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# The Clinical Relationship of the Immune and Antioxidant Systems in Chronic Obstructive Bronchitis in Young Men and Adolescents

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**Abstract** **Relevance.** Respiratory diseases occupy a leading place in the pathology of childhood and adolescence, differing in their significant prevalence and tendency to recurrent course. The leading role in the formation of a protracted course of inflammatory diseases of the respiratory tract in young men and adolescents belongs to immunological mechanisms, in which a wide range of cytokines are involved, which are responsible for the activation, proliferation, and chemotaxis of various cells. **The purpose of the study**. The study of the clinical relationship between the production of IL-8, IL-1β and the antioxidant system in the serum of peripheral blood in chronic obstructive bronchitis in young men and adolescents. **Materials and methods**. The study involved 53 adolescents and youths suffering from chronic obstructive bronchitis aged 11 to 25 years. The control group consisted of 22 healthy individuals of adolescence. Verification patients with chronic obstructive bronchitis was carried out according to the international classification of WHO. **Results and its discussion.** The main symptoms of chronic obstructive bronchitis in young men and adolescents were coughing and sputum production for most days for at least three consecutive months for more than two years. The examination revealed symptoms of a general nature, such as sweating, weakness, fever, decreased mental and physical potential. Analysis parameter cytokine status in the studied patients with chronic obstructive bronchitis in adolescence found high production of IL-8 by immunocompetent cells. **Conclusions.** The data on the immunological mechanisms of the pathogenesis of chronic obstructive bronchitis in adolescence allow us to recommend a new differentiated approach to the diagnosis and thereby to the pathogenesis treatment of the disease, which prevents the development of inflammation in the respiratory tract in patients with chronic obstructive bronchitis.

**Keywords** Youth, Adolescents, Immune and antioxidant systems, Chronic obstructive bronchitis

## 1. Relevance

Respiratory diseases occupy a leading place in the pathology of childhood and adolescence, differing in their significant prevalence and tendency to recurrent course [1, 4]. The leading role in the formation of a protracted course of inflammatory diseases of the respiratory tract in young men and adolescents belongs to immunological mechanisms, in which a wide range of cytokines are involved, which are responsible for the activation, proliferation, and chemotaxis of various cells.

One of the extremely important in the regulation of many body functions is endogenous IL-1β [1,2,5]. It has been established that IL-1β initiates the involvement of a wide range of cells in the inflammatory response and is considered to be the central early “ pro-inflammatory " cytokine, whose competence includes not only the regulation of hematopoiesis and immunogenesis, but also the management of both local and systemic inflammatory reactions of the body. Interleukin-8 is one of the active pro-inflammatory α- chemokines, is released in the focus of inflammation and expression the surface of the endothelium. In the available literature there is evidence of an increase in the level of IL-8 in the blood of patients with systemic inflammation, including chronic obstructive bronchitis [3,5].

A whole class of substances was found, united under the common name "antioxidants." The insufficiency and disruption of the endogenous antioxidant system leads to the accumulation of products of free radical lipid peroxidation, which determines the intensity of a pathological process and is clinically accompanied by the development of a nonspecific endogenous intoxication syndrome [2,5,6].

The literature available to us does not adequately cover the features of the antioxidant system in the blood in chronic obstructive bronchitis in adolescents, while the function of

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the anti-radical defense system that ensures the utilization of reactive oxygen species undoubtedly plays an important role in the development and progression of the pathological process in the bronchopulmonary system. In this regard, it was interesting to study the activity of the antioxidant enzymes catalase and peroxidase in chronic obstructive bronchitis in adolescents.

In clinical practice, in recent years, the problem of chronic obstructive bronchitis in young men and adolescents is becoming increasingly important, which is associated with a persistent tendency to increase the number of adolescents with complaints of this disease, treatment inefficiency, uncertainty of prognosis, and lack of knowledge of the direction of the inflammatory process with this pathology.

## 2. The Purpose of the Study

The study of the clinical relationship between the production of IL-8, IL-1β and the antioxidant system in the serum of peripheral blood in chronic obstructive bronchitis in young men and adolescents.

## 3. Materials and Methods

The study involved 53 adolescents and youths suffering from chronic obstructive bronchitis aged 11 to 25 years. The control group consisted of 22 healthy individuals of adolescence. Verification patients with chronic obstructive bronchitis was carried out according to the international classification of WHO (X-revision, ICD-10). The examination included an assessment of general clinical research methods (interrogation, study of objective status, a routine pair of clinical tests - a general blood test, a general urinalysis, a general sputum analysis, an x-ray of the chest organs). A mandatory method was the study of the ventilation function of the lungs, which was carried out on the apparatus "SPIROSIFT-SP-5000" with automatic processing of parameters (Fukuda Denshi, Japan). Immunological studies were carried out on the basis of the Institute of Immunology of the Academic Sciences of the Republic of Uzbekistan laboratory of immunocytokines laboratory diagnostics. Determination of the level of IL-1βin blood serum was carried out by enzyme immunoassay using a test system for analysis IFA -IL-1β (ZAO Vector-Best, Russia, 2011). Determination of the level of IL-8 in serum was carried out by enzyme-linked immunosorbent assay using a test system for analysis IFA-IL-8 (ZAO Vector-Best, Russia, 2011). The state of the antioxidant system was judged by the activity of peroxidase and catalase by potentiometric determination of these enzymes. The method is based on measuring the change in the potential of the electrodes of an electrochemical cell operating by the displacement method that occurs during the oxidation reaction of 5 aminosalicylic acids with a solution of hydrogen peroxide. The data obtained were subjected to statistical processing on a Pentium IV computer using programs developed in the Excel package using a library of statistical functions with calculation of arithmetic mean (M), standard error (m), relative values (frequency,%), student criterion (t) s calculating the probability of error (p). According to the clinical variants of chronic obstructive bronchitis, 3 subgroups were identified: 1 subgroup - 26 teenagers with a mild course of the disease; 2 subgroup - 15 teenagers with moderate severity; 3 subgroup -12 severely adolescent; In total, patients with chronic obstructive bronchitis - 53 people.

## 4. Results and Its Discussion

The main symptoms of chronic obstructive bronchitis in young men and adolescents were coughing and sputum production for most days for at least three consecutive months for more than two years. The examination revealed symptoms of a general nature, such as sweating, weakness, fever, decreased mental and physical potential. Analysis parameter cytokine status in the studied patients with chronic obstructive bronchitis in adolescence found high production of IL-8 by immunocompetent cells. So, the content of the cytokine IL-8 in the serum of peripheral blood in patients with chronic obstructive bronchitis in adolescence, it was significantly increased to 76.2 ± 5.0 pg/ml at 23.9 ± 3.31 pg/ml in the control ($p < 0.01$) (table 1).

**Table 1.** Indicators of IL-8 in patients with chronic obstructive bronchitis in adolescence

| Groups | Healthy n = 22 | general group of patients n = 53 | t | p |
|---|---|---|---|---|
| IL-8 pg/ml | 23,9 ±3,31 | 76,2 ±5,0 | 5,3 | p <0,01 |

A study of the degree of production of IL-8 depending on the severity of the disease showed that the level of IL-8 in serum of peripheral blood was significantly increased. So, the concentration of IL-8 in the serum of peripheral blood in adolescents with chronic obstructive bronchitis with a severe course of 76.2 ± 5.0 pg/ml, moderate severity was 53.5 ± 2.14 pg/ml, with a mild disease - 40.6 ± 1.18 pg/ml, and in the healthy control group - 23.9 ±3.31 pg/ml (table 2).

**Table 2.** Indicators of IL-8 in patients with chronic obstructive bronchitis in adolescence with severity

| Groups | Healthy n = 22 | Sick | | | $p_{2-1}$ | $p_{3-1}$ | $p_{3-2}$ |
|---|---|---|---|---|---|---|---|
| | | Easy n = 26 | Mean n = 15 | Heavy n = 12 | | | |
| IL-8 pg/ml | 23,9 ±3,31 | 40,6 ±1,18 | 53,5 ±2,12 | 66,2 ±5,0 | p <0,01 | p <0,01 | p <0,05 |

**Table 3.** The indicators of IL-1β patients with COPD in adolescence

| Groups | Healthy n = 22 | general group of patients with COPD n = 53 | t | p |
|---|---|---|---|---|
| IL-1β pg/ml | 9,9 ±0,3 | 7,8 ±0,4 | 4,2 | p <0,02 |

**Table 4.** Indicators of IL-1β in patients with chronic obstructive bronchitis in adolescence

| Groups | Healthy n = 22 | Sick | | | $p_{2-1}$ | $p_{3-1}$ | $p_{3-2}$ |
|---|---|---|---|---|---|---|---|
| | | Easy n = 26 | Mean n = 15 | Heavy n = 12 | | | |
| IL-1β pg/ml | 9,9 ±0,03 | 7,6 ±0,08 | 6,3 ±0,06 | 5,5 ±0,04 | p <0,02 | p <0,01 | p <0,02 |

**Table 5.** Indicators of the antioxidant system in chronic obstructive bronchitis in adolescents in the phase of exacerbation of the disease

| Indicator | Healthy n = 22 | Sick n = 53 | t | R |
|---|---|---|---|---|
| Peroxidase μmol/ml ×min | 0,05 ± 0,006 | 0,01 ± 0,002 | 6,8 | 0,001 |
| Catalase μmol/L ×min | 27,9 ± 0,8 | 25,6 ± 0,5 | 1,4 | Nd |

**Table 6.** Indicators of the antioxidant system in chronic obstructive bronchitis in adolescents, depending on the severity of the disease

| Indicator | Healthy n = 22 | Sick | | |
|---|---|---|---|---|
| | | Lung n = 26 | Average n = 15 | Heavy n = 12 |
| Peroxidase μmol/ml ×min | 0,05 ± 0,006 | 0,008 ± 0,001 * | 0,009 ± 0,005 * | 0,001 ± 0,003 * |
| Catalase μmol/L ×min | 27,9 ± 0,8 | 21,7 ± 0,7 * | 22,4 ± 0,6 * | 20,8 ± 0,4 * |

Note: * - reliability in relation to indicators of healthy individuals.

**Table 7.** Indicators of the antioxidant system in chronic obstructive bronchitis in adolescents, depending on the age of the patients examined

| Indicator | Healthy n = 22 | Sick | |
|---|---|---|---|
| | | Teenagers n = 29 | Boys n = 24 |
| Peroxidase μmol/ml ×min | 0.05 ± 0.006 | 0.01 ± 0.002 * | 0.008 ± 0.001 * |
| Catalase μmol/L ×min | 27.9 ± 0.8 | 26.7 ± 0.8 * | 20.1 ± 0.4 * |

Note: * - reliability in relation to indicators of healthy individuals

**Table 8.** The correlation relationship between the immune and antioxidant systems

| Indicators | Control group n = 22 | Sick | | |
|---|---|---|---|---|
| | | Easy n = 26 | Mean n = 15 | Heavy n = 12 |
| IL-8 pg/ml | 23,9 ±3,31 | 40,6 ±1,18 * | 53,5 ±2,12 * | 66,2 ±5.0 * x |
| IL-1β pg/ml | 9,9 ±0,03 | 7,6 ±0,08 * | 6,3 ±0,06 * | 5,5 ±0,04 * x |
| Peroxidase μmol/mlhmin | 0,05 ± 0,006 | 0,008 ± 0,001 * | 0,009 ± 0,005 * | 0,001 ± 0,003 *x |
| Catalase μmol/Lhmin | 27,9 ± 0,8 | 21,7 ± 0,7 * | 22.4 ± 0,6 * | 20,8 ± 0,4 *x |

Notes: * - the significance of differences in the indicator from the control group (p <0.05)
x - significance of differences between groups
n - number of patients

It should be noted that a higher level of IL-8 cytokine concentration was observed in patients with severe chronic obstructive bronchitis. An imbalance in the cytokine IL-8 in the formation of which a significant role is played by violations of cellular immunity, is one of the leading links in the pathogenesis that determine the development of the inflammatory process in chronic obstructive bronchitis, and its elimination favorably affects the clinical course of these diseases.

Parameter analysis of the proinflammatory cytokine, in the studied patients with chronic obstructive bronchitis in adolescence, found low production IL-1β by immunocompetent cells. Thus, the serum content of peripheral blood IL-1β cytokine in patients with chronic obstructive bronchitis in adolescence was significantly reduced to 7.8 ±0.4 pg/ml at 9.9 ±0.3 pg/ml in the control (p <0.02) (table 3).

A study of the degree of IL-1β production depending on the exacerbation/remission phase showed that the level of proinflammatory cytokine in the serum of peripheral blood, regardless of the phase of the pathological process, is at an equally low level. Thus, the concentration of IL-1β in the serum of peripheral blood in adolescents with chronic obstructive bronchitis in the acute stage was 5.5 ±0.04 pg/ml, in the remission phase - 7.6 ±0.08 pg/ml, and in the healthy

group control - 9.9 ±0.03 pg/ml (table 4).

Studies of the immunological mechanisms of the pathogenesis of chronic obstructive bronchitis in adolescence have confirmed the key role of IL-1β in the development and maintenance of the inflammatory process in the respiratory tract in this pathology.

Our studies of indicators of the antioxidant system show that the activity of the peroxidase enzyme in sick adolescents with chronic obstructive bronchitis is significantly reduced, significantly differing from the average values of the control group. Contents antiperoxide enzyme catalase slightly reduced plasma in patients suffering from adolescent chronic obstructive bronchitis and constitutes 25,6 ± 0,5 compared with 27.9 ± 0.8 Control group (table 5).

To clarify the nature and degree of tension of the antioxidant system in the examined sick adolescents suffering from chronic obstructive bronchitis, the activity of peroxidase and catalase enzymes was analyzed depending on the severity of the clinical course of the disease (table 6).

An analysis of the activity of the antioxidant system enzymes in the broken groups depending on the severity of the disease revealed their significantly low rates of both peroxidase and catalase compared to the control group. The lowest level of antioxidant system enzyme activity was observed in sick adolescents with severe clinical course of chronic obstructive bronchitis in the acute phase of the disease and amounted to 0,001 ± 0,003 μmol/ml × min for peroxidase and 20,8 ± 0,4 μmol/l × min for catalase.

When analyzing the results of the study, taking into account the age of the patients, it was found that the performance of both enzymes of the antioxidant defense of the body was markedly reduced in the youthful age group of patients with chronic obstructive bronchitis (table 7).

Thus, it can be noted that the analysis of the parameters characterizing the state of the antioxidant system in the exacerbation phase with chronic obstructive bronchitis revealed a pronounced lack of antioxidant enzymes of catalase and peroxidase related to the age of the examined and the severity of the disease. Based on the fact that the change in the activity of the antioxidant system is based on very subtle metabolic mechanisms, the disclosure of which is considered as the key to understanding the deep foundations of many diseases accompanied by disorders in the respiratory system, it is advisable to consider pathogenetic substantiated methods of treating chronic obstructive bronchitis in adolescents. In the clinical group of patients with chronic obstructive bronchitis, a severe course indicated a significant decrease in the body's immune response to chronic inflammation. The correlation between the level of the antioxidant system of catalase and peroxidase, on the one hand, and IL-8, IL-1β of the immune system, on the other hand, determined a compensatory increase in the activity of inflammation (table 8).

A significant number of correlations between immunity indices and the antioxidant system of the enzyme were revealed, indices characterizing the enzymatic link of peroxidation processes, which indicates active processes in the body and indicates a pronounced inflammatory reaction.

## 5. Conclusions

- The revealed features of the activity of antioxidant defense enzymes in patients with chronic obstructive bronchitis in adolescence can be an adequate method for assessing complex relationships lipid peroxidation, antioxidant systems characteristic of the clinical course of the disease, taking into account age, as well as pathogenically substantiated antioxidant therapy.
- In patients with chronic obstructive bronchitis in adolescence, a reduced level of production of the cytokine IL-1β of the immune system in the blood serum has been established, which reveals the role of immune disorders in the pathogenesis of this disease. It was shown that chronic obstructive bronchitis in adolescents, regardless of the phase of exacerbation/remission of the disease, is accompanied by a low concentration of IL-1β in serum.
- In patients with chronic obstructive bronchitis in adolescence, an increased level of production of the cytokine IL-8 of the immune system in the blood serum has been established, which reveals the significant pathogenesis mechanisms of the disease. It was shown that chronic obstructive bronchitis in adolescents, regardless of the clinical course, is accompanied by a high concentration of IL-8 in the blood serum.

The data on the immunological mechanisms of the pathogenesis of chronic obstructive bronchitis in adolescence allow us to recommend a new differentiated approach to the diagnosis and thereby to the pathogenesis treatment of the disease, which prevents the development of inflammation in the respiratory tract in patients with chronic obstructive bronchitis.

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