Original Research Article

Study of Different Dosage of Tranexamic Acid During Cardiac Surgery on Cardiopulmonary Bypass: Incidence and Clinical Outcome

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Abstract

Objective: We conducted this clinical study to compare standard dose of Tranexamic acid with moderately high dose of Tranexamic acid in controlling bleeding and reducing transfusion requirement in primary elective mitral valve replacement surgery with cardiopulmonary bypass.
Methods:A total of 60 American Society of Anesthesiology (ASA) grade II and III patients undergoing elective mitral valve replacement surgery.**Group I** received low dose Tranexamic acid 12.5 mg/kg iv loading dose over 20 mins after anaesthesia induction followed by iv infusion 4mg/kg/hr until chest closure.**Group II** received moderately high dose Tranexamic acid 25mg/kg iv loading dose over 20 mins after anaesthesia induction followed by iv infusion 8mg/kg/hr until chest closure.**Results:** The group received moderately high dose of tranexamic acid has less bleeding compared to group which received standared dose of tranexamic acid. The groups were similar with respect to post op ventilatorysupport,blood transfusion requirement and post op nausea and vomiting.**Conclusion:** The current study establishes moderately high dose of tranexamic acid were more effective to prevent intra- op and post- op bleeding in patients undergoing mitral valve replacement surgery.

Keywords: transfusion,tranexamic acid

Introduction

Excessive perioperative bleeding is still an important risk of contemporary cardiac surgery under cardiopulmonary bypass. This bleeding tendency is associated with surgical procedure itself and is due to changes in homeostasis resulting from extra corporeal circulation. Different pharmacologic strategies have been used to reduce bleeding and need for donor blood transfusion. Perioperative bleeding remains a problem in cardiac surgery[1].
The risk of transfusion of allogenic blood products on short and long-term outcome is well documented[2,3]. Even in first time cardiac surgery the transfusion requirement is alarmingly high.Thus a multimodal approach to reduce allogenic blood transfusion is warranted.The nonspecific proteinase inhibitor aprotinin and specific plasmin inhibitor tranexamic acid both reduce intra and post-operative bleeding in cardiac surgical patients and thus, allogenic blood requirement[4].Antifibrinolytic agents are used during cardiac surgery to minimize bleeding and reduce exposure to blood and blood products

Methods and Material

Inclusion Criteria

- NYHA class II and III
- Patient of ASA grade II and III.
- Patient scheduled for elective MVR.
- Patient with EF > 40%.
- Patient who was not on Anticoagulant therapy

Exclusion Criteria

- Re-do surgery.
- DVR surgery/associated valve and CABG surgeries.
- Patient with EF < 40%.
- Patient with history of CVA and previous seizure activity.
- Patient who was already on Anticoagulant therapy.
- Known or suspected allergy to drug(tranexamic acid)

Type of Study

Prospective, Randomised, double blind study.
The study was conducted at the Department of Anaesthesiology, Gandhi Medical College and Hamidia Hospital, Bhopal. After study approval from Institutional Ethics Committee, written informed consent was obtained from all patients after explaining the nature of the clinical study and the drugs to be used,60 patients were selected for this study.
All patients underwent pre-anaestheticcheck up. Investigations included CBC, urine(R&M), blood sugar, coagulation profile,LFT, RFT,serum electrolytes,ECG,CXR,and echocardiography.
After enrolment in the study, patients were divided randomly into 2 groups of 30 each by a computer generated table.
Group I received low dose Tranexamic acid 12.5 mg/kg iv loading dose over 20 mins after anaesthesia induction followed by iv infusion 4mg/kg/hr until chest closure.
Group II received moderately high dose Tranexamic acid 25mg/kg iv loading dose over 20 mins after anaesthesia induction followed by iv infusion 8mg/kg/hr until chest closure. No antifibrinolytics were added to the priming solution in either group
Anticoagulation was achieved with 300IU/kg heparin before Cardio pulmonary bypass ,aiming for an ACT > 480 seconds.On termination

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of,Cardio pulmonary bypass heparin was reversed with protamine in 1:1 ratio, which was titrated to achieve an ACT< 140 secs or near baseline level after weaning patient from CPB.After CPB, all blood remaining in the extracorporeal circuit was returned to the patient without centrifugation and washing. None of the patients underwent postoperative auto transfusion of mediastinal tube drainage.Uniform transfusion criteria during the intraoperative period were adhered to in all patients.Chest tube drainage was measured upto 24 hours postoperatively.

Statistical Analysis

In the statistical analysis of our study, continuous variables were presented as mean for parametric data and median if the data was non parametric or skewed. Student t -test was applied for calculation of statistical significance whenever the data followed normative distribution.Categorical variables were expressed as frequencies and percentages,nominal categorical data between the groups were compared using chi-square test or fisher's exact test as appropriate. p <0.05 was taken to indicate a statistically significant difference.minitab version 17 was used for computation of statistics.

Results

The age of all patients in Group I ranged between 17 and 60 years, while in Group II, the age ranged between 24 to 63 years.

Mean age of both groups were comparable. (Group I 36.37 ± 12.03 yrs; Group II 39.23 ± 9.25 yrs; p=0.31)

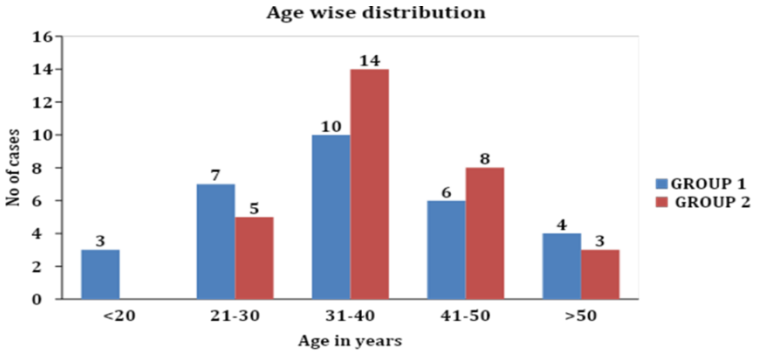

Fig 1: Age wise distribution

In the study, group i and ii were comparable in terms of bsa (1.46 ± 0.13 m^2 vs 1.43 ± 0.16 m^2 ; p = 0.4307). Therefore, no significant difference found between the groups.

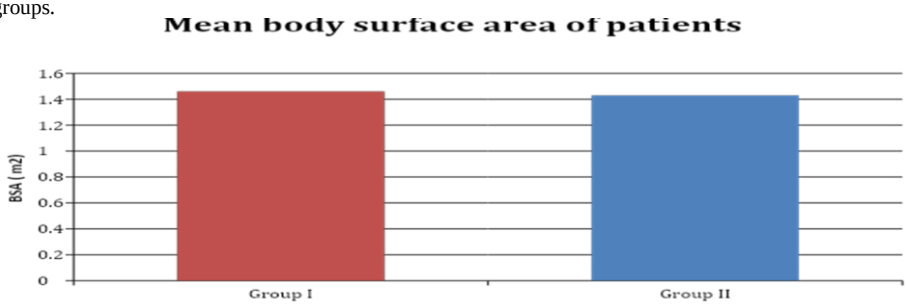

Fig 2: Mean body surface area of patients

There Was No Statistical Difference Between Group I And Group Ii In Terms Of Distribution According To Asa Ps Grade (P=0.68) And Nyha Functional Class (P=0.26)

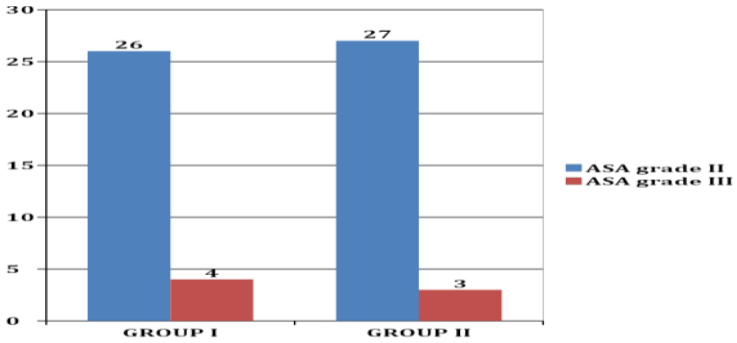

Fig 3: ASA Grading

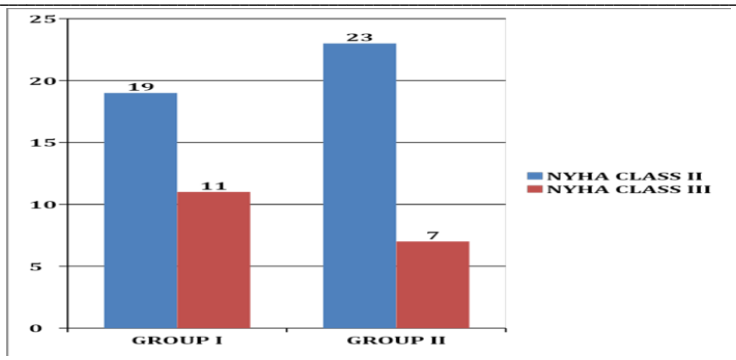

Fig 4: NYHA Class

When duration of cardiopulmonary bypass was compared between the two groups, no statistical difference was seen between group i and group ii. (122.53 ± 20.41mins vs 116.8 ± 18.13mins ; p = 0.25)

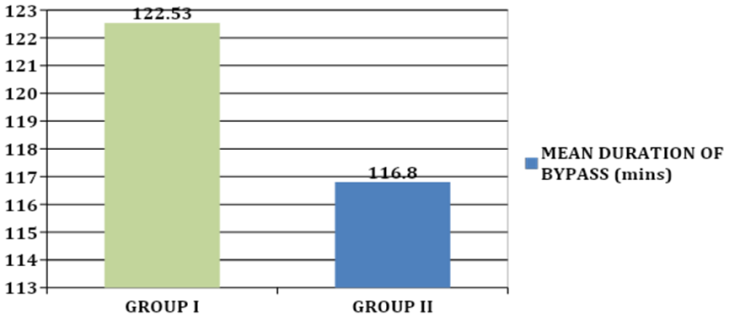

Fig 5: Mean duration of Bypass

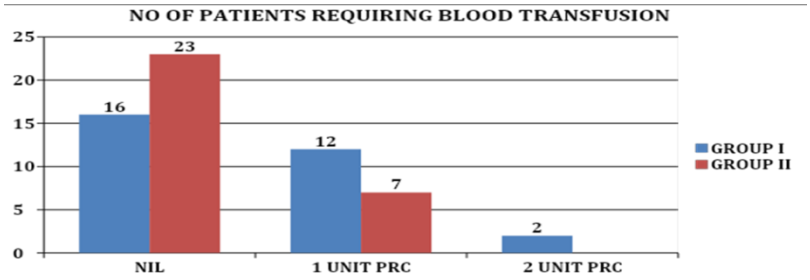

Fig 6: Number of patients requiring Blood Transfusion

Table 1: Blood Transfusion required

Transfusion	Group I	Group II	P Value
NIL	16	23	0.058
1 Unit PRC	12	7	
2 Unit PRC	2	0	
Total	30	30	

Table 2: Mean Blood Loss

Group	Mean Blood Loss	± Std. Deviation
1	386.07	122.30
2	318.33	55.34

The Mean Blood Loss of group 1 was 386 ml while it was much lower in group 2 [318.3ml] , There was significantly more blood loss in group 1 [P=0.008]

Discussion

One of the most common complications of cardiac surgery is excessive bleeding mainly caused by fibrinolysis induced by cardiopulmonary bypass (CPB) during and after cardiac surgery**.** During CPB, activation of coagulation factors induces the release of tissue plasminogen activator from endothelial cells a consequent hyperfibrinolysis.Excessive post-operative bleeding during cardiac surgery occurs in 3.6% of patients undergoing cardiac surgery and increases to 11% in those requiring more complex operations **,**Five to seven percent of patients lose more than 2 litres of blood within the first 24 hours after surgery, between 1% and 5% require re-operation for bleeding . Re-operation for bleeding increases hospital mortality

3 to 4 fold**(** Keogh and Kinsman 2004), substantially increases post-operative hospital stay and has a sizeable effect on health care costs.

Tranexamic acid is a synthetic lysine analogue that is similar to epsilon aminocaproicacid(EACA) but ten times more potent. The mechanism of action of TXA is similar to that of EACA. The usual dose for CPB patients is 1.0 g to 10.0 g intravenously. Despite a variability in dosage, there is little doubt that the 10-g dosage scheme is efficacious. In our study we used 1g (20mg/kg) of TXA. In a meta-analysis Laupacis and Fergusson found that TXA significantly decreased the proportion of cardiac surgical patients transfused. It had no effect on perioperative MI or reexploration, but these variables were not prospectively evaluated. In repeat operations, TXA is of particular benefit[5].Shore-Lesserson and coauthors demonstrated that TXA decreased blood loss and reduced transfusion by 33% in patients undergoing repeat cardiac surgery[6]Even without the requirement for re-operation, blood loss frequently leads to transfusion of allogenic blood products, which exposes patients to the risk of transfusion-related adverse effects, including allergic reactions, transfusion errors and blood-borne infections (particularly HIV and hepatitis)[7].Nevertheless, re-exploration is a strong risk factor associated with increased operative mortality and morbidity, including sepsis, renal failure, respiratory failure and arrhythmias. Concerns about transfusion safety, blood product shortages and increasing blood bank costs have generated an increasing interest in adopting risk-limiting strategies for post-operative bleeding. Therefore, antifibrinolytic agents are used during cardiac surgery with CPB to prevent excessive blood loss during and after surgery and to minimize transfusion requirements.Three antifibrinolytic agents have been used in this indication aprotinin, and two lysine analogs, Tranexamic acid and aminocaproic acids (EACA). A meta-analysis of 138 randomized, controlled clinical studies showed that blood loss sparing with any of these agents is approximately 300ml although the number of patients requiring transfusion is decreased tranexamic acid acid (TA) exerts its antifibrinolytic effect through the reversible blockade of lysine-binding sites on plasminogen molecules.Although its use is common,the optimal mode of its administration is still under discussion.

The withdrawal of aprotinin from the market has increased use of Tranexamic acid to reduce peri and post operative bleeding during cardiac surgery with Cardipulmonary bypass (CBP), and highlighted the need for an optimal dose regimen[8].

In a randomized clinical trail Horrow et al[9] reported that high doses were unnecessary for reducing blood loss and that a 10mg/kg bolus dose dose followed by 1mg/kg/hr for 12 hrs was effective and sufficient to decrease post -operative bleeding.The timing of TXA therapy has been examined by several authors. In a study bythem they found that, TXA given before the initiation of CPB decreased chest-tube drainage by 30% during the first 12 hours postoperatively and decreased the transfusion rate from 41% to 22%. Large doses were not beneficial. Administration of TXA after CPB or bleeding becomes established is a controversial practice that could lead to prothrombotic complications.A more recent study comparing the regimen of Horrow et al.with a higher dose (loading dose of 6.6 mg/kg followed by 6 mg/kg/hr and a 40 mg priming in CPB tubing)showed that postoperative mediastinal blood loss and transfusion requirement did not significantly differ between groups. Conversely, Karski et al[10]reported the superiority of a single dose of 100 mg/kg compared with 50 mg/ kg to decrease postoperative blood transfusion. Nevertheless, it is difficult to compare these studies because of differences in the administration of TA (bolus vs. bolus followed by continuous infusion).

However there is growing concerns about the safety of tranexamic acid[11]its massive use since aprotinin discontinuation has highlighted its weakness, especially with regards to neurological morbidity[12].Seizures are now a well known adverse event of Tranexamic acid There have even been reports of higher mortality and lower efficiency with Tranexamic acid than with aprotinin. In our study, we are discussing about pharmacologic strategies and so our study was conducted with the aim of comparing the two doses of tranexamic acid and its outcome on peri-operative,post operative bleeding and patients transfusion requirement in elective mitral valve replacement surgery after CPB[13,14]

Conclusion

The use of Tranexamic acid in moderately high dose i.e.25mg/kg i. v. bolus and 8 mg/kg/hr during surgery in mitral valve replacement is more effective than normal dose of Tranexamic acid.

Conflict of Interest: Nil Source of support:Nil

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