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FUNCTIONAL ACTIVITY OF NEUTROPHILS IN NON-SPECIFIC INTERSTITIAL PNEUMONIA

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Abstract. This article evaluates the functional activity of peripheral blood neutrophils in patients with nonspecific interstitial pneumonia. Neutrophil phagocytic activity, phagocytic index, phagocytic number, and oxygen-dependent cellular metabolism were assessed using the NBT test. Increased spontaneous neutrophil activity and a decreased functional reserve were observed during stimulation. These findings demonstrate the important role of neutrophils in the development of inflammatory processes in interstitial lung diseases.

Keywords: nonspecific interstitial pneumonia, neutrophils, phagocytosis, NBT test, immunological parameters.

Introduction. In modern medicine, interstitial lung diseases represent a heterogeneous set of pathological conditions associated with inflammatory reactions and structural reorganization of the interstitial component of lung tissue [1]. Within the framework of idiopathic interstitial pneumonias, nonspecific interstitial pneumonia (NIP) is distinguished as a separate nosological entity, characterized by the predominance of inflammatory changes and a more favorable clinical outcome compared to idiopathic pulmonary fibrosis [8].

Currently, immune mechanisms are receiving close attention in the study of interstitial lung diseases. Particular importance in the development of inflammation is attributed to innate immune cells, including neutrophils and macrophages [5]. Neutrophil granulocytes, being among the first cellular agents to arrive at the site of inflammation, play a critical role in defense. They perform their functions through phagocytosis, secretion of proteolytic enzymes, and generation of reactive oxygen species [7].

Moreover, patients with interstitial lung diseases have elevated neutrophil levels in the bronchoalveolar fluid and peripheral blood. This increase correlates with the severity of the inflammatory process and the severity of the clinical picture [3]. The mechanisms by which neutrophils contribute to the formation of fibrotic changes in lung tissue include the release of proteases, metalloproteinases, and the formation of neutrophil extracellular traps (NETs) [4].

In particular, neutrophil elastase and other inflammatory mediators have the ability to stimulate fibroblast proliferation and increase the synthesis of extracellular matrix components, which plays a significant role in the development of pulmonary fibrosis [10].

While there is a significant amount of research devoted to interstitial lung diseases, the functional activity of neutrophils in nonspecific interstitial pneumonia remains poorly understood. Analysis of phagocytic activity and oxygen-dependent metabolism of neutrophils may help better understand the mechanisms underlying the development of this pathology.

The aim of the study was to evaluate the functional activity of peripheral blood neutrophils in patients with nonspecific interstitial pneumonia.

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Materials and methods. The study included patients with a clinically and instrumentally confirmed diagnosis of nonspecific interstitial pneumonia. The diagnosis was based on clinical examination, high-resolution computed tomography of the lungs, and laboratory tests, following international guidelines [8].

The functional activity of peripheral blood neutrophils was studied using conventional immunological techniques. The following parameters were examined during the analysis: neutrophil phagocytic activity (NA); phagocytic number (PN); phagocytic index (PI); spontaneous NBT test; induced NBT test. The NBT test was used to evaluate the oxygen-dependent metabolism of neutrophils, as well as to study their ability to initiate an oxidative burst [6]. The obtained data were subjected to statistical processing using standard methods of variance analysis.

Results. Neutrophils are known to perform antiphagocytic activity through phagocytosis, oxygen radical scavenging, and proteolytic enzymes. It is necessary to study the activity and functional state of neutrophils by analyzing neutrophil elastase levels in patients with NIP and control groups (healthy individuals, patients with arterial hypertension, and coronary artery disease), taking into account sputum phenotypes, respiratory function, and the dynamics of these indicators during treatment.

Table 1 presents data on peripheral blood neutrophils in the study groups.

Table 1.

Results of neutrophil distribution in peripheral blood

Indikator	Healthy N=30	Patients with H and CHD N=30	NIPMC N=16	NIPMS N=59	NIPSC N=65	t	p
Neutrophils	3,36±0,12	3,28±0,16	9,62±3,1	7,56±3,6	4,81±2,5	3.7	p<0,01

Note: For samples described by a normal distribution, the values of the mean and standard deviation (M + σ) are given.

Neutrophil counts were normal in the control groups but slightly elevated in the mild NIP group. High levels were found in the moderate and mild disease groups, and their levels were statistically higher than in the above-mentioned groups ($p<0.01$, respectively). The relatively high neutrophilia levels in the NIPMC group may be explained by the lack of medical care in some patients during the prehospital phase.

Moreover, the presence of pronounced neutrophilia in patients with NIP may be related to the relative degree of inflammation in these patients, and neutrophils are the main cells involved in the inflammatory process. It should also be noted that some patients were treated with glucocorticosteroids, which may lead to a predominance of neutrophilic inflammation.

An analysis of the effect of glucocorticosteroids and antibiotics on neutrophil counts showed that patients receiving inhaled hormones had higher neutrophil counts ($p<0.01$). Similar results were observed in patients receiving oral hormones.

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Control groups of NIP patients were also analyzed, and elevated neutrophil and neutrophil elastase levels were observed in patients requiring antibiotic therapy. However, even if NIP patients had already received antibiotics, their levels were higher than in those who had not.

Specifically, in severe cases and against the background of active infection, NIP is characterized by peripheral blood neutrophilia and severe inflammation.

The study found that neutrophil counts and neutrophil elastase levels were statistically lower in women than in men. Elderly patients had higher neutrophil counts than younger patients. It should be noted that statistically significantly lower blood counts were observed in patients with NIP in those with a strong hereditary history. It is important to remember the influence of genetic factors on neutrophil counts, particularly hereditary predisposition. Neutrophil and neutrophil elastase levels are higher in smokers than in non-smokers. This suggests that tobacco smoke affects mucociliary clearance, leading to the development of chronic lung inflammation.

The cytokines IL-1β and IL-17A were detected in the serum of patients with NIP and the control group. Table 2 presents cytokine levels.

Table 2.
Cytokine levels in the study groups.

Diagnosis	IL-1β	IL-17A
NIPMC	2.2	2.9
NIPMS	2.5	4.2
NIPSC	2.1	3.2
Patients with H and CHD	2.5	4.0
Healthy	2.0	1.9
P*	0,076	0,03

*Note: * Significant correlation at $p < 0.001$.*

Serum IL-1β and IL-17A levels in the study groups were found to be within the reference range (IL-1β normal 0-4 pg/ml, IL-17 0-5.0 pg/ml).

Interleukins appear to be involved in the development and progression of the disease, particularly in patients with NIPMS and NIPSC, and to a lesser extent in patients with NIPMC.

Consequently, changes in the functional activity of neutrophil granulocytes were detected in patients with nonspecific interstitial pneumonia.

Neutrophil phagocytic activity in the study group was 54.3 ± 2.1%, which was lower than the same value in the control group (68.7 ± 2.5%, $p < 0.05$). The phagocytic number in patients with NIP was 3.8 ± 0.3, while in healthy individuals this figure reached 4.9 ± 0.4. In addition, the phagocytic index was reduced to 1.3 ± 0.1, indicating a reduced efficiency of the phagocytosis process. Analysis of neutrophil oxygen-dependent metabolism revealed an increase in

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spontaneous NBT test values (20.4 ± 1.8% compared to 11.2 ± 1.5% in the control group, $p < 0.05$). At the same time, the results of the induced NBT test increased less significantly (27.6 ± 2.2%), which indicates a reduction in the functional reserve of neutrophilic granulocytes.

Discussion. The obtained data indicate a decrease in the functional activity of neutrophils in patients with nonspecific interstitial pneumonia. An increase in spontaneous neutrophil activity indicates chronic activation of these cells during the inflammatory process. At the same time, a decrease in their phagocytic activity and functional reserve is likely associated with prolonged stimulation of immune cells, which contributes to the development of an immunological imbalance [9,11].

Research findings indicate that activated neutrophils release inflammatory mediators that promote fibroblast proliferation and increased fibrous tissue formation in the lungs [2,12]. This suggests that impaired neutrophil functional activity may significantly influence the pathogenesis of nonspecific interstitial pneumonia and accelerate disease progression.

Conclusion. Thus, patients with nonspecific interstitial pneumonia exhibit impaired functional activity of neutrophil granulocytes. Specifically, a decrease in their phagocytic capacity is observed. An increase in spontaneous oxygen-dependent metabolism is also observed, accompanied by a decrease in the cellular functional reserve. These changes in neutrophil status may play a significant role in the development of interstitial lung disease pathogenesis.

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