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THE FEATURES OF THE IMMUNE STATUS OF CHILDREN WITH CHRONIC OBSTRUCTIVE BRONCHITIS ON THE BACKGROUND OF CYSTIC FIBROSIS

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ABSTRACT

Background: Despite of the complex organization and the perfection of the defense mechanisms of the mucous membranes, various pathogens overcome all barriers and penetrate into the internal environment of the body and cause disease. This may contribute to a variety of internal and external factors that have an adverse effect on the mucous membranes of the respiratory tract and its defense mechanisms. **Objective:** The aim of the study was to examine the features of immunological reactivity in chronic obstructive bronchitis in children with and without cystic fibrosis. Methods: Determined lymphocytes with CD3, CD4, CD8, CD16, CD20, CD25, CD HLA-DR, CD95 phenotypes. It was held an examination of 56 children with chronic obstructive bronchitis (COB). Of these, In 18 children experienced COB on the background of cystic fibrosis. **Result:** Carried immunological studies have shown that the presence of cystic fibrosis exacerbate immunodeficiency Children with COB, who significantly reduced the level of T-lymphocytes and subpopulation of CD4 + - and CD8 + cells, while the level of B lymphocytes was increased. **Conclusion:** The results showed that the development of immunopathological conditions in children with chronic obstructive bronchitis on the background of cystic fibrosis has its own characteristics, and to a greater extent due to the insolvency of a functional immune cells.

KEYWORDS: Chronic obstructive bronchitis, cystic fibrosis, immune system.

INTRODUCTION

In recent years, young children significantly increased the incidence of obstructive bronchitis with lingering course. The problem is compounded by the fact that this category of children have a high incidence of bronchial obstruction case again a few weeks after discharge from the hospital, which subsequently leads to the formation of recurrent obstructive bronchitis or asthma.[1,2,4,6]

What are the main factors of chronic obstructive bronchitis in children? The most significant of these are the persistence of the pathogen and the immune dysfunction. It is known that the persistence of the virus and / or intracellular pathogen amid increased sensitivity of the bronchial tree to the infection causes chronic inflammation. Any re-infection of viral or bacterial etiology contributes to the development of acute inflammation with chronic. In this case, the classical inflammation circuit is broken: and phagocytes that contain persistent infectious agent, unable to cope with the newly received antigens; there is a faulty or defective presentation of T-cell recognition, which ultimately leads to prolonged and recurrent course of the disease.[6]

An important role in the recurrence of obstructive bronchitis play diseases associated with congenital disorder of lung development. One of such disease is - cystic fibrosis (CF). WHO estimates that 45-50 thousand children with cystic fibrosis in the world are born annually, and the number of heterozygous carriers of the disease in the tens of millions. Cystic fibrosis (CF) – is one of the most frequent inherited monogenic diseases with multiple organ manifestation.[3,5,9,10]

A special place among the causes that contribute to chronic inflammatory process is given to the defects of immunological defense. Recent studies provide compelling evidence of significant changes in the immune status of patients with chronic lung diseases.[7,8]

The aim of the study was to examine the features of immunological reactivity in chronic obstructive bronchitis in children with and without cystic fibrosis.

MATERIALS AND METHODS

Under our supervision there were 56 children who came to the Department of Pulmonology RSSPMC Pediatrics Ministry of Health of Uzbekistan. Of these 38 children were with acute exacerbation of COB and 18 children with COB on the background of cystic fibrosis. Age of examined children was between 4 - 8 years. The control group consisted of 20 healthy children of the same age.

The diagnosis of chronic obstructive bronchitis (COB) was determined in accordance with the WHO criteria. The survey consisted of the collection of clinical and anamnestic data on the basis of COB and cystic fibrosis.

The material for immunological studies served the venous peripheral blood. Mononuclear cells were isolated by standard metod in the density gradient ficoll - verografin. Immunological studies were carried out studying the quantitative determination of CD3, CD4, CD8, CD16, CD20, CD25, CD HLA-DR, CD95 lymphocyte phenotype with monoclonal LT Series antibodies (LLP "Sorbent", Moscow, Russia). The concentration of immunoglobulin was determined by a well-known method of radial immunodiffusion by Manchini (The monospecific serum of the Institute by Gamaleya N.F., Moscow). Statistical processing of the results of the study were performed using standard methods of variation statistics.

RESULTS AND DISCUSSION

On admission to the hospital, the main complaints of sick children (according to parents) were cough, especially on awakening at 100% (56) of sick children; low-grade body temperature for 3-5 days - at 89.2% (50) children; decreased of appetite - at 30.3% (17) children; lethargy - at 41.1% (23); sweating - at 67.8% (38) children.

In the history of the sick children frequent colds (SARS, influenza) suffered in the past are fixed in 72% cases, inflammatory diseases of the upper respiratory tract (acute bronchitis, acute pneumonia, diseases of ENT-organs).

As can be seen from the data presented in bronchopulmonary pathology the immunological parameters differ from the parameters of the control group. Thus, decreased level of white blood cell is observed in the group of children with the COB ($P < 0,05$), while there was an increased level of white blood cells ($P < 0,05$) in the group of children with CF. (Table1).

Table 1. Some Characteristics Of The Immune System In Children With Chronic Obstructive Bronchitis The Background Cystic Fibrosis, (M ± m)

Parameters	Control group,n=20	COB, (I gr.), n=38	COB + CF, (II gr.),n=18
White blood cells, abs.	6200 ± 73	5980 ± 115 *	8970 ± 95 *
Lymphocytes,%	32,6 ± 0,9	36,3 ± 1,2	28,4 ± 1,1
Lymphocytes, abs.	2021 ± 53	2170 ± 116*	2547 ± 107
$CD3^+$, %	54,8± 1,2	46,8 ± 1,1*	42,9 ± 0,9*
$CD3^+$, абс	1108 ± 29	1015 ± 13	1092 ± 24
$CD4^+$, %	32,3 ± 0,8	26,3 ± 0,9*	24,5 ± 0,4*
$CD4^+$, абс	653 ± 21	570 ± 16 *	624 ± 18
$CD8^+$, %	22,1 ± 0,6	23,8 ± 0,8	15,6 ± 0,5 *
$CD8^+$, абс	447 ± 12	516 ± 19*	397 ± 10*
$CD16^+$, %	14,7 ± 0,5	18,6 ± 0,6*	7,8 ± 0,7*
$CD16^+$, абс	297 ± 7,1	403 ± 6,4 *	199 ± 14
$CD20^+$, %	18,5 ± 0,8	25,4 ± 0,9*	34,5 ± 0,9 *
$CD20^+$, абс.	3746 ± 13	551 ± 63*	853 ± 61*
Phagocytosis, %	49,4 ± 1,4	44,9 ± 0,8*	42,3 ± 0,8*

Note: * value is valid in relation to the control group ($P < 0,05$ - 0,001).

The Comparative characteristics of the relative content of T-lymphocytes in the circulating blood of examined children with COB revealed significant reductions, but the most profound deficits observed in children with CF, and COB ($P < 0.01$), although the analysis of the absolute values of the number of CD3 + -cells children in the group was on the level of the control values, and in children with COB - a tendency to decrease. It is known that the absolute content of the cells is very labile and is changed in accordance with fluctuations in peripheral blood leukocytes.

The Analysis of the results of the lymphocyte subpopulations study showed that COB is characterized by reduced levels of T-helper / inducer. The deeper deficit relative importance of CD4 + lymphocytes was observed in the COB on background of CF. The content of CD8 + -cells at COB in combination with CF was reduced ($P < 0.01$). CD4 + lymphocytes, carrying out their helper function, help, at first, B cells turn into plasma cell antibody-; Second, CD8 + lymphocytes - in mature cytotoxic T-cell; at third, macrophages carry hypersensitivity effects. These functions of T-lymphocytes / helper realized due to the fact that they are in turn divided into two subpopulations - Th1 and Th2 types of operating different helper function through cytokine-production of various interleukins.[6] The cytotoxic immune response plays an important role in protecting the body against intracellular pathogens and includes ulcerative - NK-cells and antigen-specific adaptive immune response element – CTLs.[7] Significantly lower expression of CD16 antigens on B

lymphocytes from patients we studied children with CF compared to controls may be indicative of a weak resistance.

When the studying of nonspecific protection factor it have been identified that the functional failure of phagocytes is widespread in sick children (P <0,001). The phagocytic reaction initiates an immune response: reduction of phagocytic activity of protection, of course, provides a low level immune response, including humoral, delay of assimilation products, violation of balance and tolerance to self-antigens.[8]

The B-system presented by quantitative content of B lymphocytes with CD20 molecule and the level of immunoglobulin of IgG, IgA, IgM. CD20 + classes - lymphocytes are directly involved in the specific immune defense reactions of the organism.[7,8] Comparative characteristics of circulating CD20 + -cells showed that the COB the level of these cells was significantly increased (P <0.01) with the maximum value in children with COB in combination with CF (P <0,001). Analysis of absolute values showed the same trend (P <0.01). These results suggest that activation bronchitis typical B-cell component of the immune system against imbalance in the population of T-lymphocytes, particularly in cystic fibrosis.

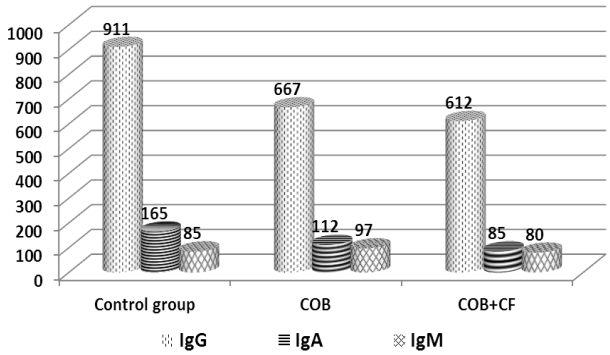

Fig.1. The concentration of immunoglobulins of the main classes in the examined children (mg / %).

The Research of the concentrations of major classes of G, A and M immunoglobulins showed that the COB takes place IgG and IgA synthesis decrease (P <0.05) (Figure 1). As for the IgM, its content is characterized by a significant increase in the group of children with the COB (P <0.05), and the COB in combination with CF have observed a decrease of IgM synthesis (P <0.05). As is known, this type of antibodies generated against infectious agents, activates complement and enhances phagocytosis and.[7] Perhaps the increased synthesis of IgM in children with COB is associated with the presence of infection.

For the activation of T-lymphocytes requires at least two consecutive processes. The first signal is provided by binding of MHC-associated peptides with the T-cell receptor. The second activation signal causes the expression of IL-2 receptors (CD25) on T lymphocytes that facilitates the exit of cells in S-phase of the cell cycle with subsequent cell replication.[8] The analysis of the results showed that in COB observed a significant decrease in the expression of the early activation markers - CD25 + -cells (P <0.05), and increased late activation markers (HLA-DR +, P <0,05 and CD95 + P <0,01). And, when combined with CF, COB level lymphocyte receptor for IL-2 is reduced to 1.35 times (P <0.05), with the COB - 1.25 times (P <0.05). (Table 2).

Table 2. Contents of Lymphocyte Activation Marker In The Examined Children, (M ± M)

Parameters	Control group, n=20	COB, (I gr.), n=38	COB + CF, (II gr.),n=18
CD25+, %	17,3 ± 0,5	13,8 ± 1,0 *	12,8 ± 0,5 *
CD95+, %	27,6 ± 0,8	32,9 ± 0,8*	33,8 ± 1,0*
CDHLA -DR+, %	23,5 ± 0,6	28,4 ± 0,7*	30,7 ± 0,9*

Note: * value is valid in relation to the control group (P <0,05 - 0,001)

Thus, the expression of the activation markers HLA-DR and CD95 on lymphocytes the sick children bronchopulmonary diseases is increased compared with that of healthy children. Increasing the number of lymphocytes expressing antigens CD95 and HLA-DR, indicate the stability of the activation process.

Apoptosis - is a form of programmed cell death characterized by DNA damage under the influence of the endonuclease. Formed in this apoptotic bodies undergo phagocytosis. Apoptosis is as an important component of immunological processes such as proliferation and differentiation. The level of lymphocyte apoptosis

receptor in our studies has examined groups of children with COB significantly increased. Moreover, children with CF + COB - more significantly (P <0, 01).

The results of our studies have shown that the development of immunopathological conditions in children with chronic obstructive bronchitis on the background of cystic fibrosis has its own characteristics, and to a greater extent due to the insolvency of a functional immune cells. It was found that chronic bronchitis with different etiologies correspond to certain immune disorders, determine the severity and extent of disease progression. One can not exclude the important role of functional disorders on the part of these effector cells, such as macrophages, involved in antigen processing and presentation to naive T-helper lymphocytes, since, at this stage there is a number of regulatory developments, determine the direction of the immune response.[7,8]

Thus, the data suggest a significant pathogenic role of immune disorders in the formation of a chronic inflammatory process in bronchopulmonary diseases in children. The complexity of the pathogenesis, the cascade of pathological processes and the variety of implementation mechanisms, as well as the depth of immune damage indicate the need for long and intensive immunotherapy to achieve persistent clinical and immunologic remission.

REFERENCES

1. Abdusalyamov A.A. Tukhvatulin R.R. Prospects for improving pediatric Uzbekistan // Pediatriyaning dolzarb muammolari: Tes.rep.Rep. scien. conf. 27-29 September 2000 Tashkent, 2000; 12.
2. Akhmedova D.I., Ashurov D.T., Arifov G.A. Risk factors for the development of bronchial obstruction syndrome in infants // Pediatrics. - T, 2000; 2-3: 52-53.
3. Bradley J., Moran F. Physical training for cystic fibrosis (review) Cochrane Database Syst Rev. 2008; p. CD002768. [PubMed].
4. Kamilov RT The incidence of Tashkent children from 7 to 14 years, according to the uptake in medical institutions // J. Pediatriya. (Pediatrics J.)-Tashkent, 2000; 2-3: 128-130.
5. Kapranov N.I. Shabalova L.A., Kashirskaya N.Y. et al. Cystic fibrosis. Current achievements and problems. Guidelines. Moscow, 2005.
6. Kokosov A.N. "Chronic bronchitis and obstructive pulmonary disease: an analytical essay." Ter. Archive, 2000; 3: 75-77.
7. Lukashevich M.G., Sizyakina L.P., Savisko A.A. Clinical and immunological features of repeated episodes of obstructive bronchitis in children // Russian journal Allergy. 2012; 2: 23-27.
8. Soloviev Yu.A., Sennikova L.V., Grishina L.V., Starostin N.M. Kozhevnikov V.S., Sennikov S.V., Shirinsky V.S. The balance of cytokines and changes in the immune status of patients with chronic bronchitis // Allergy and Immunology 2003; 4(1): 5-11.
9. O'Sullivan B.P., Freedman S.D. Cystic fibrosis. Lancet 2009; 373 (9678): 1891-1904. doi: 10.1016 / S0140-6736 (09) 60327-5. [PubMed] [Cross Ref].
10. van de Weert-van Leeuwen P.B., Slieker M.G., Hulzebos H.J., Kruitwagen C.L., Van der Ent C.K., Arets H.G. Chronic infection and inflammation affect exercise capacity in cystic fibrosis. Eur Respir J. 2012; 39(4): 893-898. doi: 10.1183 / 09031936.00086211. [PubMed] [Cross Ref].