

Comparison of Outcome of Bleeding with Single and Dual Antiplatelet Therapy in Beating Heart Surgery

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ABSTRACT

Objective: To compare the outcome of Bleeding with Single and Dual Antiplatelet Therapy in Beating Heart Surgery

Methodology: A total of 102 cases between 25 to 60 years, of either gender, advised CABG procedure and suitable for beating heart surgery were included in the study. Whereas those with known bleeding diathesis, not suitable candidate for beating heart surgery and with concomitant valvular heart disease were excluded from the study. These cases were enrolled through wards of Cardiothoracic Surgery Department, Shaikh Zayed Hospital, Lahore. Three groups were formed A,B and C. Group-A was assigned to DAPT, Group-B was SAPT (single anti platelet therapy) and Group "C" was on DAPT that is ASPRIN 75 mg and CLOPIDOGREL 75mg till the time of surgery. Control group A was compared with group B (SAPT) and group C (DAPT) for bleeding risk. The indications of blood products transfusion was assessed by baseline HCT platelet counts, PT and APTT. The CABG was carried out through a full sternotomy incision, under general anesthesia by using routine cardio protective measures and surgical techniques. Operating surgeon decided for on pump or off pump CABG. All patients were assessed and managed in ICU after Coronary artery bypass grafting. Duty doctor and anesthetist decided about transfusion of any allogenic blood product. Transfusion decision was made on the basis of routine laboratory values of APTT, ACT, and INR of PT, as well as on Hb. and HCT levels. Moreover, the need of non-self blood products was predicted.

Results: In our study, mean age was calculated as 52.65+7.48 years, 50.32+5.68 years and 48.47+5.96 years respectively, 61.76%(n=21) in Group-A, 52.94%(n=18) in Group-B and 44.12%(n=15) in Group-C were male whereas 38.24%(n=13) in Group-A, 38.24%(n=16) in Group-B and 55.88%(n=19) in Group-C were females, comparison of Perioperative blood loss as 597.29+129.26 in Group-A, 643.18+65.42 in Group-B and 654.70+59.16 in Group-C, p value was 0.02.

Conclusion: We concluded that Dual Antiplatelet Therapy have more chances of Peri-Operative bleeding as compare to heparin only or Single Antiplatelet Therapy in Coronary artery bypasses grafting on Beating heart. However, it has advantage of short pre procedure stay, reduced chances of ischemic events, less chance of canula related cellulitis and less chances of HIT. Whereas the cases administered with Heparin alone are having a greater chance of canula related cellulitis, expensive, prolonged pre procedure hospital stay with increased chances of HIT (Heparin induced thrombocytopenia).

Keywords: CABG , Perioperative bleeding, Dual Antiplatelet Therapy, Single Antiplatelet Therapy

INTRODUCTION

The need for reckless blood products is highly required for heart disease patients undergoing cardiac procedures, particularly those on APD treatment.¹ Low dose of Aspirin (ASA) 81mg reduces the risk of peri operative myocardium infarction, acute renal injury and mortality without increasing bleeding risk and use of dual Antiplatelet therapy(APD) increases bleeding risk.² Individuals with underlying clotting factors defects experience more bleeding , including plt (platelet) disorders. Although plt are needed for pedigree coagulation, more plt activity (high rebound platelet activity following withdrawal of APD) can produce severe and endangering-life thromboembolic (VTE) features such as (DVT) and (PE)in eminent risk heart disease patients.³ Especially, heart disease (CHD) patients with features of (ACS) often present with high clot formation in vascular endothelium. To prevent (VTE) events in such greater risk patients, thrombo prophylaxis (APD and anticoagulant therapy) is usually prescribed as

baseline management. After all, this therapy halt and disrupt clotting activity of blood coagulation factors including plt function by multiple mode of action during coronary surgery and in the early post-operative recovery period.⁴ In such scenario, to compensate for lost of haemostatic factors and RBC require transfusion of blood product , and to prevent acute anemia. However, not only monetary value implications, blood component therapy produce transfusion related side effects such a comes with the risk of complications such as alumnization and dilutional thrombocytopenia and hypocalcemia.⁵ Thus, in display case where cardiac operation is elective, and thrombocyte treatment can be stopped transiently to allow Plt precursor convalescence pre-operatively is required. Even though, loss of blood can be reduced and therefore, the transfusion requirement, however it produce high risk of blood clotting and myocardial ischemia during the pre and peri-operative period when the patients are not on APD treatment.⁶ Assessing the preoperative coagulation profile in patients planned for undergoing the coronary surgery (particularly those on APD) is important to help the risk assement of hemorrhage and VTE. Preoperative CBC and

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coagulation blood tests can aware of urgent decisiveness for transfusion of patients come through CABG, whereas (POCT) postoperative platelet function test (PFT) can help to monitor patient recovery and need of blood transfusions.⁷ Group meetings of these objectives check that not only accurately and reliably assess Plt function, but must also provide short turnaround time. By making careful clinical decisions to be made relatively quickly, POCT (PFT) platelet function testing can achieve significant reduction of severe bleeding, risk of ischemia and complications of DIC during coronary surgery in patients on indefinite APD.⁸ Moreover to improve clinical results for coronary surgery patients, some studies have determined that POCT, PFT has significantly decreased both the rate of transfusions and blood components (RBC unit, FFP and platelet units) used.⁹

In case of urgent need of surgical revascularization, patient has to undergo surgery with high risk of bleeding under full antiplatelet therapy. It must be kept in mind that high bleeding risk can turn into thrombotic risk, especially under circumstances when measures are taken to improve homeostasis only. In patients with a semi-urgent surgery decision to stop one or both antiplatelet (at least 5 days prior to surgery) is taken by the different involved specialties about risk evaluation of thrombosis versus bleeding.

METHODOLOGY

A total of 102 cases between 25 to 60 years, of either gender, advised CABG procedure and suitable for beating heart surgery were included in the study. Whereas those with known bleeding diathesis, not suitable candidate for beating heart surgery and with concomitant valvular heart disease were excluded from the study. These cases were enrolled through wards of Cardiothoracic Surgery Department, Shaikh Zayed Hospital, Lahore. Three groups were formed A, B and C. Group-A was assigned to DAPT, Group-B was SAPT (single anti platelet therapy) and Group "C" was on DAPT that is ASPRIN 75 mg and CLOPIDOGREL 75mg till the time of surgery. Control group A was compared with group B (SAPT) and group C (DAPT) for bleeding risk. The indications of blood products transfusion was assessed by baseline HCT platelet counts, PT and APTT. The CABG was carried out through a full sternotomy incision, under general anesthesia by using routine cardio protective measures and surgical techniques. Operating surgeon decided for on pump or off pump CABG. All patients were assessed and managed in ICU after Coronary artery bypass grafting. Duty doctor and anesthetist decided about transfusion of any allogenic blood product. Transfusion decision was made on the basis of routine laboratory values of APTT, ACT, and INR of PT, as well as on Hb. and HCT levels. Moreover, the need of non-self blood products was predicted.

In Group-A, the first control group "A" in which DAPT (dual anti platelet therapy) was stopped at least 5 days prior to surgery and shifted to intravenous low molecular heparin. Group-B, Second group "B" was on SAPT (single anti platelet therapy) that is ASPRIN 100 mg till the time of surgery and Group "C" was on DAPT that is ASPRIN 75 mg and CLOPIDOGREL 75mg till the time of surgery. Control group A was compared with group B (SAPT) and group C

(DAPT) for bleeding risk. The indications of blood products transfusion was assessed by baseline HCT platelet counts, PT and APTT. Coronary artery bypass grafting was carried out through a full sternotomy incision, under general anesthesia by using routine cardio protective measures and surgical techniques. Operating surgeon decided for on pump or off pump CABG. All patients were assessed and managed in ICU after Coronary artery bypass grafting. Duty doctor and anesthetist decided about transfusion of any allergenic blood product. Transfusion decision was made on the basis of routine laboratory values of APTT, ACT, and INR of PT, as well as on Hb. and HCT levels. Moreover, the need of non-self blood products were predicted. The outcome variable were studied.

RESULTS

Age distribution of the participants shows that 20.59%(n=7) in Group-A, 20.59%(n=7) in Group-B and 38.24%(n=13) in Group-C were between 25-45 years of age whereas 79.41%(n=27) in Group-A, 79.41%(n=27) in Group-B and 61.76%(n=21) in Group-C were between 46-60 years of age, mean+sd was calculated as 52.65+7.48 years, 50.32+5.68 years and 48.47+5.96 years respectively. Regarding gender distribution, 61.76%(n=21) in Group-A, 52.94%(n=18) in Group-B and 44.12%(n=15) in Group-C were male whereas 38.24%(n=13) in Group-A, 38.24%(n=16) in Group-B and 55.88%(n=19) in Group-C were females. Body mass index of the patients was calculated as 25.68+5.52 in Group-A, 28.32+4.72 in Group-B and 28.0+6.70 Group-C.

Frequency of associated morbidities shows that all cases in Group-A, B and C had hypertension, no case in COPD in all groups whereas dyslipidemia was recorded in 17.65%(n=6) in Group-A, no case in Group-B and 2.94%(n=1) in Group-C. Frequency of history of myocardial infarction was recorded in 50%(n=17) in Group-A, 23.52%(n=8) in Group-B and 32.35%(n=11) in Group-C.

Mean Perioperative Hb was 13.56+2.12 Group-A, 14.24+2.04 Group-B and 13.67+2.02 in Group-C, p value was 0.34, these findings after the surgery was recorded as 11.27+0.79 in Group-A, 11.59+0.82 in Group-B and 11.85+0.88 in Group-C, p value was 0.01.

Perioperative creatinine levels were recorded as 1.12+0.55 in Group-A, 1.04+0.23 in Group-B and 1.12+0.39 in Group-C, p value was 0.61, whereas postoperatively these findings were 1.33+0.86 in Group-A, 1.2+0.43 in Group-B and 1.17+0.65 in Group-C, p value was 0.55. Comparison of platelet count was done, it shows that 244.24+56.89 in Group-A, 252.68+74.79 in Group-B and 258.29+46.97 in Group-C, p value was 0.63, these findings were recorded postoperatively as 228.94+47.54 in Group-A, 236.97+58.88 in Group-B and 243.65+55.52 in Group-C, p value was 0.54. Perioperative blood loss as 597.29+129.26 in Group-A, 643.18+65.42 in Group-B and 654.70+59.16 in Group-C, p value was 0.02. We also compared mean pack cell transfusion, it shows 5.82+1.88 in Group-A, 6.21+2.01 in Group-B and 6.71+2.32 in Group-C, p value was 0.22. Regarding drain volume at first 24 hours of the surgery shows 685.0+272.80 in Group-A, 860.59+157.46 in Group-B and 867.94+69.36 in Group-C, p value was 0.0007. (Table No. 1)

Comparison of other outcome variables shows that 91.18%(n=31) in Group-A, 100%(n=34) in Group-B and 97.06%(n=33) in Group-C were discharged, no case was

re-opened whereas 8.81%(n=3) in Group-A, 2.94%(n=1) in Group-C whereas no case in Group-B was died. (Table No. 2).

Table 1: Comparison of All Groups

| Creatinine | Group-A (n=34) | | Group-B (n=34) | | Group-C (n=34) | | P value |
|-----------------------|----------------|--------|----------------|--------|----------------|-------|---------|
| | Mean | SD | Mean | SD | Mean | SD | |
| Perioperative | 1.12 | 0.55 | 1.04 | 0.23 | 1.12 | 0.39 | 0.61 |
| Post operative | 1.33 | 0.86 | 1.2 | 0.43 | 1.17 | 0.65 | 0.55 |
| Platelet count | | | | | | | |
| Perioperative | 244.24 | 56.89 | 252.68 | 74.79 | 258.29 | 46.97 | 0.63 |
| Post operative | 228.94 | 47.54 | 236.97 | 58.88 | 243.65 | 55.52 | 0.54 |
| Blood loss | | | | | | | |
| Perioperative | 597.29 | 129.26 | 643.18 | 65.42 | 654.70 | 59.16 | 0.02 |
| Pack cell transfusion | 5.82 | 1.88 | 6.21 | 2.01 | 6.71 | 2.32 | 0.22 |
| Drain volume | 685.0 | 272.80 | 860.59 | 157.46 | 867.94 | 69.36 | 0.0007 |

Table 2: Comparison of other Outcome Variables (n=102)

| Outcome | | Group-A (n=34) | | Group-B (n=34) | | Group-C (n=34) | | P value |
|------------|-----|-----------------|-------|-----------------|-----|-----------------|-------|---------|
| | | No. of patients | % | No. of patients | % | No. of patients | % | |
| Discharged | Yes | 31 | 91.18 | 34 | 100 | 33 | 97.06 | -- |
| | No | 3 | 8.82 | 0 | 0 | 1 | 2.94 | |
| Re-open | Yes | 0 | 0 | 0 | 0 | 0 | 0 | -- |
| | No | 0 | 0 | 0 | 0 | 0 | 0 | |
| Died | Yes | 3 | 8.82 | 0 | 0 | 1 | 2.94 | -- |
| | No | 31 | 91.18 | 0 | 0 | 33 | 97.06 | |

DISCUSSION

In selected group of patients of coronary artery disease (CAD),Coronary artery bypass graft (CABG) surgery showed improved survival as compared to medical therapy. Antiplatelet therapy has pivotal role in medical management and significant reduction in thrombotic events was noticed. Different regimen of antiplatelet therapy is in vogue for different indications but most studied are dual anti platelet therapy (DAPT) that is aspirin and thienopyridine derivatives which adenosine diphosphate receptor antagonist and single antiplatelet therapy (SAPT).DAPT reduces thrombotic events more effectively than SAPT in those patients who received revascularization by percutaneous intervention (PCI) for acute coronary syndrome (ACS).Regardless of treatment options like medical management, thrombolytic treatment ,PCI or CABG, for ACS patients ,DAPT gave similar benefits in all the groups. In addition to Aspirin use of antiplatelet like clopidogrel or ticagrelor is recommended in recent guidelines for all the ACS patients either treated by ischemia guided or early invasive strategy, until contraindication. However, those who were receiving DAPT within 5 days of CABG surgery were having higher Perioperative bleeding risk. At the cost of this high bleeding risk with DAPT, patient got benefit of reduced thrombotic ischemic events. Although by replacing DAPT,reduced bleeding risk noticed with heparin infusion but at the cost of higher ischemic events. Effects of rapid acting and short duration intravenous antiplatelet therapy which may be used in selected patients are under trials as an alternate.at the moment its still challenging to decide the regimen and timing of surgery to avoid fatal ischemia prior to surgery and major perioperative bleeding.

Considering the fact that it is also important to control the peri operative bleeding in the cases which have been placed under beating heart surgery, however, there is no

particular study carried out on this specific local population so this study has its importance.

It is noted that multiple blood transfusion is needed for the patients being operated for the CABG. Surgeons are trying to find the new ways to reduce the loss of blood during the procedure. Antiplatelet therapy is found to be important in the reduction of blood loss during the procedure. If we find that continuing Antiplatelet therapy is effective then all the patients who have been advised for CABG could be allowed to continue Antiplatelet therapy.

The results of our study reveals that Perioperative blood loss as 597.29+129.26 in Group-A, 643.18+65.42 in Group-B and 654.70+59.16 in Group-C, p value was 0.02.

A previous study by Zenko Nagashima et al. in 2017 evaluated the dual antiplatelet treatment in urgent surgery regarding bleeding complications and found no significant difference in DAPT vs SAPT group in terms of OPCABG (53% VS 47%) and Intra Aortic Ballon Pump insertion (67% vs 75%). Patients who were given Perioperative pack cell transfusion, fresh frozen plasma, intra operative drain volume and total bleeding output within two days after surgery were same in number in both groups. Although number of Perioperative platelet transfusions were significantly high in DAPT vs SAPT group (50% vs 18%).⁹

Another study, CURE trial (n=2072) revealed significant reduction in stroke, MI and cardiovascular mortality in group of patients who were taking clopidogrel prior to CABG surgery (14.5% for clopidogrel, 16.2% for placebo; RR 0.89 [95% CI 0.71 to 1.11]) but with mild rise in life threatening bleeding as compared to placebo (5.6% for clopidogrel and 4.2% for placebo; RR 1.30 [95% CI 0.91 to 1.95]).¹⁰

In CLARITY-TIMI28 trial promising effects were noted when clopidogrel was added to aspirin in 3491 patients with STEMI, who received thrombolytic therapy.¹¹ subsequently among the patients (12%,n=419) who were referred for CABG surgery, there was no significant difference in minor

or major bleeding in both groups who were receiving clopidogrel within 5 days of surgery compared to non-receiver. CREDO trial, which was done to evaluate effect of one month (short term) and twelve months (long term) use of clopidogrel in post PCI patients, also endorsed the same finding of no significant rise in Perioperative bleeding among patients (n=83) who subsequently underwent CABG surgery who were receiving clopidogrel.¹²

On the other hand conflicting data of observational studies about bleeding in CABG surgery patients who were taking clopidogrel may be explained by identifying different systematic differences like surgical expertise, type of CABG surgery (off pump or on pump), elective Vs urgent surgery, indication of surgery, patient co morbidity, preoperative thrombolysis or anticoagulation, physician bias and preoperative use of blood products¹³⁻¹⁴ several study explained increased rate of mortality, re exploration, post operative bleeding, transfusion and length of hospital stay was associated with treatment with clopidogrel prior to CABG surgery.¹⁵⁻¹⁷ a large study¹² evaluated retrospective data of 596 ACS patients of 14 hospitals who were in early use group (taking clopidogrel within 5 days of CABG surgery) vs non receiver. 298 patients who were in early use group experienced increase in re-opening, major bleeding and length of hospital stay. A regression analysis also documented the same results of highest risk of re opening and bleeding in patients who were taking clopidogrel within 5 days of CABG surgery, in contrast a Canadian study on 451 patients¹⁸ showed no significant difference major bleeding and mortality among patients who were taking clopidogrel (n=189) within 5 days of CABG surgery vs those who never took clopidogrel or drug stopped more than 5 days prior to surgery (n=262).

Another series of 332 patients¹⁹ who were taking clopidogrel within 5 days of CABG surgery suggested there was no association of re opening and fall in hematocrit more than 15% but modest use of red cell transfusion may attribute to surgical skill of surgeons.

Another interesting finding was demonstrated in an observational study²⁰ that beating heart CABG surgery was associated with less bleeding (P<0.01), transfusion requirement (P<0.02) and hospital stay (P<0.03) as compared to increased risk in patients who underwent conventional cardiopulmonary bypass CABG surgery.

The result of our study justified the fact that Dual Antiplatelet Therapy have more chances of Perioperative bleeding as compare to heparin only or Single Antiplatelet Therapy in Coronary artery bypasses grafting on beating heart. However, it has advantage of short pre procedure stay, reduced chances of ischemic events, less chance of canula related cellulitis and less chances of HIT. Whereas the cases administered with Heparin alone are having a greater chance of cannula related cellulitis, expensive, prolonged pre procedure hospital stay with increased chances of HIT (Heparin induced thrombocytopenia).

CONCLUSION

We concluded that Dual Antiplatelet Therapy have more chances of Peri Operative bleeding as compare to heparin only or Single Antiplatelet therapy in Coronary artery bypasses grafting on Beating heart. However, it has advantage of short pre-procedure stay, reduced chances of

ischemic events, less chance of canula related cellulitis and less chances of HIT (Heparin induced thrombocytopenia). Whereas the cases administered with Heparin alone are having a greater chance of canula related cellulitis, expensive, prolonged pre procedure hospital stay with increased chances of HIT.

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