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EFFECT OF CARDIOPULMONARY BYPASS DURATION ON POSTOPERATIVE MEDIASTINAL BLEEDING WITH COAGULOPATHY IN CORONARY ARTERY BYPASS GRAFT (CABG) SURGERY

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Contribution

AK conceived, designed and did statistical analysis. RT, AN and AK did data collection and manuscript writing. AK did review and final approval of manuscript. All authors contributed equally.

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ABSTRACT

Objective: To determine the effect of cardiopulmonary bypass (CPB) duration as a risk factor in the incidence of postoperative mediastinal bleeding with coagulopathy in elective CABG surgery.

Methodology: Our study was cross-sectional and retrospective done at Department of Cardiac Surgery and Anaesthesia at the National Institute of Cardiovascular Diseases, Karachi, from 1st February 2013 to 31st January 2015. The demographic, operative and postoperative data were collected. The time for CPB and aortic cross clamp time was noted. Postoperative mediastinal bleeding was measured through the mediastinal drains. The patients' prothrombin time /international normalized ratio (PT/INR), activated partial thromboplastin time (aPTT), platelet count and haemoglobin were documented and the patients with significant mediastinal bleeding with raised PT/INR, aPTT and thrombocytopenia were treated conservatively with fresh frozen plasma, platelets and blood or surgical re-exploration if required. Analysis of Variance (ANOVA) was used to analyse the data and a $p \leq 0.05$ was considered statistically significant.

Results: Total of 110 patients were included in the study. Our study revealed that the mean CPB time (minutes) was 75.2±11.6 minutes (range: 62 to 137 minutes). In 5 patients (4.55%) the CPB time was greater than 100 minutes. Post-operative mediastinal bleeding was increased in 4 (3.64%) out of the five patients in whom the cardiopulmonary bypass time was greater than 100 minutes ($p<0.05$). Mean postoperative mediastinal bleeding of 1.5 ml//kg/hour occurred when the immediate postoperative blood platelet count was less than or equal to 90 X 10^9/l ($p < .05$). In all these 4 patients the PT/INR,APTT was raised above normal and there was thrombocytopenia (coagulopathy). Out of these 4 patients 3 (2.73%) patients were successfully treated conservatively with transfusion of fresh frozen plasma and platelets, while 01 (0.91%) patient required surgical re-exploration as he developed cardiac tamponade.

Conclusion: Prolonged cardiopulmonary bypass time is a risk factor for post CABG mediastinal bleeding with coagulopathy.

Key Words: Coronary artery bypass graft surgery, Mediastinal bleeding, Coagulopathy.

INTRODUCTION

One of the most common cardiac surgery procedures is coronary artery bypass graft (CABG) surgery. In on pump CABG surgery cardiopulmonary bypass is used. In coronary artery bypass graft surgery postoperative mediastinal bleeding is an important complication of cardiopulmonary bypass. Therefore, the increased duration of cardio-pulmonary bypass is a risk factor for transfusion of whole blood and blood products. The increase in mediastinal bleeding after cardiopulmonary bypass in cardiac surgery has been known to result indisorders of the coagulation pathway resulting in coagulopathy.[1,2] Coagulopathy with thrombocytopenia, qualitative platelet disorders and clotting factors abnormalitiesmay be caused by priming the cardiopulmonary bypass circuit with crystalloid solution which causes hemodilution. Moreover, fibrinolysis is activated by the activation of intrinsic and extrinsic coagulation pathways and activation of platelets. Fibrinolysis is also caused by dysfunction of platelets resulting from administration of systemic heparinand inadequate heparin reversal.[3,4] Moreover, use of cell savers may result in decreased levels of coagulation factors and platelets. Fibrinolysis is indicated with increased levels of INR, APTT, D- dimers and decreased factors VIII and I.

Postoperative mediastinal bleeding associated with coagulopathy is treated using fresh frozen plasma and platelets which results in reduced postoperative morbidity and mortality. The conservative treatment of postoperative mediastinal bleeding with fresh frozen plasma, platelets and blood is especially useful for reducing the requirement of surgical re-exploration. Surgical re-exploration for mediastinal bleeding increases postoperative morbidity and mortality. The conservative treatment however entails the possible risk of transfusion related complications.[5]

This study was carried out to identify the effect of cardiopulmonary bypass duration on postoperative mediastinal bleeding associated with coagulopathy in patients undergoing CABG surgery in our population.

METHODOLOGY

This cross sectional study was carried out in the Department of Cardiac Surgery and Anaesthesia at the National Institute of Cardiovascular Diseases, Karachi, from 1st February 2013 to 31st January 2015. Our study included patients of both genders who were in the age range of 32-78 years and were undergoing isolated elective CABG surgery. We excluded those patients who had abnormal PT/INR, aPTT and platelet count (coagulopathy), chronic renal failure, history of myocardial infraction, emergency surgery, past history of stroke or transient ischemic attack, history of atrial fibrillation and ejection fraction less than 35%.The demographic, operative and postoperative data was collected. For the CABG surgery the patient's informed consent was taken and the surgery was carried out under general anaesthesia. Non-invasive and invasive monitoring was done. Conduits (left internal mammary artery and great saphenous vein) were harvested.

CABG surgery was performed with median sternotomy and cardiopulmonary bypass using the standard procedure with ascending aortic and two stage venous cannulation and nonpulsatile flow was established. Myocardial protection was achieved with systemic moderate hypothermia and cardiac arrest was achieved with antegrade cold blood cardioplegia. The left internal mammary artery (LIMA) was grafted to the left anterior descending artery. The great saphenous vein was utilized to graft the other coronary arteries. The time for cardiopulmonary bypass and aortic cross clamp time was noted. The patients were then weaned off cardiopulmonary bypass and protamine was administered. Meticulous hemostasis was done and mediastinal drains were placed. Patients were then transferred to the intensive care unit. Invasive and non-invasive monitoring was done and the postoperative mediastinal bleeding was measured through the mediastinal drains. The patients' PT/INR, aPTT, platelet count and haemoglobin were documented and the patients with significant mediastinal bleeding with raised PT/INR, aPTT and thrombocytopenia were treated conservatively with FFPs, platelets and blood or surgical re-exploration if required.

The data was analysed using the SPSS version 16.0 software. Frequencies and percentages were calculated for the qualitative data. Mean and standard deviation were calculated for age, cardiopulmonary bypass time and aortic cross clamp time. Analysis of Variance (ANOVA) was used to analyse the data and a $p \leq 0.05$ was considered statistically significant.

RESULTS

The demographic data in our study showed that the age of the patients ranged from 32 years to 78 years (mean ± SD: 66.3±23) (Table 1). Out of 110 patients 87 (79%) patients were males and 23 (21%) were females. About 13 patients (11.7%) had diabetes mellitus type II and 15 patients (13.9%) were hypertensive. None of the patients had a history of stroke/transient ischemic attack or coagulation abnormalities. About 25 (23%) patients were smokers and all were male patients, 90 (82%) patients had an ejection fraction of 40% to 50% and 20 (18%) patients had an ejection fraction of 35% to 39%.

Table 1: Baseline Characteristics of Study Population (n=110)

Demographic Variables	n (%)
Age range (years) , (Mean ± SD)	32-78 (66.3±23)
Male : Female	87 (79%) : 23 (21%)
Diabetes mellitus	13 (11.7%)
Hypertension	15 (13.9%)
Smokers	25 (23%)
Ejection Fraction 35% to 39%	20 (18%)
Ejection Fraction 40% to 50%	90 (82%)

The operative data in our study revealed that the cardiopulmonary bypass time was 75.2±11.6 minutes with the range being 62 to 137 minutes (Table 2). In five patients (4.55%) the cardiopulmonary bypass time was greater than 100 minutes. The mean aortic cross-clamp time was 56.2±1.9 minutes. About 91 (82.5%) patients had three vessel disease and 19 (17%) patients had left main plus three vessel disease. The left internal mammary artery (LIMA) was grafted to the left anterior descending (LAD) artery in 107 (97%) of patients, but in 03 (03%) patients the LIMA was harvested but was not used because the blood flow was inadequate. The mean number of grafts per patient were 3.5±0.5.

Table 2: Operative Data of Study Population (n=110)

Operative Variables	n (%)
CABG time (minutes) Mean ± SD, Range (minutes)	75.2±11.6 minutes 62-137 minutes
Patients with cardiopulmonary bypass time > 100 minutes	05 (4.55%)
Mean aortic cross-clamp time (minutes)	56.2±1.9 minutes
Three Vessel Disease	91 (82.5%)
Left main + three vessel disease	19 (17%)
LIMA grafted to LAD	107 (97%)
Mean number of grafts per patient	3.5±0.5

About 105 patients in whom the cardiopulmonary bypass time was less than 100 minutes had mean postoperative mediastinal bleeding of 0.75ml//kg/hour.Out of the five patients in whom the cardiopulmonary bypass time was greater than 100 minutes, four (3.64%) patients had post operative mean mediastinal bleeding of 1.5 ml//kg/hour. Using analysis of variance (ANOVA) the data showed statistical significance ($p < 0.05$). In all these four patients the PT/INR, aPTT was raised above normal and there was thrombocytopenia;using the analysis of variance (ANOVA) test, mean postoperative mediastinal bleeding of 1.5 ml//kg/hour occurred when the immediate postoperative blood platelet count was less than or equal to 90×10^9/l ($p < .05$). Out of these four patients with significant postoperative mediastinal bleeding three (2.73%) patients were successfully treated conservatively with transfusion of fresh frozen plasma and platelets, while 01 (0.91%) patient required surgical re-explorationas he developed cardiac tamponade. The cardiac tamponade was diagnosed based on clinical signs, chest X ray and trans-thoracic echocardiography. The mean intensive care unit stay was 4±2.1 days and the mean hospital stay was 8±3.4 days.

DISCUSSION

Mediastinal bleeding can be classified as medical or surgical. The etiology of mediastinal bleeding may be surgical bleeding sites, heparin effect (residual or rebound), excessive protamine administration, platelet dysfunction, thrombocytopenia, clotting factor deficiency and fibrinolysis. Post CABG mediastinal bleeding resulting from prolonged extracorporeal circulation is usually associated with abnormalities in the coagulation profile and haemostatic pathways that is categorized as medical bleeding.[6] The initial management strategy in postoperative mediastinal bleeding is to identify the cause and then to treat according to the etiology.[1] There are a number of risk factors for postoperative mediastinal bleeding including known coagulopathies such as von Willerbrand's disease and uremia. Postoperative mediastinal bleeding may be prevented with meticulous hemostasis technique. Physiological control of mediastinal bleeding is achieved through activation of the clotting pathway and platelets. Abnormalities of the coagulation pathway may cause significant postoperative mediastinal bleeding.[7] The incidence of life threatening postoperative mediastinal bleeding after cardiac surgery ranges from 5 to 25%.[6] Our study showed that 01 (0.91%) out of the 110 patients required surgical re-exploration for postoperative mediastinal bleeding caused by coagulopathy, and this comparableto the results demonstrated in other studies.[4,8]

Cardiopulmonary bypass causes acquired decreased platelet count and qualitative platelet dysfunction resulting in postoperative mediastinal bleeding.[6,9-12] The postoperative

mediastinal bleeding may be caused by the cardiopulmonary bypass circuit, systemic hypothermia and heparin and other drugs.[8] The decrease in the number of platelets is caused by the priming solutions resulting in haemodilution, or it may be due to the adhesion of the platelets to the cardiopulmonary bypass tubing surface.[6,8] Moreover thrombocytopenia also result from aggregation of platelets and the elimination of abnormal platelets by the reticulo-endothelial system. [6,8]

In our study of the 110 patients 5 (4.55%) patients developed postoperative mediastinal bleeding in whom the cardiopulmonary bypass time was greater than 100 minutes. About 105 patient in whom the cardiopulmonary bypass time was less than 100 minutes had mean postoperative mediastinal bleeding of 0.75ml//kg/hour. Out of the five patients in whom the cardiopulmonary bypass time was greater than 100 minutes four (3.64%) patients had postoperative mean mediastinal bleeding of 1.5 ml//kg/hour. Using analysis of variance (ANOVA) the data showed statistical significance ($p < 0.05$). In all these four patients the PT/INR, aPTT were raised above normal and there was thrombocytopenia; using the analysis of variance (ANOVA) test, mean postoperative mediastinal bleeding of 1.5 ml//kg/hour occurred when the immediate postoperative blood platelet count was less than or equal to 90 X 10^9/l ($p < .05$). Out of these four patients, three (2.73%) patients were treated successfully conservatively with transfusion of fresh frozen plasma and platelets while one (0.91%) patient required surgical re-exploration for cardiac tamponade. The cardiac tamponade was diagnosed on the basis of clinical signs, chest X-ray and trans-thoracic echocardiography. Our findings are supported by other studies that showed prolonged cardiopulmonary bypass time to be a significant factor causing postoperative bleeding requiring management with blood and blood products.[4,6,13-15] The contact of heparinised blood with the chest wound and to the synthetic surfaces of the cardiopulmonary bypass circuit results in thrombosis, activation of platelets and the coagulation pathway and fibrinolytic proteins, resulting in decreased levels of haemostasis.[6]

By reducing the time of cardiopulmonary bypass and utilizing strategies to prevent thrombocytopenia and qualitative platelet disorders we can decrease the incidence of postoperative mediastinal bleeding. By decreasing postoperative mediastinal bleeding we can reduce the requirement for transfusion of blood products and surgical re-exploration, hence we this strategy can decrease the postoperative morbidity and mortality.

CONCLUSION

Prolonged cardiopulmonary bypass time is a risk factor for post CABG mediastinal bleeding with coagulopathy.

REFERENCES

1. Despotis GJ, Hogue CW Jr. Pathophysiology, prevention, and treatment of bleeding after cardiacsurgery: a primer for cardiologists and an update for the cardiothoracic team. Am J Cardiol1999-;83(4):158-308.
2. Yamada T, Yamamoto S, Tagawa M, Kotake Y.Comprehensive haemostasis analysis during cardiopulmonary bypass with Sonoclot analyzer and glass bead activated heparinase test. Anesth Analg2004;98:1-134.
3. Khuri SF, Valeri CR, Loscalzo J, Weinstein MJ, Birjiniuk V, Healey NA, et al. Heparin causes platelet dysfunction and induces fibrinolysisbefore cardiopulmonary bypass. Ann ThoracSurg 1995;60(4):1008-14.
4. Miana LA, Atik FA, Moreira LF, Hueb AC, Jatene FB, Auler JO, et al. Risk factors of post operative bleeding after adult cardiac surgery. BrazJ CardiovasSurg 2004;19(3):169-82.
5. World Health Organization.The clinical use of blood in medicine, obstetrics, paediatrics, surgery and anaesthesia, trauma and burns. Geneva: WHO; 2001.
6. Theusinger OM, Felix C, Spahn DR. Strategies to reduce the use of blood products: an European perspective. CurrOpinAnaesthesiol 2012;25(1):59-65.
7. Welsby I. Specific variants of genes predictbleeding after heart surgery [Online]. 2005 [cited on 2017, May 24th]. Available from URL: www.newsmedical.net/id=9787.
8. Baue AE, Geha AS, Hammond GL. Glenn's thoracic and cardiovascular surgery.5th ed. US: Prentice-Hall International Inc.; 1991. p.1550-1.
9. Philip RB, Elijah WM. Post operative bleeding after coronary artery bypass surgery with cardiopulmonary bypass. AnesthAnalg2002; 95(5):1466-72.
10. Bagge L, Lilienberg G, Nyström SO, Tydén H.Coagulation, fibrinolysis and bleeding after open heart surgery. Scand J ThoracCardiovascSurg1986;20(2):151-60.
11. Kunitomo R, Tsurusaki S, Suzuki R, Takaji K, Moriyama S, Hagio K, et al. Predictive factors for platelet number after cardiopulmonary bypass andpostoperative blood loss. ASAIO J2002;48(6):671-4.
12. Suzuki Y, Hillyer P, Miyamoto S, Niewiarowski S, Sun L, Rao AK,et al. Intergrilin prevents prolonged bleeding times after cardiopulmonary bypass.Ann ThoracSurg1998;66(2):373-81.
13. Scott BH1, Seifert FC, Glass PS, Grimson R. Blood use

in patients undergoing coronary artery bypass surgery: impact of cardiopulmonary bypass pump, hematocrit, gender, age, and body weight. Anesth-Analg2003;97(4):958-63.

14. Kakaiya R. Cardiopulmonary bypass surgery in idiopathic thrombocytopenic purpura.Inst Transfus-Med2004;2:1-5.

15. Kataria TC. Long cardiopulmonary time predicts postoperative bleeding despitestrict utility of transfusion algorithms. Anesthesiology 2002;96;129-37.