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A comparative study between intravenous alone and combined intravenous and intra-articular administration of tranexamic acid in primary total knee replacement patients

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ABSTRACT

Background: With the better understanding of the total knee arthroplasty, the number of patients with extremes of ages and advanced comorbidities undergoing total knee arthroplasty are increasing. The most common post-operative complication remains the blood loss. The intravenous use of tranexamic acid was initially thought to decrease the blood loos. Over the past years, intra-articular administration of Tranexamic acid is also being used to reduce the blood loss. Now there is an increasing trend to combine the intravenous and intra-articular route for tranexamic acid in patients undergoing total knee arthroplasty. There are very few studies that evaluates or compares the intravenous and combination of intravenous and intra-articular route of tranexamic acid in total knee arthroplasty patients.
Methods: Two Hundred and two patients with severe knee osteoarthrosis planned for total knee arthroplasty were selected in accordance to inclusion and exclusion criteria. Patients were divided into Group A and B and was administered with combination of intravenous and intra-articular tranexamic acid for Group A patients and intravenous tranexamic acid for Group B patients .The outcome was measured in terms of blood loss in post-operative day one calculated using classical Nadir Method.
Results: The blood loss were found to be 328.04±178.9 ml in Group A and 362.88±220.408 ml in Group B. The p value was found to be greater than 0.005 and hence the difference in post-operative blood loss in both group was not statistically significant.
Conclusions: There is no difference between the combination of Intra-venous Transexmic and Intra-articular Tranexamic acid when compared with intravenous Tranexamic acid in reducing blood loss in patients undergoing total knee arthroplasty.

Keywords: Blood loss, Intra-articular, Intravenous, Total knee arthroplasty, Tranexamic acid

INTRODUCTION

Total knee arthroplasty (TKA) has been found to be the most definitive and frequent surgical procedure in patients with osteoarthritis. However, it is strongly associated with heavy blood loss and consequently followed by a blood transfusion. The geriatric population who remains the major population who undergoes total knee arthroplasty is vulnerable to dangerous risk following blood loss during the procedure and subsequent adverse effects from blood transfusion. A study by Kim et al, from 2011-2018 in East Asian Population has shown drastic increase in patients above age of 70 years undergoing total knee arthroplasty.[1] In addition to post-operative blood loss, thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) developed in patients

undergoing TKA are another life-threatening complication. Tranexamic acid (TXA) was widely found to be effective in reducing blood loss by inhibiting fibrinolytic activity when taken intravenously and orally.[2,3]

Various approaches such as tourniquet, hypotensive anaesthesia and various medical treatments have been evaluated to make TKA an even safer procedure. A very recent approach is the use of TXA.[4] TXA is a hemostatic substance inhibiting the transformation of plasminogen to plasmin, therefore prohibiting fibrinolys is a reducing blood loss.[5]

Consequently, TXA is a prime candidate for minimizing cases of postoperative anaemia and ultimately decreasing transfusion rates. However, the optimal TXA dosage, whether TXA dosage should be weight based and the ideal timing and route of TXA administration are subjects of continuous contention with conflicting study findings present throughout the literature.[6,7]

The IV route of administration remains the enduring clinical standard, although more recent studies have indicated that topical administration (intra-articular IA) may be superior in limiting not only overt blood loss but also bleeding into the surrounding tissue.[8,9] In addition, IA TXA has been reported to reduce both inflammation at the surgical site and the risk of TXA's systemic side effects. IA administration of TXA does not affect artificial joint functor wear.[10]

While many studies have focused on the effectiveness of intravenous TXA reducing intraoperative and postoperative blood loss there is a need to evaluate the effectiveness of combining intra-articular and intravenous administration and its advantages over intravenous administration alone during TKA.

This study aims to compare the advantage of combining the intravenous and intra-articular administration of tranexamic acid in terms of blood loss with intravenous route of tranexamic acid in patients undergoing total knee arthroplasty.

METHODS

Ethical approval and informed consents

The present study was carried out after getting adequate approval from Institutional Ethical Committee of Pushpagiri Medical College, Thiruvalla. The study was carried out after attaining informed consent from all patients. The study was carried out in accordance with the international standard on clinical trials and good clinical practice regulations.

Inclusion criteria

All patients undergoing unilateral total knee arthroplasty under spinal epidural anaesthesia. Patients were included after explaining the details of the study and have given consent for the same. Patient were assured that their medical and personal details will not be shared with any third party

Patient population

This prospective case study included a total of 202 patients divided into Group A and Group B who underwent total knee arthroplasty in Pushpagiri Medical College, Thiruvalla between 2022-2024. Group A patients were administered with intravenously 1 g tranexamic acid given 1 hour prior to surgery and another 1 g 3 hours after 1st dose and intra-articularly 1.5 gm is given through drain after tight closure of joint capsule. Group B patients were administered with 1g tranexamic acid is given 1 hour prior to surgery and 2 more doses of 1g in 3 hours interval. Excluded patients include those with knee flexion deformity >20 dg, varus and valgus deformity >20deg, allergic to tranexamic acid, anemia- Hb <8gm/dl, severe cardiovascular and respiratory disorders, renal or hepatic disorders.

Outcome evaluation

The blood loss was calculated using a mathematical formula according to Hb (grams per litre), height, weight, sex. Patient blood volume (PBV) is calculated according to the classic method of Nadler and colleagues. For males: PBV= (366.9 h 3) + (32.19 w) +604.1 (ml). for females: PBV= (356.9 h 3) (33.08 w) +183.3 (ml) (h: height in metres, W: weight in kilograms).

Hb loss is estimated using the formula. Hb loss=PBV×(Hb i-Hbe) 0.001+Hb t (Hbi: Hb concentration before surgery, Hb e: Hb concentration on post-op day 1, Hb t: Amount of Hb transfused grams (one unit of red cell suspension was considered to contain 5 g/l of Hb). Blood Loss=1000×Hb loss/Hbi (ml).

Statistical analysis

Blood loss analysed and presented as mean and standard deviation for patients who underwent total knee arthroplasty. A p value of less than 0.05 was considered as statistically significant.

RESULTS

Table 1 displays demographic data. The mean age group of Group A was 63.78 years and Group B was 63.90 years. Out of 51 study patients, 41 were females in group A and 40 were females in group B. All patient were diagnosed with grade 4 osteoarthritis knee.

Pre-operative hemoglobin

The mean pre operative hemoglobin value of group A was 12.1922 gm/dl with a standard deviation of 1.096 gm/dl. The minimum hemoglobin in group A is 9.2 gm/dl and

maximum hemoglobin is 14.8 gm/dl pre-operatively. The mean pre operative hemoglobin value of group B was 12.2078 gm/dl with a standard deviation of 1.283 gm/dl. The minimum hemoglobin in group A is 9.2 gm/dl and maximum hemoglobin is 15.10 gm/dl pre-operatively.

Post-operative hemoglobin

The mean post operative hemoglobin value of group A was 11.0314 gm/dl with a standard deviation of 1.897 gm/dl. The minimum hemoglobin in group A is 9.8 gm/dl and maximum hemoglobin is 14.8 gm/dl pre-operatively.

The mean post operative hemoglobin value of group B was 11.0608 gm/dl with a standard deviation of 1.171 gm/dl. The minimum hemoglobin in group A is 9.2 gm/dl and maximum hemoglobin is 14.40 gm/dl pre-operatively

Post-operative blood loss

The mean blood loss in group A is 328.05 ml with a standard deviation of 178.90 ml. The range was 100 ml to 910 ml. The mean blood loss in group B is 362.88 ml with a standard deviation of 220.408 ml. The range was 100 ml to 850 ml.

Table 1: Demographic data (n=51).

Demographic data	Group A	Group B
Age (in years)		
Mean	63.25	63.9
Range	51-78	51-78
Sex (%)		
Male	80.4	78.4
Female	19.6	21.6

Table 2: Results (n=51).

Results	Group A	Group B
Pre-operative haemoglobin (gm/dl)		
Mean	12.19	12.2
Range	9.2-14.8	9.2-15.10
Post- operative haemoglobin (gm/dl)		
Mean	11.03	11.06
Range	9.8-14.8	9.2-14.40
Blood loss (ml)		
Mean	328.04	362.88
Range	100-910	80-850

DISCUSSION

This comparative study was done among 102 patients who underwent total knee arthroplasty in a tertiary care hospital in South Kerala with the objectives of comparing the effect of combining intravenous and intra-articular TXA in reducing blood loss and the incidence of blood transfusion comparison to intravenous TXA. There were 51 patients included in each group. In the present study, the mean age of the study participants was found to be 63.78±6.813 years in group A and 63.90±6.853 years in Group B. Majority of them were females (80.4% in Group A and 78.4% in Group B). The pre- operative haemoglobin in the present study was 12.192±1.09 gm/dl in Group A and 12.2078±1.283 gm/dl in Group B. There was no statistical difference between the 2 groups. All patients who underwent total knee arthroplasty had Haemoglobin above 9 gm/dl, thus no patients required blood transfusions pre-operatively. The blood loss in both groups were calculated using the classic method of Nadler and colleagues. The means were found to be 328.04±178.9 ml in group A and 362.88±220.408 ml in Group B. The p value was found to be greater than 0.005 and hence the difference in post-operative blood loss in both group was not statistically significant. This was contrast to aim of the present study.

The results of present study are not in agreement with randomized trial by Adravanti et al.[11] Their study in 2017 in 100 patients had revealed synergistic effect of intra-venous and intra-articular TXA had better reduction in blood loss than the intravenous route alone. The present study shows no difference in both groups. The quest to find the protocols to streamline the use of TXA in controlling blood loss in TKA has led Zhang et al, in 2019 to conduct a study in 150 people. His study showed the combination of IV and IA TXA reduced blood loss better than intravenous alone.[12] There are many studies in determining the ideal route of using TXA in TKA in controlling blood loss. The study by Amin et al from 2016-2018 showed no difference in IV and IA TXA.[13] This was in agreement with our present study that showed no added advantage of using combination IV and IA TXA. TXA remains Instrumental in reducing blood loss in TKA when used in

IV, IA or combination IA and IV routes.[9] TKA remains the ideal management of advanced knee osteoarthritis. There are many studies that aim that reducing blood loss in TKA as it remains the major complication of TKA. As the majority of the TKA population belongs to the geriatric population, blood loss can lead to major cardiac and respiratory complications. To counter act the severe blood loss associated with TKA, use of tourniquet or normalizing haemoglobin pre-operatively were all used by Orthopedicians. TXA remains the forefront pharmacological intervention to reduce blood loss in TKA patients.[10]

TXA when used intra-articular route can avoid the systemic side effects of intra-venous TXA. Intra-articular route can also reduce the local inflammation and thereby decreasing pain and increasing functional outcome. On the contrary, the intravenous route of TXA when given pre-operatively can reduce the blood loss during the surgery. It can reduce the operation time and reduce the overall blood loss. As many studies have proven the efficacy of both combination of IV and IA and IV route, there are number of studies that align with same result of the present study. In a study conducted by Buntting et al, there were no significant differences in blood transfusion and haemoglobin drop between the two methods of administration.

This study is limited by the number of study population when the scope of the study could be expanded to a larger population group. With advancement of robotic arthroplasty, the mean operation time could vary and this would affect the blood loss. With learning curve, the mean operation time of the surgeons could decrease and this was not considered for the study. There is multiple approach to the procedure with some group of surgeons opting not to use tourniquet while the majority of the surgeons make use of the tourniquet for the procedure. This can change the outcome of the study. Use of tranexamic acid in TKA will remain the main stay in reducing blood loss. There needs to be more studies with larger study groups to establish the ideal route of administration of TXA.

CONCLUSION

The study compared the effectiveness of the combination of intravenous and Intra articular route of TXA with intravenous TXA with regards to blood loss and the need for blood transfusion in patients undergoing TKA. For this study, we found that there is no significant difference between the two modes of administration of TXA. The blood loss in both study groups was found be similar. Thus, no mode of administration was found to be superior to other mode of administration. Therefore, there needs to be further research involving a larger group of study population to assess the merits and demerits of each route of administration of TXA.

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