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The Relationship Between ICS LABA Administration and Blood Eosinophil Levels in COPD Patient at USU General Hospital

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ABSTRACT

Introduction: Blood eosinophil count may predict treatment response in patients with chronic obstructive pulmonary disease (COPD) during acute exacerbations. However, the ability of blood eosinophil counts in stable status to predict eosinophilic.

Method: This was a cohort retrospective study performed Juni-August 2022 to Juni-August 2023. Subject were COPD patients who were treated at the outpatient using ICS LABA therapy. Blood samples measured blood eosinophil levels first and control.

Results: Based on Wilcoxon test test, there was a significant positive positive correlation of eosinophil counts between ICS LABA Administration and Blood Eosinophil Levels in COPD Patient at USU General Hospital.

Conclusion: We demonstrated association between ICS LABA Administration and Blood Eosinophil Levels in COPD Patient (p value = 0.02).

Blood, Eosinophilia, Exacerbation, COPD, GOLD

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide with a substantial and increasing economic and social burden. COPD prevalence, morbidity and mortality vary across countries. COPD prevalence is often directly related to tobacco smoking prevalence, but in many countries, outdoor, occupational and household air pollution (from burning wood and other biomass fuels) are important risk factors for COPD.[1,2]

Blood eosinophils are an important biomarker that varies substantially over time in patients with COPD. In COPD patients, blood eosinophils are considered an important biomarker for determining treatment strategies. In addition, blood eosinophil count has also been recognized as an important biomarker for identifying patients at risk for exacerbations and for treatment with ICS in patients with COPD.[3]

A number of studies have shown that blood eosinophil count predicts the magnitude of the effect of ICS (added to routine maintenance bronchodilator treatment) in preventing future exacerbations. In patients with moderate to very severe COPD exacerbations, ICS combined with LABAs are more effective than either component alone in improving lung function, health status, and reducing exacerbations.[4]

ICS-containing regimens have little or no association with blood eosinophil counts <100 cells/μL, and therefore this threshold may be used to identify patients with low likelihood of benefit from ICS treatment. A blood eosinophil count threshold of ⩾300 cells/μL identifies the upper end of the sustained relationship between eosinophils and ICS, and may be used to identify patients with greatest likelihood of benefit from ICS treatment.[4]

Blood eosinophil levels may also be associated with intrinsic and extrinsic factors, such as medications, allergic sensitivities, obesity, and smoking. However, it is unclear whether blood eosinophils vary similarly in patients with COPD; furthermore, there are no studies that have addressed changes in blood eosinophils over time and how they reflect the severity of COPD disease.[5]

METHOD

This study was a retrospective cohort analysis performed June-August 2022 to June-August 2023 using medical records. Population is all COPD Patient at the Polyclinic USU General Hospital based on history taking, physical examination and supporting examination.

Subject were 44 COPD patients who were treated at the outpatient using ICS LABA therapy. Inclusion criteria is patients diagnosed with COPD (age >40 years), received inhaler therapy, and who blood eosinophils were examined. Exclusion criteria in this study is patient who do not have complete medical record data, patient with a history of allergies, parasitic infection, autoimmune and other atopic disease, patient who use therapy such as biological agents and immunotherapy. Blood samples measured blood eosinophil levels. Blood samples measured blood eosinophil levels first and control.

Univariate analysis to obtain the characteristics of the research subjects. Categorical data will be assessed in the form of percentages (%) while numerical data uses the mean or standard deviation (SD) if the data is normally distributed. If the data is not normally distributed, use the median and interquartile. To assess whether the data is normally distributed or not, the Kolmogorov-Smirnoff test will be carried out. Bivariate analysis to assess the relationship between ICS LABA and Blood Eosinophil Levels in COPD Patients at the USU Hospital Polyclinic using the paired T-test, as a substitute for non-parametric statistics with the Wilcoxon test.

RESULTS

Based on 44 subjects, we can be seen the 34 patients were male (77.3%) and 10 patients were female (22.7%). The subject age group consisted of 11 patients aged 40-60 years (25%) and 33 patients aged >60 (75%). There were 5 patient (11.4%) without comorbidities and 39 patients (88.6%) with a comorbidities with 10 patients (22,7%) having a history of Diabetes mellitus, 12 patients (27,3%) having hypertension, 14 patients with CHF (31.8%) and having Cancer as 3 patients (6,8%). Initial eosinophils with a median value of 40.89 (0.00-407.5) and advanced eosinophils with a median value of 0.00. (0.00-65.67).

Table 1. Frequency distribution of research subjects.

Subject Characteristic	n (44)
Gender, n (%)	
Male	34 (77.3%)
Female	10 (22.7%)
Age Group, n (%)	
40-60 years old	11 (25%)
>60 years old	33 (75%)
Comorbidities, n (%)	
Diabetes Melitus	10 (22.7%)
Hipertension	12 (27.3%)
CHF	14 (31.8%)
Cancer	3 (6.8 %)
No comorbidities	4 (11.4 %)
Eosinophil, median (IQR)	
Eosinophil first	40.89 (0.00 - 407.5)
Eosinophil control	0.00 (0.00 - 65.67)

The results of the normality test for initial eosinophil levels and continued eosinophils in this study showed a p value = 0.00 (p <0.05) so it was concluded that the distribution of eosinophils was not normal so that the Wilcoxon non-parametric test was performed on 2 paired groups. From the data analysis with the Wilcoxon Test, it showed that ICS LABA therapy had a value: 0.002 (p <0.05) so there was a significant relationship between the results of initial and continued eosinophil levels after ICS-LABA therapy.

Table 2. Results of the Wilcoxon Test Relationship between ICS LABA Administration and Eosinophil Levels in COPD Patients

Subject Charateristic	Median (IQR)	P value
Eosinophyl		
First	40.8 (0.00 - 407.5)	0.002
Control	0.00 (0.00 - 65.67)	

* *Wilcoxon test*

DISCUSSION

From the data analysis with the Wilcoxon Test, it shows that ICS LABA therapy has a p value = 0.02 (p <0.05), so there is a significant relationship between the results of initial and continued eosinophil levels after ICS-LABA therapy. In a previous study conducted by Mohamed (2016), there was a decrease in eosinophils after ICS-LABA administration. The decrease in eosinophils proves the immune response in COPD conditions.[14]

However, it is different from the results of previous studies conducted by a Canadian group assessing 60 COPD patients in a 6-month study using LABACS and LABA monotherapy. Although subjects who received LABACS therapy had a significant reduction in CD8 cells and macrophages compared to LABA monotherapy, there was no difference in the number of eosinophils in the two treatment groups.[15]

This decrease proves that there is an immune response mediated by eosinophils that is closely related to the occurrence of COPD. In addition, a decrease in eosinophils indicates an improvement in COPD conditions with the therapy given. 17 The magnitude of the decrease in eosinophils can be an indication of the COPD phenotype that occurs, whether it is a neutrophilic or eosinophilic phenotype. The appropriate phenotype will have a tendency to decrease more slowly, because the immune response to this phenotype is very high. A very high immune response will also worsen the condition of the disease. This study shows that there is a response to improving the condition of pro-inflammatory cells in COPD therapy which is characterized by a statistically significant decrease in eosinophil levels. This is in line with the suspicion that eosinophil cells play an important role in the pathogenesis of COPD which is mediated by remodeling and inflammatory responses.

Consumption of steroid drugs significantly reduces blood eosinophil levels and the effect will persist for more than 24 hours after consuming a single dose of the drug. The effectiveness of ICS LABA drugs is influenced by many factors such as structural changes in the respiratory airway, mucus hypersecretion and decreased recoil elasticity due to alveolar damage which can reduce the effectiveness of this drug. Epidemiological studies and post-hoc test results from clinical trials of corticosteroid treatment for COPD showed a relationship between the number of blood eosinophils and the risk of COPD exacerbations, death and response to systemic corticosteroids.[16]

CONCLUSION

There was a significant relationship between ICS LABA administration and blood eosinophil levels in COPD Patients.

DECLARATIONS

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CONSENT FOR PUBLICATION

This study was approved by Ethical Committee of Universitas Sumatera Utara, Medan, Indonesia, on Agustus 23, 2023. No : 911/KEPK/USU/2023. The sampels provided the consent to participated in the study.

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None

COMPETING INTERESTS

The authors declare that there is no conflict of interest in this report.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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