of Deep Vein Thrombosis (DVT), cardiac ailments, and renal diseases. The rationale behind this exclusion was to ensure a more focused examination of the effects of Tranexamic Acid (TXA) in a specific patient cohort.

Limitations

Our study had few limitations. First, our study had relatively small sample size. Secondly, the absence of a placebo group or control group might limit the ability to make direct comparisons and draw definitive conclusions regarding the efficacy of TXA in reducing blood loss during orthopedic surgeries. Thirdly, it's noteworthy that differences in the dosage and timing of TXA administration between the topical and IV groups might have contributed to the observed variations in blood loss and hemoglobin decline. These differences in administration methodologies could potentially influence the study outcomes. Also, a cost-benefit analysis was not conducted within the scope of this study. Future research endeavors should consider integrating this analysis to provide a comprehensive understanding of the economic implications of utilizing TXA in these surgical settings. Another aspect to acknowledge is that our study solely focused on symptomatic DVT cases. This approach might have led to an underdiagnosis of thrombotic events compared to studies where Doppler ultrasound was routinely employed, as demonstrated in the research

conducted by Wei and colleagues. Addressing these limitations and considering these points in future studies can potentially provide more comprehensive insights into the optimal use, efficacy, and safety of TXA across diverse patient groups undergoing orthopedic surgeries.

CONCLUSION

The present study suggests that both IV and topical tranexamic acid are effective and safe in reducing blood loss and preventing a significant drop in hemoglobin levels after total hip arthroplasty and total knee arthroplasty. While IV TXA appeared more effective in preventing hemoglobin drop in THA, other outcomes did not show a statistically significant difference between IV and Topical TXA in THA and TKA. No thromboembolic complications were observed, indicating the safety of both administration routes. However, due to the small sample size, further research is needed to compare the efficacy and safety of both methods, especially in patients with perceived contraindications to TXA. Larger, better-designed trials are necessary to establish the optimal dosage and delivery method for topical TXA in orthopedic surgeries.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Garg RN, Dubey R, Kundu S, Gupta D, Vaje SS. Assessment of the safety and efficacy of intravenous versus topical tranexamic acid in patients undergoing primary total hip and knee arthroplasty surgeries with respect to decreasing peri-operative blood loss and blood transfusion rates: a prospective and comparative study. Int J Res Orthop 2024;10:352-7.