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The Differences of Platelet Count, Mean Platelet Volume and Pletelet Distribution Width in Preterm Newborns with and without Patent Ductus Arteriosus

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Keyword:
PDA,
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Abstract

Background: Patent ductus arteriosus (PDA) is the most common congenital heart disease in prematur newborn. The role of platelet in closure of ductus arteriosus remains controversial.

Purpose: To evaluate difference of platelet count, mean platelet volume (MPV), and platelet distribution width (PDW) in premature newborn with and without PDA.

Methods: This was cross-sectional that collected from medical record of premature newborn who hospitalized in Perinatology Unit of Adam Malik Hospital from November 2017 to September 2019. The diagnose of PDA was taken from echocardiograhy data. Platelet indices was found from laboratory's result that was performed in 24 hours of life.

Result: A total of 73 preterm newborns consist of 35 newborns with PDA and 38 newborns without PDA. There was significantly difference of platelet count in both groups which the mean of platelet count in PDA groups was 152,765.71/µl (SD 71,792.46) and in non PDA groups was 274,456.05/µl (SD 121,360.88). However, there was no significatly difference of MPV and PDW in both groups (P= 0.22, P= 0.79). We also found that low platelet mass index and low ratio RDW to platelet were related to PDA.

Conclusion: There is significantly difference of platelet count in preterm newborns with and without PDA which the mean platelet count in newborns with PDA were significant lower than in newborns without PDA.

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INTRODUCTION

Ductus arterious is a vascular structure in normal uteroplacenta that connect the proximal of descending aorta and pulmonary artery.[1] In term newborn, the functional closure of ductus arteriosus will occur spontaneusly 50% within 24 hours, 90% within 48 hours, and 100% within 72 hours after birth. [2] This disorder is more common in premature infants with the incidence of 8 per 1000 births than in term 1 babies per 1,000 live births.[3] The study, by Division of Perinatology, Ciptomangunkusomo Hospital in Indonesia, reports the incidence of PDAs in premature newbons was 14%.[4]

The presence of Patent ductus arteriosus (PDA) can increase morbidity and mortality rates in premature newborns. Systemic circulation hypoperfusion can cause necrotizing enterecolitis (NEC) and renal insufficiency in preterm infants.[5] Intraventricular hemorrhage (IVH) can also occur due to reperfusion of cerebral blood flow.[6] Early detection and management of premature newborns with PDA, will improve clinical outcomes, shorten the duration of mechanical ventilator, and reduce the length of stay.[7]

Etcler et al who were the first study that hypotesize about role of platelet in closure of ductus arteriosus. Vascular injury due to vasoconstriction of lumen ductus arteriosus will trigger the reactivity of platelet and continually begin the process of remodelling of ductus arteriosus. Activated platelet will form of platelet aggregation and continue to platelet plug, which further influence the permanentlyclosure of the ductus arteriosus.[8] This theory has also been proven by several studies that reported of relationship of thrombocytopenia in the first 24 hours of life and the incidence of PDA in premature infants.[9-11] Nonetheless, there are also several studies that reported there is no relationship of platelet counts and PDA events in preterm newborns.[12,13]

Beside of platelet counts, the reactivity of platelet can be assessed from mean platelet volume (MPV) and platelet distribution width (PDW) values. These parameters have been investigated that related to platelet activity in cardiovascular disease, so we can be assumed that these parameters are also related with the incidence of PDA in preterm newborns.[14,15] There is no study in Indonesia that reported the relationship of platelet counts, MPV and PDW as predictive factors in preterm newborn with PDA.

METHODS

Subjects

This was cross sectional study with retrospective design. Data were collected from medical record data of all preterm newborn who have been hospitalized in Perinatology Unit in Adam Malik Hospital, Medan, Indonesia. Our hospital is the biggest tertiary and teaching hospital in Sumatera Island, Indonesia. The medical record was collected from January 2017 to September 2019. We have concluded all of the preterm newborn, was defined by gestational age from Ballard Score less than 37 week of gestational age. The diagnose of PDA was established from the echocardiograhy examination. We also collected data about prenatal and antenatal condition, delivery methods, birth weight, the using of respiratory support, mortality and the length of stay in perinatology unit. The laboratory data was collected in the first 24 hours of life. We excluded all of the preterm newborns that have mayor congenital disorder and congenital heart disease beside PDA.

Statistical Analysis

Data was statistically analyzed using SPSS software version 22.0 (Statistical Package for Social Sciences) for windows. Descriptive statistics were expressed in the form of mean ± standard deviation (SD); while for categorical data they were presented in the form of frequency. Comparisons between groups for continuous variables, normally distributed data were performed by T-test or Mann–Whitney test for the not normally distributed data with P-value of (< 0.05) was considered as a significant difference.

Ethical Considerations

Our study was approve by Ethical Commision of Medical Faculty of Sumatera Utara University.

RESULTS

A total of 73 preterm newborns were included in this study with 35 subjects with PDA and 38 subjects without PDA. From all of the subjects, 41 subjects were female, 45 subjects have gestational ages between 33-36 weeks, and 58 subjects were delivery in sectio caesaria. The incidence of asphyxia neonatorum occurred in 29 subjects with PDA and 35 subjects without PDA. The average length of stay for preterm newborns with a PDA were 20 (SD 13.21) days whereas the preterm infants without PDA were 19.1 (SD 11.82) days. During the treatment period, 41 subjects used nasal continuos positive airway pressure (CPAP) and 25 subjects used mechanical ventilator,

Tabel 1. Charateristic demograhips of subjects

Karakteristik	PDA (n= 35)	No PDA (n= 38)
Sex		
Male, n	15	17
Female, n	20	21
Gestational age, n		
<32 week	13	15
33-36 week	22	23
Birth weight, gram, mean (SD)	1,564.0 (368.85)	1,445.1 (443.92)
<1,000 gr, n	0	5
1,000-1,500 gr, n	18	19
>1,500-2,500 gr, n	17	14
Delivery methods		
Spontaneous delivery, n	9	6
Sectio caesaria, n	26	32
Ashyxia neonatorum, n	29	35
Platelet count in 24 hours, n		
< 50,000/µL	3	
≥ 50,000-149,000/µL	13	
≥150,000/µl	19	38
Respiratory support		
CPAP, n	20	21
Mechanical Ventilator, n	9	16
Length of stay, day, mean (SD)	20.0 (13.21)	19.1 (11.82)
Outcome		
Discharge	27	23
Death	8	15
Hasil ekokardiografi		
Diameter of ductus arterious, n		
≤ 1.5 mm (small)	3	-
1.5-3 mm (moderate)	28	-
3-5 mm (large)	4	-

Tabel 2. Differences of platelet counts in preterm subjects with and without PDA

Subjects	Mean platelet counts (SD)	Mean difference (CI 95%)	P
PDA (n = 35)	152,765.7/µL (71,792.46)	121,690.3 (74,641-168,738.74)	0.001
No PDA (n = 38)	274,456.1/µL (121,360.88)		

Unpaired t test

and 23 of subjects were died. From the platelet indices in 24 hours of life, all of preterm subjects with PDA have platelet count more than 150,000/µl. Based on the diameter of the ductus arteriosus, the most common type of PDA is a moderate PDA (1.5-3 mm). The demographic characteristics of the subjects are shown in table 1.

The mean of platelet count in PDA groups was 152,765.7/µL (SD 71,792.46), lower than non PDA groups with 274,456.1/µL (SD121,360.88) (Table 2). From statistical analysis, there is a significant difference of platelet count in preterm subjects with and without PDA (P=0.001). On the contrary, there is no significant difference of MPV and PDW in both groups (P=0.220, P=0.792) (Table 3 and Table 4). The differences of other hematology parameters in preterm infants with and without PDA, can be seen in table 5.

Tabel 3. Differences of MPV in preterm subjects with and without PDA

Subjects	Mean MPV (SD)	Mean difference (CI 95%)	P
PDA (n = 35)	11.1 fL (2.37)	0.512 (0.313-1.338)	0.220
No PDA (n = 38)	10.7 fL (0.92)		

Unpaired t test

Table 4. Differences of PDW in preterm subjects with and without PDA

Subjects	Mean PDW (SD)	Mean difference (CI 95%)	P
PDA (n = 35)	11.9 (2.06)	0.128 (0.84-1.09)	0.792
No PDA (n = 38)	11.8 (2.08)		

Unpaired t test

Tabel 5. Differences of other hematology parameters in preterm infants with and without PDA

Hematology Parameter	PDA (n=35)	No PDA (n= 38)	Mean difference (CI 95%)	P
Hemoglobin, g/dl, mean (SB)	14.7 (3.74)	14.3 (2.96)	0.378 (1.19-1.94)	0.632[a]
Hematocrit,%,mean (SD)	43.1 (10.65)	41.5 (8.16)	1.6 (2.79-6.02)	0.467[a]
Leukocyte,/µl,mean (SD)	12,456.0 (7,746.87)	12,398.7 (5,105.93)	57.1 (2,982.07-3,096.17)	0.970[a]
RDW,%, mean (SD)	17.3 (3.55)	17.4 (2.78)	0.2 (1.31-1.65)	0.816[a]
Platelet mass index median, (min-maks)	2,059.93 (54-1,483)	2,497.1 (1,686-32,307)	1,595.22 (238.07-3,428.51)	0.001[b]
Ratio RDW/platelet (RPR), %, mean (SD)	0.26 (0.567)	0.07 (0.023)	0.19 (0.01-0.37)	0.038[a]

[a] Unpaired t test

[b] Mann Whitney

DISCUSIONS

The objective of this study was to evaluate the differences of platelet count in preterm infants with and without PDA. In our study, we found that there is significant difference of platelet count in both group where the mean of platelet count in PDA subjects were significant lower than in no PDA subjects. Our findings were confirmed by previous study which reported that there is correlations of thrombocytopenia in 24 hours of life and the incidence of PDA in pretem newborn. Beside that, there were also study reporterd inversely.

Our findings also confirmed that there is no significant difference MPV and PDW in both groups. These findings also support by the study from Kahvecioglu *et al* and Dani *et al*.[16,17] Study of Bednarek *et al* reported that hyporeactive *platelet in* preterm infants in first week of life and become normal reactivity in 10-14 days of life.[18] Platelet hyporecativity in preterm infants is also caused by a lack of α-adrenergic receptors on platelets.[19] These receptors function as receptors on activated platelets to bind to other receptors in the process of platelet adhesion. In addition, platelets in preterm infants produce fewer adhesion granules such as glycoprotein IIIa / IIb.[20]

Platelet activity examination using flow cytometry has a good level of sensitivity and specificity in premature infants.[21,22] The relationship of platelet hyporeactivity in preterm infants with the incidence of PDA has been investigated by Kahvecioglu *et al* which reported platelet in premature infants with PDA showed hyporectivity to the primary ADP agonist and caused prolongation of the formation of platelet aggregation and occlusion.[16]

Platelet mass index parameters are obtained from calculations [platelet count x MPV / 1000]. In our study, there was a significant difference in the value of platelet mass index in preterm infants with and without PDA, where the platelet mass index value was lower in preterm infants with PDA compared to without PDA.

This is consistent with previous studies where platelet mass index is low associated with the incidence of hsPDA in preterm infants. Large young platelets have a greater mass index. In addition, young platelets contain more adhesion and ADP molecules so that they are more active and aggregated than normal platelets. [23]

Another platelet parameter that has been investigated in relation to PDA in preterm infants is the RDW to platelet ratio (red distribution width to platelet / RPR ratio). Red cell distribution width is a measurement of variation in the size of erythrocytes (anisocytosis). Increased RDW levels in adults are associated with an increased risk of mortality in patients with heart failure and other chronic diseases.[24] A retrospective cohort study by Bekmez *et al* reported that the RPR had a 71% sensitivity level and 92% specificity in diagnosing the incidence of hsPDA in preterm infants with a value of the cut off point is 0.13% .[25]

In our study, we found a significant difference in the value of ratio RDW to platelet (RPR in preterm infants with and without PDAs which the RPR value in the group of preterm infants with PDA was higher than in the preterm infants group without PDA. An increase in RPR values in newborns (> 0.816%) is associated with neonatal early-onset sepsis.[26] The known risk factors for onset neonatal sepsis are chorioamnionitis, maternal urinary tract infections, premature rupture, and vaginitis. Neonatal sepsis is a risk factor that has been studied in association with PDA events in preterm infants.[27]

This study provided data on platelet indices as a predictive factor for PDA in preterm infants. Our study were taken based on the medical record data so that selection and information bias can occur. Because of the limitations of medical record data, this study has not been able to provide information about the role of these platelet parameters in the success of PDA pharmacological therapy. Further cohort studies that can be developed from this study are expected to provide information on the role of platelet parameters in the successful closure of PDA with pharmacological therapy.

CONCLUSIONS

There is significant difference of platelet count in preterm infants with and without PDA which the platelet count in preterm infants with PDA is significant lower that in preterm infants without PDA. There is no significant difference of MPV and PDW in both groups. We also identified that low platelet mass index and low RpR is significant related with preterm infanst with PDA.

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CONFLICT OF INTERESTS :

There was no conflics of interest in this research.

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