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Estimation of efficacy on tranexamic acid in reducing peri-operative blood loss in patient undergoing hemiarthroplasty

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Abstract

Introduction: Hip fracture surgeries are associated with substantial blood loss, exposing patients to postoperative anemia. The severity of anemia is related to reduced functional recovery, which is related to long-term mortality. Patients undergoing hemiarthroplasty surgeries require 1 to 2 pints of blood transfusion post operatively. There are many transfusion related health hazards. Tranexamic acid is a less expensive pharmacological agent that interferes with fibrinolysis and reduces blood loss in hemiarthroplasty surgeries. The aim of this study is to evaluate the efficacy of intra-venous administration of tranexamic acid in patients who underwent hemiarthroplasty with regards to blood loss at peri and post-operative period.

Materials and Methods: Patients with fracture neck of femur, above 60 years who primarily presented to Emergency medical service medicine in our institution fulfilling the inclusion criteria were included in our study. After obtaining the informed consent, patients were grouped into two categories; group 1 and group 2. Group 1 intervention: Placebo- 50 ml of normal saline intravenously was administered 10 minutes before starting the surgery. Group 2 intervention: Study-Tranexamic acid -1500mg diluted in 50ml normal saline intravenously was administered 10 minutes before the surgery. Intra-operative blood loss was assessed by collecting the number of fully soaked mopping pads, gauze pieces and the quantity of irrigation fluid after subtracting the amount of saline wash. Post operatively the efficacy was assessed by evaluating the hemoglobin and packed cell volume values. The blood collected in the drain on day 1 and 2 were also analysed and compared between the control group and the study group.

Result: In our study we included 40 patients who had undergone hemiarthroplasty for neck of femur fracture. Intra operatively we did PRBC transfusion for 11 patients in the control group and 3 patients in the study group. Postoperatively 2 patients received PRBC transfusion in the control group and none of the patients received PRBC transfusion in the study group. The post surgery blood loss was also very minimal in the control group as compared to the study group.

Conclusion: In our study, there was a significant amount of blood loss reduction in tranexamic acid administered group when compared to the placebo group. Tranexamic acid was cost effective and safer when compared to blood components. Tranexamic acid was useful and effective in reducing intra-operative blood loss and reduces the need for blood transfusion post-operatively. Tranexamic acid should be considered for routine use in hemiarthroplasty surgery to decrease blood loss.

Keywords: Tranexamic acid, hemiarthroplasty, blood loss

Introduction

Femoral neck fractures are frequent injuries in a trauma centre and have a high incidence in the geriatric population^[1]. Paralleling trends of demographic data forecasts, their incidence will continue to increase in the near future. Especially in the elderly, neck of femur fractures is a significant healthcare problem. Therefore, definitive treatment for neck of femur fractures is essential. Osteoporosis is the major cause for the femoral neck fractures, hence along with the surgical management for fracture, medical management should also be provided for osteoporosis management. The World Health Organisation (WHO) has defined osteoporosis as, bone mineral density (BMD) falling -2.5 or below the standard deviations of the mean found in young adult women^[2].

At present, surgery is the mainstay of care for fracture neck of femur. Younger patients (20-50 years) are routinely treated by closed reduction and internal fixation (CRIF), the treatment of older patients with neck of femur fractures largely depends on multiple conditions such as patient's physiological activity, personal preferences and experience of the surgeon.

Globally, orthopaedic surgeons treat older (50+ years) patients similar to younger patients (20-50 years) by CRIF using cannulated cancellous screws or dynamic hip screw in contrast to reconstruction surgery such as hemiarthroplasty (unipolar and bipolar hip hemiarthroplasty) [3]. The goal of surgery is to provide stable, pain free, mobile joint. Hip fracture surgery will be associated with substantial blood loss, exposing patients to postoperative anaemia. The severity of anaemia is related to reduced functional recovery, which leads to long-term mortality [4].

Approximately half of the population undergoing surgery for hip fracture require erythrocyte transfusion with a mean of 3 units of red blood cell (RBC). Transfusion of allogeneic RBCs is not free of adverse events and has an increased risk of postoperative infections [5-7].

The aim of this study is to assess the efficacy of intra-venous administration of tranexamic acid in patients undergoing hemiarthroplasty with regards to blood loss at peri and post-operative period.

Methodology

This is a prospective observational study. It was conducted in a tertiary care centre in South India. We conducted our study from January 2016 till December 2018. We had a total of 40 patients in our study. The patients were selected based on the inclusion criteria. The inclusion criteria were patients above 60 years of age, neck of femur fracture planned for hemiarthroplasty who presented to the Emergency medical service. The exclusion criteria were patients who were on anti-coagulant therapy, coronary artery diseases / cerebrovascular accident/ uncontrolled hypertension, revision surgeries, neuro-muscular disorders and pathological fractures. After obtaining informed consent, these patients were then grouped into two categories group 1 and group 2. Patients were prospectively randomized, between the control and intervention group within each stratum by computer-generated permuted block randomization of sizes 2, 4, or 6 using SAS 9.4 which was pre-prepared (SAS Institute Inc., SAS 9.1.3 Help and Documentation, Cary, NC: SAS Institute Inc., 2002-2004) by a statistician. The trial ensured concealment of allocation as the Principle Investigator (PI) was provided with opaque, serially numbered sealed envelopes for the serially numbered eligible patients before baseline assessment. One envelope was opened by the principle investigator (PI) in the presence of the participant. A note inside the envelope invited the participants either to attend intervention or the standard practice.

Group 1 intervention

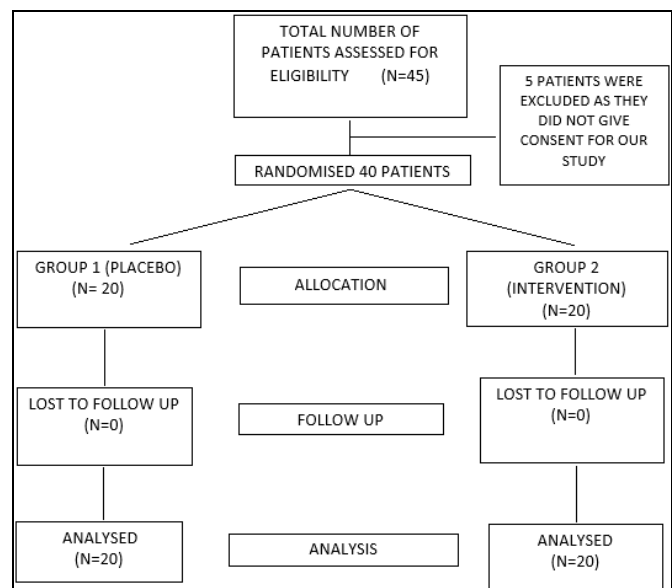
Patients in control group were administered with placebo, 50 ml of normal saline intra-venously administered 10 minutes before starting the surgery. Intraoperatively blood loss was assessed by collecting the number of fully soaked mopping pads and gauze pieces and the quantity of irrigation fluid subtracting the amount of wash given. Post operatively all patients were assessed by evaluating the hemoglobin and packed cell volume values. Blood collected in the drain on

day 1 and day 2 were also analyzed and were compared between the control group and the study group.

Group 2 intervention

Patients in the study group were administered with the constant dose of Tranexamic acid (1500mg diluted in 50ml normal saline) intra-venously administered 10 minutes before the surgery. Intraoperatively blood loss was assessed by collecting the number of fully soaked mopping pads and gauze pieces and the quantity of irrigation fluid subtracting the amount of wash given. Post operatively all patients were assessed by evaluating the hemoglobin and packed cell volume values. Blood collected in the drain on day 1 and day 2 were also analyzed and were compared between the study group and the control group.

The data obtained was entered in Microsoft Excel and analyzed in Epi Data analysis V2.2.2.184 software. The continuous variables age, hemoglobin values (pre and post-surgery), PCV values (pre and post-surgery), liters of suction fluid and washed fluid and drain amount were reported as Mean (SD). The categorical variables such as groups (those who received and not received tranexamic acid), gender, side of surgery, mode of injury, Garden's type of fracture, cement usage, type of prosthesis, number of units of blood transfusion done (pre, intra and post surgery), number of mopping pad and gauze pads used, were reported as proportions. The association between continuous variables and the groups (those who received and not received tranexamic acid) were assessed using independent t-test and the association between categorical variable and groups were assessed using Chi Square test or Fishers exact test. The p value of <0.05 was considered for statistical significance.



Algorithm for patient selection

A total of 40 patients with neck of femur fracture were included this study on the basis of pre-defined inclusion and exclusion criteria after informed consent. All patients were recruited through the EMS. These 40 patients, included in our study were randomised in two groups. The mean age in the control group was 65.3 years and in the study group was 68.9 years.

Table 1: Gender distribution of both groups

| Gender | Control group (N=20) | | Study group (N=20) | | Total number of the participants | P value |
|--------|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| Male | 7 | 35.0 | 11 | 55.0 | 18 | 0.633 |
| Female | 13 | 65.0 | 9 | 45.0 | 22 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 1 shows the distribution of gender, where the control group had 13 females as (65%) majority. While in the

study group there was a male preponderance of 11 patients forming 55% of the study group.

Table 2: Mode of injury among both groups

| Mode of injury | Control group (N=20) | | Study group (N=20) | | Total number of the participants | P value |
|----------------|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| Domestic fall | 18 | 90.0 | 17 | 85.0 | 35 | 1.000 |
| RTA | 2 | 10.0 | 3 | 15.0 | 5 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 2 shows the most common mode of injury in the control and study population. The most common mode of

injury in both the study groups was domestic fall.

Table 3: Cement used among participants of both groups

| Cement used | Control group (N=20) | | Study group (N=20) | | Total number of the participants | P value |
|-------------|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| No | 14 | 70.0 | 11 | 55.0 | 25 | 0.327 |
| Yes | 6 | 30.0 | 9 | 45.0 | 15 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 3 shows the usage of cement in both the groups. We used cement for 30 % of the patients (n=6) in

control group and 45% of patients (n=9) in the control group.

Table 4: Garden type among study participants of both groups

| Garden type | Control group (N=20) | | Study group (N=20) | | Total number of the participants | P value |
|-------------|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| Type I | 0 | 0.0 | 1 | 5.0 | 1 | 0.723 |
| Type II | 3 | 15.0 | 4 | 20.0 | 7 | |
| Type III | 13 | 65.0 | 11 | 55.0 | 24 | |
| Type IV | 4 | 20.0 | 4 | 20.0 | 8 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 4 shows the incidence of the type of Garden's classification in both the groups. Both the groups have

majority of type 3 fracture, 65% (n=13) in control group and 55% (n=11) in the study group.

Table 5: Number of transfusion done intra operatively among the two groups

| Number of blood transfusion done intra operatively | Control group (N=20) | | Study group (N=20) | | Total number of the participants | P value |
|--|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| 0 | 9 | 45.0 | 17 | 85.0 | 26 | 0.027 |
| 1 | 9 | 45.0 | 2 | 10.0 | 11 | |
| 2 | 2 | 10.0 | 1 | 5.0 | 3 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 5 shows the intra operative transfusion in both the groups. In the control group patients had 1 pint of packed red blood cell (PRBC) transfusion in 45% (n=9) of

cases and 2 pints in 10% (n=2) of cases, whereas in the study group only 10% (n=2) of cases had 1 pint of PRBC transfusion and 5% (n=1) with 2 pints of PRBC transfusion.

Table 6: Number of blood transfusion had done post operatively among both the groups

| Blood Transfusion Post-Operatively | Control Group (N=20) | | Study Group (N=20) | | Total Number of the Participants | P value |
|------------------------------------|----------------------|------------|--------------------|------------|----------------------------------|---------|
| | Number | Percentage | Number | Percentage | Number | |
| 0 | 18 | 90.0 | 20 | 100.0 | 38 | 0.349 |
| 1 | 1 | 5.0 | 0 | 0.0 | 1 | |
| 2 | 1 | 5.0 | 0 | 0.0 | 1 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 6 shows the post operative transfusion in both the groups. In the control group only 2 patients had PRBC transfusion. One patient had 1 pint and another patient had 2

pints of PRBC transfusion. None of the patients received PRBC transfusion post surgery in the study group.

Table 7: Type of prosthesis of both the groups

| Type of prosthesis | Control Group (N=20) | | Study Group (N=20) | | Total number of the participants Number | P value # |
|--------------------|----------------------|------------|--------------------|------------|--|-----------|
| | Number | Percentage | Number | Percentage | | |
| Bipolar | 17 | 85.0 | 15 | 75.0 | 32 | 0.429 |
| AMP | 3 | 15.0 | 5 | 25.0 | 8 | |
| Total | 20 | 100.0 | 20 | 100.0 | 40 | |

The above table 7 shows the implants that we used in both the study groups. We used Bipolar prosthesis for majority of the cases in both the groups. Implants were chosen based on the

age and the physiological activity of the patients before the fracture.

Table 8: Postoperative Hemoglobin & PCV values of participants of both groups

| | Control Group (N=20) | | Study Group (N=20) | | P value |
|---------------------------------------|----------------------|--------------------|--------------------|--------------------|---------|
| | Mean | Standard deviation | Mean | Standard deviation | |
| Post-operative Hemoglobin values g/dl | 10.4 | 1.2 | 10.6 | 1.1 | 0.694 |
| Post-operative PCV | 31.0 | 3.4 | 30.5 | 2.8 | 0.622 |

The above table 8 shows the post operative hemoglobin and the PCV values of the the control and the study group. The

mean hemoglobin value in the control group was 10.3 and 10.6 in the study group.

Table 9: Amount of drain collected in day 1 & day 2 among both the groups

| | Control group (N=20) | | Study group (N=20) | | P value |
|---------------------|----------------------|--------------------|--------------------|--------------------|---------|
| | Mean | Standard deviation | Mean | Standard deviation | |
| Drain day one in ml | 222.5 | 85.2 | 160.5 | 55.4 | 0.010 |
| Drain day two in ml | 74.2 | 14.4 | 74.0 | 16.7 | 0.960 |
| Total drain in ml | 296.7 | 93.7 | 234.5 | 66.2 | 0.020 |

The above table 9 shows the amount of drain collected on post operative day 1 and day 2. In the control group a mean value of 222.5ml was obtained on day one and 74.2ml on day 2. In the study group a mean value of 55.4 was obtained on day one and 16.7ml on day 2.

synthetic derivative of amino acid lysine that exhibits an antifibrinolytic effect through reversible blockade of the binding sites in lysine on plasminogen, thereby reducing the conversion of plasminogen to plasmin (fibrinolysis) enzyme that degrades the fibrin clots and fibrinogen. Its biological half-life is 2 hours. Elimination is through renal, via glomerular filtration; 90% of the dose is excreted within 24 hours after intravenous administration of 10mg/kg. It acts as a competitive inhibitor of plasminogen and a noncompetitive inhibitor of plasmin at higher concentrations. The mechanism of action is similar to that of aminocaproic acid but tranexamic acid is around 10 times more effective *in vitro* than aminocaproic acid.

Discussion

Neck of femur fractures are common in older age group for which hemiarthroplasty is the widely preferred surgical option. This procedure involves extensive soft tissue release and medullary reaming leading to excessive blood loss. Various studies have shown the efficacy of i.v tranexamic acid in the control of blood loss following hemoiarthroplasty, total hip replacement and total knee replacement. It is a

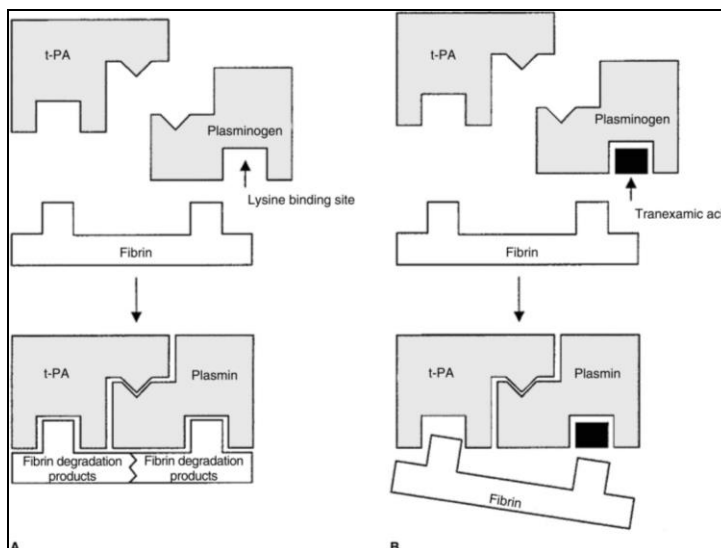


Fig 1: Tranexamic Acid Binding Pathway

Tranexamic acid binds readily than aminocaproic acid to both strong and weak receptors of the plasminogen molecule in a ratio corresponding to the difference in potency between the compounds. Tranexamic acid does not show any effect at a dosage of 10mg per ml of blood, but when it is titrated at a dose more than 10mg per ml, it helps in the prolongation of thrombin time.

After i.v administration of 1gm, the plasma concentration time curve shows triple the exponential of decay in the terminal elimination phase with a half-life of about 2 hours. The initial volume is distributed in 9 to 12 litres. Renal excretion is the main route of elimination through glomerular filtration. The entire renal clearance is equal to the plasma clearance (110 to 116 mL/min) and more than 95% of the drug dose is excreted as unchanged drug in the urine. On administration of 10mg per kg body weight of i.v tranexamic acid, there will be an elimination of 90% of the drug in 24 hours.

The antifibrinolytic concentration of tranexamic acid in blood serum is for 7-8 hours, in joint fluid serum for about 3 hours and in other tissues for around 17 hours [8-11].

There is an increased risk of renal insufficiency due to accumulation by tranexamic acid. In case of upper urinary

tract bleeding, patients can develop clot formation and might obstruct the ureter due to tranexamic acid infusion. Venous and arterial thrombosis or thromboembolism has also been reported in patients managed with tranexamic acid. There are also other studies with eye related complications such as central retinal artery and central retinal vein obstruction. Patients with a past history of thromboembolic events are more prone for venous or arterial thrombosis. Tranexamic acid is contraindicated concomitantly with factor IX complex concentrates or anti-inhibitor coagulant concentrates, as there is an increased chance for thrombosis.

Patients with disseminated intravascular coagulation, who require treatment with tranexamic acid, must be under strict supervision of a physician experienced in treating this disorder. There is no clear evidence of mutagenic activity in several *in vitro* and *in vivo* test systems. The common side effects of tranexamic acid are nausea, vomiting, dizziness, diarrhea, vision changes, seizures [8-11].

In our study we included 40 patients (n=40) who underwent hemiarthroplasty. The mean age of patients who underwent hemiarthroplasty with tranexamic acid was 68.9 and without tranexamic acid was 65.3.

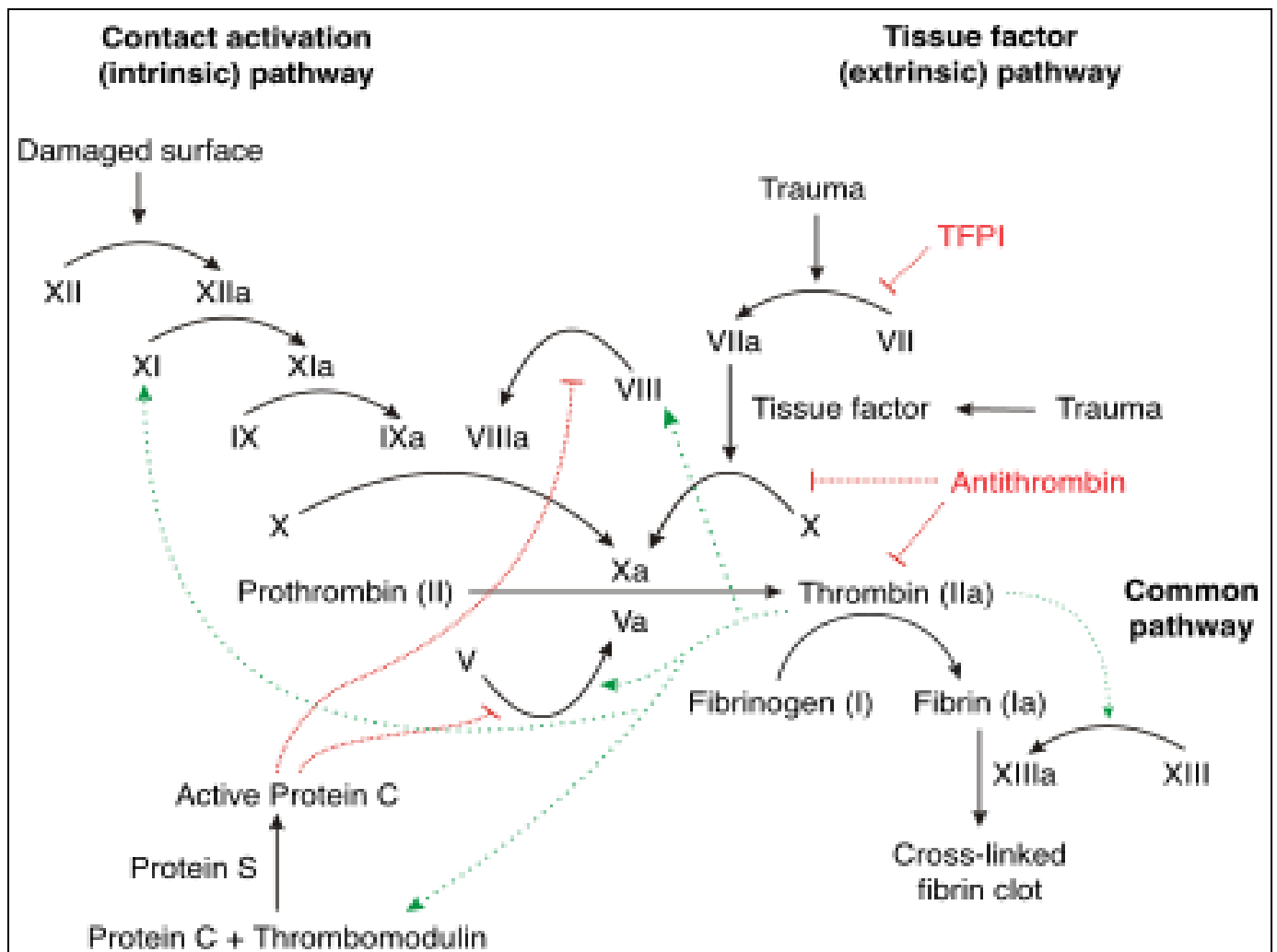


Fig 2: Normal Coagulation Pathway

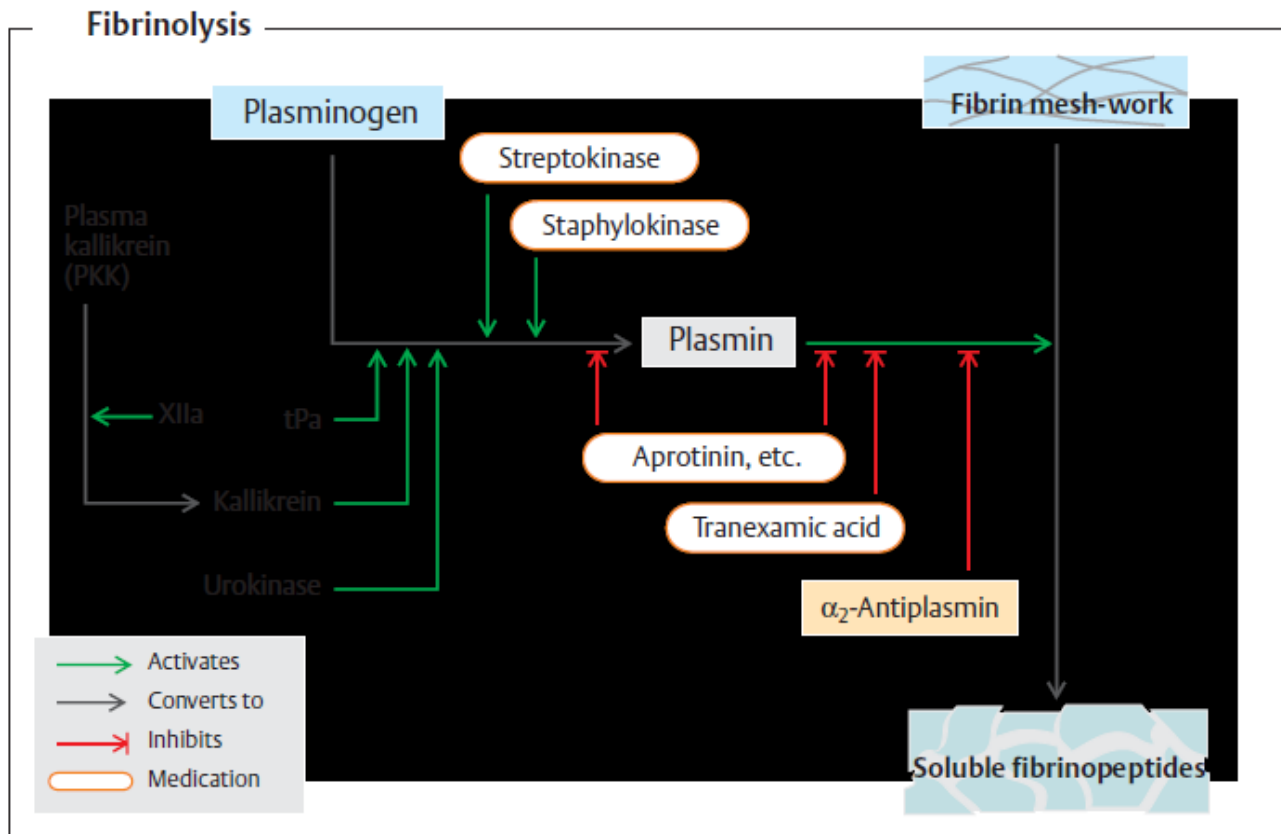


Fig 3: Action of Tranexamic Acid in Fibrinolysis Pathway

In our study 11 patients were transfused with PRBC intra operatively in the control group whereas only 3 patients from the study group received intra op transfusion and 2 patients from the control group also received post-operative transfusion while the study group did not receive transfusion post operatively. In a study by Zufferey *et al.* [12], out of 57 patients from tranexamic acid group and 53 patients from the placebo group, 24 patients received transfusion from the tranexamic acid group and 32 patients from the placebo group. In a similar study by Mohib *et al.* [13], from 50 patients in each group, 9 (18%) patients from the study group required transfusion whereas in the control group 21 (42%) patients received transfusion ($p=0.009$).

The post-operative hemoglobin in our study was 10.4 g/dl in the control group and 10.6g/dl in the study group. In a study by Mohib *et al.* [13] the post-operative hemoglobin values in the control group was 8.9 +/-2.4g/dl, and 10.2 +/-2.4g/dl in the study group ($p=0.007$).

In our study we had an average post-operative blood loss of 296.7ml in the control group and 66.2ml of blood loss in the study group. In a study by Dinakar Rai *et al.* [14], out of 17 patients from the study group had 207.05ml of post-operative blood loss, and 329.68ml of blood loss in the control group.

In our study we did not experience any complications. In study by Olli L Korkala *et al.* [15], 3 complications occurred in the study group, 1 patient had superficial wound infection, 1 patient developed transient dyspnea on post operative day 3 and 1 patient developed pyelonephritis on post operative day 30 in the study group. In the control group 1 patient developed bladder retention which was managed with supra pubic catheterization and another patient developed acute gluteal eczema. In another study by Zufferey *et al.* [12], the infection rate was 25% in the study group and 38% in the control group. In a study by Wang *et al.* [16], out of 124 patients, they were categorized into 3 groups. These three

groups were divided in 1:1:1 ratio. First group was placebo group, second group was 10mg/kg i.v tranexamic acid infusion group and third group was 15mg/kg i.v tranexamic acid infusion group. In the second group 1 patient developed asymptomatic venous thromboembolism. We did not experience any complications in our group.

Conclusion

In our study there was significant reduction in the amount of blood loss in tranexamic acid administered group when compared to the placebo group. Tranexamic acid was useful and effective in peri-operative blood loss and reduces the need for blood transfusion post-operatively. Tranexamic acid can be considered for hemiarthroplasty surgery to decrease blood loss.

Limitations in this study

- Small sample size.
- No randomization was done.
- Single centre study.
- Multicentric large studies have to be carried out to improve the outcome of results.

References

1. Ossendorf C, Scheyerer MJ, Wanner GA, Simmen H-P, Werner CM. Treatment of femoral neck fractures in elderly patients over 60 years of age - which is the ideal modality of primary joint replacement? *Patent Saf Surg.* 2010; 4(1):16.
2. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. *World Health Organ Tech Rep Ser.* 1994; 843:1-129.
3. Meta-analysis comparing arthroplasty with internal fixation for displaced femoral neck fracture in the elderly.

- PubMed - NCBI [Internet]. [Cited 2017 Nov 29]. Available from:
<https://www.ncbi.nlm.nih.gov/pubmed/19552922>
4. Lawrence VA, Silverstein JH, Cornell JE, Pederson T, Noveck H, Carson JL. Higher Hb level is associated with better early functional recovery after hip fracture repair. *Transfusion (Paris)*. 2003; 43(12):1717-22.
 5. Eriksson BI, Bauer KA, Lassen MR, Turpie AG. Steering Committee of the Pentasaccharide in Hip-Fracture Surgery Study. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med*. 2001; 345(18):1298-304.
 6. Klein HG, Spahn DR, Carson JL. Red blood cell transfusion in clinical practice. *Lancet Lond Engl*. 2007; 370(9585):415-26.
 7. Carson JL, Altman DG, Duff A, Noveck H, Weinstein MP, Sonnenberg FA *et al*. Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair. *Transfusion (Paris)*. 1999; 39(7):694-700.
 8. Mohseni K, Jafari A, Nobahar MR, Arami A. Polymyoclonus seizure resulting from accidental injection of tranexamic acid in spinal anesthesia. *Anesth Analg*. 2009; 108(6):1984-6.
 9. Murkin JM, Falter F, Granton J, Young B, Burt C, Chu M. High-dose tranexamic Acid is associated with nonischemic clinical seizures in cardiac surgical patients. *Anesth Analg*. 2010; 110(2):350-3.
 10. Bruce-Brand R, Dragomir R, Baker J, Harty J. Cerebrovascular infarction following bilateral total knee arthroplasty and tranexamic acid administration. *Acta Orthop Belg*. 2013; 79(3):351-4.
 11. Furtmüller R, Schlag MG, Berger M, Hopf R, Huck S, Sieghart W *et al*. Tranexamic acid, a widely used antifibrinolytic agent, causes convulsions by a gamma-aminobutyric acid (A) receptor antagonistic effect. *J Pharmacol Exp Ther*. 2002; 301(1):168-73.
 12. Zufferey PJ, Lanoiselee J, Chapelle C *et al*. Intravenous tranexamic acid bolus plus infusion is not more effective than a single bolus in primary hip arthroplasty: a randomized controlled trial. *Anesthesiology*. 2017; 127(3):413-422.
 13. Mohib Y, Rashid RH, Ali M, Zubairi AJ, Umer M. Does tranexamic acid reduce blood transfusion following surgery for inter-trochanteric fracture? A randomized control trial. *J Pak Med Assoc*. 2015; 65(11-3):S17-S20.
 14. Shiva, Dinakar Rai, Shyam Sundar. Effect of the Tranexamic Acid in Reducing the Blood Loss in the Orthopaedic Surgery. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* e-ISSN: 2279-0853, p-ISSN: 2279-0861. 2015; 14(2)VIII:22-26.
 15. Raimo Niskanen O, Olli Korkkala L. Tranexamic acid reduces blood loss in cemented hip arthroplasty: A randomized, double-blind study of 39 patients with osteoarthritis. *Acta Orthopaedica*. 2005; 76(6):829-832.
 16. Wang F, Zhao KC, Zhao MM, Zhao DX. The efficacy of oral versus intravenous tranexamic acid in reducing blood loss after primary total knee and hip arthroplasty: A meta-analysis. *Medicine (Baltimore)*. 2018; 97(36):e12270.