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# Blood Count of Eosinophil Polymorphonuclear Leucocytes and Bronchial Hyperreactivity in Chronic Obstructive Pulmonary Disease

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## ABSTRACT

**Introduction:** Polymorphonuclear eosinophil leucocytes (eosinophils) are found in increased numbers in the circulation and sputum in asthma patients, usually in relation to the severity of asthma but it is the question whether they have a significant role in the development and level of bronchial hyperreactivity in patients with chronic obstructive pulmonary disease (COPD).

**Objective:** to show the role of the eosinophils in the development and level of BHR in patients with COPD and so in the severity of illness. **Material and methods:** We observed 240 patients with COPD treated in Clinic for Pulmonary Diseases and TB «Podhrastovi» Sarajevo during five years: from 2012 to 2016. They were divided into groups and subgroups according to the first registration of BHR in the course of illness and to the number of exacerbations of the disease in one year. The number of blood eosinophils was measured at the onset of exacerbation of the disease before switching on any therapy, at the beginning and at the end of the research. **Results:** we did not find any significant difference in the eosinophil blood count between the COPD patients with and without BHR, nor according to the time of the first registration of BHR in the course of illness nor according to the number of exacerbations of illness per one year. There was not statistically significant difference in eosinophil count (increase-drop) within any of the groups or subgroups, or between the groups and subgroups between the first and last test.

**Conclusion:** There is not significant correlation between the eosinophil blood count and the level of BHR, number of exacerbations and the severity of COPD.

**Keywords:** polymorphonuclear eosinophil leucocytes, BHR, COPD.

## 1. INTRODUCTION

Bronchial hyperreactivity (BHR) is condition in which airways show a much bigger bronchoconstrictive response to various provocative specific and non-specific agents than it is normal (1). In the condition of BHR these agents in small quantities, much under the threshold of normal reactivity, get to development of more expressive airway obstruction expressed as bronchospasm (1, 2). If the degree of BHR is higher it is easier to provoke bronchospasm (1, 3). Bronchial inflammation, which is caused by various mechanisms, is a fundament for development of BHR (1, 2, 3).

Eosinophils, a prominent feature of asthma, are found in increased numbers in the circulation and sputum, usually in relation to the severity of asthma (4). It is the question whether eosinophil polymorphonuclear leucocytes have a role in the development of inflammation of bronchial mucosa in patient with COPD

and whether they have a role in the development of BHR in COPD and influence the severity of disease.

Eosinophils are end-stage cells derived from the bone marrow under the influence of granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-3, and the late differentiation factor IL-5 (5). The selective recruitment of eosinophils into the airway is mediated by a multistep process directed by  $T_H2$  cytokine-producing T cells (6).

The eosinophil specific basic proteins, which are stored in the distinctive secondary granules, are major basic protein eosinophil cationic protein (ECP), eosinophil peroxidase (EPO), and eosinophil-derived neurotoxin. All of these proteins are toxic to bronchial epithelial cells. Eosinophils, with mast cells and basophiles, are the most prominent source of cysteinyl-leukotrienes and eosinophils also release a diverse range of cytokines (7).

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Absolute eosinophil blood count is 30-350 x10<sup>9</sup>/L. Eosinophils blood % is 0.0-6.0. This range may vary slightly in different laboratories. A count of more than 500 eosinophils per microliter of blood is generally considered as eosinophilia in adults. Corticosteroids reduce the number of eosinophilic granulocytes in the blood (8).

## 2. AIM

Aim of article was to show the role of the eosinophils in the development and level of BHR in patients with COPD and so in the severity of COPD.

## 3. MATERIAL AND METHODS

Research observed 240 patients with COPD treated in Clinic for Pulmonary Diseases and TB «Podhrastovi» Sarajevo during five years: from 2012 to 2016, and 180 patients had registered BHR, and 60 had not. Patients with BHR were divided into groups and subgroups according to the time of the first registration of BHR expressed as bronchospasm in the course of disease and to the number of exacerbations of the disease within one year. The first group (I) consists of patients with BHR registered in the first year of the diagnosis of COPD, second group (II) of patients with BHR registered from 1 to 3 years, and third group (III) consists of patients with COPD where BHR is registered more than 3 years after the diagnosis of COPD. Each group was divided into subgroups according to number of exacerbations of the disease in one year as follows: (a) one or less exacerbations during one year, (b) 2-3, and (c) more than 3 exacerbations of disease during one year. Patients without BHR were divided into subgroups according to the number of exacerbations during one year. The number of blood eosinophils was measured at the onset of exacerbation of the disease before switching on any therapy, at the beginning and at the end of the research. No-one patient was under corticosteroid therapy for more than 7 days (neither parenteral, nor oral, nor inhalatory) before the time of blood testing for blood cell counts.

## 4. RESULTS

The number and the changes of number of blood eosinophils between first and last examination in COPD patients with registered BHR are showed on Table 1 and Figure 1. The number and the changes of number of blood eosinophils between first and last examination in all COPD patients with and without registered BHR are showed on Table 2 and Figure 2.

There is not statically significant difference in number and in the changes of number of blood eosinophils (increase-drop) in COPD patients with BHR according to

EOSINOPHILS ( n x10 <sup>9</sup> /L )				
Number of exacerbations per year	First examination (mean value)	Last examination (mean value)	Difference	Significance of difference
<b>Patients with BHR</b>				
<b>I Group:</b> time of registration of BHR : 0-1 year ( 60 patients)				
a) 1 or less exacerbations	0,236	0,242	0,006	non.sign
SD	0,2785	0,2576	0,1674	
b) 2-3 exacerbations	0,190	0,178	-0,012	non.sign.
SD	0,1356	0,1463	0,1926	
c) more than 3 exacerbations	0,195	0,222	0,027	non.sign.
SD	0,2401	0,2223	0,2187	
Total	0,205	0,313	0,008	non.sign
SD	0,2217	0,2137	0,1943	
<b>II Group:</b> time of registration of BHR 1- 3 years ( 60 patients)				
a) 1 or less exacerbations	0,235	0,181	-0,054	non.sign.
SD	0,2562	0,1670	0,1785	
b) 2-3 exacerbations	0,199	0,158	-0,041	non.sign.
SD	0,2022	0,1526	0,1501	
c) more than 3 exacerbations	0,204	0,184	-0,020	non.sign.
SD	0,1608	0,1642	0,2131	
Total	0,212	0,174	-0,038	non.sign.
SD	0,2047	0,1578	0,1785	
<b>III Group:</b> time of registration of BHR – more than 3 years ( 60 patients)				
a) 1 or less exacerbations	0,193	0,186	-0,007	non.sign
SD	0,1289	0,1195	0,1127	
b) 2-3 exacerbations	0,328	0,261	-0,067	non. sign.
SD	0,4325	0,2512	0,3183	
c) more than 3 exacerbations	0,178	0,222	0,044	non.sign
SD	0,1953	0,3009	0,3549	
Total	0,233	0,221	-0,012	non.sign
SD	0,2810	0,2232	0,2669	
All patients with BHR	0,216	0,204	-0,012	non.sign
SD	0,2370	0,2006	0,2158	

Table 1. The average number of eosinophils according to the time of the first registration of BHR in the course of COPD and to the number of exacerbations of disease in one year in patients with registered BHR. SD= standard deviation

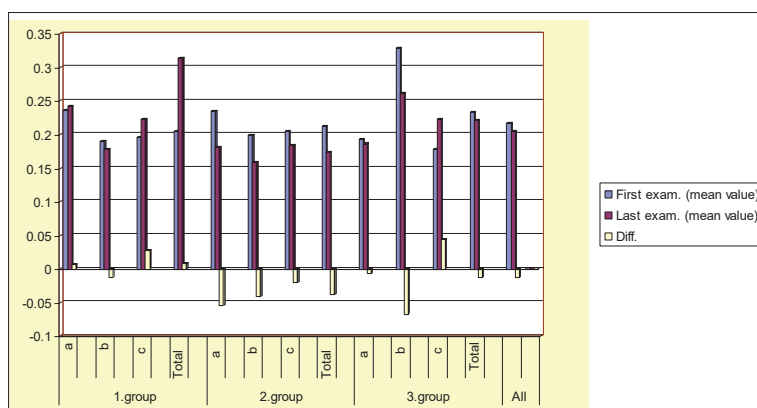


Figure 1. Number of blood eosinophils in COPD patients according to the time of registration of BHR in the course of disease and to the number of exacerbations per year. Legend: groups (time of registration of BHR): 1. = 0-1 year, 2. = 1- 3 years, 3. = more than 3 years after the diagnosis of COPD; subgroups: a= 1 or less, b=2-3, c= more than 3 exacerbations per year

the number of exacerbations per year and to the time of registration of BHR (Table 1).

In patients with registered BHR there is not a statistically significant difference in the number of eosinophils between patient groups according to the time of BHR registration in the evolutionary course of the disease. The mean change in the eosinophil count between the first and last examinations is not statistically significant

EOSINOPHILS (n x 10 <sup>9</sup> /L)				
Number of exacerbations per one year	First examination (mean value)	Last examination (mean value)	Difference	Significance of difference
<b>COPD patients with BHR (180 patients)</b>				
a) 1 or less exacerbations	0,220 SD 0,2221	0,203 0,1854	-0,017 0,1518	non.sign
b) 2-3 exacerbations	0,235 SD 0,2786	0,197 0,1873	-0,038 0,224	non.sign.
c) more than 3 exacerbations	0,193 SD 0,2037	0,210 0,2249	0,017 0,2525	non.sign.
Total	0,216 SD 0,2370	0,204 0,2006	-0,012 0,2158	non.sign
<b>COPD patients without BHR (60 patients)</b>				
Number of exacerbations per one year	First examination (mean value)	Last examination (mean value)	Difference	Significance of difference
a) 1 or less exacerbations	0,113 SD 0,1138	0,170 0,2537	0,057 0,2165	non. sign.
b) 2-3 exacerbations	0,139 SD 0,1501	0,148 0,1071	0,009 0,1909	non. sign.
c) more than 3 exacerbations	0,222 SD 0,2841	0,251 0,3876	0,0229 0,3480	non. sign
Total	0,157 SD 0,1957	0,189 0,2423	0,032 0,2538	non.sign.
<b>All patients with COPD (with and without BHR)</b>				
	0,203 SD 0,2299	0,201 0,2104	-0,002 0,2253	non. sign.

Table 2. Average number of eosinophils according to the number of exacerbations of COPD during one year in patients with and without registered BHR

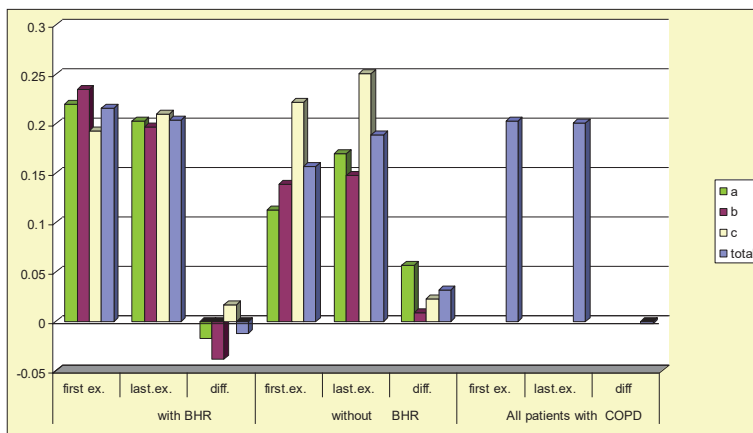


Figure 2. Number of blood eosinophils in all COPD patients according to the number of exacerbations per year. Legend: subgroups: a= 1 or less, b=2-3, c= more than 3 exacerbations per year. Ex=examination, diff. = difference

in any group, nor is there a statistically significant difference between individual patient groups and subgroups.

There is not statically significant difference in number and in the changes of number of blood eosinophils (increase-drop) in COPD patients with BHR and without BHR, regardless of the number of exacerbations per year (Table 2).

There is not a statistically significant difference in the number of eosinophils between patients with and without BHR.

There is not a statistically significant difference in the number of eosinophils according to the number of exacerbations of the disease per year, both in those with and those without BHR (at the last examination) (Figure 2).

The average change in the number of eosinophils (increase-drop) between the first and last examinations

is not a statistically significant in any group depending on the number of exacerbations. There is no statistically significant difference in the change of the number of eosinophils between the first and last examinations between patients with and without BHR, and among the groups according to the number of exacerbations of disease.

## 5. DISCUSSION

While there is a plausible role of eosinophils in causing inflammation and BHR in the allergic asthmatics (4) it is a question whether eosinophils have a similar role in COPD.

Although eosinophils and mast cells are important effector cells in asthma, neither has been ascribed a prominent role in COPD (9). In exacerbations of COPD airway wall eosinophilia has been observed at a level similar to that found in asthma (10, 11) with an associated increase in RANTES (CCL5) expression by airway subepithelial and epithelial cells (10). In stable COPD, increased eosinophil counts have been found in sputum (12), BAL fluid (13) and in the airway wall (14). Increased levels of eosinophilic cationic protein (ECP) in BAL fluid (15) and induced sputum (16) have also been observed. Many studies have failed to confirm that any airway eosinophilia occurs in COPD (17, 18, 19, 20), while others have suggested that the eosinophils, even if they are present, are not activated (21, 22).

Eosinophils, a prominent feature of asthma, are found in increased numbers in the circulation and sputum, usually in relation to the severity of asthma (4). Patients with asthma with higher blood eosinophil counts experienced more asthma attacks than those with lower eosinophil counts (23).

It is the question whether eosinophils have a role in the development of inflammation of bronchial mucosa in patient with COPD and whether they have a role in the development of BHR in COPD.

BHR is condition in which airways show a much bigger bronchoconstrictive response to various provocative specific and non-specific agents than it is normal (1). If the level of BHR is higher there is bigger number of exacerbations of disease (1, 2, 3) which indicates that the disease is more severe.

In this research we have tried to show whether there is the connection between the eosinophil blood count with the time of development of the BHR in the course of COPD, with the number of exacerbations of illness per year, with the level of BHR, that is whether there is a link between eosinophil blood count and the severity of the disease. We did not find any correlation between the blood count of eosinophils, as opposed to neutrophils (24), and the development and the level of bronchial hy-

perreactivity; number of exacerbations and so the severity of COPD.

## 6. CONCLUSION

Eosinophilic granulocytes have no role in the onset and level of bronchial hyperactivity, nor in the number of exacerbations of the disease in COPD, so eosinophil blood count cannot be an indicator of the severity of the disease in COPD patients as opposed to asthma.

- **Conflict of interest:** none declared.
- **Author contribution:** Vesna Cukic made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data. She prepared final version to be submitted and revised version to be published.

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