



ORIGINAL RESEARCH PAPER

Anaesthesiology

COMPARISON BETWEEN EPSILON AMINOCAPROIC ACID AND TRANEXAMIC ACID IN REDUCING POSTOPERATIVE BLOOD LOSS IN VALVULAR HEART SURGERIES

KEY WORDS: Post-operative bleeding, Epsilon Aminocaproic Acid, Tranexamic Acid

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ABSTRACT

This study was done to compare the effects of Epsilon Aminocaproic Acid (EACA) and Tranexamic Acid (TXA) in reducing postoperative blood loss in adult patients of ASA Grade III and IV, undergoing valvular heart surgeries on Cardiopulmonary Bypass (CPB). Patients were randomly divided into 3 Groups A, B and C of 30 each. Group A received Normal saline (placebo), Group B received EACA 100 mg/kg over and Group C received TXA 10 mg/kg over 15 min. These 3 groups were comparable in terms of age, sex, CPB time. Postoperative data showed that cumulative blood loss was significantly greater ($P < 0.05$) in the control Group A, as compared to Group B and C. Between Groups B and C, there was no statistically significant difference in blood loss at 24 hours post-operatively. There were no re-explorations in any groups. No complications associated with these drugs were found in this study.

A. Introduction

The excessive blood loss after cardiac surgery is a major problem in surgeries performed on a cardiopulmonary bypass.¹ Cardiopulmonary bypass (CPB) affects the haemostatic balance and predisposes patients to an increased risk of microvascular bleeding.² Blood contact to non-biological components of the CPB circuit activates coagulation, inflammation, fibrinolysis and injury to the cellular components of blood despite heparinization.³ Excessive postoperative bleeding may lead to surgical re-exploration thus increasing morbidity and mortality.

Antifibrinolytic drugs prevent primary fibrinolysis and preserve platelet function by preventing platelet activation. The most commonly used antifibrinolytic agents are synthetic lysine analogs Epsilon Aminocaproic Acid (EACA) and Tranexamic acid (TXA). These are small molecular weight synthetic antifibrinolytic of the amino-carboxylic acid. They saturate the lysine binding sites of plasminogen and tissue plasminogen activator thus displacing it from the fibrin surface and inhibiting the proteolytic action of the serine-histidine enzyme site of plasminogen/plasmin.⁴

TXA is 7-10 times more potent than EACA and plasma half-life of both is 80 to 120 min. Both TXA and EACA have shown efficacy to reduce post-operative blood loss during cardiac operations.⁵ The aim of this study was to establish which drug is better in decreasing the postoperative blood loss and requirement of blood products.

B. Materials and Methods

Ninety patients aged between 18 and 60 years, admitted to Sri Sathya Sai Institute of Higher Medical Sciences, Puttaparthi – Andhra Pradesh, undergoing valvular heart surgeries were included in the study. A prospective, controlled, randomised, single blinded study was conducted with the approval of study protocol by the hospital ethical committee. Patients were randomly divided in three groups of Group A (Normal saline – placebo: Control group), Group B (Epsilon Aminocaproic Acid) and Group C (Tranexamic Acid).

- **I. Inclusion criteria**
- ASA - Grade III and grade IV
- Age - Between 18 years to 60 years
- Sex - Both male & females
- Patients with valid informed consent
- Patient scheduled to undergo elective single valve replacement surgery on CPB

• **II. Exclusion criteria**

- Patient refusal to participate in the study
- ASA grade I and II
- Patients undergoing emergency surgery
- Patients with history of renal failure or neurological events.
- Patients receiving platelet inhibitors like aspirin, clopidogrel or

heparin infusion.

- Pregnant and Lactating women
- Redo surgeries

All the patients underwent thorough pre-anaesthetic evaluation on the day prior to surgery. Written informed consent was obtained from each patient before the procedure. Patients were randomly divided in following groups.

Group A: 30 ml of Normal Saline (placebo) diluted to 50 ml by Ringers Lactate solution.

Group B: 100 mg/Kg of EACA, diluted to 50 ml by RL solution.

Group C: 10 mg/Kg of Tranexamic Acid diluted to 50 ml by RL solution.

After induction of anaesthesia the patients were infused the first dose of 50 ml of prepared solution as per above mentioned group in the peripheral line over 15 minutes. Once on CPB, same doses of drugs were repeated second time. Once the protamine reversal was complete, the patients were again infused with the same doses of drugs third time over 15 minutes in the peripheral line. Time when the protamine reversal was complete and time when the sternum was closed was noted. This gave the time for sternal closure. All surgeries were performed by same surgical team.

In ICU, Activated Clotting Time (ACT) was repeated at 6th hour, along with platelet counts for all patients and noted. If the ACT was > 140 , protamine was given according to institute's protocol. Chest tube drainage and use of blood and blood products in first 24 hours postoperatively was noted.

Analysis of variance (ANOVA) was used to find the comparability of study parameters among three groups of patients, Post-hoc Tukey test was used to find the significance pair wise. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale among groups. The quantitative data were expressed in terms of mean \pm standard deviation. The P values < 0.05 were considered significant.

C. Observation and Results

Patient characteristics (age, sex and weight) were similar in all three groups and they were comparable. In Group A (78.87 ± 7.62 minutes), Group B (82.90 ± 8.59 minutes) and Group C (83.03 ± 8.18 minutes), there was no statistically significant difference in CPB time ($P = 0.085$).

The mean sternal closure time (Figure – 1) in Group A was 51.50 ± 4.69 minutes which was more as compared to 39.67 ± 7.46 minutes in Group B and 40.03 ± 7.57 minutes in Group C which was statistically significant ($P < 0.001$) although the difference in mean sternal closure time between Group B and Group C was statistically insignificant.

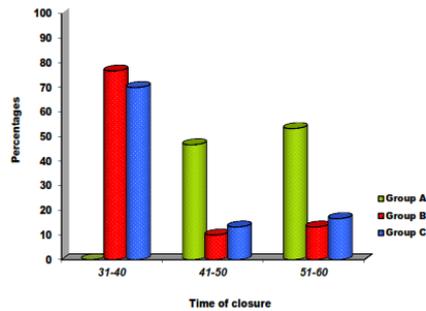


Figure - 1 : Sternal closure time

There was statistically significant ($P < 0.001$) higher requirement of Whole Blood transfusion (Figure – 3) postoperatively among the patient of Group A (325.00 ± 63.4 ml) compared to Group B (231.25 ± 48.53 ml) or Group C (233.75 ± 35.83 ml). There was no statistically significant difference between Group B and Group C ($P > 0.05$).

The usage of Fresh Frozen Plasma (Figure – 3) was higher in Group A (220.00 ± 32.07 ml) but the difference was not statistically significant as compared to Group B (192.00 ± 23.88 ml) or Group C (190.00 ± 20.82 ml). There was no statistically significant difference between Group B and C.

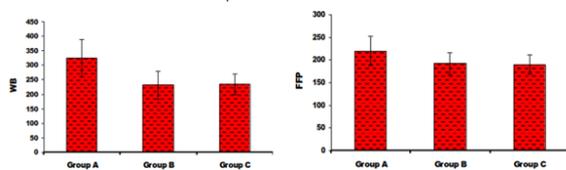


Figure - 3: Usage of Whole Blood & Fresh Frozen Plasma

In this study, there were no re-explorations observed in any of the three groups.

A.Discussion:

Antifibrinolytic therapy using EACA and TXA provide a pharmacological means for reducing postoperative blood loss and transfusion requirements. The present study was undertaken to compare the efficacy of these two drugs in patients undergoing valve surgeries on CPB.

This study shows that mean sternal closure time required was significantly more ($P < 0.001$) in Group A when compared with Group B or C. Similar findings were observed in a study conducted by Chauhan, Gharde, Bisoi, Kale & Kiran (2004)¹ and in a study by Ravindranath, Raghuram, Reddy, Rajeev & Sarma (2002)⁶ on patients undergoing open heart surgeries on CPB, statistically significant difference in chest closure time was found among EACA group (102 ± 23.1 min) and Control Group 135 ± 29.0 min ($P < 0.01$).

At 6th hour postoperatively, this study showed a significant statistical difference in the ACT among the three groups (Group A 134.73 ± 7.33 seconds, Group B 126.93 ± 7.66 seconds and Group C 125.20 ± 8.90 seconds; $P < 0.05$) but in the study by Chauhan et al. (2004)¹ no significant statistical difference was found between the three groups.

Platelet counts measured at 6th hour postoperatively were preserved in all the three groups with no significant statistical difference between them, which excludes the platelet related causes of bleeding in these patients. Similar results were seen in other studies.^{1,6,7}

Brown, Birkmeyer & O'connor (2007)⁸ observed that EACA resulted in 240 mL less blood loss ($P < 0.001$) and TXA resulted in 285 mL less blood loss ($P < 0.001$). Del Rossi, Cernaianu, Botros, Lemole & Moore (1989)⁹ using a low dose of EACA found a significant decrease in mediastinal drainage (617.2 ± 43.9 ml) in EACA group as compared to (83.2 ± 23.2 ml) control group ($P < 0.05$). Vander Salm et al.¹⁰ also reported a reduction in chest

tube drainage in patients undergoing cardiac surgery on CPB, who received EACA prophylactically as compared to the group receiving Placebo ($P < 0.05$). Horrow et al.¹¹ studied TXA in a prophylactic manner prior to skin incision for primary CABG surgery and observed 12 hour post-operative blood loss of 496 ml in the TA group compared to 750 ml in the placebo group. But in contrast, a study by Ghavidel et al. (2009)¹² blood loss was more in Placebo group as compared to EACA and TXA group, the difference was not statistically significant ($p=0.55$).

In this study, there was statistically ($p < 0.001$) significant more loss of blood in chest tube drainage for 24 hours postoperatively between the control group (675.33 ± 64.69 ml) and EACA group (344.83 ± 63.10 ml), TXA group (339.33 ± 58.93 ml). There was no statistically significant difference between EACA group and TXA group. In a meta-analysis by Ferraris et al. (2007),¹³ there were statistically significant reductions in transfusion requirement in patients receiving EACA or TXA.

In this study, there were no re-explorations for any non-surgical bleeding in all three groups. However, in a study of Del Rossi et al. (1989)⁹ showed that the patients, who receive EACA, had a less incidence of exploration as compared to Control group. Katsaros, Petricevic, Snow, Woodhall, & Van Bergen (1996) observed that as compared to 4.7% patients of the control group, only 0.96% of the patients in TXA group required exploration for excessive bleeding. However, this difference was statistically insignificant ($P > 0.05$).

B.Conclusion:

From this study, it can be concluded that Epsilon Aminocaproic Acid and Tranexamic Acid both are equally effective in patients undergoing valve surgeries on Cardiopulmonary Bypass and their use is associated with decreased post-operative bleeding, decreased use of blood and blood products.

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