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RESEARCH ARTICLE

Platelet Profile in Patients with Status Asmaticus in Kebumen

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ABSTRACT

BACKGROUND: *Asthma has been considered as type 1 hypersensitivity disease, but actually asthma involves a variety of inflammatory factors. Based on pro-inflammatory cells, asthma is classified into eosinophilic, non-eosinophilic, neutrophilic, and non-neutrophilic. Platelet plays a role in pathophysiology of asthma through inflammation. However, platelet profile in patients with asthma have not been established.* ***OBJECTIVE:*** *to determine the platelet indices of patients with status asmaticus of different phenotypes.*

METHODS: *a cross-sectional study was conducted among a minimum sample size of 67 patients. Data were collected from medical records of patients in RSUD Kebumen. Platelet indices included mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT).*

RESULTS: *There was no significant difference in the value of MPV and PDW in patients with eosinophilic and neutrophilic asthma (p> 0.05). But, there was a significant difference in PCT between the two groups (P <0.05)*

CONCLUSION: *There was difference only in plateletcrit (PCT) between patients with eosinophilic and netrophilic asthma.*

Keywords: *Asthma, platelets, MPV, PDW, PCT*

INTRODUCTION

Asthma is a reversible disease affecting airway. More than 300 million people worldwide have asthma with morbidity and mortality between 1-8% and 250 thousand deaths per year. The majority of asthma patients are women (Panek et al., 2016). The number of asthma attacks is highly variable and influenced by the climate, so that asthma attacks take place according to the cycle. Climate not only affects the number but also the severity of asthma attacks. Hot and dry climate has been shown to decrease the number of attacks but not the severity (Correia Junior et al. 2017). In addittion, asthma is also affected by physical activity. Epidemiological studies on asthma conducted on athletes showed that asthma tend to attack athletes who exercise at a high ventilation (Selge et al., 2016). Three conditions underlying asthma include reversible airway obstruction -either spontaneously or with treatment-, airway inflammation, and increased responsiveness respiratory tract due to various stimuli (Gorczynski & Stanley, 2013). Studies showed that many pro inflammatory cells in airway mucosa were found in biopsies of the epithelial tissue and lumen vessel bronchial blood (Lukawska et al. 2014). Vascular tissue increment in the airway affect the severity of asthma attacks (Chung & Ferrara 2011; Harkness et al. 2014).

Asthma is classified into eosinophilic, non-eosinophilic, neutrophilic, and non-neutrophilic. The classification is based on the character of eosinophils and neutrophils found in patients with asthma. Patients with eosinophilic asthma tend to have severe attacks. Airway remodelling in this type is more severe than in asthma patients with non eosinophilic phenotype (Fahy, 2009). This is possible because the neutrophils will encourage the activity of inflammatory mediators and vascularization in asthma.Asthma always characterized by remodeling of airway tissue. This remodelling is related to the pathological changes in asthma due to exposure of inflammatory mediators. The active mast cells mainly secrete histamine, proteases, leukotrienes, prostaglandins, platelet activating factor, and various cytokines including vascular endothelial growth factor (VEGF). The presence of histamine will cause contraction of airway smooth muscle, mucosal edema, and increased mucous secretion. Leukotrienes together with prostaglandins and cytokines will cause mucosal inflammation. Protease and the formed reactive oxygen

species (ROS) resulted from inflammation lead to the damage in the respiratory tract tissue and replaced with new, non-functional tissue. This condition causes a chronic asthma becomes more severe (Lieberman & Anderson 2007). Inflammatory conditions also play an important role in airway remodeling in asthma. Biopsy results also indicate that in asthma, solid vascular network is formed in sub epithelial layer. The evaluation of broncho alveolar lavage (BAL) shows a great number of pro vascularization molecules, vascular endothelial growth factor (VEGF). Vascular endothelial growth factor (VEGF) is a molecule that stimulates the expansion of vascular tissue, vasodilatation, and plasma leakage (Harkness et al. 2015).

Platelet is a fragment of the megakaryocytes cytoplasm in the blood, ranging from 1-4 um and having no nuclei. Platelets have been associated with hemostasis (Theml et al., 2004 and Hoffman, 2013). Platelet activity can be determined by several indices such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT). Increased MPV reflects the impaired platelet function and activation due to the emergence of megakaryocytes as compensation for chronic impaired production of platelets.Function of platelets can not be replaced by their precursors, namely megakaryocytes, resulting in functional defect. Plateocrite can be used as predictors of bleeding in addition to the number of platelets in the case of thrombocytopenia. The increase in platelet distribution width (PDW) indicates platelet anisocytosis (Wiwanitkit 2004); (Tekçe et al. 2015). Other studies have shown that MPV can not be used to determine the asthma phenotype (Nacaroglu et al. 2016). Experimental studies in mice have shown that platelets affect the expression of pro angiogenic mediators. Mice with suppressed platelet activity were not able to show sufficient angiogenesis (Harkness et al. 2015). This is presumably because platelets are part of the inflammatory activators. The lack of activators causes a decrease in the incidence of inflamation. In fact, angiogenesis is triggered by inflamatory mediator. Platelet involvement in remodelling in asthma has been well studied but not the platelet profile using a complete blood tests. This is a preliminary study to a long-term study to develop an anti-platelet as a treatment for asthma.

RESEARCH METHODS

This study was a cross-sectional study on medical records of a total of 67 adult patients with asthma hospitalized in Kebumen general hospital between January 2016 and December 2016. Inclusion criteria were all adult inpatients with asthma in Kebumen general hospital. The exclusion criteria of this study were asthma patients undergoing oral steroid treatment before admission to hospital. The samples were divided into two groups: eosinophils of 47 (61.84%) and neutrophils group of 20 (26.32%) patients. Data taken in this research included medical history and physical examination including a history of asthma, the condition of the attacks, and the current therapy of asthma. The laboratory data included complete blood test results. The blood sample was taken from cubital vein and then inserted into the tube EDTA and screened using a hematology analyzer Mindray. The results produced a complete data include platelet indices.

STATISTICAL ANALYSIS

Based on the normality test, data were normaly distributed. Thus, chi-square test were then performed. The data were considered significant if $p < 0.05$. The ethical clearence was obtained from Committee of ethics, Faculty of Medicine, Universitas Islam Indonesia (31/Ka.Kom.Et /70/KE/X/2016).

RESULTS

The study entrolled 67 inpatients of Kebumen general hospital. There were 17 (25. 37%) male and 50 female (74.63%) subjects. The mean age of the subjects included in this study was 44 years. The majority of the subjects did not use reliever regularly during the attack (79.10%). 3 subjects (4.48%) used controller. The detail characteristics of the subjects is presented in Table 1. The most common reliever was salbutamol. The controllers used were dexametason and budesonide. The status was classsified into 4 categories namely eosinophilia, netrophilia, eosinophilia netrophilia, and non eosinophilia netrofilia. The table shows the largest proportion was in the neutrophilia group (44.74%). Chi-square test showed a significant difference ($p = 0.002$).

Platelet indices were then evaluated. There was a significant difference in levels of plateletcrit (PCT) between neutrophilic and eosinophilic status ($p= 0.0011$). The mean plateletcrit (PCT) of neutrophilia was smaller than eosinophilia.

DISCUSSION

This study showed that there were more patients with neutrophilic than eosinophilic asthma.This finding supports previous study (Fahy, 2009). Eosinophils itself is a marker of immune activity against parasitic and allergic diseases (Mehta & Hoffbrand, 2014). The increase in eosinophils in asthma has been associated with bronchial mucosal damage and other

Table 1. Characteristics of the Subjects

Characteristics	Eosinophilic	Netrophilic	Eosinophilic + Netrophilic	Non Eosinophilic + Netrophilic	Total	P
Gender						
• Man	4	10	0	3	17 (25.37%)	0.6391
• Woman	12	24	4	10	50 (74.63%)	
Age	44.81	42.68	44.75	46.62		0.859
Reliever						
• Yes	2	7	3	2	14 (20.89%)	0.0459
• No	14	27	1	11	53 (79.10%)	
Controller						
• Yes	0	2	1	0	3 (4,48%)	0.1414
• No	16	32	3	13	64 (95.52%)	
Total number	16 (21. 05%)	34 (44.74%)	4 (5. 26%)	13 (17.11%)		0, 002
Platelet count	294.300 ± 77.150	280.526 ± 74.539				0.5114
Mean Platelet Volume	9.9 ± 0.28	10.45 ± 1.25				0.5921
Platelet Distribution Width	10.6 ± 0.42	12.43 ± 2.70				0.4205
Plateletcrit	0.33 ± 0.01	0.24 ± 0.01				0.0011

hiperresponsivity. Studies indicated a relationship between eosinophilic asthma phenotype and severe inflammation (Berry et al., 2007). Eosinophils affect the pathophysiology of asthma by increasing the released inflammatory mediators such as Major Basic Protein (MBP), cysteinyl leukotrienes (CysLTs), Reactive oxygen species (ROS), and cytokines. This increase has been shown to cause a more severe inflammatory reaction in asthma (Athari & Athari, 2014). Mediator released also led to the survival of eosinophils from apoptosis leading to increased in eosinophils (Walsh, 2000). This process is mediated by granulocyte-macrophage colony-stimulating factor (GM-CSF), released by platelets (Btech, 2015).

Neutrophil has the same role as eosinophil in bronchial hiperactivity. Patients with netrophilic asthma experience more severe asthma due to methacholine reactivity (Fahy, 2009). Neutrophils also play a role in vascular remodeling in asthma. Thus, it has been assosiated with the status of patients with chronic asthma (Harkness et al., 2015). Neutrophilic characters has been associated with respiratory syncytial virus (RSV) (Tauro et al., 2008; Hansbro et al., 2008).

The presence of more severe inflammation manifest in platelet activity. Platelet will have an increased activity, indicated by the size of the granules leading to increased secretion of chemokine. Physically, platelets have been shown to seemingly bigger so that increase MPV (Somuk et al., 2014). However, the effect of MPV on the type of eosinophilic asthma has not been established (Tuncel et al. 2012). Some studies showed that PDW shown a better response than MPV and can be a specific marker of coagulation (Vagdatli et al., 2010).

Platelet indices including MPV, PDW, and PCT can be used as a predictor of worsening asthma (Sun et al,. 2014). However this finding does not supports the previous study among children (Tural Kara et al., 2015). This present study found a significant difference in PCT between eosinophilic and neutrophilic asthma phenotype (0.33 ± 0:01 vs. 0:24 ± 0:01). Plateletcrit describes the number of circulating platelet of specific blood volume. Plateletcrit is similar to hematocrite (Ugur, 2014). The process of platelet activity appears on plateocrite. This is because that the body response in platelets appear on this unit (Ergelen & Uyarel, 2014; Akpinar et al., 2014).

This difference might have been due to the difference in the study subjects used. Research showed immunological response in children is stronger than that of adult (Balduini & Noris, 2014). Changes in platelet indices has been strongly associated with some

diseases in children (Ergul et al., 2016; Tuncel et al., 2012; Buyukyilmaz et al., 2014; Sun et al. 2014; Shah et al. 2017).

This study has shown a significant difference in the levels of PCT between the study groups. The study provided an overview of the opportunities the use of PCT in predicting asthma phenotype.Although this study has met the minimum sample size, there was a significant difference in another test (number of platelets, MPV, and PDW). Further studies using a largerer number of subjects to find out more about whether there are differences in the group.

CONCLUSION

The majority of the research subjects had neutrophilic asthma and only few had eosinophilic asthma. In addition, there was a significant difference in the PCT level in both study groups.

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