ORIGINAL ARTICLE

New GOLD COPD Guideline 2019: How We Deal With It? (Inhaled Corticosteroid Use and Blood Eosinophil Count)

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ABSTRACT

Background: Blood eosinophils may predict response to inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD), where ICS is recommended in patients at high risk of exacerbations by the Global Initiative for COPD (GOLD) strategy. It can help clinicians to estimate the likelihood of beneficial preventive responses to the addition ICS to regular bronchodilator treatment, and thus can be used as a biomarker in conjunction with clinical assessment when making decisions regarding ICS use. This study aims to compare therapeutic data with blood eosinophil count in COPD patients.

Method: Data were collected from consecutive COPD outpatients in Bukit Asam Medika Hospital starting from March 1st, 2019 until June 30th, 2019 and dr. H. Mohamad Rabain Hospital starting from Oct 1st, 2019 until Dec 27th, 2019. We collected demographics, anthropometrics, smoking history, therapy, dynamic lung volumes, the Medical Research Council scale (MRC), CAT score, and blood eosinophil count.

Results: From 57 data collected, 24 patients (42,1%) were having blood eosinophil count ≥300. Patients who have more exacerbation in COPD Group C were 33,3% and 63,2% in COPD Group D. The proportions of ICS-treated COPD Group D patients and blood eosinophil count of <300 and ≥300 was 63,9% and 36,1%, respectively.

Conclusion: This study may provide information and characteristic of COPD patient in Indonesia rural area and showed who may have benefit to ICS therapy based on recommendation GOLD COPD 2019. Blood eosinophils counts is a low-cost biomarker and may help clinicians to made decision therapy.

Keywords: COPD, ICS, blood eosinophil count

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide that induces an economic and social burden that is both substantial. In 2010, the number of COPD cases was 384 million with a global prevalence of 11,7%. Globally, there are around three million deaths annually.[1–4]

Exacerbations in COPD are major contributors to worsening lung function, impaired quality of life, emergency healthcare use and COPD-related mortality.[5] Regular use of inhaled corticosteroids (ICS), either alone or in combination with a long-acting β2-agonist (LABA), reduces the risk of chronic obstructive pulmonary disease (COPD) exacerbation. These drugs are effective agents for the prevention of COPD exacerbations and improvement of lung function. They also have various effects on health status, but they are associated with adverse events, as pneumonia being the most concerning.[6]

Several recent studies have shown that blood eosinophil counts predict the magnitude of the effect of ICS (added on top of regular maintenance bronchodilator treatment) in preventing future exacerbation. Therefore, in Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019, blood eosinophil counts can help clinicians estimate the likelihood of a beneficial preventive response to the addition of ICS to regular bronchodilator treatment, and thus can be used as a biomarker in conjunction with clinical assessment when making decisions regarding ICS use.[1]

Indonesia do not yet have definitive data of COPD prevalence. The survey results of non-communicable diseases by the General Directorate of Eradication of Non-Communicable Diseases in five provincial hospitals in Indonesia (West Java, Central Java, East Java, Lampung, and South Sumatra) in 2004, COPD contributes at the most to morbidity (35%), followed by bronchial asthma (33%), lung cancer (30%), and other 2%.[7] As the GOLD 2019 application, this study aims to compare therapeutic data with blood eosinophil count in COPD patients.

METHOD

The research will be conducted in an observational descriptive from consecutive COPD outpatients in Bukit Asam Medika Hospital starting from March 1st, 2019 until June 30th, 2019 and Dr. H. Mohamad Rabain Hospital starting from Oct 1st, 2019 until Dec 27th, 2019.

Study participants will be patients suffering from COPD as defined by the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guidelines,[1] more than ≥40 years old, recruited from Bukit Asam Medika Hospital, Tanjung Enim, Muara Enim District, South Sumatra, Indonesia between 1 March until 30 June 2019 and Dr. H. Mohamad Rabain Hospital Muara Enim District, South Sumatra, Indonesia between 1 October until 27 December 2019. Patients will be excluded for refusal to participate, cannot perform spirometry, and unwilling or unable to provide informed consent.

The following data and measurements will be recorded:

- Demographics and anthropometrics, smoking history, and drug therapy.
- Dynamic lung volumes, assessed after bronchodilation and expressed as absolute and percent of predicted values according to The Pneumomobile Project Indonesia.
- The subjective sensation of breathlessness will be evaluated by means of the Medical Research Council (MRC) scale.
- Indonesian Version of the COPD Assessment Test (CAT) score.
- Blood eosinophil count.

RESULT

This study describes the main parameters namely therapeutic data and blood eosinophils in COPD patients, as well as several characteristics. These characteristics include gender, age, education, Brinkman index, duration of diagnosis, nutritional status (BMI), degree classification based on GOLD, and COPD group. There are 57 patients has been assessment. The characteristics of research subjects can be seen in Table 1.

The range age of the population was 55 until 64 years; approximately 96,5% of respondents were male. The most research population is junior high school education (33,3%). Brinkman index of patients is dominated by moderate and heavy. Most of respondents were old patient. Respondents with body mass index underweight was 45,6% and normal weight was 43,9%. Respondents with GOLD I, II, III, and IV constituted 7,0%, 36,8%, 38,6%, and 17,5% of the population, respectively. Respondents in group A same with group B is 1,8% and groups C, D constituted 33,3% and 63,2% of the population, respectively. In blood eosinophil count <300 cells/µL was 57,9%.

Table 1. Characteristics of COPD Patient

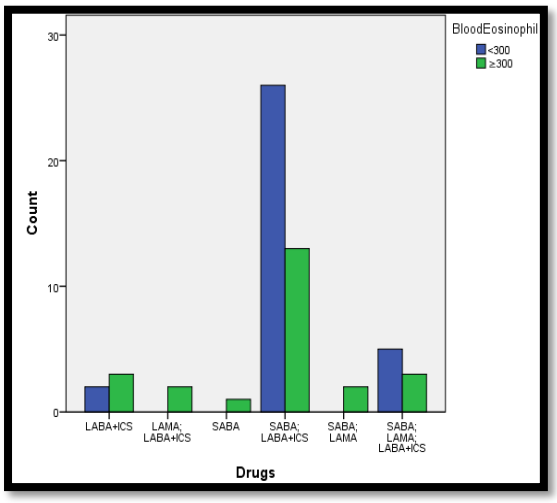
Variable	Frequency	Percent
Sex		
Man	55	96.5
Woman	2	3.5
Age		
40-54	13	22.8
55-64	25	43.9
65-69	10	17.5
≥70	9	15.8
Education		
Uneducated	14	24.6
Elementary School	7	12.3
Junior High School	19	33.3
Senior High School	15	26.3
Diploma	1	1.8
Master Degree	1	1.8
Brinkman Index		
Never	5	8.8
Mild	1	1.8
Moderate	26	45.6
Heavy	25	43.9
Duration of Diagnosis		
New	25	43.9
Old	32	56.1
Body Mass Index		
Underweight	26	45.6
Normal weight	25	43.9
Overweight	5	8.8
Obesity	1	1.8
GOLD		
I	4	7.0
II	21	36.8
III	22	38.6
IV	10	17.5
COPD Group		
A	1	1.8
B	1	1.8
C	19	33.3
D	36	63.2

Table 1. Characteristics of COPD Patient (cont.)

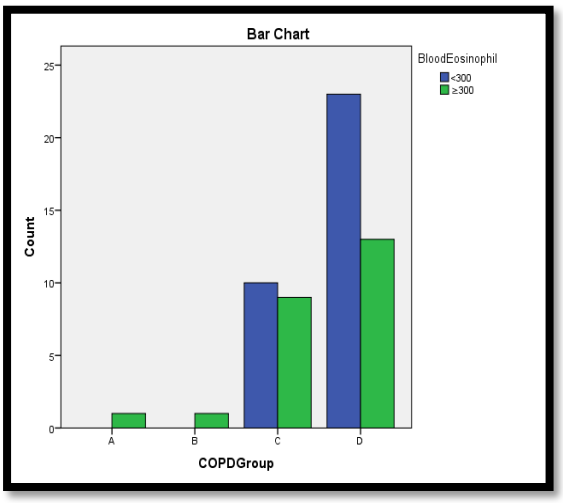
Variable	Frequency	Percent
Blood Eosinophil		
<300	33	57.9
≥300	24	42.1
Drugs		
SABA	1	1.8
LABA+ICS	5	8.8
SABA; LABA+ICS	39	68.4
SABA; LAMA	2	3.5
LAMA; LABA+ICS	2	3.5
SABA; LAMA; LABA+ICS	8	14.0

Table 2. Drugs and COPD Group Crosstabulation

Drugs	Blood Eosinophil		Total
	<300	≥300	
LABA+ICS	2 (6.1%)	3 (12.5%)	5 (8.8%)
LAMA; LABA+ICS	0 (0.0%)	2 (8.3%)	2 (3.5%)
SABA	0 (0.0%)	1 (4.2%)	1 (1.8%)
SABA; LABA+ICS	26 (78.8%)	13 (54.2%)	39 (68.4%)
SABA; LAMA	0 (0.0%)	2 (8.3%)	2 (3.5%)
SABA; LAMA; LABA+ICS	5 (15.2%)	3 (12.5%)	8 (14.0%)
Total	33 (100.0%)	24 (100.0%)	57 (100.0%)



Graphic 1. Drugs Distribution by Blood Eosinophil Count



Graphic 2. Blood Eosinophil Count by COPD Group

The proportions of COPD patients who had an inhaler drug are shown in Table 2.

In group A there were 1 respondent (2.9%) using SABA, and group B 1 (2.9%) respondent using

SABA; LABA + ICS. 10 (29.4%) of respondents in group C were divided into 7 respondents (20.6%) using SABA; LABA + ICS, 2 (5.9%) of respondents use SABA; LAMA, and 1 respondent (2.9%) use triple therapy. Therapy in group D is dominated by SABA; LABA + ICS were 16 (47.1%) respondents while 6 (17.6%) respondents used triple therapy. ICS is recommended in patients at high risk of exacerbations by the Global Initiative for COPD (GOLD) strategy. The highest use of ICS in group D was 22 respondents (64.7%).

Comparison between ICS use and Blood Eosinophil Count can be seen in Graph 1. Respondents who received single ICS therapy is 3 (60%) of 5 respondents and ICS in dual therapy is 15 (57.7%) of 26 respondents who had a blood eosinophil count ≥300 cells/μL. While respondents who received ICS in triple therapy with blood eosinophil count ≥300 cells/μL are 3 (37.5%) of 8 respondents.

Graphic 2 shows the proportions of blood eosinophil count by COPD group patients. There was a higher proportion of respondents with blood eosinophil counts of ≥300 cells/μL in COPD Group D 13 (36,1%) respondents. But compared with blood eosinophil count <300 cells/μL in COPD Group D, higher than blood eosinophil counts of ≥300 cells/μL is 23 (63,9%) respondent. The proportions of respondents with blood eosinophil counts of ≥300 cells/μL in COPD Group A, B, and C were 1 (4,2%) respondent, 1 (4,2%) respondent, and 9 (37,5%) respondent, respectively.

DISCUSSION

This study shows therapeutic data, blood eosinophils count, and several characteristics in COPD patients. These characteristics include gender, age, education, Brinkman index, duration of diagnosis, nutritional status (BMI), degree classification based on GOLD, and COPD group. The efficacy, safety and positioning of ICS in the treatment of patients with COPD is much debated, since it can result in clear clinical benefits in some patients ("friend") but can be ineffective or even associated with undesired side effects, *e.g.* pneumonia, in others ("foe").[8]

The use of blood eosinophils as a biomarker in COPD is based on the premise that they reflect and correlate with tissue eosinophilic inflammation in pulmonary airways and parenchyma.[9] *Post hoc* and pre-specified analyses of chronic obstructive pulmonary disease (COPD) randomized controlled trials have shown that higher blood eosinophil counts predict greater

inhaled corticosteroid (ICS) effects on exacerbation prevention.[10] The clinical relevance of a blood eosinophil cut off in the management of COPD remains uncertain because blood eosinophils are not stable throughout the disease course. A recent publication reported that the association of higher eosinophil counts with exacerbations is not consistent.[11]

The rate of pneumonia was marginally higher in those with <2% blood eosinophils than those with ≥2% blood eosinophils, echoing findings from a *post hoc* analysis that suggested rates of pneumonia were slightly lower in patients with COPD with higher eosinophil counts and putatively more responsive to ICS.[1,12] The threshold of a blood eosinophil count > 300 cells/µL identifies the top of the continuous relationship between eosinophils and ICS, and can be used to identify patients with the greatest likelihood of treatment benefit with ICS.[1] The IMPACT trial and observational study in UK and US patients with COPD shows that assessment of blood eosinophil count and smoking status has the potential to optimize ICS use in clinical practice in patients with COPD and a history of exacerbations and should be considered while making treatment decisions.[13,14]

The use of blood eosinophil counts to predict ICS effects should always be combined with clinical assessment of exacerbation risk (as indicated by the previous history of exacerbations). Other factors (smoking status, ethnicity, geographical location) could influence the relationship between ICS effect and blood eosinophil count, but remains to be further explored. The mechanism for an increased ICS effect in COPD patients with higher blood eosinophil counts remains unclear. There is insufficient evidence to recommend that blood eosinophils should be used to predict future exacerbation risk on an individual basis in COPD patients.[1]

The problem in Indonesia regarding inhalation therapy in COPD patients is the high price of inhalation drugs. Although that has been helped by the national health insurance system, for LAMA inhalation is still relatively expensive, therefore the regulation of its administration is very difficult. Based on the GOLD COPD 2019 therapy algorithm, LAMA is the first choice in COPD group C and D therapy. While the administration of LABA + ICS therapy is only in COPD group D by considering blood eosinophil count.

CONCLUSION

This study may provide information and characteristic of COPD patient in Indonesia rural area and showed who may have benefit to ICS therapy based on recommendation GOLD COPD 2019. Blood eosinophils counts is a low-cost biomarker and may help clinicians to made decision therapy.

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