Vitamin D and the importance of its deficiency in the development of broncho-obstructive syndrome in young children

Ruzmetova S.U.

Assistant of the Department of 3-pediatrics and medical genetics of the Samara State Medical University.

Abstract: *The article is devoted to the problem of broncho-obstructive syndrome and the role of vitamin D in the development of respiratory pathology in young children. The main extraskeletal mechanisms of the anti-infective action of vitamin D are described. Data on the possible use of vitamin D as a preventive measure and adjuvant therapy for broncho-obstructive syndrome in young children are presented.*

Key words: *young children, bronchoobstructive syndrome, vitamin D.*

Abstract: *The article is devoted to the problem of broncho -obstructive syndrome and the role of vitamin D in developing of respiratory pathology in young children. The main extraskeletal mechanisms of antiinfectious actions of vitamin D have been described. The data about the possibility of using vitamin D as a prevention and adjuvant therapy of broncho -obstructive syndrome in young children are presented.*

Key words: *young children, broncho-obstructive syndrome, vitamin D.*

Pathology of the respiratory system, including broncho -obstructive syndrome (BOS) in young children, remains one of the pressing problems of modern pediatrics. It is known that acute lower respiratory tract infections are one of the leading causes of childhood mortality in the world and account for about 1.4 million deaths in children under 5 years of age every year.

In the pediatric population, according to O. I. Lasitsa (2004), bronchial obstruction occurs in almost 30% of children. Respiratory infections are the most common cause of BOS development in young children [1]. It should be noted that

the frequency of BOS in acute respiratory diseases (ARI) in children of the first year of life has grown today to 50% and more, while 40% of children experience at least one episode of BOS before reaching school age [2]. BOS of infectious genesis most often occurs in obstructive bronchitis and bronchiolitis . In the world literature, the distinction between acute obstructive bronchitis and bronchiolitis is not recognized by all pulmonologists [1]. For example, in the USA, any first episode of BOS of viral etiology in a child under 2 years of age is called bronchiolitis . Among viruses, the leading role is played by respiratory syncytial virus (RSV) (in half of the cases), adenovirus, parainfluenza virus [1].

In children under 5 years of age, most foreign scientists describe three types of wheezing : early transient wheezing , late-onset wheezing, and persistent early-onset wheezing (before age three). According to another classification, three wheezing phenotypes are distinguished in childhood: early transient wheezing, non-atopic wheezing, or IgE -associated wheezing/asthma [5, 11].

According to Yu. L. Mizernitsky (2010), subsequently, against the background of an acute respiratory infection a significant number of young children (54 %) repeated episodes of obstructive bronchitis are possible, not accompanied, however, by the development of bronchial asthma. Recurrent BOS is defined as three or more episodes of broncho-obstruction [7] , but some authors define recurrent BOS as BOS with a frequency of episodes of more than one in the last 12 months [6]. Foreign scientists have found that the prevalence of recurrent BOS among 30,093 children aged 12 to 15 months was 24% in Latin America and 15% in Europe.

Among the known risk factors for repeated episodes of BOS, such as family history of allergies , manifestations of atopy , eosinophilia , the role of vitamin D (25(OH)D, VD) and the significance of its deficiency in the tendency to frequent respiratory diseases are currently being actively studied. Historically, VD was associated only with diseases of the skeletal system, including calcium-phosphorus and bone metabolism, osteoporosis , fractures, and the state of the muscular system [9]. However, the biological role of VD is not limited to the

regulation of bone metabolism. 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 (VDR), which are widely represented in the body and have been found in at least 40 organs and tissues. Due to the wide distribution of VDR in tissues, in addition to the main function, the extraskeletal effects of VD are of great scientific interest.

Some studies suggest that VD deficiency, namely a decrease in the concentration of 25(OH)D in the blood serum below 20 ng / ml, may contribute to the severe course of respiratory infections in young children. A group of Canadian scientists found that among children with bronchiolitis or pneumonia who were hospitalized in the intensive care unit, the average level of 25(OH)D in the blood serum was significantly lower compared to a group of children who were treated in the pediatric department (20 ng/ml and 35 ng /ml, respectively) [10]. Science M. et al . [Science M. et al ., 2013] demonstrated that low levels of VD (below 30 ng /ml) increased the risk of ARI by 50% in children aged 3–15 years. The above-mentioned large-scale clinical studies confirm the importance of VD in providing anti-infective immunity.

To date, the following mechanisms of anti-infective action of VD are known, which are realized through the direct and indirect influence of active metabolites of this vitamin on the functional state of innate and acquired immunity. VD takes an active part in the functioning of the innate immune system due to the production of antimicrobial peptides (AMP), which play an important protective role against respiratory pathogens such as viruses, bacteria and fungi. In humans, cationic AMPs functioning in the respiratory tract are represented by two main molecular families, which are organized by defensins (β-defensins-2) and cathelicidins (hCAP-18 and LL-37) [11] . Cathelicidin is active against gram-positive and gram-negative flora, fungi and mycobacteria, and therefore patients with serum 25(OH)D levels less than 20ng/ml may be prone to the development of pneumonia, sepsis, and neuroinfections . Another proposed mechanism for

vitamin D -mediated effects on the respiratory system involves adaptive immunity, including modulation of antigen-presenting cells such as macrophages. Moreover, VD is a direct and indirect regulator of T cells. It is known that the expressed VDR gene is found in activated proliferating T lymphocytes, monocytes, macrophages and histiocytes, which ensures the differentiation of monocytes and prelymphocytes to their mature forms capable of producing sufficient amounts of interleukins (IL), growth factors and other Ca-dependent mediators of immunogenesis [12] . It is through the increase in T - activity that regulatory lymphocytes VD plays an important role in maintaining the balance between Th 1 and Th 2 types and affects the release of cytokines . Under the influence of calcitriol, there is a decrease in the expression of Th 1 - (IL-2, TNF-α, IFN-γ), Th 9 - (IL-9) and Th 22 - (IL-22) cytokines , but an increase in the production of anti-inflammatory Th 2 -associated cytokines (IL-3, IL-4, IL-5, IL-10) [8] . In addition to T cells, some studies indicate the suppression of the production of immunoglobulins by B cells, including IgE , under the influence of 1,25 (OH) 2 D [4, 8]. It has been established that activation of VDR inhibits the expression of IgE in B cells and enhances the expression of IL-10, which is important for preventing the development of atopy [3].

Given the numerous extraskeletal effects of vitamin D, in particular on the immune system and pulmonary function, the issue of the possible use of vitamin D as an adjuvant therapy for acute respiratory infections, including BOS, is relevant in order to improve the clinical course, reduce the recovery period, and prevent the development of repeated episodes of BOS in young children. It has been proven that the target concentration of 25 (OH) D in the blood serum of children should correspond to a level of more than 30 ng / ml to ensure all the positive effects of this vitamin on the body. To achieve the target level of 25 (OH) D in the blood serum, at least 1700 IU of vitamin D per day is required. Double-blind randomized A placebo-controlled study in Japanese schoolchildren aged 6–15 years showed that taking 1200 IU/day of vitamin D3 in winter and early spring helps prevent the occurrence of influenza and asthma attacks [11].

Thus, at present, the understanding of the role of vitamin D in the human body has significantly expanded. The development of vitamin D deficiency can contribute to the development and worsen the course of respiratory diseases in childhood. However, there is a need for further research to study all mechanisms of vitamin D effect on lung function in young children with BOS, which have not been sufficiently studied to date. For example, studying the level of vitamin D provision among children depending on the season, respiratory morbidity; establishing the frequency of vitamin D deficiency in children with episodic and repeated BOS, identifying the relationship between serum vitamin D level, severity and frequency of repeated episodes of BOS in young children.

Bibliography:

1. Belykh N.A. Modern approaches to diagnostics and therapy of broncho-obstructive syndrome of infectious genesis in children / N.A. Belykh, L.A. Zalivnaya // Actual infectology . - 2015. - V.6, No. 1. - 88-93.

2. Yulish E.I. On risk factors for the development of broncho-obstructive syndrome in young children / E.I. Yulish , Yu.A. Soroka, O.E. Chernysheva // Child health. - 2012. - V.41, No. 6. - P.85-88.

3. Bantz Selene K. The Role of Vitamin D in Pediatric Asthma/ Selene K. Bantz , Zhou Zhu, and Tao Zheng // Annals of Pediatrics and Child Health. – 2015. –Vol.3, No.1. R.1-7. – Journal access mode: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4415725/

4. Immune Modulation by Vitamin D and Its Relevance to Food Allergy / Noor HA Suaini , Yuxia Zhang, Peter J. Vuillermin [et al.] // Nutrients. – 2015. – No. 7.–R.6088-6108. doi:10.3390/nu7085271.

5. Global strategy for asthma management and prevention (updated 2014): Global Initiative for Asthma (GINA). [Electronic resource] URL: http: // www.ginasthma.org (date of access 27.01.2016).

6. MarkChungWaiNg.Recurrentwheezeandcoughinyoungchildren:isit asthma?/ Mark Chung Wai Ng, Choon How How // Singapore Med J. - 2014. - Vol.55, No. 5. – R.236-241 .

7. Prevalence, severity, and treatment of recurrent wheezing during the first yearoflife:across-sectionalstudyof12,405LatinAmericaninfants/Javier Mallol , Dirceu Solé , Luis Garcia-Marcos [et al.] // Allergy Asthma Immunol . – 2016. – Vol. 8, No. 1. – R. 22-31. http://dx.doi.org/10.4168/aair.2016.8.1.22.

8. Vojinovic Jelena . Vitamin D—update for the pediatric rheumatologists/ Jelena Vojinovic , Rolando Cimaz // Pediatric Rheumatology. – 2015. – No. 13. – R. 2-9. doi:10.1186/s12969-015-0013-0.

9. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomized trials / Evropi Theodoratou , Ioanna Tzoulaki , Lina Zgaga [et al.] //BMJ. – 2014. – Vol. 348. – R.1–19 . doi : 10.1136/bmj.g2035.

10. Vitamin D deficiency in young children with severe acute lower respiratory infection / JD McNally, K. Leis, LA Matheson [et al.] // Pediatr . Pulmonol . – 2009. – No. 44. – R. 981-988

11. Vitamin D. – 3rd ed. / edited by David Feldman, J. Wesley Pike, John S. Adams – CA: Elsevier, 2011. – 2189pp.

12. Vitamin D and 1,25(OH) 2 D Regulation of T cells / Margherita T. Cantorna , Lindsay Snyder, Yang-Ding Lin [et al.] // Nutrients. – 2015. – No. 7. – R.3011-3021 .