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Research Article

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Outcome of Plasma Fibrinogen Level and Postoperative Bleeding Following OPCAB Surgical Patients

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Abstract

Background: *Bleeding is a major concern after cardiac surgery and also a significant cause of morbidity and mortality. Postoperative mediastinal bleeding in patients undergoing cardiac surgery is still one of the most common complications. Objective: To find out Outcome of Plasma Fibrinogen Level and Postoperative Bleeding Following OPCAB Surgical Patients.*

Methods: *This comparative cross-sectional study was carried out at the Department of Cardiac Surgery in BSMMU hospital from March, 2017 to August, 2019. The study population was 60, with 2 (two) groups having 30 patients in each. Patients from both the groups underwent OPCAB. Statistical analysis of different characteristics between the patients of both groups was done to draw a conclusion.*

Results: *This study total sixty (60) patients who underwent off-pump coronary artery bypass graft surgery were evaluated in this study. Postoperative care at ICU was given to the patients of both groups as per standard hospital protocol. The findings of the study obtained from data analysis presented in the following pages. Among the study population mean age in group A was 55.43±8.53 years and in group B was 59.63±6.86 years. The difference in age between two groups was statistically significant ($p<0.05$). There was no statistical significance of gender between the two study groups ($p>0.05$). The mean BMI in group A was 24.13±2.49 kg/m² and that in group B was 24.62±3.71 kg/m². The findings were statistically not significant ($p>0.05$). Shows the comparison of postoperative variables between group A and B patients. Amount blood loss in 1st 12 hours immediate after surgery in group A and B were 185.67±35.20 ml and 219.67±57.32 ml respectively. Post-operative*

blood transfusion in group A and B were 2±0.53 units and 2.5±0.68 units respectively, which was statistically significant (p<0.05. There were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality. The most valuable predictor for increased postoperative bleeding after OPCAB.

Conclusion: *In conclusion the efficacy were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality. Pearson co-efficient correlation test showed an inverse relationship between plasma fibrinogen level and postoperative bleeding following OPCAB. Fibrinogen concentration level was associated with increased postoperative bleeding in patients undergoing off-pump coronary artery bypass grafting surgical patients*

Keywords: Fibrinogen, Blood Transfusion, Post-Operative Outcomes, Topical Tranexamic Acid, OPCAB Surgery

Introduction

Coronary artery disease (CAD) is one of the most scrutinized diseases in medical science and coronary revascularization is the most studied intervention. Coronary artery disease (CAD) results from narrowing of the coronary arteries. The narrowing is caused by thickening and loss of elasticity of arterial walls. When this narrowing is sufficiently severe, it limits blood flow to the myocardium. At primary stage, the disease limits only coronary flow reserve (increase inflow that normally accompanies increased myocardial oxygen demands) but when sufficiently advanced, CAD reduces blood flow through the affected artery even at rest. In its most severe form, atherosclerotic CAD occludes the coronary artery [1]. Initially, for revascularization of the coronary arteries in CAD, coronary artery bypass surgeries were performed using cardiopulmonary bypass with cardioplegic arrest [2]. To reduce postoperative complications caused by systemic inflammation, off-pump coronary artery bypass (OPCAB) was introduced into clinical practice in the early 1990s [3]. During off-pump surgery, the coronary artery grafts are placed on coronary arteries of a beating heart using intra-coronary shunts, thereby avoiding aortic cross clamping and CPB. Benefits of OPCAB are early extubation, reduced perioperative blood transfusion, hospital stay and mortality [4]. In spite of having several advantages, OPCAB is still accompanied with a risk of complications such as bleeding, infections, stroke, and myocardial infarction with heart failure, renal insufficiency and pulmonary dysfunction [5]. Bleeding is a common and severe complication after cardiac surgery. It may be caused by surgical factors or disturbed hemostasis or combination of both. Disturbed postoperative hemostasis may be related to impaired coagulation, increased fibrinolysis or platelet dysfunction [6]. Fibrinogen is a key protein in hemostasis synthesized by the liver. It is also known as clotting factor I (one) and it circulates in plasma at a concentration of 2.0-4.5 gm/L. In healthy human adults, about 2-5 gm of fibrinogen is synthesized daily and the same amount is catabolized. The plasma half-life of fibrinogen in normal humans has been estimated to be 3-5 days. Fibrinogen is converted in plasma by thrombin into fibrin, which under the influence of factor XIII is formed into a meshwork at the site of tissue damage to minimize blood loss and stimulate tissue repair. Fibrinogen is the final clotting factor activated in the coagulation cascade during hemostasis [7]. Fibrinogen binds to the specific platelet receptor, which is important for incorporating platelet aggregation [8]. Thus, in primary hemostasis it supports formation of platelet plug and in secondary hemostasis the formation of insoluble fibrin clot. Fibrinogen and fibrin also interact with other adhesive glycoproteins, hemostatic factors and blood cells forming a complex system that constitutes the process of hemostasis. Therapeutic fibrinogen substitution is based on products derived from human plasma, such as fresh-frozen plasma (about 2-3 mg/ml), cryoprecipitate (about 200-250 mg/unit) or fibrinogen concentrate (dose: 70mg/kg body weight). However, there were significant inverse correlation between postoperative bleeding and preoperative fibrinogen levels [9].

Objective

To find out Outcome of Plasma Fibrinogen Level and Postoperative Bleeding Following OPCAB Surgical Patients.

Materials & Methods

This comparative cross-sectional study was carried out at the Department of Cardiac Surgery in BSMMU hospital from March, 2017 to August, 2019. The study population was 60, with 2 (two) groups having 30 patients in each. Patients from both the groups underwent OPCAB. Statistical analysis of different characteristics between the patients of both groups was done to draw a conclusion.

Data Collection

All patients admitted in Cardiac Surgery Department, BSMMU with coronary artery disease scheduled for OPCAB were considered as study population (without exclusion criteria). Patient who fulfilled the inclusion criteria and willing to enroll in the study was included in the study after receiving the proper consent. The specimen was platelet-free plasma or platelet poor plasma. Amount of specimen needed from each subject is 1 ml of plasma. To obtain this, after all aseptic precaution, venous blood sample was collected from each study subject in a disposable plastic syringe and immediately transferred to a sterile 2.7 ml blue-top (3.2% sodium citrate) tube. Then, the tube was gently moved upside down for several times to mix the whole blood with 3.2% sodium citrate. Blood was not drawn from a heparinized line. To avoid contamination of the sample with tissue thromboplastin or heparin, venipuncture was done very carefully to avoid any trauma. In case blood was drawn from an indwelling catheter, it was flushed with 5 ml of saline and the first 5 ml of blood collected was discarded. If drawn with a butterfly setup, a discard was made first to remove air from tubing. Tubes were labeled with patients name, ID number & collection date and sent to BSMMU Hematology laboratory immediately for centrifugation & further procedure. Standard anesthetic techniques of induction and maintenance were followed for all procedures.

Data Analysis

Statistical analysis was conducted using Statistical Package for Social Science (SPSS) version 23.0 for windows software. Comparisons between groups were made with Student's t-test, Chi-Square test and Fisher's exact test. The results were presented in tables. Observations were recorded as statistically significant if a p-value is ≤0.05.

Results

This study total sixty (60) patients who underwent off-pump coronary artery bypass graft surgery were evaluated in this study. Post-operative care at ICU was given to the patients of both groups as per standard hospital protocol. The findings of the study obtained from data analysis presented in the following pages.

Comparison of demographic and anthropometric variables:

Among the study population mean age in group A was 55.43±8.53 years and in group B was 59.63±6.86 years. The difference in age between two groups was statistically significant ($p<0.05$). There was no statistical significance of gender between the two study groups ($p>0.05$). The mean BMI in group A was 24.13±2.49 kg/m² and that in group B was 24.62±3.71 kg/m². The findings were statistically not significant ($p>0.05$) [Table-1].

Table 1: Comparison of demographic and anthropometric variables: (N=60)

Variables	Group Group A(n=30)	Group B(n=30)	p value*
[a]Age (In years) Mean ± SD Range	55.43±8.53 (42 to 72)	59.63±6.86	0.012[s]
[b]Sex Male Female	 23 (76.66%) 07 (23.33%)	 18 (60.0%) 12 (40.0%)	0.165[ns]
[a]BMI (kg/m2) Mean ± SD	24.13±2.49	24.62±3.71	0.548[ns]

Table in the parentheses indicate percentage. Data were analyzed using, [a]Student's t-test and was presented as mean ± SD. [b]Chi-square test (χ^2) was used to measure the level of significance. *p>0.05 was considered not to be significant. n= number of subjects, s= significant, ns= not significant, BMI = Body Mass Index.

Comparison of postoperative variables regarding blood loss:

Table 2 shows the comparison of postoperative variables between group A and B patients. Amount blood loss in 1st 12 hours immediate after surgery in group A and B were 185.67±35.20 ml and 219.67±57.32 ml respectively, which was statistically significant ($p<0.05$). Amount blood loss in 1st 24 hours after surgery in group A and B were 306.00±73.37 ml and 370.33±69.65 ml respectively, which was also statistically significant ($p<0.05$). Total drain collection after surgery in group A was 792.33±160.32 and in group B was 905.33±137.03 ml, which was statistically significant ($p<0.05$).

Table 2: Comparison of postoperative variables regarding blood loss: (N=60)

Variables	Group Group A(n=30)	GroupB(n=30)	p value*
Blood loss in 1st 12 hours (ml) Range	185.67±35.20 (140-380)	219.67±57.32	0.008[s]
Blood loss in 1st 24 hours (ml) Range	306.00±73.37 (180-550)	370.33±69.65	0.001[s]
Total drain collection (ml) Range	792.33±160.32 (530-1700)	905.33±137.03	0.005[s]

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, s= significant.

Comparison of postoperative outcome variables:

Table 3 shows that among the study population, difference between the postoperative ventilation time of the two groups was not statistically significant ($p>0.05$). Post-operative blood transfusion in group A and B were 2±0.53 units and 2.5±0.68 units respectively, which was statistically significant ($p<0.05$). Duration of ICU stay following surgery was longer in group B patients (64.37±11.98 hours) compared to group A patients (58.5±9.06 hours), which was statistically significant ($p<0.05$). Difference between the duration of hospital stay of the two groups was also statistically significant ($p<0.05$).

Table 3: Comparison of postoperative outcome variables: (N=60)

Variables	Group Group A(n=30)	Group B(n=30)	p value*
Postoperative ventilation time (minutes)	401.5±33.84	415.83±47.16	0.181[ns]
Postoperative blood transfusion (units)	2±0.53	2.5±0.68	0.002[s]
Duration of ICU stay (hours)	58.5±9.06	64.37±11.98	0.037[s]
Duration of hospital stay (days)	9.03±0.99	10.97±1.56	0.028[s]

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, s= significant, ns= not significant, ICU=Intensive Care Unit.

Discussion

The study was conducted at BSMMU hospital, Shahbagh, Dhaka, Bangladesh included a total number of 60 patients undergo-

ing OPCAB as per the inclusion and exclusion criteria. The patients were divided into two groups (Group A and Group B; 30 patients in each). Alagha and associates found a clear threshold for the plasma fibrinogen level postoperative bleeding following OPCAB of 3.1gm/L. OPCAB was performed and postoperative ICU care was given to the patients of both groups as per standard protocol. The demographic variables of the participating patients were recorded and analyzed. The mean age for group A was 55.43±8.53 years and group B was 59.63±6.86 years respectively, the difference was statistically significant (p=0.012). The age range of the patients of this study was from 42 years to 72 years. This study observed that the incidence of low plasma fibrinogen and postoperative bleeding were more common in old age. A similar study showed plasma fibrinogen level and relation to age was statistically significant (p=0.015) which was carried out by Ucar and colleagues [10]. In group A, approximately two third of the population were male 23 (76.66%) and one third 07 (23.33%) were female. In group B, Male were 18 (60%) and 12 (40%) respectively. Male patients were predominant in both the groups. The distribution of gender between the groups were not statistically significant (p=0.16). Ucar and associates also found insignificant (p=0.87) relationship between fibrinogen and gender (male gender=400.7±123.0 versus female gender=395.6±148.1) [10]. A study done by Blome and colleagues in 2005 included ninety-eight (n=98) patients undergoing CABG showed that sex distribution had no significant influence (p=0.389) on postoperative bleeding [11]. When average BMI was compared between the two groups, it was 24.13±2.49 kg/m2 in Group A and 24.62±3.71 kg/m^2 in Group B. The difference was statistically insignificant (p=0.548). This finding correlates to this study of Kim and colleagues, where they found BMI distribution among the groups was not significant (p=0.096) [12]. Presence of diabetes mellitus as a risk factor between two groups were also analyzed statistically but was found to be of no significance (p=0.121). Alagha and associates found distribution of diabetic patients between the two groups were not statistically significant as a risk factor (p=0.07) [10]. Distribution of hypertensive patients between group A and group B was analyzed. Group A had 20 (66.7%) hypertensive patients and group B had 19 (63.3%). This distribution was not statistically significant (p=0.787). The finding of Kim and colleagues correlates with current study, in which p=0.058 for hypertension [12]. In this study, Group A had 03(10%) patients of COPD whereas group B was comprised of 04(13.33%) COPD patients. In that study, the mean platelet count of two groups were 264±90 $\times 10^3$/cumm of blood and 240±85 $\times 10^3$/cumm of blood respectively which was statistically significant (p<0.001) [11]. In current study it was found that, the mean PT of the two groups were 12.29±0.68 seconds and 12.34±0.65 seconds with mean APTT of group A 33.83±3.02 seconds and group B 33.17±2.70 seconds. No significant association was found between PT (p=0.758) and post-operative bleeding. The association of APTT was also statistically insignificant (p=0.371). These findings also correlate with the findings of Blome and Colleagues [13]. The difference in ACT after heparinization and ACT after heparin neutralization between the two groups was statistically not significant (p>0.05). Mean ACT after Heparinization was 357.9±31.26 seconds in group A and 389.1±26.86 seconds in group B (p=0.142). The average ACT after Heparin neutralization in both groups were 123.27±9.17 seconds and 129.47±8.24 seconds (p=0.332). Similar findings were observed in the study done by Rosin and Holt [13]. Operative time to perform OPCAB on patients of group A and B were also compared statistically. The mean time taken to complete OPCAB in group A was 4.38±0.57 hours and that of group B was 4.53±0.66 hours, which was statistically not significant (p=0.347). Comparison of number of distal grafts performed on patients of group A and B was also not significant (p=0.324). These findings correspond to the study conducted by Jeppsson and associates [12]. In present study, mean blood loss in 1st 12 hours in group A was 185.67±35.20 ml and 219.67±57.32 ml in group B and the difference was statistically significant (p=0.008). And the difference between mean Blood loss in 1st 24 hours in the two groups was (306±73.37 ml in group A and 370.33±69.65 ml in group B, range 180-550 ml) statistically significant (p=0.001). These findings are also found in the retrospective study done by Alagha and associates. The difference of postoperative bleeding in 1st 24 hours following OPCAB was statistically significant (p=0.01) [11]. In the study done by Ucar [11], and associates, chest drainage was a mean of 972 ml (range, 240-2445 ml) and there were negative linear relation between the fibrinogen levels and the postoperative bleeding. This relation was statistically significant ($r = -0.897$, $p<0.001$) which correlates with current study [11]. The mean post-operative blood transfusion in group A and B were 2±0.53 units and 2.5±0.68 units respectively, which was statistically significant (p<0.05). These findings correspond to the study conducted by Tettey and associates [14]. The distribution of mean postoperative ventilation time in the two groups was not significant (p=0.181). This is comparable to the study conducted by Birla and associates [15]. The mean ICU stay of the patients of group A and group B (58.5±9.06 hours and 64.37±11.98 hours respectively) was observed and longer duration of ICU stay of the group B patients were statistically significant (p=0.037). This finding is similar to the finding (p=0.023) of Kim and colleagues. A logistic regression analysis was done to assess the predictive value of plasma fibrinogen level, age, platelet count for postoperative bleeding following OPCAB. Among the other variables plasma fibrinogen level was the most valuable predictor of postoperative bleeding following OPCAB (OR 2.960, 95% CI, 1.009-8.678, p=0.048). This is similar to the information provided by Alagha and associates [10]. There were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality in present study.

Conclusion

In conclusion the efficacy were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality. Fibrinogen concentration level was associated with increased postoperative bleeding in patients undergoing off-pump coronary artery bypass grafting surgical patients. Plasma fibrinogen level appears to be a useful predictor of postoperative bleeding in patients undergoing OPCAB. Its preoperative level may indicate us to take necessary steps to prevent postoperative bleeding as well as reduce the rate of ICU stay. This study demonstrated fibrinogen levels are associated with increased postoperative bleeding following OPCAB fibrinogen determination may be a useful screening tool to identify individuals at added risk for excessive bleeding after OPCAB [16].

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