A Comparative Study between Tranexamic Acid and Epsilon-Amino-Caproic Acid in Reducing Post-Operative Bleeding in Patients Undergoing on Pump CABG Surgeries

Rajeev Nair, Satish Kumar Mishra*, Parli Raghavan Ravi and Avanish Bhardwaj

Department of Anesthesiology and critical care Command hospital Airforce, Bangalore, India

*Corresponding author: Satish Kumar Mishra, Department of Anesthesiology and critical care Command hospital Airforce, Bangalore, India, E-mail: mdsatish08@gmail.com


Received date: November 09, 2020; Accepted date: November 23, 2020; Published date: November 30, 2020

Abstract

The amount of strain that cardiac surgery exerts on blood bank services is an example that emphasizes the need for multimodal blood conservation strategy. The most common factor which is being attributable to increased bleeding after cardiac surgery is hyperfibrinolysis. Therefore the use of antifibrinolytics during high risk cardiac surgery becomes inevitable. Commonly used antifibrinolytic include Tranexamic Acid (TA) and Epsilon-Amino-Caproic Acid (EACA). The aim of our study was to compare the effectiveness of both TA and EACA in reducing post-surgical bleeding in on-pump CABG surgeries and to assess the post-operative complications associated with its use. Material and Methods After obtaining informed written consent, approval of ethics and research committee patients who were scheduled for on-pump CABG were included in the study. Patients were divided into two groups randomly by using a computer generated randomized block design namely group TA (n=40) and group EACA (n=40). TA group received tranexamic acid at a dose of 10 mg/kg IV over 20 min at the time of induction then 1-2 mg/kg in CPB prime followed by 1 mg/kg/hour infusion during surgery. Group EACA received EACA in a dose of 100 mg/kg/IV over 20 min at the time of induction then 5-10 mg/kg in CPB prime followed by 10 mg/kg/hour infusion during surgery. Patients were assessed for blood loss and were monitored for fibrinogen level and D-dimer levels, Re-exploration and post-operative complications. Result Primary outcomes like bleeding at 4 hours, there was no significant difference between the groups but when total bleeding at 24 hours was compared there was a significantly lesser bleed in group TA group compared to group EACA (p=0.0022).The requirement of PRBC in group TA was for 3 patients, whereas in EACA group 4 patients required PRBC (p>0.05).There was no significant difference in the rate of post-operative complications between the groups (p>0.05). Conclusion from our study we concluded that both TA and EACA effectively inhibits fibrinolysis during on pump CABG surgery and thus results in decreased post-operative bleeding. When compared between the two, TA was slightly better with respect to post-operative bleeding at 24 hours. Our study also re-emphasized the fact that neither of the...
post-operative bleeding[5,6]. Similarly EACA is a synthetic lysin analog which reduces the rate of plasmin formation and further decreases the degradation of fibrin to fibrin degradation product (FDP) [7]. Apart from this EACA also has a platelet sparing action which leads in inhibition of plasmin mediated platelet injury [8].

Both TA and EACA have been shown to decrease post-operative bleeding associated with CPB. However there are no large studies comparing the effectiveness of both drugs in patients undergoing on-pump CABG surgeries. The aim of our study was to compare the effectiveness of both TA and EACA in reducing post-surgical bleeding in on-pump CABG surgeries with regards to the amount of blood loss at 4 hours and 24 hours as the primary outcome. The secondary outcome of our study included the rate of transfusion of Packed Red Blood Cell (PRBC), Fresh Frozen Plasma (FFP) and platelets, re exploration rates, post-operative D-dimer and fibrinogen levels.

Materials and Methods

After obtaining informed written consent, approval of ethics and research committee patients who were scheduled for on-pump CABG were included in the study. This study was carried out between June 2019 to February 2020. Patients with concomitant valvar heart disease, recent Myocardiac Infarction (MI<4 wks) Ejection Fraction<40%, Preexisting neurological, pulmonary or hepatic dysfunction were excluded from the study. Patients were divided into two groups randomly by using a computer generated randomized block design namely group TA (n=40) and group EACA (n=40). In both the group under strict aseptic precaution under local anesthesia a wide bore peripheral IV cannula, right radial artery cannulation and right femoral artery cannulation was done for continuous hemodynamic monitoring. Anesthesia was induced with Inj etomidate (0.2 mg/kg), Inj Fentanyl (3-5 ug/kg) and Inj Rocuronium (0.8-1 mg/kg). After induction of patient right internal jugular vein cannulation was done with 7.5 Fr triple lumen catheter and PA catheter was inserted. Anesthesia was maintained with air and oxygen (50%), sevoflurane (1%-3%) and Inj Atracurium (0.5-1 mg/Kg). After sternotomy and heparinization CPB was established once ACT was >420 Sec. TA group received tranaxamic acid at a dose of 10 mg/kg/IV over 20 min at the time of induction then 1-2 mg/kg in CPB prime followed by 1 mg/kg/hour infusion during surgery. Group EACA received EACA in a dose of 100 mg/kg/IV over 20 min at the time of induction then 5-10 mg/kg in CPB prime followed by 10 mg/kg/hour infusion during surgery. Later Inj Protamine was administered to reverse the effect of Heparin. After the completion of surgery patients were shifted to ICU and were assessed for blood loss at 4 hours and 24 hours after shifting. Indication for transfusion of PRBC was a haemoglobin level of <8 gm/dl. FFP was transfused if post-operative drain was >250 ml/ hour in first hour. Platelet transfusion was indicated if platelets counts were <50000/mm3. The degree of fibrinolysis was measured by Thromboelastography (TEG), (Hemostasis system, Haemoscope corporation USA). Other parameters which were monitored included fibrinogen level and D-dimer levels at 4 hours and 24 hours. Re-exploration of case was considered if the bleeding was >300 ml/hour in first 2 hours or if >200 ml/hour for 4 consecutive hours, with normal coagulation data. Patients were also observed for post-operative complications like MI, Stroke, Deep Vein Thrombosis (DVT), renal dysfunction and seizures for 72 hours (Figure 1).

![Figure 1: Randomization group allocation and assessment of patients.](image)

Statistical analysis was done with SPSS software version 19.0 normality of the test were checked using Kolmogorov-smirnov test. The values which were obtained were analyzed and were expressed as mean ± Standard Deviation (SD) and median ± range. For continuous variables for parametric data, Independent’s tests were used and for nonparametric data Mann-Whitney u test were used. For categorical data, Chi-Square test or fisher’s exact test were used. AP value of <0.05 was considered to be statistically significant.

Result

Demographic variables like age, weight, height, male-female ratio were comparable in both groups (Table 1). The cross clamp time and duration on CPB were also comparable in both groups (Table 2). Primary outcomes like bleeding at 4 hours, there was no significant difference between the groups but when total bleeding at 24 hours was compared there was a significantly lesser bleed in group TA group compared to group EACA (p=0.0022). The requirement of PRBC in group TA was for 3 patients, whereas in EACA group 4 patients required PRBC (p>0.05). One patient in each group required FFP transfusion (p>0.05).Both the groups did not require any platelet transfusion and the transfusion rate was non-significant between the groups. Both the groups had no re exploration due to excessive bleeding (Table 3). There was no significant difference in the rate of post-operative complications between the groups (p>0.05) (Table 4).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group (n=40)</th>
<th>TA</th>
<th>Group (n=40)</th>
<th>EACA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>68 ± 2</td>
<td>67 ± 3</td>
<td></td>
<td></td>
<td>0.967</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>74 ± 3</td>
<td>76 ± 4</td>
<td></td>
<td></td>
<td>0.271</td>
</tr>
<tr>
<td>Height (Cm)</td>
<td>165 ± 3</td>
<td>162 ± 6</td>
<td></td>
<td></td>
<td>0.118</td>
</tr>
<tr>
<td>M/F (Gender)</td>
<td>26/14</td>
<td>28/12</td>
<td></td>
<td></td>
<td>0.739</td>
</tr>
<tr>
<td>TA=Tranaxamic Acid; EACA=Epsilon-Amino-Caproic-Acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Baseline Demography.
investigate at 4 hours between the groups however at 24 hours there was a fibrinolysis attributable cardiac surgeries [11]. In our study we found that there was no significant difference between both the groups with lesser bleeding in group TA compared to group EACA. This may be due to the fact the TA is 10 times more potent than EACA [12]. Similar findings were obtained in a study comparing TA and EACA with placebo conducted by Karski et al. [13]. Chauhan et al. [14] and Faure et al. [15] while comparing both the drugs showed that there was no significant difference in the rate of post-operative transfusion of PRBC, FFP/Platelet or the rate of re-exploration for excessive bleeding, which was comparable with our study. Post-operative blood transfusion after CABB is associated with increased long term mortality [16]. Therefore the role of these drugs in reducing the transfusion rate after on pump CABB is very significant. There were no differences in the rate of post-operative complications between the groups. Hardy et al. in his study while comparing both the drugs did not find any significant difference between the drugs with regards to post-operative thromboembolic complications [17]. There are controversies with regards to the dosing of the drug. A high dose (20 mg/kg) TA is associated with increased risk of post-operative seizures and therefore a low dose (10 mg/kg) regime is recommended [18]. Armelin et al. compared the low dose and high dose TA regime and found no difference with respect to amount of post-operative blood loss or transfusion requirement [19]. In our study we used low dose TA dosing and did not find any significant post-operative complications.

### Conclusion

Based on the results of our study it can be concluded that both TA and EACA effectively inhibits fibrinolysis during on pump CABB surgery and thus results in decreased post-operative bleeding. When compared between the two, TA was slightly better with respect to post-operative bleeding at 24 hours. Our study also re-emphasized the fact that neither of the drugs led to any additional risk of post-operative thrombotic complications and thus can potentially become a standard of care for blood conservation in patients undergoing on pump CABB.

### References


