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Safety and efficacy of topical tranexamic acid over intravenous tranexamic acid in reducing blood loss and transfusion rates in hip and knee arthroplasty

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ABSTRACT

Background: Tranexamic acid (TXA) is increasingly used in orthopedic surgery to reduce blood loss. Hence the present study was undertaken to compare the efficacy of topical TXA and intravenous (IV) TXA in reducing blood loss and transfusion rate in primary total hip and total knee arthroplasty.
Methods: Total of 31 cases undergoing either primary THA (23 cases) or TKA (8 cases) during a study period from June were enrolled. Outcome measures were drained output, transfusion rate, drop in haemoglobin (Hb) and blood loss measured by Nadler et al formula.
Results: In THR group, 12 (52.17%) cases and in TKA group, 3 (37.5%) cases were managed using IV TXA whereas 11 (47.82%) and 5 (62.5%) cases were managed using topical TXA in THR and TKR group respectively. The mean drain output was greater among IV TKR group (261.66±129.60 ml) as compared to topical TKR group (210±129.49 ml). In THR drain output in IV group was 216±104.08 ml. In both the groups, mean blood loss was lower in cases where IV TXA was administered as compared to topical TXA, ($p>0.05$). The mean drop in Hb was greater after topical administration of TXA in both the groups as compared to IV administered TXA. In THR group, 9 (39.13%) patients required blood transfusion. In sickle cell disease patients, we found more blood loss and drain output as compared to non-sickle cell disease (SCD) patients.
Conclusions: Both IV and topical TXA are clinically effective and safe in decreasing calculated blood loss, Hb drop after THA and TKA.

Keywords: TXA, Topical, Intravenous, Blood loss, Drain output, Transfusion, Haemoglobin, Sickle cell disease, Arthroplasty

INTRODUCTION

Arthroplasty is one of the most common surgeries in orthopedics today.[1] The perioperative blood loss (anemia) and transfusion related (hemolysis, immunosupression) risks is of major concern for patients undergoing arthroplasty. So, in order to reduce the risks associated with blood loss and transfusion, other method, such as use of a synthetic antifibrinolytic agent called TXA used.[2-4] But which route of TXA is safe and effective is not proven yet, so the present study was conducted to compare the efficacy of topical TXA and IV TXA in reducing blood loss and transfusion rates in arthroplasty.

METHODS

After obtaining institutional ethics committee approval and written inform consent from all the patients, this prospective randomized hospital based analytical study was conducted in department of orthopaedics government

medical college Nagpur, India from July 2018 to July 2020. Total 31 cases undergoing either primary THA or TKA during 24 months, that fulfilling the inclusion and exclusion criteria were included in the study.

Inclusion criteria

All patients undergoing primary TKR and THR were included in the study.

Exclusion criteria

Patients with history of allergy to TXA, preoperative severe hepatic or renal dysfunction, previous cardiac or respiratory disease, thrombocytopenia (if <1, 50,000), pregnancy; breast feeding, pre-op HB <10, patient age >80 years and patients with previous history of thrombotic events were excluded from the study.

Topical TXA in THA (Group B)- all THA was performed with posterior approach. Major bleeder was identified and cauterized in a standard fashion. After acetabular preparation the acetabulum bathed with 20 ml of TXA solution at a concentration of 3 gm TXA per 100 ml saline and kept for 3-5 min. Then uncemented acetabular component was impacted. After femoral canal broach preparation, 20 ml of TXA solution was placed in the femoral canal for 3-5 minutes with the help of drain tube. The uncemented femoral stem was impacted into the femoral canal. After the reduction of the final hip components, the external rotator and capsule was repaired in all cases. Deep fascia, subcutaneous and skin closure was performed in the standard fashion over a drain. Rest 60 ml of TXA solution injected in hip with the help of drain tube and the drain tube was clamped for 3-5 minutes. After 5 minutes, drain tube was removed and drain was not kept (Figure 1).

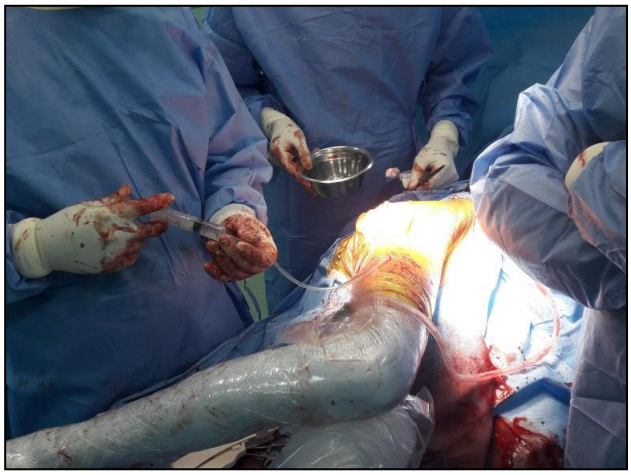

Figure 1: Topical use of TXA in THR.

Topical TXA in TKA (Group B)-all total knee arthroplasty was performed through standard medial parapatellar approach under tourniquet control. After cementation of all components and placement of final polyethelene the torniquet was released. Hemostasis then achieved followed by placement of deep drain and closure of the arthrotomy and parapateller incision. After closure, inject 3 gm TXA 100 ml of normal saline in knee with the help of drain tube. The drain was clamp for 1 hour and then be released. All drains were removed on the day following the surgery (Figure 2).

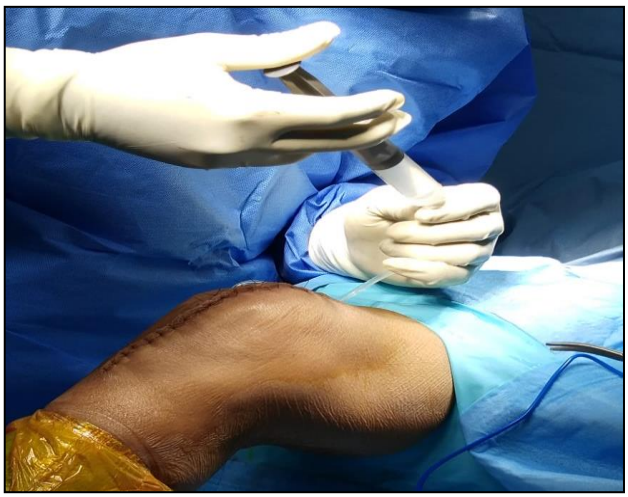

Figure 2: Topical use of TXA in TKR.

Intravenous TXA in THA and TKA (Group A)-patients in IV TXA group received TXA in two 1 gm doses. The first IV dose was given before the incision, and the second was given 3 hours after the first IV dose in THR and TKA.

Outcome measurements: drain output at 24 hours was measured with beaker, number of patients needs transfusion (if Hb <10 gm%), drop in Hb (prop Hb-lowest Hb) after 24 hrs of surgery and complication (Symptomatic DVT, Cerebrovascular accidents Arterio-occlusive events (such as MI) during hospital stay. The mean calculated blood loss was measured by Nadler et al formula after the procedures (Figure 3).[5]

Figure 3: Drain output measurement.

Data collection and analysis- the data was collected with the help of standard, pre-validated, semi-structured case record proforma. The collected data was entered with the help of Microsoft Excel spreadsheets and analyzed by using SPSS. Parametric tests were used for quantitative data (t test), while non-parametric tests were used for qualitative data (Chi-square test). Differences in observations with p less than 0.05 were considered as significant.

RESULTS

A total of 31 cases were admitted under department of orthopaedics at tertiary care center during the study period of two years. THR was performed among 23 cases (74.19%) whereas TKR was performed among 8 cases (25.80%). The majority of study subjects were males (23; 74.19%), and (8; 25.80%) patients were females. Most of the subjects belonged to 26-35 and 46-55 years of age group (25.80%), followed by 36-45 years (19.35%), with the mean age of patients was 46.67±13.48 years (Table 1).

Table 1: Distribution of study subjects according to their age.

Age group (Years)	Number	Percentage (%)
15-25	1	3.22
26-35	8	25.80
36-45	6	19.35
46-55	8	25.80
56-65	4	12.90
66-75	4	12.90
Total	31	100

In THR group, 12 (52.17%) cases were managed using IV TXA and 11 (47.82%) cases were managed using topical TXA while in TKR group, 3 (37.5%) cases were managed using IV TXA and 5 (62.5%) cases were managed using topical TXA, (Figure 4).

The mean drain output was greater among IV TKR group (261.66±129.60 ml) as compared to topical TKR group (210±129.49 ml) which was not statistically significant (p=0.47). In THR drain output in IV group was 216±104.08 ml.

In THR and TKR group, mean blood loss was lower in cases where IV TXA was administered as compared to topical TXA. In both the groups, mean calculated blood loss was statistically insignificant (p>0.05) as shown in (Table 2).

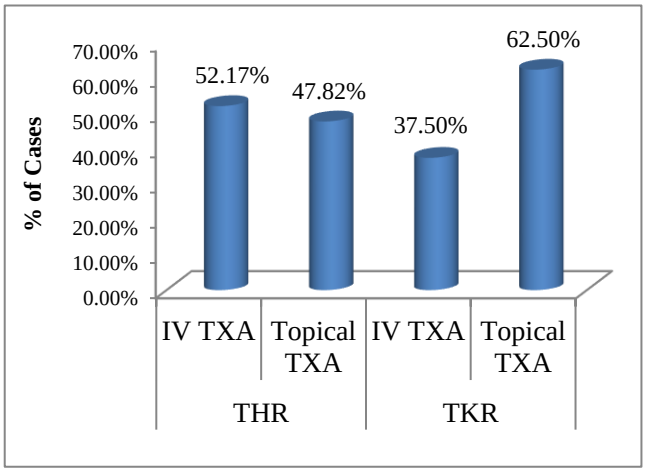

Figure 4: Mode of administration of TXA.

The mean drop in haemoglobin was greater after topical administration of TXA in both the groups (THR and TKR) as compared to IV administered of TXA. In THR group, 9 (39.13%) patients required blood transfusion while in TKR group, none of the patient required blood transfusion (Table 3).

We observed that 3 (9.67%) cases presented with history of SCD. The blood loss and drain output was comparatively lower in those patients who did not have SCD. The 66.66% cases with SCD required blood transfusion, while only 25% cases among the patients who did not have SCD required blood transfusion. Statistically only mean drain output and blood loss was significant, (p<0.05) (Table 4).

Table 2: Mean calculated blood loss.

Procedure	Mode of administration of TXA	Mean calculated blood loss	Min	Max	P value
THR	IV	765.41±441.16	443	2042	0.36
	Topical	819.09±244.9	474	1182	
TKR	IV	431.33±117.77	331	561	0.21
	Topical	491.4±81.69	386	580	

Table 3: Mean drop in haemoglobin and blood transfusion.

Procedure	Mode of administration of TXA	Mean drop in Hb	P value	No. of patients in whom blood transfusion done, (%)	P value
THR	IV	1.98±0.57	0.041	4 (33.33)	0.55
	Topical	2.98±0.84		5 (45.45)	
TKR	IV	1.63±0.70	0.24	0 (0)	-
	Topical	1.98±0.62		0 (0)	

Table 4: Distribution of outcome parameter according to presence of SCD.

Parameters	Sickle cell disease		P value
	Yes	No	
Mean drain output (ml)	366.66±152.75	220±105.65	0.023
Mean calculated blood loss (ml)	1158.33±783.18l	659.67±238.38	0.006
Mean drop in haemoglobin (mg/dl)	2.23±0.65	2.13±0.75	0.412
Blood transfusion (%)	2 (66.66)	7 (25)	0.13

DISCUSSION

TKA and THA are associated with significant peri-operative bleeding that can cause hematomas and sometimes acute anemia requiring blood transfusion with potential risks and costs.[6] To reduce this blood loss during orthopedic surgery TXA is increasingly used. However, the dosage and type of administration are still controversial, and possible side effects such as nausea, headache and hypercoagulation, although rare, may occur.[7,8] A study measuring the plasma levels of plasminogen in peripheral blood suggests that the effect of TXA is greater at the site of the surgical wound than in the peripheral blood.[9] Despite the numerous published studies and trials, there remains no consensus regarding the most effective regimen, dosage, safety and method of delivery of TXA in THA and TKA. Therefore, present study was carried out to compare the efficacy of topical TXA and intravenous TXA in reducing blood loss and transfusion rate in THA and TKA. There was male predominance observed in this study as similar to previous studies conducted by Gomez-Barrena et al and Keyhani et al.[10,11] The majority of patients belonged to 26-35 and 46-55 years of age group (25.80%) with mean age of patient was 46.67±13.48 years which is comparable with the study done by Patel et al where the mean age of patient was 42 years.[12]

In THR group, 52.17% cases were managed using IV TXA and 47.82% cases were managed using topical TXA. While in TKR group, 37.5% cases were managed using IV TXA and 62.5% cases were managed using topical TXA. In Bobin Mi et al study there were 653 patients treated with IA TXA, and 655 patients treated with IV TXA.[13] Also, in Wei et al study 32 patients each treated with topical TXA and IV TXA.[14] The drain output was greater among IV TKR group (261.66±129.49 ml) as compared to topical TKR group (210±129.49 ml) which was not clinically significant. These findings are correlated well with the other studies.[13,15-17]

In both THR and TKR group, mean blood loss was comparatively lower in cases where IV TXA was administered as compared to topical TXA which was not clinically significant. These results are in accordance with the previous studies.[11,13,15-19] The mean drop in haemoglobin was greater after topical administration of TXA in THR group as compared to IV administered TXA and difference was statistically significant. Similarly, in TKR group, mean drop in haemoglobin was comparatively lower in cases where IV TXA was administered as compared to topical TXA was administered and it was not statistically significant. These findings are correlated with the earlier studies.[11,13,16,17,20] We observed that in THR group 45.45% cases required blood transfusion where topical TXA was administered whereas 33.33% cases required blood transfusion where IV TXA was administered. In TKR group, none of the patient required blood transfusion. Our results are comparable with the study done by Bobin et al, Abdel et al and Zyla et al.[13,15,19] In SCD patients we found that more blood loss and drain output as compared to non SCD patient and also use of IV TXA in sickle cell patient was safe in this study. We did not report any major post-operative complications such as myocardial infarction, symptomatic deep venous thrombosis or pulmonary embolism.

Limitations

The current study excluded high risk patients such as patient with previous DVT events cardiac and renal diseases.

Dose and timing of administration of TXA different in topical and IV group which may cause of difference in blood loss and drop in haemoglobin.

Sample size was small and lacked of placebo group or control group.

No cost benefit analysis was done for this study; future studies should be design to include this also.

We only considered the symptomatic DVT. This may result in the under diagnosis of thrombotic events in this study as in other studies Wei and colleagues Doppler ultrasound routinely used.

Use TXA in sickle cell disease patients needs further large studies.

CONCLUSION

From the results of present study, it can be concluded that both IV and topical TXA are clinically effective and safe in decreasing calculated blood loss, haemoglobin drop after THA and TKA. However, IV TXA appear to be statistically effective than topical TXA in prevention of drop of haemoglobin in THA and rest outcome not statistically significant in THA and TKA. No thromboembolic complications were found in study, so both routes of TXA administration was safe. Sample size

was small so, more studies are needed to compare the efficacy and safety profile of topical and IV TXA, especially in patient with SCD and perceived contraindications to TXA. Also, larger and better designed future RCTs are required to establish the optimum dosage and method of delivery of topical use of TXA.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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