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Immune parameters in patients with asthma

Introduction. Bronchial asthma (BA) - a genetically determined chronic inflammation of airways, characterized by presence of inverse bronchial obstruction, allergic processes of the mucous membrane of respiratory tract and bronchial hypersensitivity to environmental factors [1, 2].

Today it is proved that the development of asthma is associated with hyperreactivity of large and small bronchi caused by chronic inflammation, which is coordinated by type 2 T-helper lymphocytes (Th-2). The initial actions that lead to the dominance of Th-2, are not fully understood [3, 4, 5].

Aim and methods. The aim of the work was to study the immune status of patients with asthma. 112 adult patients with bronchial asthma were examined. All patients underwent subsequent immune studies (studies of functional activity of phagocytes, absorptive activity, cytolytic effect of natural killer cells, determining the number of T-and B-lymphocytes in the peripheral blood, parameters of humoral immunity, interferon induction and titration, tumor necrosis factor (TNF) titration).

Oxygen-dependent bactericidal activity of peripheral blood neutrophils was determined by nitro blue tetrazolium reaction. Phagocytosis activity was assessed by the ability of phagocytes to absorb St. aureus cells. The activity of natural killer (NK) was determined in the cytotoxic reaction in which the suspension culture cells L-929 were the targets.

Relative and absolute number of T-(CD3 +, CD4 +, CD8 +, CD3 + / HLA-DR +), B cells (CD19 +) and SD3-/HLA-DR + cells was determined in the peripheral blood by flow cytofluorometry method on the FACStarPlus device. The content of immunoglobulins G, A and M in serum was studied by radial immunodiffusion method using monospecific serums against human immunoglobulins. Number of TNF in serum was determined by index of cytotoxicity.

Results. The group of patients with asthma included 50 men, mean age 35,8±2,0 years and 62 women, mean age 36,5±1,7 years. The control group consisted of 96 healthy individuals. According to Table 1, patients with mild, moderate and severe persistent asthma showed a reduction in NK activity of blood mononuclear cells compared to the control group and patients with intermittent asthma.

Table 1

Indicators of cellular immunity (M±m) in patients with asthma of different degrees of severity

Data	Asthma			
	Intermittent	Persistent		
		Mild	Moderate	Severe
NK activity, %	43,2±3,7	39,0±4,3*	32,8±3,2*°	32,1±3,7*°
Monocytes: Phagocytic number (MPN), %	55,9±3,4*	53,9±3,4*	48,6±3,5*	34,6±3,2°

Phagocytic index (PI), conv	5,6±0,6*	5,5±0,6*	3,8±0,7	3,1±0,7
Neutrophils: NPN, %	79,9±3,5*	75,9±3,6	69,0±3,8	67,7±3,6
PI, conv	7,9±0,8	7,2±0,7	6,1±1,0	6,0±1,1
NBT test, %	16,4±2,5	15,8±3,1	17,8±2,2*	24,2±4,8*
Stim. NBT, conv	1,8±0,2	1,7±0,2	1,5±0,2*	1,3±0,2*

* - p<0.05 compared with control group; ° - p<0.05 compared with intermittent asthma

In intermittent asthma serum interferon mean values were within normal limits (Table 2). In persistent asthma of different degree of severity elevated levels of this index were found, compared with control group (6,2±0,4) log (2), and the highest interferon values were observed in patient with severe persistent asthma.

Normal values of serum interferon in patients with intermittent asthma were accompanied by normal values of NK activity, and increased rates of interferon in patients with persistent asthma were accompanied by inhibition of the function of NK cells, indicating a more pronounced imbalance antiviral protection at persistent asthma. It is not excluded that elevated levels of serum interferon is the result of compensatory mechanisms that occur due to insufficient NC.

Table 2

Indicators of natural killer activity and serum interferon (M±m) in patients with asthma of different degrees of severity

Data	Asthma			
	Intermittent	Persistent		
		Mild	Moderate	Severe
Interferon, log (2)	8,8±2,1	17,3±2,5*°	12,8±1,0*	28,8±1,6*°
NK activity, %	43,2±3,7	39,0±4,3*	32,8±3,2*°	32,1±3,7*°
TNF, %	4,6±1,3	10,4±2,2*	21,1±2,2*°	12,6±1,6*°

* - p<0.05 compared with control group; ° - p<0.05 compared with intermittent asthma

Values of TNF in intermittent asthma were within normal limits, and in persistent asthma were increased, compared with the average values of this index in the control group (4,2±0,8%). But if the level of interferon in severe asthma was significantly higher compared with moderate asthma, the level of TNF in severe asthma was significantly lower compared with moderate asthma (Table 3). It is known that TNF induces the synthesis of IFN-γ by NK-cells and is a co-stimulator IL-2-dependent production of interferon-γ leukocytes, which, in turn, can activate cells of the phagocytic system and NC. It is not

excluded that the relative reduction of TNF in severe asthma is one of the manifestations of exhaustion of compensatory mechanisms.

To explore the physiological role of serum interferon and tumor necrosis factor in the immunopathogenesis of asthma, correlation analysis between the levels of serum interferon and TNF and the number of acute viral infectious diseases of the upper respiratory tract (ARI), which was defined by a survey a year later was conducted. An expressed inverse relationship between the level of serum interferon and frequency of ARI (K = -0.60) was discovered, indicating that higher values of this parameter helped protect against ARI in patients with asthma. The correlation coefficient between the level of TNF and frequency of ARI was slightly negative (K = -0.7), which does not allow to give a definite answer about the protective value of this indicator in asthma.

As seen from Table 3, higher values of serum interferon were associated with a lower incidence of ARI in intermittent, mild and moderate persistent asthma, indicating a protective role of this index. In severe persistent asthma the correlation coefficient was even slightly positive, ie, according to our data, higher levels of interferon in severe asthma hardly contributed to protection against ARI, and possibly supported the activation of eosinophils. The highest correlation coefficients were found between the frequency of acute respiratory infections and levels of serum interferon (K = -0.60), NK activity (K = -0.56), spontaneous NBT-test (K = -0.36).

Table 3

The correlation coefficients (K) between the frequency of acute respiratory infections and immune parameters in patients with different severity types of asthma.

Data	K between the frequency of acute respiratory infections and immune parameters			
	Intermittent	Persistent		
		Mild	Moderate	Severe
NK activity	- 0,58	- 0,58	- 0,56	- 0,16
Serum interferon	- 0,33	- 0,26	- 0,72	0,03
TNF	- 0,45	- 0,40	0,03	0,72
Spontaneous NBT-test	- 0,27	- 0,27	- 0,38	- 0,14

As shown in Table 3, decreased NK activity and NBT test were associated with frequent acute respiratory diseases in intermittent and mild and moderate persistent asthma. This connection was not found in severe asthma. Elevated level of serum IFN contributed to protection against ARI in moderate asthma. In severe asthma, according to our data, elevated levels of IFN hardly contributed to protection against ARI. That is, if in mild intermittent and persistent asthma higher values of TNF and interferon could contribute to protection against ARI, then in moderate asthma - most likely not.

Conclusion. Reduction in NK activity of blood mononuclear cells in patients with mild, moderate and severe persistent asthma is apparently associated with infection-dependent component (usually viral) in the pathogenesis of the disease. Probable reduction of stimulated NBT reaction in patients with moderate and severe asthma indicates exhaustion of functional reserves of phagocytes. Normal levels of serum interferon and TNF were found in patients with intermittent asthma, compared with control group, mean values were significantly higher in patients with mild, moderate and severe persistent asthma. In mild asthma (intermittent and persistent) higher values of serum interferon and TNF were associated with lower incidence of ARI, apparently contributing to protection against viral infections. A similar relationship was marked for interferon in moderate asthma. However, in patients with severe asthma the relationship between ARI frequency and values of serum IFN and particularly TNF was positive, indicating a need for a differentiated approach to immunotherapy with different severity types of asthma.

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SUMMARY

Immune parameters in patients with asthma

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The article is dedicated to researching of conditions of factors of nonspecific resistance of organism in patients with bronchial asthma. Damage of intensity of absorbtive function of neutrophils, activation of metabolism of neutrophils and monocytes of peripheral blood, coupled with a decrease in bactericidal functional reserve of monocytes prevailed in clinical manifestations of immune deficiency at bronchopulmonary diseases. Suppression of interferon genesis was combined with deviations of indicators of cellular and humoral immunity, and leukocyte production of tumor necrosis factor.

Key words: bronchopulmonary system, immune system, cytokines.