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Vitamin D level and its importance in children with bronchial asthma

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To gain MD and PhD medicine

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Introduction:

Theme's Actuality

Modern medicine is constantly renewable and developing science. Scientists are constantly telling us about new methods of treatment of diseases. Despite significant success in this direction, the timely detection and prevention of the disease is the priority of modern medicine.

According to the information provided by the National Center for Disease Control and Public Health under the Ministry of Labor, Health and Social Affairs of Georgia, the first place among the leading causes of illness in children 0-15 year olds, on the first place is the respiratory system - 60.4%. New cases of respiratory system disease have increased since 2004 from 150 to 500 .

Bronchial asthma is the most common chronic disease in the respiratory tract and is a global health problem in children (1). In 90% of cases, asthma is diagnosed for age 6. During the last 20-30 years, the clinically diagnosed asthma rate in children and adolescents has increased from 9 to 17%.

Due to the study of ISAAC , asthma frequency ranges from 5 to 36.8% (The International Study of Asthma and Allergies in Childhood). Especially high asthma prevails in developed countries.

334 million people on the Earth suffers from asthma and this number may reach 400 million by 2025. The prevalence of bronchial asthma increases especially in children. In developed countries, 1-2% of the health care total volume expenses comes on asthma. Disease affects every aspect of the patient's life.

Asthma and other allergic diseases are a major health problem throughout the world (Masoli M, Fabian D, 2014). Asthma remains the most common disease in children's population and prevalence is especially high in developed countries (Mannino DM, Homa DM, 2013).

In some countries, the prevalence of asthma increases annually. For example, in the UK, asthma prevalence is 15-35%.

According to the latest data, about 250000 people suffering asthma die every year, while the correlation between the death rate and the prevalence of the disease is weakly correlated.

Economic expenses are related to the direct costs-economical costs of medical expenses (hospitalization, cost of medical preparations, etc.) and indirect medical expenses - absence of school or service, ineffectiveness of work, premature mortality. In case of inadequate treatment, losses are higher and mainly depend on the effectiveness of the prevention and control of the disease.

Studies are actively undertaken to identify asthma prevalence in developed countries. The most relevant is the so called Hygiene Theory. According to this hypothesis, Western-type small family members are in contact with microbes, which in turn lead to changes in immune response and Th2 / Th1 equilibrium disorders, respectively, atopia and bronchial asthma. Although this hypothesis is approved experimentally, the important factors for developing asthma may be obesity, poor living conditions, infections, etc. In the last two decades scientific interest of vitamin D significance has increased immensely. It is well known that Vitamin D participates in bone metabolism and calcium homeostasis, but at the same point latest research suggests its possible importance in allergic diseases (Masoli M, Fabian D 2014). The first direct evidence of the role of vitamin D in allergy and asthma development was adopted by the human genetic studies. Two parallel survey revealed a statistically significant relationship between vitamin D VDR0029 receptor gene (responsible for predisposition to allergies and asthma) polymorphism and asthma (Raby BA, Lazarus R, 2004).

Experimental studies have been established that vitamin D-'s affects immune system. Matheu et al (2003) study showed vitamin D- y Th2 allergic response inhibition effect in a mouse model with pulmonary eosinophilic inflammation. Topiliski et al (2004) In vitro study using Th2 asthma mice - model revealed that vitamin D reduces the inflammatory answers inactivation and decreases production of IL-4 in bronchoalveolar lavage fluid.

Vitamin D plays an important role in regulating the immune system [1.10.12] Vitamin D low level reduces the formation of Th1 cells and increases Th2 cell proliferation, which itself increases the number of IL-4, IL-5 and IL-12 cell quantity. Interleukins IL_4, IL-5 and IL-13 are related to the number of eosinophiles in the peripheral blood and total IgE blood serum levels.

According to a research, the 25 (OH) D low level in blood serum is correlated with increased asthma prevalence and hospitalization. Studies are actively underway for determining correlation between vitamin D levels and etiological and trigger factors of bronchial asthma. (Room dust, vegetable and animal allergens, tobacco smoke, environmental pollution, etc).

In particular, a significant reduction in the formation of immunoglobulin E by B lymphocyte cells was revealed after Vitamin D. The research also found that the reduction of immunoglobulin E production by B lymphocyte cells resulted in the addition of Vitamin D and VDR agonists [1.5.7.].

Chinellato I, Piazza M. (2010) study in children has shown connection between low level of vitamin D and low lung function and high reactivity of physical activity.

Xystrakis et al (2006) study reported that subscription of vitamin D in asthma patients makes neutralization of steroid resistanceAccording to Harvard Medical School study (Augusto A. Litonjua, 2010) the growth of level of vitamin D is perspectives measure in the primary prevention of asthma, avoid steroid resistance and prevent aggravation of illnesses Bogaczewicz J, Jeziorkowska R (2013) studies have shown a relation between vitamin D deficit and the frequency and severity of atopic

dermatitis. Vitamin D affects the immune system, lung development and function. To answer these issues further research is essential. At the same point, modern lifestyle, food and daily activity leads to high prevalence of vitamin D deficiency, even in the southern countries. All the above mentioned consideration defies scientific novelty of vitamin D study in Georgian population, to evaluate vitamin D level and its importance in children with bronchial asthma.

The aim of the study:

The aim of the study is to determine the level of vitamin D in children with bronchial asthma, considering comorbid and asthma control status.

The main tasks of the study:

1. Formation of the basic and the control group, clinical characterization of patients with bronchial asthma;

2. Determination of Vitamin D level in blood serum of individuals in the basic and control group;

3. Determination of the correlation between vitamin D level and asthma control status;

4. Determination of the correlation between vitamin D level and pulmonary function;

5. Determination of the correlation between vitamin D level and atopic markers.

6. Determination of the correlation between vitamin D level and comorbid conditions.

7. Comparison of Vitamin D level in the control and basic group.

Scientific novelty of the work

At first in Georgia

- Vitamin D status in children with bronchial asthma was established.

- Comorbid conditions and risk factors were studied.

- The frequency of vitamin D deficiency was detected.

- The relation between vitamin D level, asthma control status and atopic lung function was determined.

Practical value of the study

From practical point of view, Vitamin D deficiency as a risk factor for disease formation and / or severe progress, as well as treatment-resistant cases was assessed. The study is available for practicing physicians and has useful recommendations to achieve better control of bronchial asthma.

I Literature Review

1.1. Bronchial asthma prevalence in children

Bronchial asthma is problem, of a global importance, which is due to the growing epidemiological indicators of this disease. As a result, asthma frequency and mortality rates is increased.

Asthma is one of the most common chronic diseases in the world . Asthma is the most common chronic disease in childhood. Mortality rates vary from 0.0 to 0.7 per 100,000 population in children. Asthma prevalence is especially high in developed countries, although some developing countries have high prevalence of asthma too.

1.2. Triggers and risk factors of bronchial asthma

According to the American Lung Association, the risk factors for asthma are the following: family history, viral infections, allergy, professional factor, smoke, air pollution and obesity. Some prenatal risk factors, such as mother's smoking, diet, meals, stress, and antibiotics, may affect the development of allergies and bronchial asthma. Factors such as breastfeeding, allergens, family size and structure, gender can also be one of the risk factors for allergy and asthma development.

1.3. Vitamin D synthesis and physiological activity in the body.

Vitamin D is not only a vitamin but also a prohromone. Vitamin D does not synthesized in our body. It synthesized by the sun's rays in the skin, or we take it through the food. It is known that it is enough to get sunbathing twice or three times a week, 5-10 minute, to get the body syntheses an adequate amount of Vitamin D. However, Vitamin D stock supplies very quickly, especially during the winter season.

1.4 Vitamin D status in the world.

To determine the status of vitamin D, studies are actively going on in the world. To determine the vitamin D status, is necessary to measure 25(OH)D level in blood serum. Vitamin D in the blood serum is differentiated as follows: The normal level of vitamin D - 30 - 100 ng / ml: Vitamin D Insufficiency - 20 - 30 ng / ml; Vitamin D deficiency - <20.0 ng / ml. When vitamin D is more than 100 ng / ml, hyper D vitaminosis develops. While the blood serum vitamin D is less than 20 ng / ml, clinically revealed D hypovitaminosis.

Vitamin D status changes according to the geographic location, season and populations skin color. In general population, Vitamin D level in the blood serum is much higher in Northern Europe than in the Southern countries, and higher in the western regions than in the East.

Therefore, despite the abundance of literature, is not yet established the vitamin D level and its correlation with bronchial asthma, as well as comorbid conditions and lung function in our region. There is no predictive value of Vitamin D supplementation, which gives the basis for further research. The goal of our study was to determine the level of vitamin D as

well as its assessment in children on bronchial asthma. In addition, it is essential to establish correlation between comorbid conditions, lung function and asthma control status in children with bronchial asthma.

II. Study Materials and Methods:

One centric clinical trial was performed on the base of Sachkhere Medical Center. The main group was formed. Fifty patients with bronchial asthma, were involved in the main group. Diagnosis and control of asthma in the patients produced by the GINA guideline.

The control group included 20 persons, without allergic history at the time of the study, a reported episode of bronchial asthma attack, and severe infectious symptoms over the past month.

In the study process, all individuals were performed the quantitative determination of vitamin D in blood serum. (Chemiluminescensional analysis).

2.1 Inclusion criteria

1. Age - from 6 to 15 years

2. Confirmed Bronchial asthma by using clinical- instrumental examines. Diagnosis and control of asthma in the patients produced by the GINA guideline.

3. Healthy people, who were involved in the control group, did not have an allergic reaction , an episode of bronchial asthma attack and the acute infectious manifestation during the last month prior to the study.

4. Confirmation consent of a parent or a guardian about the participation in the study.

2.2. Exclude criteria

1.Vitamin D intake within one month prior to research.

2.Associated somatic disease

3.Severe chronic infections

2.3. Studies

1. Determine the vitamin D level in blood serum

2. Determine the Total IgE level in blood serum.

3. Determine the lung function by spirometry test.

4. Skin allergen samples for allergens (including tip-dermatophagoides farinae, cow's milk protein, ambrosia) by skin prick tests.

From the passport data during the study age and sex were evaluated . By the asthma control status the persons were divided into two groups: controlled and uncontrolled bronchial asthma. We have received information about social-hygienic factors. These are: parents' education; Living conditions for individuals; Assessment of living conditions; Exist dust collectors in the apartment; The existence of plants and animals in living conditions was also assessed; In order to evaluate the social hygiene factor, we have received information about the school and/or nursery school absence .

During the study within biological factors, we got information about pregnancy and newborn period of persons. The existence of chronic infection lesions, medication or nutrient allergy during pregnancy was revealed.

We received the necessary information on the peculiarities of childbirth and the newborn period. For example: whether or not the caesarean intake was taken, the first child was or second, the timely or premature. Also we studied the anthropometric data during the birth and feeding period.

It is important to know about the first year illness of individuals, in which system the pathological condition was revealed. It is important to know about the hereditary. The hereditary was revealed in the first row, or in distant relatives.

During the questionnaire, we received significant information about the comorbidities, as well as triggers and risk factors.

Individual map-questionnaire has include test results, that was made during the study.

III Study results

3.1 Own material characterization

60% of the study individuals were between 6 and 10 years (n-30; p-0.00), and 11-15 year olds were 40% in the basic group (n-20; p-0.002).

Among the study groups involved in the main group were male, 54% of total number (n-27; p-0.00), while females were 46% of the study individuals. (n-23; p-0.00).

Individuals involved in the basic study group are divided into two groups: controlled bronchial asthma 62% (n-31; p-0.00) and uncontrolled bronchial asthma 38% (n-19; p-0.039).

3.2 Bronchial asthma, comorbid conditions and risk factors in children with asthma

During the first stage of the research in persons, who were involved in the basic group, bronchial asthma, its comorbid conditions and risk factors has been studied,.

Statistically correct correlation has been observed during allergic rhinitis and allergic conjunctivitis. Specifically: the symptoms of allergic rhinitis at the time of bronchial asthma are reliable $P < 0.05$, OR = 17.250. (95% CI: lower-1.730; upper-172.036)

3.3. Pulmonary function and disease control in children with bronchial asthma.

The first phase of single-centered clinical trial study was performed in Sachkhere Medical Center. 50 individuals involved in the basic group, have undergone complete allergic research. All individuals were tested by Total IgE level in blood serum. In most cases, the IgE level of blood serum varies between 500-600 KU / l.

Individuals, involved in the basic group, were studied by lung function using spirometry testing. The children had decreased lung function, in most obstruction type. In most 56% of the children had mild quality obstructive lesions in medium and low-caliber bronchas (n-28; mean-0.56; f-24.09; p-0.001). All researchers were treated with the skin prick-tested with allergens. Allergic reactions have been reported at the highest dose of dermatophagoides farinae - 84% (n-42; p-0.001). In 10% of cases, the researchers identified a positive allergic response to ambrosia (n-5; p-0.00). In relatively less intensity, only 6% of all cases of allergy to cow's milk proteins (n-3; p-0.078) were revealed. At the next stage of the study, all researchers were diagnosed with vitamin D levels of blood serum. Vitamin D level in the blood group of people involved in the basic group is quantitatively distributed as follows: In 68% of cases (n-34) the vitamin D deficiency (mean-18.78610) was revealed. 32% of the researchers (n-16) had a insufficient of vitamin D. As for the normal number of Vitamin D in the blood serum, none of the individuals involved in the basic group did not had any symptoms.

In controlled asthma group Vitamin D is an average indicator of mean-20.72-ng / ml. As for the uncontrolled bronchial asthma, the researchers found that the subgroup had a significantly lower level of blood serum - mean-15.04 ng / ml. The researchers found that the controlled bronchial asthma subgroup had almost equal numbers as a deficiency. In 48% of cases, vitamin D deficiency (n = 15) was revealed, and in 52% Vitamin D was

diagnosed with vitamin D deficiency in blood serum (n = 16). As for the uncontrolled bronchial asthma group, the majority of researchers have been shown to have a severely expressed deficiency of Vitamin D insufficient in the blood serum 95% of cases (n = 18). Only 5% showed a vitamin D in blood serum (n = 1).

According to the results of the study D deficiency in a reliable correlation with uncontrolled bronchial asthma and decreased lung function. (p-0.039); In addition, neither the total serum of the serum Total-IgE (p-0.793) nor the positive effect on the room dust ticks according to the skin prick test (p-0.50) is associated with the vitamin D deficiency of blood serum.

3.4. Vitamin D level and comorbid conditions in children with bronchial asthma

At the next stage of the study, the level of vitamin D in the blood serum, the correlation between the comorbid conditions and the correlation between risk factors was assessed. The following correlations were identified: the accompanying atopic dermatitis was reported by statistically significant Vitamin D deficiency in the blood serum rather than other comorbid conditions, including allergic rhinitis (P-0.08), sinusitis (P-0.54) and urticaria (P- 1.00) and conjugate (P-0.20).

Risk factors and vitamin D correlation rates have been identified as: Risk factors such as medical and nutrient allergies at the first year of life (P-0.039) and the history of asthma hereditary predisposition (P-0.039) is associated with vitamin D deficiency in blood serum.

3.5 .Vitamin D is computed in the main and control group.

At the next stage of the study, we determinate the quantity of vitamin D in the blood serum of the persons involved in the control group. Vitamin D is an average indicator of mean-26.30. In 80% of cases, the insufficiency of vitamin D 20 ng / ml-30 ng / ml was determined and only 20% of the individuals had vitamin D normal level in blood serum. It is noteworthy that vitamin D deficiency was not identified in the control group.

According to statistical d ata, children with bronchial asthma have relatively low levels of vitamin D. (X^2 = 6.78; F-0.022;) The chances of odds were studied (OR -13.5, 95% CI 1,42-128.25; p = 0.011). The results obtained confirm the connection between the given factor (vitamin D) and the likelihood of the disease (bronchial asthma).

Chapter IV

Summarize and analyze the results obtained

The work was based on the study of 70 individuals on the base of Sachkhere medical center. There were 50 children in the basic group, who were registered at the Sachkhere Medical Center in Children's Allergy department. On the other hand, the individuals were divided into two subgroups: controlled and non-controlled asthma sub-groups. There was also a control group forming involving 20 conditionally healthy people. The study of comorbid conditions has shown that the most common condition in bronchial asthma is allergic rhinitis in 84% of cases (n-42; 84%; t-12.04; p-0.004).

According to the results obtained, the blood serum of the children involved in the basic group was found to be significantly lower vitamin D level (mean = 18.7ng / ml), than in the control group (mean = 26.30ng / ml). The correlation between the bronchial asthma and the vitamin D deficiency in blood serum was revealed.

According to the results of the study, vitamin D deficiency is associated with relative correlation between asthma control and decreased lung function (p-0.039); In addition, neither the Total-IgE level (p-0.793) nor the positive test on the room dust according to the skin prick test (p-0.50), is not associated with the vitamin D deficiency of blood serum. The individuals found that accompanying atopic dermatitis were statistically high levels of vitamin D in the blood serum rather than other comorbid conditions including P-0.08, sinusitis (P-0.54) (P-0.20). Risk factors such as alimentary and medicine allergy in the first year of life (p-0.039 x2- 4.24) and genetically predisposition of bronchial asthma (p-0.039; x2- 2.42 are reliable correlation between vitamin D deficiency in blood serum.

Conclusions:

1. Conducted studies have shown that the main importance of bronchial asthma symptoms in patients involved in the basic group is leading allergic rhinitis (n-25; p-0.004, OR-17.25); Sinusitis - (n-19; p-0.094, OR-7.08) and allergic conjunctivitis - (n-16; P-0.031, OR-5.4). Allergic rhinitis and allergic conjunctivitis are correlated with the main illness and in the case of sinusitis statistical reliability has not been established.

2. The presence of vitamin D deficiency predicts an increased risk of asthma in children. The study showed that most children with asthma had vitamin D deficiency, in contrast to the children involved in the control group. (OR = 1.35, 95% CI (1,14-1.58) P = 0.011; X^2=6.78; F-0.022).

3. Vitamin D deficiency is associated with reliable correlation between the alimentary and medicine allergy in the first year of life child's age (p-0.039) and asthma hereditary predisposition (p-0.039), when the correlation with manifestation of pregnancy pathology (p-0.21) was not found.

4. Vitamin D deficiency is associated with atopic dermatitis and medical allergy, while correlation with allergic rhinitis (p-0.172) and urticaria (p-1.00) was not indicated.

5.Vitamin D deficiency is associated with relative correlation between asthma control and decreased lung function (p-0.039); In addition, total IgE level (p-0.793) and increased sensitivity to dust mite (p-0.50) is not associated with vitamin D deficiency in blood serum.

For the first time in Georgia:

- Vitamin D status was established in children with bronchial asthma.

- The frequency of vitamin D deficiency was detected.

- Comorbid conditions, risk factors and their correlation with Vitamin D deficiency has been studied in children with bronchial asthma.

- Correlation with vitamin D levels, asthma control status, atopic markers and lung function indicators also has been studied.

Practical recommendations:

- Timely recognition of risk factors and medical involvement is important to avoid comorbid conditions during bronchial asthma. Besides, it is an integral part of asthma management.

- Due to the results obtained, the presence of vitamin D deficiency predictably increases the risk of asthma in children. The study showed that most children with bronchial asthma had vitamin D deficiency, in contrast to the children involved in the control group.

- In addition, the level of vitamin D in blood serum correlates with the level of asthma control and decreased lung function.

- Therefore, by increasing the level of vitamin D in blood serum ,can improve the control status of disease and lung function in children with bronchial asthma.

Attachment

List of published papers

1. L. Bugadze. L.Jorjoliani. N. manjavidze Bronchial asthma, comorbidities and risk factors in pediatric patients. Experimental & Clinical Medicine N5 2017 Pg. 65-69 www.jecm.ge; www.interpharm.edu.ge

2. L. Bugadze. L.Jorjoliani. N. manjavidze. clinical importance of vitamin d determining in children with bronchial asthma. Experimental & Clinical Medicine N4 201 Pg. 81-85 www.jecm.ge; www.interpharm.edu.ge

3. L. Bugadze. L.Jorjoliani. N. manjavidze Vitamin D level and comorbid conditions of children with bronchial asthma. Experimental & Clinical Medicine N5 2018 Pg. 68-73 www.jecm.ge; www.interpharm.edu.ge

4. L.Bugadze. N.Manjavidze L. JorJoliani. Asthma control status and lung function in relation to vitamin D level in children with bronchial asthma. Georgian Medical News N10 (283) 2018 Pg 115-118 www.geomednews.org