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Significance Of Pro-Inflammatory Cytokines (Il-8, Ifnγ) In Prediction Of The Course In AD, COPD, and ACO

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Relevance: Asthma and chronic obstructive pulmonary disease (COPD) are a major public health problem and a leading cause of morbidity and mortality worldwide. Asthma and COPD are the most common chronic respiratory diseases, each with a specific pathophysiology. Usually, asthma is characterized by chronic inflammation of the airways with reversible symptoms, while COPD is characterized by persistent respiratory changes in the bronchopulmonary system. The importance of the need for its further study is beyond doubt, since this pathology significantly reduces the quality of life of patients, being a serious medical and social problem. Most previous studies have shown that patients with ACO have more severe respiratory symptoms, frequent exacerbations, poor quality of life, high mortality, increased use of healthcare resources, and a higher prevalence of comorbidities than patients with isolated asthma or COPD. As recommended by the GINA experts, ACO is characterized by three major criteria: (1) long-term smoking, (2) chronic airflow limitation, (3) documented history of asthma and three minor criteria: (1) documented history of atopy or allergic rhinitis, (2) decreased volume forced exhalation in 1 second (FEV 1) ≥ 12% and ≥ 200 ml or (3) an increase in blood eosinophils. The diagnosis is made in the presence of 2 major or 1 major and 2 minor criteria. and a higher prevalence of comorbidities than patients with isolated asthma or COPD. As recommended by the GINA experts, ACO is characterized by three major criteria: (1) long-term smoking, (2) chronic airflow limitation, (3) documented history of asthma and three minor criteria: (1) documented history of atopy or allergic rhinitis, (2) decreased volume forced exhalation in 1 second (FEV 1) ≥ 12% and ≥ 200 ml or (3) an increase in blood eosinophils. The diagnosis is made in the presence of 2 major or 1 major and 2 minor criteria. and a higher prevalence of comorbidities than patients with isolated asthma or COPD. As recommended by the GINA experts, ACO is characterized by three major criteria: (1) long-term smoking, (2) chronic airflow limitation, (3) documented history of asthma and three minor criteria: (1) documented history of atopy or allergic rhinitis, (2) decreased volume forced exhalation in 1 second (FEV 1) ≥ 12% and ≥ 200 ml or (3) an increase in blood eosinophils. The diagnosis is made in the presence of 2 major or 1 major and 2 minor criteria. (3) a documented history of asthma and three secondary criteria: (1) a documented history of atopy or allergic rhinitis, (2) a decrease in forced expiratory volume in 1 second (FEV 1) ≥ 12% and ≥ 200 ml, or (3) an increase in blood eosinophils . The diagnosis is made in the presence of 2 major or 1 major and 2 minor criteria. (3) a documented history of asthma and three secondary criteria: (1) a documented history of atopy or allergic rhinitis, (2) a decrease in forced expiratory

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volume in 1 second (FEV 1) ≥ 12% and ≥ 200 ml, or (3) an increase in blood eosinophils . The diagnosis is made in the presence of 2 major or 1 major and 2 minor criteria.

The issue of fundamental importance in modern practical medicine is the relationship between the formation of the layering of chronic diseases, such as asthma and COPD, with the processes occurring in the bronchopulmonary system or with changes in the immune system. According to many authors, the cause of overlap or layering of bronchial asthma and chronic obstructive pulmonary disease are various immune disorders that cause a decrease in the body's resistance to microbial infection. The study of cytokines shows their significant and diverse role in the development of immune, allergic and inflammatory reactions in respiratory diseases. Emerging new data on the nature and functions of these mediators complement the understanding of the pathogenesis of pulmonary diseases.

Purpose of the study: identify the most important cytokines in the prognosis of the course of PAH

Materials and methods of research: We have studied clinical and immunological parameters in 159 patients with BA, COPD and ACO.

Of 159 patients: 62 patients were diagnosed with bronchial asthma, 67 patients with COPD, 30 patients with an overlap of asthma and COPD

The diagnosis was established according to clinical and functional data in accordance with the international consensus (GINA-2021) for the diagnosis and treatment of bronchopulmonary diseases. The diagnoses were verified on the basis of a thorough history taking, clinical, laboratory (general blood count, urine), biochemical blood test, bacteriological examination of sputum, instrumental (chest x-ray, electrocardiography, spirography, peak fluometry). Particular attention was paid to the prescription of the pathological process, past and concomitant diseases, and the tendency to allergic reactions.

The inclusion criteria for the study were patients with an established diagnosis of BA, COPD, ACO aged 18 to 75 years.

Exclusion Criteria:

- heart disease (acute myocardial infarction)
- the presence of cerebrovascular diseases (stroke, transient ischemic attacks
- malignant neoplasms
- severe kidney or liver failure
- Pregnancy or breastfeeding in women
- severe endocrine pathologies
- severe autoimmune condition

Quantitative assessment of the levels of IL-4, IL-8, TNFα, IFNγ was carried out using test systems (LLC "Cytokin", St. Petersburg) by enzyme-linked immunosorbent assay.

Statistical processing of the obtained data was carried out by the Fisher-Student variation statistics method and Pearson's χ^2 test was used.

Research results: In our studies, we conducted a comparative analysis of pro- and anti-inflammatory cytokines in the studied groups (IL-4, IL-8, TNFα, IFNγ). According to many authors, cells synthesizing Th2-type cytokines dominate in the airways affected by asthma. CD8+ cells, eosinophils, and mast cells produce IL-4, which in turn possibly causes bronchial tree hyperreactivity. Our data confirm that the levelIL-4 was the highest in the BA group - 28.6 ± 1.7 pg/ml, which was significantly higher by 3.97 times than in the COPD

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group and 1.25 times more than in the PBAH group. (P<0.01).

In chronic obstructive pulmonary disease and ACO, an increase in the content of IL-8 in sputum is observed, which is associated with the involvement of neutrophils in the focus of inflammation. In our study, the concentration of IL-8 was high in the ACO group - 39.6 ± 1.1 pg/ml, which was significantly higher by 2.1 times compared with the BA group and 1.42 times higher in COPD.(P<0.01).

When studying the concentration of tumor necrosis factor, there were no significant differences between the BA and COPD groups; in the ACO group, the concentration TNFα was increased 1.3 times compared with other groups (46.2 ± 1.7 pg/ml).(P<0.01).The increase in the level of TNFα in the ACO group is possibly associated with a more intense inflammatory process in the lungs.

Interferon gamma is an indicator of the Th1 immune response, which is more characteristic of a non-allergic inflammatory process. Level IFNγ was reduced in all the studied groups, but its lowest concentration was observed in the BA group 11.7±0.6.(P<0.01).

The results obtained reflect the type and intensity of airway inflammation. The high values of the studied cytokines confirm their role in bronchial remodeling and contribute to the irreversibility of obstruction in these pathologies. Perhaps this is due to the chronic course of both eosinophilic and neutrophilic airway inflammation. Undoubtedly, these cytokines play an important role in the pathogenesis of BA, COPD, ACO and can serve as markers of the severity of the pathological process.

Our studies revealed that among the groups examined in the group of patients with ACO, the levels of pro-inflammatory cytokines - IL-8 and IFNγ undergo a sharp change. In this regard, we considered it appropriate to calculate an index that combines these indicators, according to the following formula: IPCD = IL-8 / IFNγ. Calculations showed that in practically healthy people (control group) IPCD was less than 1 and amounted to 0.6±0.15. with ACO = 3.19±0.17.

Analysis of the result of the index of the prognosis of the course of the disease (IPCD) showed that among the examined, an increased index corresponded to a more severe clinical condition. So, for example, in patients with ACO with IPCD equal to 3.19 and higher, there was a higher percentage of complications, a severe protracted course in combination with symptoms of intoxication.

Findings: Thus the ratioIL-8 and IFNγ provide important information about the state of the immune system not only at the time of the examination, but also allows predicting the further course of the disease. The study of these cytokines will help the doctor in determining the choice and duration of the necessary therapy.

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