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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

THE ROLE OF VITAMIN D IN THE PATHOGENESIS AND TREATMENT OF ATOPIC BRONCHIAL ASTHMA IN CHILDREN

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GENERAL CHARACTERISTICS OF THE RESEARCH

The Relevance of the Research: In the modern era, a trend of increasing prevalence of bronchial asthma on a global scale is observed. Epidemiological research indicates that approximately 350 million individuals worldwide suffer from bronchial asthma, with this number projected to reach 400 million by 2025[1] When left untreated, this chronic disease significantly reduces the quality of life for individuals of all age groups, leading to early disability and even death. From this perspective, bronchial asthma remains a global issue within the healthcare system.

Epidemiological research data reveals that the prevalence of bronchial asthma among children varies from 1.5% to 20% in different countries. In Azerbaijan, based on epidemiological indicators, the prevalence of bronchial asthma among children is approximately 3.2%.[2] Currently, the atopic form of bronchial asthma is more common among children. The increased risk of bronchial asthma among children is associated with its wide heterogeneity in pathogenesis and the polymorphic nature of its clinical course.[3]

In recent years, there has been an increase in the number of children with severe bronchial asthma worldwide. Achieving complete control over the disease is often not possible for most children with atopic bronchial asthma. This is due to additional risk factors that can affect the effectiveness of basic therapy or the presence of

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[1] Global Initiative for Asthma. Global strategy for asthma management and prevention: Updated 2019 [Electronic resource] - 1 December 2022 – 200 p. URL: https://ginasthma.org/wp-content/uploads/2019/06/GINA2019-main-report-June-2019-wms.pdf–

[2]Фассахов, Р.С. Терапия бронхиальной астмы в режиме SMART: исследования в реальной клинической практике // - Москва: Медицинский совет, - 2016. №15, - с. 23-26.

[3]Эюбова, А.А. Клинико-эпидемиологические особенности бронхиальной астмы у детей в различных регионах Азербайджана / А.А. Эюбова, Г.Г. Кабулов // Аллергология и иммунология, - Москва: - 2007. т. 8, №2, - с.191-192.

comorbidities. Vitamin D deficiency is one of these factors.[4] The molecular mechanisms of vitamin D's impact on the immune system, apoptosis, cardiovascular system, reproductive system, and other systems are considered among the achievements of recent years.[5] Contemporary literature links vitamin D deficiency among children to exacerbating various diseases. Up to 50% of the world's population suffers from some degree of vitamin D deficiency.

The study of vitamin D deficiency in children has become a pressing issue. While traditionally regarded as a regulator of calcium and phosphorus metabolism in the body, recent years have seen reports of its involvement in various biological processes, including immune system regulation. Notably, vitamin D's "non-classical" effects on various organs and systems are widely discussed in the literature. Special attention is given to the study of vitamin D and its deficiency in various diseases, including bronchial asthma[6]

Researchers from the University of Pennsylvania in the USA associate vitamin D with the pathogenesis of bronchial asthma, emphasizing its role in the differentiation of Th1 and Th2 lymphocytes, as well as its role in correcting the imbalance between them.[7] The presence of vitamin D receptors (VDR) identified in lymphocytes is believed to influence the proliferation of Th2 cells and stimulate the synthesis of interleukins (IL-13, IL-17, IL-10, IL-4) derived from them. Additionally, vitamin D weakens the functional activity of B lymphocytes, enhancing the activity of Th1 lymphocytes and increasing the synthesis of IL-2.

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[4] L.İ. Uşaqlarda bronxial astma. metodik vəsait / L.I. Allahverdiyeva, - 2010.

[5] Leiter, K. Vitamin D receptor polymorphisms are associated with severity of wheezing illnesses and asthma exacerbations in children / K. Leiter, K. Franks, M. L. Borland // J. Steroid BiochemMol Biol., – 2020. no 201, – p. 105–692.

[6] Захарова, И.Н. Известные и неизвестные эффекты витамина Д / И.Н. Захарова, С.В. Яблочкова, Ю.А. Дмитриева // Вопросы современной педиатрии, - 2013, 12 (2), - с. 20-25.

[7] Ашерова, И.К. Нарушение метаболизма витамина D у детей и подростков с муковисцидозом / И.К. Ашерова, О.Б. Ершова, Е.А. Охапкина [и др.] // Педиатрия. Журнал им. Г. Н. Сперанского, – 2016. 91 (2), – с. 34–39.

Vitamin D blocks the differentiation pathway of T-helper cells into the Th-17 subpopulation, inhibiting neutrophil inflammation in the bronchial mucosa, thereby reducing the severity of severe bronchial asthma clinically. The multifaceted role of vitamin D, especially its involvement in regulating the immune response during bronchial asthma, establishes its importance as a significant factor affecting the severity of the disease.

Recent immunological research has highlighted the prognostic significance of cytokine levels in the blood during bronchial asthma. Assessing the levels of anti-inflammatory and pro-inflammatory cytokines in order to evaluate the severity and prognosis of the disease is essential for determining the effectiveness of treatment. Despite numerous scientific studies investigating the measurement of cytokine levels in the blood during bronchial asthma, specific details regarding their mechanism of action remain unclear. For example, in the literature, the imbalance in the levels of IL-13, IL-17, and IL-2 during asthma exacerbation and severe courses is explained as contributing to the pathogenesis of asthma and the selection of effective treatment modalities.[8]

Thus, during vitamin D deficiency in bronchial asthma, the existing cytokine imbalance carries a compensatory nature, exacerbating the development of allergic inflammatory processes and leading to a more acute and chronic course.

The modification of treatment for children with bronchial asthma represents one of the key challenges in modern pediatrics and allergology. It has been established that the diversity of treatment principles for bronchial asthma is due to the complexity of the disease's pathogenesis. In this context, it is emphasized that in order to achieve continuous remission, it is necessary to clarify certain factors contributing to the disease. Increasingly, researchers suggest that, in addition to basic therapy for bronchial asthma, the use of vitamin D may be a promising approach for certain conditions.

[8] Chambers, E.S. The impact of vitamin D on regulatory T cells / E.S. Chambers, C.M. Hawrylowicz // Curr Allergy Asthma Rep., - 2011. v.11, - p.29-36.

The relevance of the problem of vitamin D deficiency and its co-occurrence with atopic form bronchial asthma primarily stems from the wide prevalence of these two pathological conditions. The data obtained not only contribute to the study of the role of vitamin D as a perspective factor in the pathogenesis of bronchopulmonary diseases but also offer a basis for optimizing the use of vitamin D in the modification of the treatment of such diseases. [9]

Object and subject of the Research:

85 patients diagnosed with atopic bronchial asthma were the object of the study, the clinical and immunological characteristics of vitamin D in the treatment and pathogenesis of the disease in these patients were studied as the subject of the study.

The Aim of the Research: to research the clinical and immunological characteristics of vitamin D in children with atopic form bronchial asthma and to evaluate its therapeutic effectiveness.

The Tasks of the Research:

1. To determine and clinically evaluate vitamin D levels in the blood of children with atopic form bronchial asthma depending on the severity of the condition.
2. To determine interleukin IL-2, IL-13, and IL-17 cytokine levels in the blood, which affect the severity of bronchial asthma.
3. To examine the indicators of cellular (CD cells) and humoral (A, M, G, E) immunity in children with bronchial asthma.
4. To evaluate the clinical and immunological effectiveness of vitamin D preparations containing cholecalciferol in children with bronchial asthma.
5. To study the correlation between immune indicators and vitamin D levels in children with bronchial asthma.

Research methods. Clinical, laboratory, instrumental, and statistical methods are the research methods.

[9] Mathyssen, C. Vitamin D supplementation in respiratory diseases: evidence from randomized controlled trials / C. Mathyssen, G. Gayan-Ramirez, R. Bouillon // JanssensPol Arch Intern Med., – 2017. 127 (11), – p. 775–784.

The Main Provisions of the defense are as follows:

- Vitamin D deficiency in children with atopic form bronchial asthma is considered one of the risk factors for disease exacerbation.

- Immunological changes in children with atopic form bronchial asthma, occurring against the backdrop of vitamin D deficiency, manifest as alterations in cellular and humoral immune indicators.

- In children with atopic form bronchial asthma and vitamin D deficiency, changes in the cytokine profile require correction, with significant fluctuations in the levels of both pro-inflammatory and anti-inflammatory cytokines.

- Correction of vitamin D deficiency with vitamin D preparations containing cholecalciferol in children with atopic form bronchial asthma enhances the clinical and laboratory effectiveness of basic therapy.

The Scientific Novelty of the Research:

- The relationship between vitamin D and immunological indicators in the diagnosis of children with atopic form bronchial asthma, as well as its effects on the clinical course, severity, and stages of the disease, has been elucidated for the first time.

- The research has revealed the presence of cytokine imbalances, particularly interleukin IL-2, IL-17, and IL-13, contributing to the persistence of the inflammatory process during bronchial asthma.

- The study has identified the specific characteristics of vitamin D and its role in compensatory imbalances among certain cytokine cascades in children with atopic form bronchial asthma.

- The immunotherapeutic effectiveness of vitamin D preparations containing cholecalciferol in children with atopic form bronchial asthma has been studied for the first time.

The Theoretical and Practical Importance of the Research:

The research of immunological indicators and their correlation with vitamin D in the early diagnosis of atopic form bronchial asthma adds diagnostic criteria, enabling individualized treatment approaches and contributing to the adequate management of the disease.

This research study was planned and carried out with the aim of increasing the effectiveness of treatment with vitamin D deficiency in blood serum of patients with atopic bronchial asthma.

The treatment included basic anti-inflammatory treatment and vitamin D depending on the level of vitamin D deficiency. According to the results of the research, increasing the clinical effectiveness in children with atopic bronchial asthma by adding vitamin D with basic treatment allows for an individualized approach to treatment.

The Approval of Research and Application in practice:

The main findings of the dissertation were presented at the following conferences:

"IX World Asthma Allergy & COPD Forum. X CIS Congress on Allergology and Immunology" (poster presentation in Saint Petersburg, Russia) in July 2016. "Azerbaijan Republic Society of Allergology, Immunology, and Immunorehabilitation" conference on November 23, 2018. International conference on "Modern Aspects of Allergology and Clinical Immunology" on November 23, 2019. "XIII Republic Scientific Conference of Doctoral Students and Young Researchers Dedicated to the 650th Anniversary of Imadaddin Nasimi" on December 3, 2019.

The results of the research are applied in the practical work of the AMU's Therapeutic Clinic, Children's Clinical Hospital No. 6, and the Department of “Pediatric Diseases II”, contributing to the diagnosis and treatment of pediatric patients.

The name of the institution where the Research study was performed. The research was carried out at the Therapeutic Clinic of Azerbaijan Medical University and Children's Clinical Hospital No. 6.

Published Scientific Works:

Based on the research results, 17 scientific works have been published, including 7 articles and 10 abstracts.

The Volume and Structure of the Dissertation:

The dissertation consists of introduction (10412 marks), 5 chapters, conclusions (3164 marks), practical recommendations (520) and literature list. Chapter I - review of literature (47669 marks), Chapter II - materials and methods of research (17743

marks), Chapter III - results obtained from research (20001 marks), Chapter IV - discussion of research results (18217 marks), Chapter V - conclusion of research (54072 marks) are dedicated. The total volume of the dissertation with marks (excluding the bibliography, pictures and tables) was 166277 marks. The dissertation is compiled on a computer in 144 pages, illustrated with 21 tables and 30 pictures. The literature list included 226 bibliographic sources (2 of them in Azerbaijani, 1 in Turkish, 41 in Russian, 182 in English).

THE MATERIALS AND METHODS OF THE RESEARCH

In accordance with the set objectives and tasks, the research was conducted at the 6th Children's Clinical Hospital in Baku and the Teaching Therapeutic Clinic of Azerbaijan Medical University. For the research, 4 infants and 81 children with moderate to severe persistent atopic asthma were enrolled in the study group. The medical histories of the enrolled patients were investigated, and a total of 85 children (60 (70.6%) boys, 25 (29.4%) girls) between the ages of 4 and 17, with recurrent bronchial asthma attacks, were included. Additionally, 20 healthy children (12 (60.0%) boys, and 8 (40.0%) girls) were included in the control group.

The diagnosis of bronchial asthma was established based on comprehensive data collection, including general and allergological history, and clinical, laboratory, and instrumental examinations. The core of the examination program comprised the analysis of anamnestic data, clinical manifestations of the disease, and the results of laboratory and instrumental examination methods. The research included the determination of cytokine levels (IL2, IL13, IL17), membrane markers of immune-competent cells (CD3, CD4, CD8, CD19, CD16/56, CD8), the level of vitamin D (25(OH)D3), X-ray of the thoracic organs, and external respiratory function testing.

The inclusion criteria for the children in the research were as follows:

- Persistent mild and moderate-to-severe atopic asthma.
- Age between 4 and 17 years.
- Disease duration of at least 2 years.

- Confirmation of bronchial asthma diagnosis based on functional tests.

- Elevated total IgE levels in the blood and confirmation of specific IgE based on examination results.

The exclusion criteria for the children in the research were as follows:

- Severe persistent atopic bronchial asthma.

- Vitamin D or multivitamin complex intake within the last 6 months prior to examination.

- Presence of chronic somatic diseases.

- Pathological conditions in the respiratory system.

- Occurrence of respiratory tract infections in the 12 months before the start of the research.

Children in the control group were selected based on the following criteria:

- Age between 6 and 17 years.

- Absence of bronchial asthma diagnosis.

- Absence of allergic diseases in the medical history.

- No pathological conditions in the respiratory system.

- IgE levels <100 IU/ml.

The severity of bronchial asthma was evaluated according to the Global Strategy for Asthma Management and Prevention (GINA 2017).

Criteria for diagnosing bronchial asthma included:

- Patient complaints and anamnestic information (cough, shortness of breath, wheezing, recurrent attacks of suffocation, expiratory wheezing during breathing, symptom occurrence or exacerbation after contact with triggers, positive allergic history).

- Clinical-functional data (expiratory wheezing during auscultation, reversible bronchial obstruction).

- Information from the allergological examination.

The confirmation of the atopic form of bronchial asthma was based on an increase in total IgE levels in the blood and the results of specific IgE examinations.

The form, severity level, and duration of the disease were determined based on the classification criteria of bronchial asthma

according to GINA (2017). Patients were categorized into mild (4 individuals) and moderate-to-severe (81 individuals) forms based on the requirements for bronchodilators, the frequency of nighttime symptoms, and lung function indicators. Clinical, functional, and laboratory examinations of patients with bronchial asthma were conducted according to generally accepted methods.

The criteria for mild asthma were determined based on the following signs:

- Symptoms occurring more than once a week but less than once a day
- Nighttime symptoms occurring 1-2 times per month
- Exacerbations leading to decreased physical activity and disrupted sleep
- FEV1 or PEF ≥ 80%

Four children with persistent mild bronchial asthma presented with weekly exacerbations and monthly nighttime symptoms, normal FEV1, and PEF ≥ 80%. Good control of asthma was achieved with treatment in the 1st and 2nd steps.

The criteria for moderate-to-severe asthma were determined based on the following signs:

- Daily symptoms;
- Exacerbations limiting physical activity and causing sleep disturbances
- Nighttime symptoms occurring more than once a week
- Daily use of short-acting inhaled β2-agonists
- FEV1 or PEF representing 60-80% of the predicted value

In 81 children with persistent moderate-to-severe bronchial asthma, expiratory wheezing, involvement of accessory respiratory muscles in respiration, various wheezing sounds heard during lung auscultation, exacerbations occurring 1-2 times per week and 2 times per month at night, normal values of NZS and OFV1 in the range of 60-80%, and less than 80%, respectively, were observed. Good control of moderate-to-severe persistent bronchial asthma was achieved in the 3rd step of treatment.

A comprehensive analysis of medical histories was conducted for all children. Life, disease, allergy, and family histories were meti-

culously documented. The duration of the disease, triggering factors, previous treatment, and its effectiveness were noted. The onset of the disease, considered as the year when the diagnosis was made by the physician-allergist, ranged from 2 to 5 years (3.7 ± 0.9 years).

For laboratory examination, venous blood samples were collected from the elbow vein in the morning on an empty stomach for all measured parameters. The blood was collected into vacuum tubes with red caps, and EDTA was used as an anticoagulant activator and gel.

Immunological tests were performed at the "Immunology" laboratory of Azerbaijan Medical University using an automatic flow cytometry system on the "Coulter Epix XL" device (Beckton Dickinson, USA). The research was carried out by following the standard procedure for mononuclear cell fractions. The surface phenotypes of cells were determined using monoclonal antibodies. Fluorescein isothiocyanate (FITC) was used in the fluorochrome labeling region. The cell staining and fixation procedure was carried out according to the manufacturer's instructions and standard methods. Using standard beads (Beckton Dickinson, USA), the absolute and relative quantities of T- (CD3+) and B- (CD19+) lymphocyte populations, as well as T-helper/inducer (CD4+), T-suppressor/cytotoxic (CD8+) subpopulations, and T-killer (CD16/56+) cell indicators were determined. CellQuest software (Becton Dickinson, USA) was used for data analysis, utilizing forward scatter (FSC) and side scatter (SSC) light scattering parameters.

The concentrations of class A, M, and G immunoglobulins in the blood serum were determined using the enzyme-linked immunosorbent assay (ELISA) method with “ИФА-БЕСТ” test systems (the production of the Closed Joint-Stock Company “Вектор-Бест”, Russia) according to the manufacturer's instructions. The determination of total immunoglobulin E (IgE) levels was performed using the “İgE-ИФА-БЕСТ-стрип” kit (the production of the Closed Joint-Stock Company “Вектор-Бест”, Russia) from standard commercial kits. The analysis was conducted using the sandwich variant of enzyme-linked immunosorbent assay (ELISA).

The concentration of 25 (OH) D3 in the blood serum was determined using the immunoassay method on the analyzer of Roche Diagnostics (Germany). The level of vitamin D was selected based on the following indicators: 30-100 ng/ml - normal, 20-29 ng/ml - mild deficiency, 10-19 ng/ml - moderate deficiency, less than 10 ng/ml - severe deficiency (insufficiency). Levels above 100 ng/ml were considered vitamin D hypersufficiency. For pharmacological correction of vitamin D deficiency, 40 patients received daily doses of 2-4 drops (1500-3000 IU/day) of Tridrop preparation containing vitamin D (total treatment dose: 45,000-90,000 IU). The vitamin D level in the blood serum was determined before the treatment course and 3 months after treatment.

All collected data were analyzed statistically, taking into account modern recommendations, using variation, discriminant, dispersion, and correlation methods. All calculations were performed in Microsoft Excel 2016 spreadsheets and processed using SPSS-22 statistical software. The results were summarized in tables and diagrams.

THE RESULTS OF THE RESEARCH AND THEIR DISCUSSION

Under our observation, there were 85 children with persistent atopic mild and moderate-severity bronchial asthma. The duration of the disease ranged from 2 to 5 years, with an average of 3.7±0.9 years. Among children with mild asthma, 50.0% (n=2) were aged 4-7 years, and 50.0% (n=2) were aged 7-12 years. In the group of children with moderate-severity bronchial asthma, 24.7% (n=21) were aged 4-7 years, 49.4% (n=42) were aged 7-12 years, and 21.2% (n=18) were aged 12-17 years. The mean age of children with bronchial asthma was 10.2±0.4 years, while in the control group, it was 10.1±0.8 years.

During the analysis of the medical history, special attention was paid to family allergic history. Out of the observed children, 85.8% (n=75) had a family history of allergic diseases. Among them, 30.6% (n=26) had both parents or close relatives with allergic reac-

tions. In the history of 32.9% (n=28) of the patients, aggravation by paternal lineage and in 24.7% (n=21) by maternal lineage was noted.

Based on the anamnestic data and examination results, almost all children showed polyvalent sensitization. Sensitization to household allergens (including 11 children (12.9%) sensitized to dust allergens and 6 children (7.1%) sensitized to epidermal allergens) was observed in 20.0% (n=17) of the children. Food allergies were observed in 64.7% (n=55) of the examined children.

In 68 (92%) of the examined children, there was an increase in total immunoglobulin E (IgE) in the peripheral blood. The mean level of total IgE was 597.4±103.8 IU/ml.

Children with bronchial asthma also had a high prevalence of comorbid allergic diseases. During the analysis of allergic pathologies, 45.9% (n=39) of children were found to have comorbid diseases of atopic origin. Allergic rhinitis was the most common comorbid disease among children with bronchial asthma, observed in 37.65% (n=32) of cases. Atopic dermatitis was observed in 8.25% (n=7) of children with bronchial asthma. Comorbid allergic diseases were not observed in 54.1% (n=46) of the patients. Identifying comorbid pathologies in children with bronchial asthma helps determine the correct approach to the complex treatment of the disease, develop preventive measures aimed at reducing the exacerbation of concomitant p;2athologies, and thereby increase control over bronchial asthma.

The clinical picture of the disease was typical for the studied pathology. Generally, patients' repeated episodes of difficult breathing, especially in children and their parents, were concerning. Expiratory-type dyspnea, a feeling of heaviness in the chest, and cough (ranging from distressing dry to productive sputum cough) were common symptoms. This symptomatology intensified in the evening and early morning hours and, along with fluctuations in the number of attacks during the day, often carried a variable character. The examined children were admitted to the hospital with complaints of cough, rapid fatigue, and physical inactivity associated with shortness of breath. Patients reported difficulties in falling asleep and waking up at night due to coughing, which led to nighttime awakenings.

Cough accompanied by shortness of breath and a small amount of sputum characterized the first day of the disease.

During clinical examination, allergic signs were observed: dry skin (36.5% - 31 children), nasal congestion (78.8% - 67 children), periorbital shadows (23.5% - 20 children), and persistent conjunctivitis (65.9% - 56 children). Nasal obstruction ranged from mild (32.9% - 28 children) to severe (24.7% - 21 children). Children also complained of itching and sneezing (75.3% - 64 children). During the admission period, the chest shape of the chest organs changed from a normal cylindrical shape (79.4%) to an emphysematous barrel shape (20.6%). Expiratory dyspnea with the involvement of auxiliary muscles was observed in all children. Percussion revealed box-like pulmonary resonance in the majority of patients (83.5% - 71 children). During auscultation of the lungs, dry wheezing was heard in the harsh breath sounds, and all children had prolonged expiration, with various-caliber wet wheezing heard in 74.1% (n=63) of children. An increase in respiratory rate of more than 30% was observed in 45.9% (n=39) of children, more than 30-50% in 41.2% (n=35) of children, and more than 50% in 11.8% (n=10) of children. During an asthma attack, tachycardia was observed in 39 children (45.9%), which is a non-specific sign of hypoxia. No significant changes in the cardiovascular system were noted outside of the attacks. Oxygen saturation (SpO2) in the blood was ≥ 95% in 35 children (41.2%), and 90%-94% in 13 children (15.3%) during the examination.

Chest X-rays of the thoracic organs revealed increased lung transparency, strengthening of the lung pattern in the medial areas, bronchial root enlargement and structural changes, widening of the intercostal spaces, and a horizontal arrangement of the ribs.

In children with bronchial asthma, an absolute increase in the number of eosinophils and monocytes in peripheral blood and an elevated erythrocyte sedimentation rate (ESR) were observed.

Eosinophilia in the blood plays an important role in determining the phenotype of bronchial asthma and is considered a significant marker of atopy. Eosinophilia was observed in 80 (94.1%) of the children with bronchial asthma, while in the control group, eosinop--hils were not detected in peripheral blood. In children without comp-

laints of allergic diseases in the control group, the level of eosinophilia ranged from 0.07 to 0.22 x 10^9/L. In the patient group, the variation in this indicator ranged from 0 to 2.14 x 10^9/L. The mean value of eosinophils in children with bronchial asthma was 0.84 x 10^9/L, while in the control group, it was 0.13 x 10^9/L. When comparing both groups, significant differences were noted ($p<0.001$).

In addition to determining specific IgE levels against the main classes of allergens, the levels of total IgE were also assessed in 74 children with bronchial asthma and 20 children from the control group. In the group of children with bronchial asthma, total IgE levels ranged from 21.0 to 2830 IU/ml. This indicator differed significantly from the control group ($p=0.002$), where total IgE levels ranged from 1.0 to 94.0 IU/ml, with an average value of 33.0±5.5 IU/ml.

A positive correlation was found between the level of total IgE in peripheral blood and the quantity of eosinophils ($p=0.935$). Thus, when comparing the patient group to the control group based on the presence of eosinophilia and the level of total IgE, statistically significant differences were obtained ($p<0.001$).

Analysis of vitamin D values in the groups showed that in the control group, a normal level of vitamin D was found in 19 children (95.0%), while mild deficiency was observed in 1 child (5.0%). In the group of children with bronchial asthma, severe deficiency of vitamin D was observed in 21 children (24.7%), moderate-to-severe (severe) deficiency in 34 children (40.0%), and mild deficiency in 23 children (27.1%). Seven children (8.2%) with atopic forms of bronchial asthma had at the lower limit of normal vitamin D level. (Figure 1)

The average vitamin D level in the control group was 45.3±2.2 ng/ml, with a minimum and maximum value of 28.0 and 61.0 ng/ml, respectively.

In children with bronchial asthma, the average value of 25(OH) D3 was 17.4±0.9 ng/ml, with corresponding minimum and maximum values of 5.9 and 38.6 ng/ml. Notably, the minimum level of D vitamin in bronchial asthmatic children was 5.9 ng/ml, indicating severe deficiency, which requires pharmacological correction.

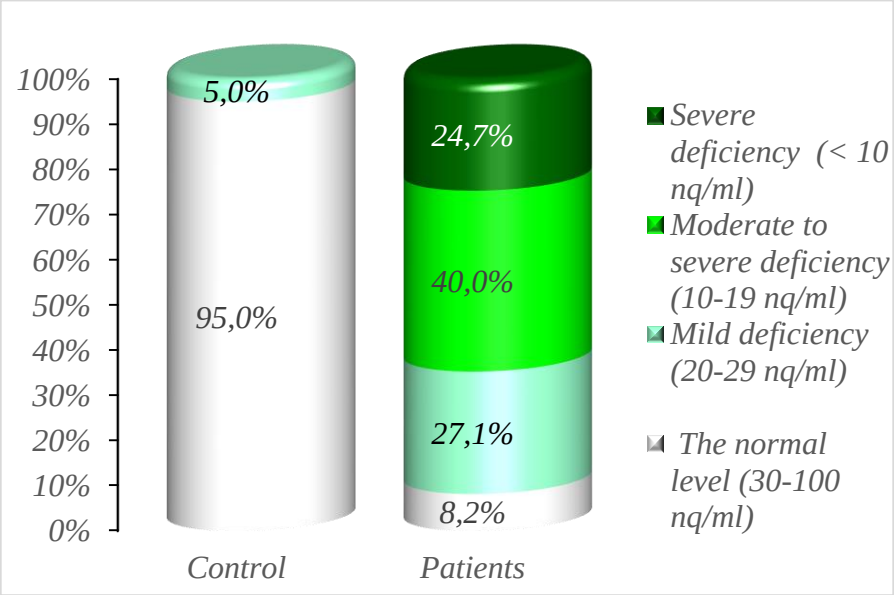

Figure 1. Levels of vitamin D in children with atopic form bronchial asthma

During the investigation of immune cell parameters, peripheral blood levels of differentiation markers CD3+, CD4+, CD8+, CD16+/CD56+, and CD19+ were determined in 34 children. Comparative characteristics of membrane markers (CD markers) in these children were studied. The results revealed that in atopic bronchial asthma, the levels of T-helper cells (CD4+) were reduced to 37.6 ± 0.6%, which was significantly lower than in the control group (40.0 ± 1.2%) ($p < 0.05$). Moreover, the levels of T-suppressor cells (CD8+) were also reduced in patients (29.5 ± 0.6%) compared to the control group (32 ± 0.8%) ($p < 0.05$). The CD4+/CD8+ T-lymphocyte ratio in patients was within the normal range (1.18 ± 0.05%), similar to that in the control group (1.23 ± 0.02, $p > 0.05$).

The study also explored natural killer (NK) cells, a population of immune cells distinct from T and B lymphocytes, which play a unique role in the immune system. NK cells are primarily involved in defending the body against foreign and altered cells. CD16+ surface

receptors were used as markers for NK cells, reflecting the overall count of NK cells. The count of activated natural killer cells was determined based on the expression of CD56+. The relative quantity of NK cells (CD16+/CD56+) in peripheral blood of bronchial asthmatic children did not significantly differ from that of the control group. The value of this indicator in patients was 12.7 ± 0.9%, while it was 12.8 ± 0.3% in control subjects ($p > 0.05$).

Comparison of B-lymphocyte levels (CD19+) in the blood showed no significant difference between bronchial asthma patients (19 ± 1.0%) and healthy individuals (16.4 ± 0.7%) ($p > 0.05$).

The comparison of humoral immunity indicators has shown that in all patients with bronchial asthma included in the study, the level of IgA in the blood serum was 1.24±0.06 g/l, which was significantly lower compared to the control group (1.74±0.11 g/l, $p<0.05$). When evaluating the level of IgM, the obtained indicator was 1.21±0.08 g/l, which was also significantly lower compared to the control group (1.78±0.14 g/l, $p<0.05$). A comparison of the IgG level revealed that in patients with bronchial asthma, this indicator was 5.9±0.1 g/l, significantly lower ($p<0.05$) than the control group (10.6±0.5 g/l). Since IgA's primary function is to defend against microbes and viruses, its decreased level can lead to the entry of viruses into cells and the fixation of microorganisms in the bronchial tree's mucus. The reduced levels of key immunoglobulins, IgG, and IgM, which are considered essential for the full formation and effectiveness of the immune response, are characterized as compensatory due to the decreased activity of the immune system compared to the control group.

During the course of the research, the characteristics of the cytokine profile (IL2; IL13; IL17) of children with atopic form bronchial asthma and vitamin D deficiency were analyzed. Significant differences were observed when comparing the indicators of children with bronchial asthma in the analysis of cytokine levels in their blood serum to those in the control group. The comparison of IL-2 levels has shown that in bronchial asthma patients with vitamin D deficiency, its level has significantly decreased compared to healthy children ($p<0.001$). Specifically, the mean concentration of this cytokine in

the blood serum of the control group children was 10.8±0.68 pg/ml, whereas in the patients, this indicator was equal to 2.5±0.3 pg/ml.

The level of IL-13 has been significantly higher in children with atopic form bronchial asthma compared to the control group ($p<0.01$). In the blood serum of the patients, the mean concentration of this cytokine was 13.8±0.8 pg/ml, whereas in the control group, this indicator was significantly lower - 5.3±0.7 pg/ml.

During the investigation of IL-17 concentration, it has been observed that its level was also relatively high in patients with bronchial asthma compared to healthy individuals. At that time, the concentration of this cytokine in the blood serum of patients was 9.4±0.8 pg/ml, while in the control group, this indicator was at a level of 5.0±0.4 pg/ml ($p<0.05$).

In conclusion, our findings suggest that in children with atopic form bronchial asthma and vitamin D deficiency, increased levels of pro-inflammatory cytokines may contribute to the chronicity and exacerbation of inflammatory processes in the bronchial-lung system, indicating a significant pathogenic mechanism.

In the investigated cytokines, both pro-inflammatory (IL-13, IL-17) and anti-inflammatory (IL-2) interleukins were present, making it essential to assess the complex balance of cytokines in the body. To do this, we calculated the integral cytokine index, which is the ratio of the average mathematical values of pro-inflammatory and anti-inflammatory cytokines. To calculate the index, we determined the values of the interleukin indices (ILI) by dividing the concentrations of interleukins in patients by their average control values:

ILI = IL_patient / IL_control

The integral cytokine index (ICI) was then calculated using the following formula:

ICI = I1 + (IL2 - 1)

Where:

IL1 is the average mathematical value of pro-inflammatory interleukins.

IL2 is the average mathematical value of anti-inflammatory interleukins.

ICI is the integral cytokine index.

The balance of cytokines was determined based on the value of ICI: when ICI ≤ 1, it indicates a normal cytokine balance, and when ICI > 1, it is considered to be disturbed[10]

It was found that in children with atopic form bronchial asthma and vitamin D deficiency, there was an imbalance in cytokines, and a deviation from normal balance was observed. The value of ICI was 1.58, which is higher than the value found in healthy children (ICI=1, $p < 0.05$). Through the conducted experiments, a graphical representation of the immunological status model in the coordinate system was established for children with atopic form bronchial asthma. In this model, each vector corresponds to an individual parameter of the immune system (Figure 2).

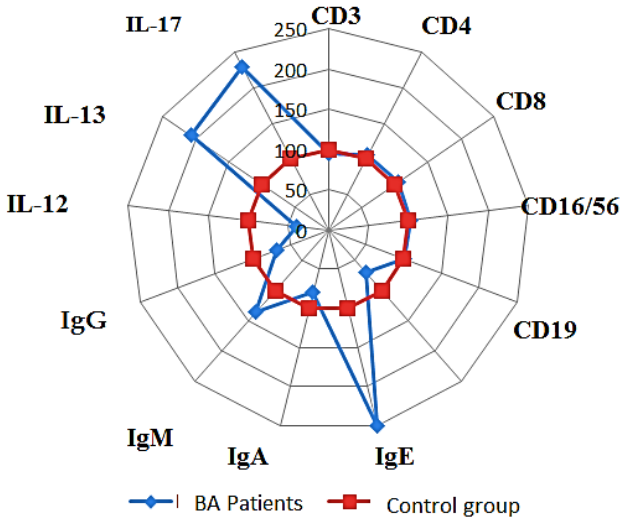

Figure 2. Graphic representation of patterns of immune status in children with atopic form bronchial asthma

A correlation analysis has revealed a significant relationship between vitamin D levels and immune system parameters in children with atopic form bronchial asthma. It has been observed that there is a relatively strong mutual relationship between vitamin D levels and

[10] Т.В.Юдина; методические рекомендации, 2012.

the immune system in the examined children. In children with atopic form bronchial asthma, a positive correlation has been found between vitamin D levels and IgA (ρ = 0,353, p = 0,002), IgM (ρ = 0.131, p = 0,265), and IgG (ρ = 0,597, p = 0,000) indicators. This means that a decrease in vitamin D concentration in the blood is statistically associated with a decrease in the levels of these immunoglobulins. A negative correlation has been found between vitamin D and total IgE levels, indicating that a decrease in vitamin D concentration in the blood is statistically associated with an increase in total IgE levels (ρ = - 0,404, p = 0,000). This reverse correlation between vitamin D and IgE suggests a relationship between vitamin D deficiency and atopic form bronchial asthma. The analysis of the correlation between the level of vitamin D in the blood and the indicators of cellular immunity is presented in Table 1.

Table 1.

Correlation between the levels of T- and B-lymphocyte subpopulations in the blood of examined children and the concentration of vitamin D.

		VitD	CD3%	CD4%	CD8%	CD19%	CD16/56%	CD4/CD8%
VitD	ρ	1,000	0,032	0,325**	0,127	-0,182	0,159	0,118
	p		0,802	0,008	0,312	0,146	0,207	0,348
CD3%	ρ	0,032	1,000	0,168	0,362**	-0,123	0,021	0,057
	p	0,802		0,181	0,003	0,329	0,867	0,650
CD4%	ρ	0,325**	0,168	1,000	0,154	-0,223	-0,082	0,213
	p	0,008	0,181		0,221	0,074	0,516	0,088
CD8%	ρ	0,127	0,362**	0,154	1,000	-0,249*	0,070	-0,048
	p	0,312	0,003	0,221		0,046	0,579	0,706
CD19%	ρ	-0,182	-0,123	-0,223	-0,249*	1,000	-0,005	0,017
	p	0,146	0,329	0,074	0,046		0,968	0,892
CD16/56%	ρ	0,159	0,021	-0,082	0,070	-0,005	1,000	0,111
	p	0,207	0,867	0,516	0,579	0,968		0,379
CD4/CD8%	ρ	0,118	0,057	0,213	-0,048	0,017	0,111	1,000
	P	0,348	0,650	0,088	0,706	0,892	0,379	

We have also explored the correlation between vitamin D deficiency and the levels of inflammatory (IL-2) and anti-inflammatory (IL-13, IL-17) cytokines in the examined children with atopic bronchial asthma. During the correlation analysis of the children's

indicators, a direct positive correlation between vitamin D deficiency and the level of IL-2 (0.363, p = 0.003) has been observed. However, there has been a significant inverse correlation between vitamin D levels and the levels of IL-13 (ρ = - 0.247, p = 0.049) and IL-17 (ρ = -0.340, p = 0.006) cytokines. Vitamin D, through its receptors identified in lymphocytes (VDR), influences Th2 cell proliferation, thereby stimulating the production of interleukins (IL-13, IL-17) derived from them.

Thus, based on the observed correlations, it can be inferred that during vitamin D hypervitaminosis, the activity of Th1 lymphocytes increases, leading to an increased synthesis of IL-2, while the activity of Th2 lymphocytes decreases, resulting in a reduction in the levels of IL-13 and IL-17. From this perspective, the increase in IL-13 and IL-17 levels during exacerbation of atopic bronchial asthma, along with a decrease in IL-2 levels, explains the selective choice of the pathogenetic and effective treatment method for asthma.

In the subsequent stages of the research, basic therapy for allergic inflammation was combined with vitamin D supplementation to correct the vitamin D deficiency. The treatment of the included patients was conducted as a stepwise asthma management: 1st step (without basic therapy), 2nd step (low doses of ICS), 3rd step (for children up to 5 years - ICS at half dose, for children over 5 years - ICS at medium/high doses).

To correct hypovitaminosis, 40 children received the Tridrop preparation, which contains vitamin D. Depending on the degree of vitamin D deficiency, they took 2-4 drops per day (1500-3000 IU daily) for one month (45000-90000 IU course treatment dose).

Before treatment, the daytime symptom frequency (asthma attacks) for the first and second groups of patients was respectively 3,31±0,30 and 3,25±0,29 (Table 2).

As seen in Table 2, the comparison groups were also evaluated in terms of the frequency of nighttime attacks before treatment. Accordingly, in the first and second groups, the weekly frequency of nighttime attacks was 1,20±0,12 and 1,33±0,12 respectively.

Table 2.

Dynamic of clinical symptoms in the treatment groups of children with atopic bronchial asthma

Parameter	Stage of examination	Unit of measurement	1 group (basic therapy)	2 groups (basic therapy + Tridrop)	P
Daytime symptoms	Before treatment	Number during the week	3,31±0,30	3,25±0,29	>0,05
	1-6 weeks		2,67±0,29	2,23±0,27	>0,05
	6-12 weeks		2,02±0,22*	1,68±0,25*	<0,05
Night symptoms	Before treatment	Number during the week	1,20±0,12	1,33±0,12	>0,05
	1-6 weeks		0,89±0,09	0,53±0,09	>0,05
	6-12 weeks		0,56±0,07	0,33±0,08	<0,05

*Note: p - statistical significance of intergroup differences; * - statistically significant differences compared to the beginning of treatment*

Significant reductions in daytime symptoms were observed in each observation group over the course of 12 weeks under basic therapy ($p<0.05$). The dynamics of these changes between the groups differed. Specifically, by the 6th week of the study, in the second group of patients receiving the Tridrop preparation under basic therapy, the frequency of daytime and nighttime symptoms had significantly decreased compared to the first group (Figure 3).

Therefore, in the second group of patients, when correcting vitamin D deficiency with the prescribed dose of the Tridrop preparation in addition to basic therapy, it was recommended based on the significant reduction in the frequency of daytime attacks by 41.0% and nighttime attacks by up to 63.4% (in the first group, it was 28.4% and 39.3%, respectively). The decrease in the frequency of daytime and nighttime symptoms in both observation groups increased the number of symptom-free days.

In the next stage of the study, the 25(OH) D3 level in peripheral blood was examined in both groups after 12 weeks of treatment. Initially and after 12 weeks of treatment, there was no significant difference in the 25(OH) D3 levels between the two groups.

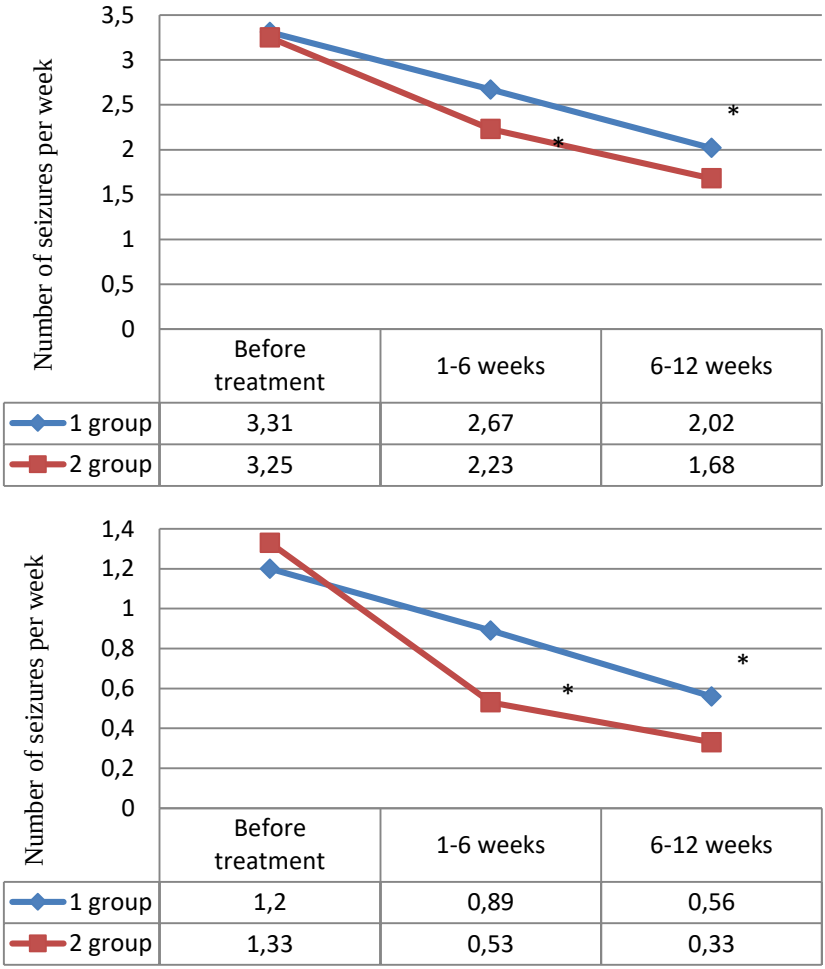

Figure 3. Dynamics of daytime and nighttime symptoms in children with atopic bronchial asthma

In the first group of children with bronchial asthma, under basic therapy, there was a partial increase in the 25(OH) D3 level, with an average increase from 17.1±1.1 ng/ml (before treatment) to 17.2±1.2 ng/ml after 12 weeks of therapy, which was statistically significant compared to the control group ($p<0.001$).

In the children included in the second group, the 25(OH) D3 level in peripheral blood before treatment was 17.8±1.4 ng/ml, which corresponded to its deficiency based on accepted classification ($p<0.001$ compared to the control group). After 12 weeks of pharmacocorrection with the Tridrop preparation, a significant increase of up to 45 % (26.5±1.3 ng/ml) on average was observed in the 25(OH) D3 level in peripheral blood ($p<0.001$ compared to the control group). It should be noted that in children with episodes of exacerbation during the treatment period, the increase in vitamin D was less pronounced.

Furthermore, variability in the dynamics of the level of eosinophils in peripheral blood during the treatment dynamics was observed, which corresponded to changes in the overall IgE levels.

The research results indicated that in the first group of patients, the total number of T-helper (CD4+) (before treatment 38.4 ± 0,9%, after treatment 40± 1.3%) and T-suppressor (CD8+) (before treatment 30,0 ± 0.8%, after treatment 33,8 ± 1,1%) lymphocytes in peripheral blood increased significantly compared to the control group (39 ± 0.9%) ($p<0.05$), leading to a rise in the CD4+/CD8+ immunoregulatory index (IRI) values to 1.24 ± 0.09 from 1,31 ± 0,06 which was statistically significant ($p<0.05$).

In the second group of patients, before treatment, there was a significant decrease in the total number of T-lymphocytes (CD3+) (before treatment 67,1 ± 1,8%) in peripheral blood compared to the control group (70.4 ± 0.7%) ($p<0.05$). After treatment, this indicator increased to 73,4 ± 1,9%

In the second group of patients, during the treatment dynamics, an important increase in the total numbers of T-helper (CD4+) (before treatment 36.8 ± 0.7%, after treatment 41± 0.6%, control group (39 ± 0.9%)) ($p<0.01$) and T-suppressor (CD8+) (before treatment 28.9 ± 0.9%, after treatment 36.4 ± 1.4%) lymphocytes in peripheral blood was observed compared to the control group (32 ± 0.7%) ($p<0.01$). In both groups, the CD4+/CD8+ ratio values during treatment (before treatment 1.11 ± 0.06%, after treatment 1.38 ± 0.04%, control group 1.23 ± 0.02%) corresponded to the average values of the norm.

When investigating humoral immunity in children with atopic bronchial asthma associated with vitamin D deficiency, it was found that the first group of children showed more favorable dynamics in the levels of IgA, IgM, and IgG in peripheral blood compared to the second group of children ($p<0.01$).

The results of the research have shown that in both groups when examining the levels of cytokines in peripheral blood during the dynamics of treatment, the indicators are presented in Table 3.

Table 3.

Comparative dynamics of cytokines in the blood during the treatment of children with atopic bronchial asthma

Indicators	Basic treatment (I group)		Basic treatment + Tridrop (II group)		Control group
	Before Treatment	After Treatment	Before Treatment	After Treatment	
IL-2, pg/ml	2,4±0,5***	2,6±0,7***	2,6±0,4 ***	6,3±0,6***^^	10,8±0,7
IL-13, pg/ml	13,8±1,0**	12,3±0,8*	13,8±1,4*#	10,3±1,7^	5,3±0,7
IL-17,pg/ml	9,2±0,8*	7,9±0,7***	9,4±1,6**##	5,3±0,7^^	5,0±0,4

*Note: *p<0.05 **p<0.01 ***p<0.001 compared to the control group;*
Compared to the pre-treatment indicators: ^p<0.05 ^^p<0.01 ^^^p<0.001;
When comparing between groups: #p<0.05 ##p<0.01 ###p<0.001.

The results of the research have determined that in Group I patients, the IL-2 level in the blood before treatment was 2.4±0.5 pg/ml ($p>0.05$). After basic treatment, this indicator increased slightly to 2.6±0.7 pg/ml but was significantly lower than the control group's indicator (10.8±0.7 pg/ml), decreasing by a factor of three.

In Group II patients, who received pharmacocorrection with the Tridrop preparation as part of their basic treatment, the IL-2 median level in the blood before treatment was 2.6±0.4 pg/ml. Compared to the healthy control group, this difference was statistically significant (10.8±0.7 pg/ml, $p<0.001$). After basic treatment with the addition of Tridrop, the IL-2 level in Group II increased to 6.3±0.6 pg/ml, which explained a significant rise when compared to Group I.

In Group I patients, the level of IL-13 was up to 2.5 times higher compared to the control group and reached 13.8±1.4 pg/ml (13.8±1.0 pg/ml in Group I) after treatment, which was statistically significant ($p<0.05$). Compared to the healthy control group, these differences were also statistically significant (5.3±0.7 pg/ml, $p<0.05$). In Group II, the IL-13 level after treatment was 10.3±1.7 pg/ml, which was significantly lower compared to Group I (12.3±0.8 pg/ml after treatment, $p<0.05$).

The level of IL-17 differed between both observation groups. In Group II, it was 9.2±0.8 pg/ml, while in Group I, it was 9.4±1.6 pg/ml, indicating an increase in Group II ($p<0.01$). These differences were statistically significant when compared to the control group (5.0±0.4 pg/ml, $p<0.05$-0.01). In Group II, the IL-17 level after treatment was 5.3±0.7 pg/ml, which was significantly lower compared to Group I (5.3±0.7 pg/ml after treatment).

After the treatment, the cytokine levels in the blood were evaluated in relation to the number of patients in both groups. When assessing the IL-2 level in the blood dynamically, it was found that, despite not reaching the normal value in 10 patients (90.9±8.7%) from Group I, it partially decreased and was higher than normal in 1 patient (9.1±8.7%). In Group II, 9 patients out of 9 (100%) had IL-2 levels that were partially close to normal, while 6 patients (66.7±15.7%) had high levels.

When examining IL-13 in patients after treatment, it was observed that among 11 patients, it partially decreased in 3 patients (27.3±13.4%) and was below average in 8 patients (72.7±13.4%). In Group II, IL-13 levels were significantly decreased in 5 patients (55.6±16.6%) and were close to normal in 4 patients (44.4±16.6%).

The IL-17 level was partially decreased in 2 patients (40.0±21.9%) in Group II and remained unchanged in 3 patients (60.0±21.9%). In Group I, the dynamics of IL-17 levels were not observed, and all patients had high levels ($p>0.05$).

The information obtained from this study indicates that applying the Tridrop preparation in the treatment scheme for children with atopic bronchial asthma has more effectively corrected the cytokine imbalance in bronchial asthma patients.

The correlation between the level of D vitamin and the indicators of immune cytokine clusters has been observed after treatment in children with atopic bronchial asthma. Specifically, after treatment, as the level of D vitamin increased, the levels of İL-2 (ρ =0,363, p =0,003) increased, the levels of IL-13 (ρ = - 0,247, p = 0,049) and IL-17 (ρ = - 0,340, p = 0,006) decreased. An inverse correlation between vitamin D and IL-13 and IL-17 was noted when evaluating the correlation between vitamin D and these cytokines in children with bronchial asthma. Consequently, the complex treatment of atopic bronchial asthma with the addition of vitamin D to vitamin deficiency has resulted in significant changes in immune indicators and positive dynamics in clinical outcomes.

Thus, in children with atopic bronchial asthma, the use of vitamin D as part of the complex treatment, in addition to correcting vitamin deficiency, has allowed for the normalization of the activity of allergic inflammatory processes. This opens up the possibility of considering it as an additional diagnostic measure in the course of research.

CONCLUSIONS

1. Depending on the severity of atopic bronchial asthma, it has been determined that the level of vitamin D varies significantly. Among patients with mild persistent bronchial asthma, the vitamin D level was 25.1 (22.3-26.72) ng/ml, while in patients with moderate to severe persistent bronchial asthma, this indicator was 17.0 (5.9-38.60) ng/ml, which was statistically significant ($p<0.01$). In patients with moderate to severe bronchial asthma, the minimal level of vitamin D was 5.9 ng/ml, indicating its severe deficiency and the need for pharmacocorrection. [6, 14]

2. During the correction of atopic bronchial asthma with the addition of the Tridrop preparation to the basic treatment, there was a significant reduction in daytime symptoms by 41.0% and nighttime symptoms by up to 63.4% (in the first group, respectively, 28.4% and 39.3%). The decrease in the number of daytime and nighttime

symptoms resulted in an increase in symptom-free days ($p<0.05$). [1,2]

3. The study of cytokine cascades such as IL-2, IL-13, and IL-17 in children with atopic bronchial asthma revealed a compensatory imbalance among them. Specifically, it was found that, compared to the control group, patients with atopic bronchial asthma had a significant decrease in IL-2 levels in their blood ($p<0.001$), while IL-13 and IL-17 levels were significantly higher ($p<0.01$). This observed cytokine imbalance is thought to play a role in the chronicization of allergic inflammatory processes. [11, 12]

4. Analysis of lymphocyte markers in children with atopic bronchial asthma revealed a statistically significant decrease in the relative amount of CD3+, CD4+, CD8+, CD16+/56+ lymphocytes, as well as an increase in the percentage of CD19+ (18±0.7%) lymphocytes compared to the control group (*$p<0.05$). Additionally, lower levels of IgA, IgM, and IgG were observed, while IgE was found to be elevated. This immune system imbalance contributed to the exacerbation of the disease clinically. [5, 8, 10]

5. By considering the role of vitamin D in the immunopathogenic mechanism of bronchial asthma, the inclusion of vitamin D-containing Tridrop preparation in the basic treatment regimen resulted in positive dynamics in clinical, immunological, and functional indicators. Vitamin D regulates the imbalance created in Th1/Th2 lymphocytes, leading to a decrease in the important protective IL-13 and IL-17 synthesis during bronchial asthma, while increasing IL-2 levels. The clinical effectiveness of the treatment was assessed through the reduction in the number of daytime and nighttime symptoms and a decrease in the percentage of ß2-agonist requirements. [7, 9, 13]

6. During the study, a direct positive correlation was found between the levels of IL-2, a cytokine involved in inflammation, and vitamin D. Correction of D hypovitaminosis led to an increase in IL-2 levels (ρ =0,363, p =0,003). Furthermore, an inverse correlation was observed between vitamin D and IL-13 and IL-17 when assessing their relationship. After treatment, as vitamin D levels increased, IL-13 (ρ = - 0,247, p = 0,049) and IL-17 (ρ - 0,340, p =

0,006) decreased. Consequently, the complex treatment of atopic bronchial asthma with the addition of vitamin D resulted in significant changes in immune indicators and positive clinical outcomes. [15, 16, 17]

PRACTICAL RECOMMENDATIONS

1. When modifying the diagnostic and treatment approaches for patients with atopic bronchial asthma, it is advisable to take into consideration the role of vitamin D in the immune system.

2. For children, it is recommended to include the measurement of vitamin D levels in blood serum as a more accurate diagnostic method for assessing vitamin D deficiency.

3. When a low level of vitamin D is identified in the blood serum of patients with atopic bronchial asthma, it is recommended to administer vitamin D supplements in the appropriate dosage in addition to basic treatment, considering the deficient level of D vitamin.

SCIENTIFIC WORKS PUBLISHED ON THE SUBJECT OF THE DISSERTATION

1. N.H.Sultanova, Cəfərova A.O. Иммуномодулирующая эффективность витамина Д у детей с атопической бронхиальной астмой / «Аллергология и иммунология » Том 17, N-2. Июнь 2016, p. 139 . A.A.Eyyubova.

2. A.A.Eyyubova, N.H.Sultanova, Cəfərova A.O. Atopik forma bronxial astmanın patogenezində vitamin D rolu / «Allerqologiya, İmmunologiya və İmmunoreabilitasiya üzrə V Azərbaycan Milli Konqresi» 21 oktyabr 2016 materialları, p. 31-34. Bakı.

3. . A.A.Eyyubova, H.H.Qabulov, N.H.Sultanova, Cəfərova A.O. Роль витамина Д в патогенезе заболеваний бронхо-легочной системы // «Azərbaycan Allerqologiya və Klinik İmmunologiya» jurnalı. Cild 4; №2, p. 38 – 43, 2016

4. N.H.Sultanova, L.İ.Allahverdiyeva, Cəfərova A.O. Uşaqlarda bronxial astma və vitamin D: suala müasir yanaşma // «Azərbaycan Allerqologiya və Klinik İmmunologiya» jurnalı Cild 5; №2, 2017, p. 28 - 34.

5. N.H.Sultanova, L.İ.Allahverdiyeva, Cəfərova A.O. Иммунокорригирующий эффект витамина D у больных бронхиальной астмой // «Медицинские новости» , 2018, p. 54 – 56.

6. Cəfərova A.O. Atopik forma bronxial astma olan uşaqlarda vitamin D-nin səviyyəsi və onun korreksiyası // «Azərbaycanın Təbabətinin müasir nailiyyətləri» jurnalı, № 4, 2018, p. 107-1107.

7. L.İ.Allahverdiyeva, N.H.Sultanova, Cəfərova A.O. Влияние фармакологической коррекции витамином D на цитокиновый ответ у детей с атопической бронхиальной астмой // «Казанский Медицинский Журнал» , том c, 2019, №1, p. 135 – 139.

8. Cəfərova A.O. Atopik forma bronxial astma xəstəliyi və vitamin D-nin çatişmazlığı olan uşaqlarda immun sistemin vəziyyətinin qiymətləndirilməsi və korreksiyasi // «Sağlamlıq» jurnalı, № 1, 2019, p. 117.

9. N.H.Sultanova, Cəfərova A.O. Atopik forma bronxial astmalı uşaqlarda vitamin D ilə sitokin sistemi arasında əlaqənin qiymətləndirilməsi / Tibbin görən gözü. Şüa diaqnostikasının aktual problemlərinə həsr olunmuş beynəlxalq praktik konfransın materialları, p. 117. 30-31 mart 2019.

10. N.H.Sultanova, Cəfərova A.O. Влияние витамина D на иммунный статус у больных атопической бронхиальной астмой / XIV Ümumdünya Böyrək gününə həsr olunmuş «Müasir Nefrologiyanın aktual problemləri » adli elmi-praktik konfransın materialları, p. 122 – 123. 14 mart 2019.

11. Cəfərova A.O. Atopik forma bronxial astma xəstəliyi olan uşaqlarda vitamin D-nin çatişmazliği ilə sitokin sistemi arasinda əlaqənin qiymətləndirilməsi / İmadəddin Nəsiminin 650 illik yubiliyinə həsr olunmuş Doktarantların və gənc tədqiqatçıların

XXIII Respublika elmi konfransının materialları, I cild, p. 121 – 122. 2019.

12. N.H.Sultanova, Cəfərova A.O. Uşaqlarda atopık forma bronxıal asmanın müalicəsində vitamin D-nin rolu / 18 iyun 2022-ci il akademik M.A.Topçubaşov adına Elmi Cərrahiyyə Mərkəzinin yaradılmasının 60 illiyinə həsr olunmuş elmi – praktiki konfransın toplusu, №2, 2022, p. 102.

13. N.H.Sultanova, Cəfərova A.O. Atopik forma bronxial astmanın müalicəsinə müasir yanaşma / "Pediatriyanın aktual problemləri" XII Beynəlxalq Elmi – Praktiki Konqres toplusu, 2022, 11-13 oktyabr, p. 23.

14. Cəfərova A.O. Uşaqlarda bronxial astmanın diaqnostikasında D vitamininin rolu / Azərbaycan Allerqoloq, İmmunoloq və İmmunoreabilitoloqların VI Milli Beynəlxalq Konqresinin toplusu, 2022, 4 noyabr, p. 22.

15. N.H.Sultanova, Cəfərova A.O. Atopik forma bronxıal astmalı uşaqlarda sitokin göstəriciləri ilə D vitaminin göstəricisi arasında korrelyasion əlaqənin xarakteristikası // Nəzəri, klinik və eksperimental morfologiya jurnalı, 2022, cild 4, № 1-2, p. 58-60.

16. N.H.Sultanova, Cəfərova A.O. Atopik forma bronxıal astmalı uşaqlarda vitamin D – nin rolu / Professor Zərifə Ağarza qızı Zeynalovanın anadan olmasının 90 illik yubileyinə həsr olunmuş elmi konfransın materialları, 2023, 3 fevral, p. 142-143.

17. N.H.Sultanova, Cəfərova A.O. Atopik forma bronxıal astmalı uşaqların immun sisteminin tənzimlənməsində vitamin D – nin rolu / Ulu Öndər Heydər Əliyevin anadan olmasının 100 illiyinə həsr olunmuş "Təbabətin aktual problemləri-2023" elmi-beynəlxalq konqres toplusu, 2023, 3-6 may.

LIST OF ABBREVIATIONS

ARI – acute respiratory infection
BA – bronchial asthma
CI – confidence interval
GINA – Global Initiative for Asthma
ICS – inhaled corticosteroid
IFN – interferon
Ig – immunoglobulin
ISI – integral cytokine index
ILI – interleukin indices
IL – interleukin
NK – natural killer cells
RR – relative risk
RXR – retinoid-X receptors
SpO2 – blood oxygen saturation
Th – T helper cells
Treg – T regulatory cells
UV – ultraviolet rays
VDR – vitamin D receptors

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