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## CYTOKINE PROFILE IS THE BIOMARKER OF THE SEVERITY OF BRONCHIAL ASTHMA

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Abstracts: It is well known that bronchial asthma (BA) is in the leading place in the structure of morbidity of respiratory organs is the most important problem of modern pulmonology.

As you know, the nature of the clinical course and severity of BA largely depends on the ac-tivity of the inflammatory process that begins with damage to the bronchial epithelium, disorders of microcirculation and the subsequent interaction of key effector cells and their mediators.

BA is accompanied by a systemic response of the organism to inflammation in the lung tis-sue and involved in this type of mediators, including Pro - and anti-inflammatory cytokines, chemo-kines, leukotrienes, prostaglandins and others, determine the mechanisms of disease develop-ment.

In the literature available to us there is a lot of information, details and evidence character-izing the role of cytokines in the development and course of BA. However, these studies presented a lot of data, but they are, in our opinion, do not allow to present a clear picture of the changes of the cytokine profile in asthma, depending on the shape and severity of the disease. In addition, there are difficulties in the interpretation of cytokine regulation in asthma because the pathogene-sis of this disease are «working» complex allergic and non-allergic mechanisms.

In this regard, exploring the use of a set of biomarkers of inflammatory activity, in particular of Pro - and anti-inflammatory cytokines for evaluation of the prognosis of BA is of great practical importance.

Bronchial asthma (BA) is accompanied by a systemic response of the organism to the in-flammation in lung tissue and involved in this type of mediators, including pro - and anti-inflammatory cytokines, chemokines, leukotrienes, prostaglandins and others, determine the mechanisms of disease development.

Key words: bronchial asthma, cytokines, chemokines, leukotrienes

Goal: investigation of the spectrum of pro - and anti-inflammatory cytokines in serum and bronchoalveolar lavage (BAL) fluid of patients with BA according to spectrum sensitization, severity and form of the disease to development criteria for the evaluation and prediction of the nature of the disease

Materials and methods: The study included 115 patients with asthma aged 19 to 67 years, pre-divshih the course of examination and treatment in the pulmonology Department of the Amur regional clinical hospital of the health Ministry of the Russian Federation. Among them was 68 (59,1%) women and 47 (40,9%) men.

Upon admission to the hospital patients to BA conducted a comprehensive survey with ap-plication of clinical, radiological, functional and laboratory methods of research.

The diagnosis of BA were staged according to the International classification of diseases, X revision (ICD – 10) and Global initiative for asthma...(GINA), given the typical clinical picture of the disease, the data allergological anamnesis, hereditary predisposition, the results of clinical, func-tional and allergological methods.

Among the patients examined 41 patients were diagnosed BA of moderate severity (SST), 42 – severe severity (TST) and 32 – steroids-dependent BA TST (TST+Sz).

The form of the disease, patients were distributed as follows: 70 patients were established combined form BA (BA-sm), and 45 – non-allergic BA (BAN). When BA-see 25 patients were BA SST, 26 – and 19 TST – TST+Sz. If you BAN 16 patients was BA SST, 16 – and 13 TST – TST+Sz.

Benchmarking results the study included 14 healthy donors (control group) aged from 24 to 44 years. At diagnosis account for the peculiarity of allergological tests with standard allergens, and conducted pricesthe fungal allergens («Allergopharma», Germany).

Levels of proinflammatory (IL-1b, IL-6, IL-8 and TNF-a) and antiinflammatory (IL-4) cytokines was determined using the method of enzyme immunoassay on a vertical photometer Multiskan MCC-340 (450 nm) using test systems ProCon company «Protein contour» (St. Petersburg).

Statistical processing of research results was performed using standard methods of varia-tion statistics with the definition of the average value (M) and standard error of the mean (m). A comparison of ranks was performed using student's t-test in cases of abnormal distribution, non-parametric criterion of Wilcoxon-Mann-Whitney. The difference between compared indicators were considered significant at $p<0.05$.

In the work investigated the cells of bronchoalveolar lavage (BAL) fluid of 18 patients with a mixed form of ASTHMA, who were divided into 2 groups depending on the severity of the disease: 10 patients with moderate and 8 – severe severity. BAL fluid was obtained during therapeutic and diagnostic bronchoscopy performed according to standard methods. BAL fluid was centrifuged at 1000 rpm for 10 min to obtain a suspension of lung cells.

The cells of BAL fluid were cultured in number of 106/ml with RPMI-1640 medium by adding 10% fetal calf serum, Gentamicin 80 μg/ml, 2mm L-glutamine, 5x10-5 mm mercaptoethanol. For stimulation of cells in BAL fluid in a parallel-hole tablet was added E. coli LPS at a concen-tration of 0.5 μg/ml.

The content of the immunoregulatory cytokines IL-1β, IL-4 and TNF-α in the conditioned culture medium of cells BAL fluid was assessed after 24 hours of incubation using a commercial test systems for ELISA («Protein contour», Saint-Petersburg) according to the manufacturer's Protocol.

Results: The increase in pro-inflammatory cytokines correlates with the severity of BA with a compensatory increase in the level of anti-inflammatory cytokine IL-4. In patients with non-allergic BA the inflammatory process is more active than the patients with allergic BA. At steroids-dependent BA set to maintain a high level of IL-8 regardless of the form of the disease, indicating the development of resistance of cells-producers to the action of glucocorticoid hormones.

The BAL fluid cells of patients with moderate BA active products pro-inflammatory cyto-kines (TNF-α), and in patients with a severe degree of IL-4. The cells of BAL fluid of patients with severe asthma, according to results LPS-induced cytokine-producing activity, pre-conditioned on increased Th2-cytokine profile (IL-4).

Conclusions: The change in the spectrum of pro - and anti-inflammatory cytokines in blood serum is a molecular marker of severity of BA course. ytokine-producing activity of macrophages and neutrophils BAL fluid determines the na-ture of the inflammation in situ.

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