Correlation between Improve Lung Function with Decrease of Eosinophil Levels in Atopic Asthma Persistent After Asthma Exercise

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Abstract

Background: Asthma is a chronic inflammation that is a serious health problem in the world, especially in developing countries, one of which is characterized by limited expiratory airflow. Expiratory limitations in asthma patients due to respiratory obstruction asthma exercise. Spirometry is the gold standard for identifying obstruction in asthmatic. The high eosinophils are one marker of allergies. One of the non-pharmacological management of asthma.

Objectives: The purpose of this study was to analyze the correlations between Forced Exhaled Volume in the first 1 second (FEV1), Forced Vital Capacity (FVC) and FEV1/FVC ratio with eosinophil levels in persistent atopic asthma

Method: The design of this study was an experiment with a sample of 39 people. Measurements of FEV1, FVC and FEV1/FVC ratio measured by spirometry H-101 and eosinophils were carried out in 2 methods namely manual and automatic. The manual procedure used eosin staining and automatically used hematology analyzer. Asthma exercises are carried out 4 times a week for 8 weeks. Statistical analysis used the Spearman test

Results: The correlation between FEV1 and eosinophil levels -0.379 with a value of 0.037; there was a correlation between FVC and eosinophils -0.462 with a value of 0.001; there was a correlation of FEV1/FVC -0.403 with eosinophils a value of 0.028
Conclusion: There was a correlation between improvement in pulmonary function with a decrease in eosinophil levels after following asthma exercises in persistent atopic asthma.

Keywords: Lung function, eosinophil, Persistent atopic asthma


1. Background

Chronic airway disease is a serious health problem in the world. Asthma is a chronic inflammation of the airways characterized by coughing, shortness of breath, wheezing, chest pain, and limitations of expiratory expiration. Asthma can interfere with activity, productivity and cause disability, which results in a decrease in quality of life. Bronchial hyperactivity (HRB) is excessive bronchial narrowing caused by direct stimuli or indirect stimuli such as allergens, chemical irritants, cold air, viral infections, and drugs. The role of the pathogenesis of the occurrence of HRB is related to the release and production of inflammatory mediators in both airway epithelial cells and airway smooth muscle cells which are the main pathogenesis of inflammation in asthma. The pathogenesis of HRB is also influenced by Th2 lymphocyte activity and mediators, especially IL-4, IL-5, IL-13, IL-10.

Interleukin-10 (IL10) produced by T-lymphocytes and lymphocytes which play a major role as anti-inflammatory and immunosuppressive. Based on research conducted by Quinn et al 2000 that IL-10 can reduce the occurrence of bronchial hyperactivity and inhibit the formation of eosinophils. Pathophysiology of allergies and asthma occurs due to airway inflammation which involves the interaction of several cell types and mediators that will cause asthma symptoms. Inhalation of antigens activates mast cells and Th2 cells in the airways. This situation will stimulate the production of inflammatory mediators such as histamine, leukotrienes, and cytokines such as interleukin 5 (IL-5).

Interleukin-5 is the main cytokine in the response of allergic pathogenesis associated with the secretion of Immunoglobulin E (IgE) by B lymphocytes by repairing IgE receptors on the cell surface. An increase in the number of eosinophils in the airways and peripheral blood in asthmatic patients is related to the severity of asthma, although allergic diseases are associated with an increase in Th2 immune responses characterized by increased IL-4, IL-5, and IL-13, cytokines. This cytokine is an
effector cell that activates eosinophils and mast cells. Based on studies conducted by Zanini et al 2015 it was mentioned that bronchial hyperactivity is associated with a decrease in FEV1. Decreased first second forced expiratory volume (FEV1), FEV1/FVC ratio (Force Vital Capacity) is an indicator of bronchial obstruction. The FEV1/FVC ratio is less than 75% -80% hence indicates the occurrence of obstruction.

According Hancox 2017 although higher eosinophils were associated with lower forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC), the association between eosinophils and spirometry were similar among participants without asthma. An increased number of blood eosinophils reflects an inflammatory reaction in airway, which might lead to development of obstructive airflow limitation. This study aims to analyze the correlation between pulmonary function FEV1, FVC, and FEV1 / FVC with eosinophils with the atopy asthma persistant.

2. Methods

The design of this study is a correlation study with a sample of 39 people taken from Margono Soekarjo hospital with asthma. The subject measured skin prick test used dermatophagoides pteronyssinus (Der p) house dust mite allergen at March 2017. The subjects of the study measured lung function using spirometry H-101. Spirometry measurements were carried out before and after asthma exercise, while eosinophil examination was carried out with 2 methods namely manual and automatic. Manual method using eosin coloring and automatic method with hematology analyzer.

Manual procedure for eosinophil examination: Prepare eosin reagent 2% plus 1: 1 acetone (5 ml), add aquadest 100 ml; Preparing blood samples with EDTA anticoagulants, taking blood to the number line 0.5; Cleanse the blood at the tip of the pipette and insert it into the solution until the line 11 (no bubbles), close the tip of the pipette with the fingers and then lift the pipette and release the rubber suction; Shake the pipette for 15-30 seconds. Eosinophil calculation: Place the cover glass on top of the counting room, shake the dilution for 3 minutes, remove the first 3 or 4 drops on the cotton or tissue and put it into the counting room with the glass cover (leave 2-3 minutes). Asthma exercise is done 4 times a week for 8 weeks (Monday, Wednesday, Friday and Saturday). The analysis was carried out by the Spearman test.
3. The Result and Discussions

A. The Correlations between FEV1 and Eosinophils

Based on Figure 1 it can be seen that the eosinophil level with FVC volume has a value of -0.462 with a value of 0.001 which shows a sloping trendline line to the left, so that there is a relationship between eosinophils and FVC with a negative relationship so that the lower eosinophils level, the higher the FVC volume.

B. The Correlations between FVC and Eosinophils
Based on figure 2 volume FEV1 with eosinophil levels has a value of -0.3379 with a value of 0.037 which shows a sloping trendline line to the left, this indicates a relationship between volume FEV1 and eosinophil levels with a negative relationship ie lower eosinophil levels higher FEV1 volume.

Based on Figure 3, the r-value between eosinophils and FEV1/FVC was -0.403 with a value of 0.028 which showed a sloping trendline line to the left. It can be said that there is a relationship between eosinophils and
FEV1/FVC with a negative relationship, namely the lower the eosinophil level, the higher the volume of FEV1/FVC.

4. Discussion

Based on figure 1 (p: 0.037), figure 2 (0.001) and figure 3 (p: 0.028) there is a relationship between eosinophils with FEV1, FVC and FEV1/FVC. There is a relationship between FEV1 and Peak Flow Expiration / PEF with levels of eosinophils in the blood.\textsuperscript{15} The findings of this study support the theory that the role of eosinophil leukocytes in obstructive pulmonary disease in allergic response suggests that an increase in the amount of eosinophils in blood reflects an inflammatory reaction in the airways, which leads to obstructive development due to limited airflow. This is also in accordance with the Hancox et al 2018 study, that there is a relationship between high levels of eosinophils in the blood and a decrease in FEV1/FVC in asthma patients.\textsuperscript{16}

According to the Satpathy study, 2013 the effects of yoga practice given every 15 minutes for 6 weeks caused a decrease in eosinophil levels and increased FEV1/FVC. Physical exercise can stimulate the parasympathetic system which causes the airway muscles to relax and dilate, resulting in an increase in FEV1/FVC.\textsuperscript{17}

Based on the results of a study by Virchow et al 1993, there was a relationship between the number of eosinophils and the degree of obstruction in asthma patients. Eosinophils are one of the leukocytes that contain several specific proteins that are in the cytoplasm as effector cells to protect the body from foreign objects, but eosinophils can also harm the body by releasing specific proteins that are cytotoxic to tissues, so inflammation can occur.

Eosinophils flow in the bloodstream to the bronchial vascular endothelium. Infiltration of eosinophils into the airways will not occur unless there is adhesion and transmigration across the bronchial vascular endothelium. This occurs due to the interaction between integrins on the surface of eosinophils and receptors on the surface of blood vessel endothelium, which includes p-selectin / p-selectin glycoprotein ligan-1 and vascular cell adhesion molecule / VCAM-1. One of the basic proteins of eosinophils is Eosinophile Cationic Protein (ECP) can increase Reactive Oxygen Species (ROS) which can be cytotoxic and disrupt the lungs that allow inflammation. This can be proven in the results of this study, that the eosinophil decline was followed by an increase in FEV1/FVC, although there is often a relationship between eosinophils in the lungs, ECP in fluid BAL, and decreased FEV1 volume in humans. decreased lung function.\textsuperscript{18,19}
Few factors are known to cause lung function decreases are pollutants, including tobacco smoke. For this study, findings that eosinophils inflammation may be another factor, exposure to environmental or occupational allergens contribute to this. And higher BMI can be associated with lower FEV1/FVC ratios in females.

5. Conclusions

There was correlation between improved lung function and decreased eosinophil levels in atopic asthma persistent after asthma exercise. In addition, we need to do exercises with the routine for non-pharmacological treatment approaches. And we need to understand more about the intrinsic and environmental drivers of eosinophil inflammation.

6. Financial support and sponsorship

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7. Conflicts of interest

There are no conflicts of interest.

8. Acknowledgements

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9. Ethical Clearance

The study received ethical approval from the Institutional Review Board of the Faculty of Medicine Universitas Indonesia (Ethical Clearance No. 998/UN. F1/ETIK/2017)

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