STUDY OF VITAMIN D LEVELS ON THE COURSE OF BRONCHO-OBSTRUCTIVE SYNDROME IN CHILDREN

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Abstract. The aim of the study was to investigate the effect of vitamin D on the course of broncho-obstructive syndrome in children and to determine its relationship with cytokine status. The study involved 86 patients aged 3 to 15 years with acute obstructive bronchitis, recurrent obstructive bronchitis and bronchial asthma. The patients underwent a single set of diagnostic studies: clinical examination, immunological study, study of the level of vitamin D in the blood serum. The results of the study showed that vitamin D deficiency was accompanied by the development of secondary immune deficiency.

Key words: broncho-obstructive syndrome, vitamin D , immune status, children.

Annotatsiya. Tadqiqotning maqsadi D vitaminining bolalarda bronxo-obstruktiv sindrom kursiga ta'sirini o'rganish va uning sitokin holati bilan bog'liqligini aniqlash edi. Tadqiqotda 15 yoshdan 86 yoshgacha bo'lgan 3 bemorga o'tkir obstruktiv bronxit, takroriy obstruktiv bronxit va bronxial astma tashxisi qo'yilgan. Bemorlarga bitta diagnostik tadqiqot berildi: klinik tekshiruv, immunologik tadqiqotlar, sarum D vitamini darajasini o'rganish. Tadqiqot natijalari shuni ko'rsatdiki, D vitamini etishmasligi ikkilamchi immunitet tanqisligining rivojlanishi bilan birga kelgan.

Kalit so'zlar: bronxo-obstruktiv sindrom , D vitamini, immunitet holati, bolalar.

Аннотация. Целью исследования было изучить влияние витамина D на течение бронхообструктивного синдрома у детей и выяснить, связано ли это с состоянием цитокинов. В исследовании у 3 пациентов в возрасте от 15 до 86 лет был диагностирован острый обструктивный бронхит, рецидивирующий обструктивный бронхит и бронхиальная астма. Пациентам было проведено одно диагностическое исследование: клиническое обследование, иммунологические исследования, исследование уровня витамина D в сыворотке крови. Результаты исследования показали, что дефицит витамина D сопровождается развитием вторичного иммунодефицита.

Ключевые слова: бронхообструктивный синдром , витамин D, иммунный статус, дети.

Introduction

Respiratory pathology, including broncho-obstructive syndrome in young children, remains one of the pressing problems of modern pediatrics. In the pediatric population, bronchial obstruction occurs in almost 30% of children.

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Respiratory infections are the most common cause of broncho-obstructive syndrome in young children [1,2]. It should be noted that the incidence of broncho-obstructive syndrome in children of the first year of life has increased today to 50% or more, while 40% of children experience at least one episode of bronchial obstruction before reaching school age [2].

Broncho-obstructive syndrome itself has a characteristic clinical picture, so there are no difficulties with its diagnosis. At the same time, broncho-obstructive syndrome can be a consequence of allergic inflammation, obstructive obstruction or hemodynamic disorders, remodeling of the respiratory tract (bronchopulmonary dysplasia, bronchial tree dystonia, congenital malformations of the respiratory tract). Most often, broncho-obstructive syndrome occurs in acute obstructive bronchitis, obstructive bronchitis with a recurrent course and bronchial asthma. Among the known risk factors for repeated episodes of broncho-obstructive syndrome, such as family history of allergies , manifestations of atopy , eosinophilia, the role of vitamin D and the significance of its deficiency in the tendency to frequent episodes of bronchial obstruction are currently being actively studied [3-9].

The potential effect of vitamin D on the course of broncho-obstructive syndrome is due to its ability to affect cellular and humoral immunity, thereby reducing the inflammatory process [10-12]. This mechanism is due to gene expression and cytokine synthesis. The point of application here are vitamin D receptors. The molecular mechanism of action of the highly active metabolite of VD - 1,25-dihydroxyvitamin D (1,25 (OH) 2D), the so-called D-hormone (calcitriol) is the interaction with specific receptors in tissues - vitamin D receptors, which are widely represented in the body and are found in many tissues: T- and B-lymphocytes, macrophages, including pulmonary alveolocytes and bronchial smooth muscle cells [13-16]. It is worth noting that the molecular mechanism of the non-classical action of vitamin D has not yet been studied. This is largely due to the insufficient number of randomized studies conducted to assess the effect of vitamin D on metabolic processes and the course of broncho-obstructive syndrome.

The aim of this study was to examine the level of vitamin D on the course of broncho-obstructive syndrome in children and determine its relationship with cytokine status.

Materials and methods. The study involved 86 patients aged 3 to 15 years. Of these, 38 children with acute obstructive bronchitis (Group I), 15 children with recurrent obstructive bronchitis (Group II) and 33 children with bronchial asthma (Group III). As a control group, 20 practically healthy children of the same age were examined.

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All patients underwent a single set of diagnostic tests: clinical examination, immunological blood test, and serum vitamin D level test. The clinical examination included collection of anamnestic data, including previous illnesses, allergy history, premorbid background of the child, and assessment of the general condition at the time of examination. The immunological test included determination of cytokine levels: IL -4, IL -8, TNF -α, IFNγ . Serum vitamin D (25-(OH)D) level was analyzed using enzyme immunoassay. According to the recommendations of the United States Institute of Medicine, vitamin D level ≥ 20 ng /ml was considered by us as sufficient vitamin D intake , 11-20 ng /ml – insufficient intake, ≤10 ng /ml – deficiency. The obtained results were processed in the Statistics 10 program, after checking the normality of the distribution using the variation statistics method using the Student t-test, differences were considered statistically significant at $P < 0.05$.

Results and discussion . After the clinical examination, it was revealed that the severity of the examined patients is significantly affected by the unfavorable premorbid background and concomitant pathology. In all three observation groups, the most common background conditions were anemia, rickets and allergic diathesis. In the group of patients with acute obstructive bronchitis, the above conditions were more significant. Delayed physical development was observed in 24.6% of patients with bronchial asthma.

On admission to the hospital, the main complaints of children with acute obstructive bronchitis and recurrent obstructive bronchitis were cough 53 (100%), shortness of breath 53 (100%), fever in 32 (61.4%) children, decreased appetite 47 (90.3%), weakness 40 (76.3%), sleep disturbance 41 (91.8%). All children with bronchial asthma complained of cough with mucous sputum - 33 (100.0%), shortness of breath - 33 (100.0%), decreased appetite - 30 (90.8%), lethargy - 31 (95.4%), asthma attacks - 26 (80.0%), sweating - 16 (49.2%), headache - 14 (44.6%). On admission to the hospital, the leading clinical manifestation of the disease in patients with acute obstructive bronchitis was respiratory failure, weakness was noted in 21 (56.0%) patients, appetite was decreased in 30 (81.3%) patients. Sleep disturbance, pallor of the skin and dyspnea were noted in 38 (100.0%) cases. Cyanosis of the nasolabial triangle was in 12 (32.0%) children. Body temperature was febrile in 7 (18.7%), subfebrile - in 11 (30.6%). The cough was dry in 30 (81.3%), wet - in 7 (18.7%) patients. During auscultation of the lungs against the background of harsh breathing, dry wheezing was heard in 29 (77.3%) patients, wet wheezing was heard in 8 (22.7%). Chest percussion revealed a box percussion sound in 30 (88.0%) patients. In children with recurrent obstructive bronchitis, the disease was characterized by an acute (subacute) onset, cough, initially dry in 90.0% and wet in 10.0% of patients. Cough upon admission

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was paroxysmal in nature, more at night, and transformed into wet on the 5th-6th day of treatment. Cyanosis of the nasolabial triangle was observed in 25.0%, and dry skin was observed in 70.0% of patients. Auscultatory signs were varied and mainly depended on the level of bronchial mucosal damage. Dry wheezing was detected in 15.0% of children, and wet conductive wheezing was detected in 85.0% of children.

The results of the cytokine status study revealed that in children with acute obstructive bronchitis, IL -4 production significantly ($P < 0.01$) increased to 18.9±0.3 pg /ml compared to healthy children (Table 1). In patients with recurrent obstructive bronchitis, the IL -4 production index was significantly ($P < 0.01$) increased to 21.3±0.3 pg /ml, which was 4.6 times higher than the norm. In patients with bronchial asthma, the IL -4 production rate was increased to 26.7±1.4 pg /ml, which was 5.8 times higher than the norm. When analyzing the IL -8 content, its reliable increase was revealed in children of all three groups: with acute obstructive bronchitis up to 32.5±2.8 pg /ml, with obstructive bronchitis with recurrent course up to 89.5±3.9 pg /ml, with bronchial asthma up to 100.9±7.7 pg /ml, ($P<0.01$), which was 5.2 times higher than the norm. Our studies on the level of IFNγ in the examined patients showed a profound deficiency in their content. Thus, in children with acute obstructive bronchitis, the serum IFNγ level averaged - 27.4±1.5 pg / ml ($P < 0.05$), with recurrent obstructive bronchitis - 21.4±1.7 pg / ml and with bronchial asthma - 14.3±1.9 pg / ml, respectively, which is 1.2-1.6-1.4 times lower than the values in practically healthy children (P in all cases from < 0.05 to < 0.001), and the most significant changes were determined in children with bronchial asthma. Impaired production of IFNγ , which plays an important role in maintaining homeostasis, is characteristic of the examined patients.

It is known that TNFα is mainly produced by monocytes and macrophages and performs many important functions. During the inflammation initiation period, it activates the endothelium, increases the expression of adhesion molecules on endothelial cells and promotes the adhesion of leukocytes to the endothelium, activates leukocytes (granulocytes, monocytes, lymphocytes), induces the production of other proinflammatory cytokines that have a synergistic effect with TNFα. In our studies, the level of TNFα was 3.5 times higher in children with bronchial asthma, compared with children in the control group ($P <0.001$), in children with acute obstructive bronchitis it was 48.7±3.5 pg /ml, recurrent obstructive bronchitis - 62.7±3.2 pg /ml versus 28.4±1.5 pg /ml in the control ($P <0.001$), which reflects the increased activity of macrophages involved in maintaining the inflammatory process.

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Table 1.

Cytokine content in children in the study groups (M± m)

Indicators	Practically healthy children n=20 (I)	Acute obstructive bronchitis n =38 (II)	Recurrent obstructive bronchitis n =15 (III)	Bronchial asthma n = 33 (IV)	R	R_1	R_2
TNFα (pg /ml)	28.4±1.5	48.7±3.5	62.7±3.2	98.4±4.5	<0.01	<0.001	<0.01
IL – 4 (pg /ml)	4.6±0.6	18.9±0.31	21.3±0.34	26.7±1.4	<0.05	<0.001	<0.01
IFNγ (pg /ml)	34.3±2.7	27.4±1.5	21.4±1.7	14.3±1.9	<0.05	<0.001	<0.01
IL-8 (pg /ml)	19.2±2.4	32.5±2.8	89.55±3.87	100.98±7.67	<0.05	<0.001	<0.01

Note:

P - reliability of differences in indicators between I and II groups of patients ;

P_1 - reliability of differences in indicators between II and III groups of patients ;

P_2 - reliability of differences in indicators between groups III and IV of patients.

According to the results of the vitamin D3 content in the blood serum, in group I of patients with acute obstructive bronchitis, 18.5% (12) of patients were found to have vitamin D deficiency, 4.0.3 % (10) with vitamin D insufficiency, and 42 % (16) of cases with sufficient vitamin D content. In group II , patients with recurrent obstructive bronchitis, 26.6 % (4) of patients were found to have vitamin D deficiency, 40 % (6) with vitamin D insufficiency, and 33.3 % (5) of cases with sufficient vitamin D levels . In Group III , Of patients with BA, 45.4 % (15) were found to have vitamin D deficiency, 36.3 % (12) were found to have vitamin D insufficiency and in 18.2 % (6) of cases with sufficient vitamin D content (Table 2).

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Table 2.

Vitamin D levels in the study groups

Groups	vitamin level D ≥ 20 ng /ml		vitamin level D 11-20 ng /ml		vitamin level D ≤10 ng /ml	
	abs	%	abs	%	abs	%
I (acute obstructive bronchitis)	16	42	10	40.3	12	18.5
II (recurrent obstructive bronchitis)	5	33.3	6	40	4	26.6
III (bronchial asthma)	6	18,2	12	36.3	15	45.4
Control group	1 0	55	6	30	4	20

Average content of vitamin D (25(OH)-D) in the blood serum of the examined children is shown in Figure 1.

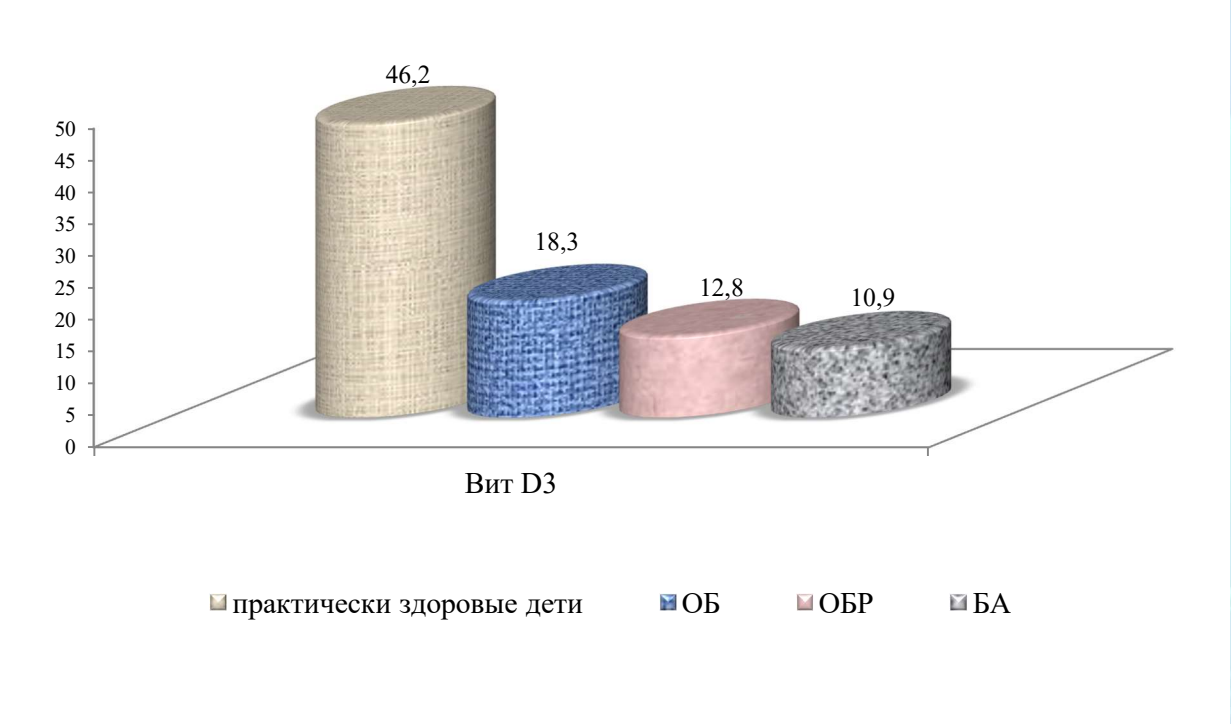


Figure 1. Average Vitamin D levels in children examined, ng / m l

As can be seen from Figure 1, the level of vitamin D $_3$ in children with bronchial asthma it was significantly reduced to 10.9±0.6 ng /ml, which is more than 4.2 times lower than the average values in healthy children (46.2±4.2 ng /ml; P<0.001) and was significantly lower compared to the values in children with acute obstructive bronchitis and recurrent obstructive bronchitis (18.3±3.2 ng /ml and 12.8±1.2 ng /ml, respectively, P<0.01).

Thus, based on the data obtained, the following **conclusions can be drawn:**

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1. The severity of the course of broncho-obstructive syndrome is associated with an aggravated premorbid background, concomitant and past diseases, which significantly aggravate the course of the underlying pathology. In broncho-obstructive syndrome, depending on the underlying disease, the level of serum cytokines changes, which is characterized by a significant increase in such cytokines as IL -4, IL -8, TNFα and a decrease in IFNγ .

D deficiency is accompanied by the development of secondary immune deficiency, which is manifested by a decrease in the phagocytic activity of cells and a decrease in interferon production. The greatest changes in immune status are observed in patients with bronchial asthma, which is characterized by an increase in IL -4, IL -8, TNFα and a decrease in IFNγ .

2. The increase in the severity of broncho-obstructive syndrome is directly proportional to the decrease in the level of vitamin D metabolites in the blood serum, which is clearly evident in children with bronchial asthma.

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