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THE ROLE OF PLATELET CONCENTRATION TRANSFUSION ON THE CORRELATION BETWEEN PLATELET NUMBER AND MAXIMUM AMPLITUDE WITH BLEEDING VOLUME POST CARDIOPULMONARY BYPASS

Ryan Bayusantika Ristandi, Nida Suraya, Leni Lismayanti, Sylvia Rachmayati

Department of Clinical Pathology, Faculty of Medicine, Padjadjaran University, Hasan Sadikin General Hospital, Bandung, Indonesia. E-mail:: ryan_b_ristandi@yahoo.com

ABSTRACT

Post-operative heart patients with Cardiopulmonary Bypass (CPB) are at risk of excessive bleeding. Excessive bleeding is mainly due to thrombocytopenia and platelet dysfunction. The volume of post-CPB bleeding without the administration of platelet concentrate correlates well with platelet count and Maximum Amplitude (MA). The administration of platelet concentrate in thrombocytopenia and platelet dysfunction post-CPB may affect the correlation of platelet count and MA which affects the volume of bleeding. The purpose of this research was to know the role of transfusion of platelet concentration post-CPB on the correlation between platelet number and MA with the volume of bleeding. The analytical observational analytic test with the cross-sectional design was conducted on secondary data from September 2015 to March 2016. A total of 44 postoperative heart patients CPB monitored up to four hours in the room Cardiac Intensive Care Unit (CICU) Dr. Hasan Sadikin Hospital Bandung. The platelet count was negatively correlated with bleeding volume (r = -0.157, p = 0.308) and the MA was negatively correlated (very weak) with bleeding volume (r = -0.171, p = 0.266). The post-CPB platelet concentrate concentration led to better patient hemostasis, as evidenced by the majority of platelet counts (97.7%) > 100,000/mm^3 and MA (84%) x ≥ x 50x mm. The post-CPB platelet concentrate causes a negative (very weak correlation between platelet count and MA with bleeding volume.

Key words: Platelet number, platelet concentrate, maximum amplitude, cardiac surgery, bleeding volume post cardiopulmonary bypass

INTRODUCTION

Basic Health Research Data in 2013 mentioned that Coronary Heart Disease (CHD) increased 1.5% compared with the data in 2007, 1.3% and CHD is the disease with the highest patients in patients with thenon-infectiousdisease.[1] In 2013, West Java Province had the highest coronary heart disease patients in Indonesia with the amount of 160.812 (5% and heart failure of 96.487 (0.3%)). Based on the age of the patients, coronary heart happened in the age of 45 – 54 years.[2]

Public Center Hospital, Dr. Hasan Sadikin, Bandung, as the center of referral for heart surgery, recorded 6.829 visits in 2015 for atherosclerosis heart disease with the sixth highest group other than accidents and malignancy. One hundred three heart operations with Cardiopulmonary Bypass (CPB) were done during the year of 2015 (1.5% heart disease).[3] The most common types of heart surgery by CPB method are Coronary Artery Bypass Graft (CABG), Mitral Valve Replacement (MVR), Double Valve Replacement (DVR), Atrial Septal Defect (ASD) correction and Ventricle Septal Defect (VSD).[4,5-9]

The use of heart-lung machine during CPB activates and consumes thrombocytes leading to thrombocytopenia and thrombocyte dysfunction. In the use of the heart-lung machine, mechanical contact (extracorporeal) happens tocause an irreversible defect of glycoprotein thrombocyte surface function for adhesion and aggregation named GpIb/IX/V and GpIIb/IIIa.[10-12] Therapeutic hypothermia during CPB causes adhesive and aggregation thrombocyte disorder. Adhesive disorder happens because during hypothermia the secretion of alpha-granule happen massively that induce the activation of Complement Receptor type 3 (liver macrophage), creating TXA2 and Gp1b phagocytosis occurs which has an essential role in the adhesive process. Aggregation defect occurs because during hypothermia tissue plasminogen activator will increase plasmin level. Plasmin causes

proteolysis of GpIIb/IIIa which functions actively in thrombocyte aggregation.[13-15] Hemodilution in heart operation with CPB causes thrombocytopenia.[16]

Excessive bleeding after CPB was caused mostly by the defect in thrombocytes compared to coagulation factor disorder. Additional management after CPB is transfusion and since thrombocytesare the highest cause compared with coagulation factor disorder, thrombocyte concentrate transfusion should be considered.[17-19] Thrombocyte defect causes excessive bleeding after CPB when there are thrombocytopenia and thrombocyte dysfunction.[10] After CPB, thrombocyte left in patient circulation will be influenced by thrombocyte concentrate transfusion.[20]

In the good wound healing process, right thrombocyte amount and function is needed. According to Roccoftzen's *et al*. research, thrombocyte concentrate transfusion has the same hemostatic function, similar to thrombocytes in the circulation but better role in thrombocyte concentrates stored 1 – 3 days compared to those stored 4 – 5 days.[19] The hemostatic effect is examined within 24 hours after transfusion. The amount of thrombocyte after CPB increases in accordance with the amount of thrombocyte. The more thrombocytes, the more thrombin will be formed. Each bag of thrombocyte concentrate contains 50 mL and will increase patient thrombocytes 5,000/mm^3.[21] Thrombocyte secretes α-granule (50 – 80 granules/thrombocyte) which influences Vascular Endothelial Growth Factor (VEGF), Platelet Derived Growth Factor (PDGF) and Epidermal Growth Factor (EGF) to accelerate the formation of clot (platelet driven angiogenesis) and increasing thrombin production (thrombin production stimulation) which plays a role in wound coverage. The fewer the number of thrombocytes the smaller the secretion of α-granule which causes VEGF, PDGF, EGF, and thrombin production to be hindered so the wound covering process becomes more difficult and the bleeding risk increases.[22]

Only checking the amount of thrombocyte does not describe the function and the activity of thrombocyte interaction with coagulation factors and natural anticoagulant protein in covering the wound. The amount of thrombocyte solely cannot reflect bleeding etiology after CPB, because according to Weitzel *et al*.[13] the bleeding risk still exists even though the number of thrombocytesis normal. The amount and function of thrombocyte influence the strength of the final clot which can be evaluated by the MA parameter from Thromboelastography (TEG) instrument. According to his research, the number and function of thrombocyte are reflected by the decrease of MA and the increase of bleeding risk. In TEG, thrombocyte and coagulation factors interactionin the process of initiation amplification propagation in the formation of the final clot which covers wound can be observed.[23] In Welsby *et al*. research was carried out on the patient after CPB before thrombocyte concentrate transfusion with the correlation result that the number of thrombocytes and MA correlates with the bleeding volume.[23]

The purpose of this research was to know the role of transfusion of platelet concentration post-CPB on the correlation between platelet number and MA with the volume of bleeding.

METHODS

Secondary data were collected from 44 patients after heart surgery with CPB in the period from September 2015 to March 2016. The data were taken from core research entitled "Analysis of Fresh Frozen Plasma Transfusion Need Based on Laboratory Examination of Standard Coagulation and Thromboelastography on Heart Disease Patient after Cardiopulmonary Bypass" The research design was the analytical observational retrospective with the design of a cross-sectional study. Bleeding volume was stated to be excessive (>400 mL in the first hour or 100 mL/hour in 4 hours consecutively). The number of thrombocytes wasreported to increase if it is was >100,000/mm^3, normal 50,000–100,000/mm^3, and decrease in <50,000/mm^3. Platelet examination is done by the impedance method. This study was carried out in Dr. Hasan Sadikin Bandung Hospital with patients who had been given informed concent.

RESULT AND DISCUSSION

The description of research subject characteristics is presented in Table 1, covering sex, Body Mass Index (BMI), age, diagnosis, action, CPB duration bleeding volume in Chest Tube Drainage (CTD), thrombocyte amount, TEG maximum amplitude and bleeding amount.

In this study the correlation of platelet counts with volume bleeding can be seen in Table 2, with insignificant results because p-value> 0.05.

In this study also can be seen TEG correlation analysis with volume bleeding can be seen in Table 3, with the results not significant because p-value> 0.05.

This research was dominated by males which

Table 1. Research subject characteristics (n = 44)

Variable	n (%)
Age	
10 – 20 years	7 (15.9)
20 – 30 years	1 (2.2)
30 – 40 years	2 (4.5)
40 – 50 years	7 (15.9)
50 – 60 years	11 (25)
60 – 70 years	15 (34)
70 – 80 years	1 (2.2)
Sex	
Male	29 (65.9)
Female	15 (34.1)
BMI	
Underweight	6 (13.6)
Normal	23 (52.3)
Overweight	15 (34.1)
Diagnosis	
Coronary Artery Disease (CAD)	29 (69.5)
Rheumatoid Heart Disease (RHD)	7 (15.9)
Atrial Septal Defect (ASD)	4 (9)
Ventricle Septal Defect (VSD)	2 (4.5)
Tetralogy of Fallot (TOF)	1 (2.2)
Mitral Valve Prolapse (MVP)	1 (2.2)
Duration of CPB	
<120 minutes	33 (75)
120 – 180 minutes	6 (13.9)
>180 minutes	4 (9.1)
Bleeding	
Excessive	3 (6.81)
No-excessive	41 (93.18)
Intervention	
CABG	29 (65.9)
Mitral Valve Replacement (MVR)	4 (9.1)
Total Valve Replacement (TVR)	3 (6.8)
ASD Closure	3 (6.8)
VSD Closure	2 (4.5)
Double Valve Replacement (DVR)	1 (2.2)
ASD Closure + MVR	1 (2.2)
CABG + DVR	1 (2.2)
Thrombocyte Amount	
Normal	43 (97.7)
Decrease	1 (2.3)
Maximum Amplitude	
Normal	37 (84)
Decrease	7 (16)

were 65.9%. This result was different from Maas *et al*. research which was dominated by females with age>50 years and were all diagnosed with CAD.[24] Estrogen deficiency in female >50 years changed cholesterol level especially LDL increase, and HDL would decrease so that it increased atherosclerosis

Table 2. Correlation ofthrombocyte amount and bleeding volume

Variable	rs (CI 95%)	p-value
Correlation between Thrombocyte amount And bleeding volume	-0.157	0.308

Note: Spearman correlation; significant if p <0.05. Sign of ** showed significant or meaningful in the statistic. r: coefficient correlation

Table 3. Correlation analysis of TEG maximum amplitude and bleeding volume

Variable	rs (CI 95%)	p-value
Correlation analysis of TEG maximum amplitude and bleeding volume	-0.171	0.266

Note: Spearman correlation; significant if p <0.05. Sign of ** showed significant or meaningful in the statistic. r: coefficient correlation.

risk and supported CAD diagnosis on Maas'research subjects. In this research, female subjects were only 15 persons (34.1%).[25] Ten of 15 female subjects were >50 years, and 70% of the subjects suffered from CAD.

The highest proportion of research subject was in the range of 60 – 70 years (34.1%) and the most diagnosis was CAD (69.5%) so that the actionstaken were dominated by CABG (65.90%). That result was in accordance with Riskesdas 2013 which found the highest heart disease in the age >60 that was 65 – 74 years.[1] Aging was connected with the change of vascular endothelial functionand heart thrombogenesis disorder so that heart disease risk increased and reached the peak in the sixth decade.[26] Average age of research subjects of Welsby *et al*. research was 60 years with CABG as the majority of action (88%).[23]

Duration of heart surgery with CPB method in this research was <120 minutes in 75% patient. In Despotis *et al*. research, it was concluded that the longer CPB duration, the more transfusion was needed which was related to hemostasis disorder including thrombocyte activity disorder exposed by heart-lung machine, hypothermia, and hemodilution.[27] This researcher also concluded that the CPB duration >120 minutes started to increase the amount and thrombocyte function which wassignificant (r = 0.66; p = 0.001) and thrombocyte function was decreased in CPB with the duration >180 minutes.

The research result showed that there was a

negative correlation between thrombocytes with the bleeding amount which was weak and not meaningful statistically (r = 0.157 and p = 0.308). The presence of a negative correlation between the number of thrombocytes with bleeding volume showed that the lower thrombocyte volume, the higher bleeding volume and vice versa. But the power which was weak showed the role of thrombocyte transfusion after CPB influenced the patient thrombocyte which also influenced the patient bleeding volume. Adequate thrombocyte amount was needed to interact with coagulation factors in the amplification phase for more thrombin formation which functioned for changing fibrinogen into fibrin and wound healing. If the amount of thrombocyte decreased, the bleeding risk could decrease because proper wound healing did not happen. Thrombocyte concentrate transfusion helps the remaining thrombocyte from surgery to functionalize well in wound healing.[19]

In this research, before entering Cardiac Intensive Care Unit (CICU), patient stabilization was done with by giving therapy or thrombocyte transfusion.[19] Thrombocyte concentrate transfusion became the only factor which influenced thrombocyte amount directly. Mostly research subjects (97.4%) had thrombocyte amount >100,000/mm^3 caused by thrombocyte concentrate transfusion treatment while stabilization process in the operating room before transferred to CICU. Thrombocyte concentrate transfusion became the only factor that influenced the thrombocyte amount directly, so in this research, it could be concluded that the role of thrombocyte concentrate was the cause of correlation between thrombocyte and bleeding volume which became negative and weak. According to Roeloffzen *et al.* research, the supply of thrombocyte concentrate transfusion caused the recovery of thrombocyte amount to become good especially after the first hour of transfusion. Thrombocyte amount increased from 11,000/mm^3 to 37,000/mm^3 with p < 0.05.[19]

The previous research in America, of Welsby *et al*. resulted in thrombocyte amount correlating well with bleeding after heart surgery with CPB (r = 0.45; p = 0.02).[23] The differences between Welsbys *et al*. with this research was the removal of check material that was done before thrombocyte concentrate transfusion. Another factor which might influence patients in the previous research was evaluation was conducted not only 4 hours post-surgery but periodically throughout 24 hours post-operation.[23] This could become the factor that could resultin differences of this research with the previous research.

This research result showed that there was a weak negative correlation between MA with bleeding volume. The presence of a negative correlation between MA with bleeding volume showed that the lower the thrombocyte amount, the higher the bleeding volume and vice versa. The weak power showed the role of thrombocyte concentrate transfusion after CPB influenced patient's amount and thrombocyte function (MA) and it had hemostasis potencies similar to patient circulation in accordance with Reoloffzen *et al*. (p ≥ 0.1).[19] In Reoloffzen, there was an increase of MA after transfusion from 44.000/mm^3 to 54.000/mm^3. Thrombocyte transferred helped the remaining thrombocytes after surgery to functioned well in wound healing. In this research thrombocyte function disorder (MA) decreased in seven patient in line with the duration process of CPB >180 minutes in 9.1% patient. Excessive bleeding happened in three patients (6.8%) while the rest was (93.18%) of normal bleeding non excessive. From three patients who experienced excessive bleeding, all had thrombocyte amount above 100,000/mm^3 but two of them had MA which was decreasing (< 50 mm). The research result was different from Welsby *et al*. research because MA correlated well with post-surgery CPB bleeding (r=0.06 and p < 0.0018).[23] This was caused by check material in Welsby's research taken before thrombocyte concentrate transfusion. The subjects in Welsby *et al*. research was more homogenous in the diagnosis and was done in countries where MA-TEG was used as the reference method of using thrombocyte concentrate transfusion. Foriester *et al*. research, resulted in maximum amplitude significantly influencing bleeding (r = 0.52; p < 0.05), but there was a difference, there were CPB and non-CPB subjects.[28] In this research, there were two research subjects with normal thrombocytes, MA decrease, and excessive bleeding. It happened possibly because of surgery coagulopathy or other hemostatic disorders (such as coagulation factor disorder) because there was no disorder in thrombocyte amount and function disorder. In this research, there were three research subjects with normal thrombocyte amount, decreasing maximum amplitude but normal bleeding (not excessive), that might be caused by normal thrombocyte amount that could cover the wound well although the function was not good. Thrombocyte concentrate transfusionbecame the only factor which influenced the thrombocyte amount directly, so this research concluded that thrombocyte concentrate

transfusion role caused very weak negative correlation between MA with bleeding volume.

CONCLUSION AND SUGGESTION

Thrombocyte concentrate distribution post-CPB cause the thrombocyte amount and MA thromboelastography to have an inversed correlation with patient bleeding volume.

The supply of thrombocyte concentrate should be given after checking the thrombocyte amount and MA thromboelastography so the thrombocyte concentrate transfusionis appropriate with the patient's needs.

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