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The course of bronchial asthma associated with metabolic syndrome in children with different phenotypes depending on vitamin D_3 level

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Objective: to establish specific features of BA course in children with various phenotypes on the background of metabolic syndrome, depending on serum vitamin D_3 level.

Subjects and methods. 106 children with BA participated in the study. 42 patients had BA associated with metabolic syndrome (MS), and 64 had BA with no MS. By the phenotype 61 (57.5 %) of patients had allergen-induced (allergic) asthma and 45 (42.5 %) – virus-induced (non-allergic) BA. The control group consisted of 44 children (the patients with MS and those without MS and BA), average age 15.5 ± 1.3 years. All the patients underwent a unified complex of diagnostic investigations: general physical examination, measurement of waist circumference and body mass index (BMI), clinical blood test, spirometry, lipid profile. Weight categories (normal weight, excess weight and obesity) were determined by percentiles (P) of BMI variation series with regard to age, as indicated in WHO recommendations. Serum 25(OH)D levels were determined by enzyme immunoassay. Vitamin D level ≥20 ng/ml was considered sufficient, 11–20 ng/ml – insufficient, ≤10 ng/ml – deficient. General and specific serum IgE levels were determined by enzyme immunoassay. The data obtained were processed with Statistica 8 program, P values of less than 0.05 were considered to indicate statistical significance.

Results. In the group of patients with vitamin D_3 level below 20 ng/ml, 19.5 % had controlled BA and 41.3 % – uncontrolled BA, while among the children with vitamin D_3 level over 20 ng/ml, 30.4 % had controlled BA and 8.6 % – uncontrolled BA ($\chi^2 = 9.12$, $P < 0.05$). Mean value of vitamin D_3 concentration in the control group was significantly higher than in the patients with BA associated with MS and BA without MS ($P < 0.05$). The relationship between OW, obesity and atopy was confirmed by high serum level of sIgE antibodies in those weight categories. High sIgE levels to allergens from the pollen of meadow grass, weeds and trees, animal epithelium, household dust mite, food and fungal allergens were determined much more frequently in the children with OW and obesity than in those with NW. In the patients with BA associated with MS and vitamin D_3 level below 20 ng/ml, FEV1 and FVLC values appeared to be significantly lower as compared to those with vitamin D_3 level over 20 ng/ml ($P = 0.002$). Inverse relationship between the most important parameters of external respiration function and BMI was established: VLC ($r_{xy} = -0.45$, $P = 0.002$), FVLC ($r_{xy} = -0.52$, $P = 0.001$), FEV1 ($r_{xy} = -0.78$, $P = 0.001$), respectively.

Conclusions. The severity of BA as well as the degree of its control in the patients with different phenotypes was found to be influenced by both the presence of MS and vitamin D_3 level. Therefore, vitamin D deficiency can be one of the risk factors of BA and MS development, and can affect the severity of both BA and MS course. Vitamin D_3 deficiency and the presence of MS greatly influence FEV1, FVLC, PEF values, decreasing the indices of external respiration in children and leading to more severe obstruction.

Ключові слова: бронхіальна астма, метаболічний синдром, діти, вітамін D3.

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Особливості перебігу бронхіальної астми на тлі метаболічного синдрому в дітей із різними фенотипами залежно від показників вітаміну D_3

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Мета роботи – встановити особливості перебігу бронхіальної астми (БА) у дітей із різними фенотипами на тлі метаболічного синдрому залежно від рівня вітаміну D_3 в сироватці крові.

Матеріали та методи. У дослідженні взяли участь 106 дітей, хворих на БА: 42 дитини з діагнозом БА в поєднанні з метаболічним синдромом (МС), 64 дитини з БА без МС. Алерген-індукований фенотип встановили у 57,5 % хворих на БА, вірус-індукований – у 42,5 %. Група контролю – 44 дитини (пацієнти з МС і без МС і БА), середній вік – 15,5 ± 1,3 року. Всім хворим виконали єдиний комплекс діагностичних досліджень: загальне фізикальне обстеження, визначення обводу талії та індексу маси тіла (ІМТ), аналіз крові клінічний, спірометрія, визначення ліпідного спектра. Вагові категорії (нормальна, надмірна вага та ожиріння) визначали за перцентилями (Р) варіаційного ряду ІМТ з урахуванням віку відповідно до рекомендацій ВООЗ. Рівні 25-(ОН)D у сироватці крові визначили за допомогою імуноферментного аналізу. Рівень вітаміну D_3 ≥20 нг/мл розцінювали як достатній, 11–20 нг/мл – недостатній, ≤10 нг/мл – дефіцит. Загальний і специфічні рівні сироваткових IgE визначили за допомогою ІФА. Результати опрацювали в програмі Statistica 8, статистично вірогідними вважали розбіжності при $p < 0,05$.

Результати. У групі хворих із рівнем вітаміну D_3 нижче ніж 20 нг/мл пацієнти з контрольованим перебігом БА становили 19,5 %, а з неконтрольованим – 41,3 %; серед хворих із рівнем вітаміну D_3 понад 20 нг/мл контрольований перебіг БА встановили у 30,4 % пацієнтів, неконтрольований – у 8,6 % ($\chi^2 = 9,12$, $p < 0,05$). Середній показник концентрації вітаміну D_3 в контрольній групі був вірогідно вищим, ніж у групах хворих на БА в поєднанні з МС і БА без МС ($p < 0,05$). У дітей із надмірною масою тіла та ожирінням значно частіше, ніж у дітей із нормальною вагою, визначали високі рівні sIgE до алергенів із пилку лучних трав, бур'янів і дерев, епітелію тварин, кліщів побутового пилу, харчових і грибкових алергенів. У хворих на БА в поєднанні з МС і показниками рівня вітаміну D_3 нижче ніж 20 нг/мл, показники $ОФВ_1$ і ФЖЄЛ виявилися вірогідно нижчими порівняно з пацієнтами з рівнем вітаміну D_3 понад 20 нг/мл ($p = 0,002$). Встановили зворотний взаємозв'язок найбільш значущих параметрів функції зовнішнього дихання з ІМТ: ЖЄЛ ($r_{xy} = -0,45$, $p = 0,002$), ФЖЄЛ ($r_{xy} = -0,52$, $p = 0,001$), $ОФВ_1$ ($r_{xy} = -0,78$, $p = 0,001$) відповідно.

Висновки. Важкість і контрольованість перебігу БА у хворих із різними фенотипами залежить як від наявності МС, так і від рівня вітаміну D_3, дефіцит вітаміну D_3, відповідно, може бути одним із факторів ризику розвитку БА і МС, а також впливати на тяжкість перебігу БА і МС. Дефіцит вітаміну D_3 і наявність МС суттєво впливають на показники $ОФВ_1$, ФЖЄЛ, ПШВ, знижуючи показники зовнішнього дихання в дітей, призводять до більш виражених обструктивних змін.

Особенности течения бронхиальной астмы на фоне метаболического синдрома у детей с различными фенотипами в зависимости от показателей витамина D_3

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Ключевые слова: бронхиальная астма, метаболический синдром, дети, витамин D3.

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Цель работы – установить особенности течения бронхиальной астмы (БА) у детей с различными фенотипами на фоне метаболического синдрома в зависимости от уровня витамина D_3 в сыворотке крови.

Материалы и методы. В исследовании приняли участие 106 детей, больных БА: 42 ребенка с диагнозом БА в сочетании с метаболическим синдромом (МС), 64 ребенка с БА без МС. Аллерген-индуцированный фенотип установлен у 57,5 % больных, вирус-индуцированный – у 42,5 %. Группа контроля состояла из 44 детей (пациенты с МС и без МС и БА), средний возраст – 15,5 ± 1,3 года. Всем больным проведен единый комплекс диагностических исследований: общее физикальное обследование, установление окружности талии и индекса массы тела (ИМТ), клинический анализ крови, спирометрия, определение липидного спектра. Весовые категории (нормальная, избыточный вес и ожирение) определяли по перцентили (Р) вариационного ряда ИМТ с учетом возраста в соответствии с рекомендациями ВОЗ. Уровни 25-(OH)D_3 в сыворотке крови, показатели общего и специфических уровней сывороточных IgE определяли с помощью ИФА. Уровень витамина D_3 ≥20 нг/мл расценивали как достаточный, 11–20 нг/мл – недостаточный, ≤10 нг/мл – дефицит. Результаты обработали в программе Statistica 8, статистически достоверными считали различия при $p < 0,05$.

Результаты. В группе детей с уровнем витамина D_3 ниже 20 нг/мл больные с контролируемым течением БА составили 19,5 %, с неконтролируемым – 41,3 %; среди больных с уровнем витамина D_3 более 20 нг/мл контролируемое течение БА установлено у 30,4% пациентов, неконтролируемое – у 8,6 % ($\chi^2 = 9,12$, $p < 0,05$). Средний показатель концентрации витамина D_3 в контрольной группе достоверно выше, чем в группах больных БА в сочетании с МС и БА без МС ($p < 0,05$). У детей с избыточной массой тела и ожирением значительно чаще, чем у детей с нормальным весом определены высокие уровни sIgE к аллергенам из пыльцы луговых трав, сорняков и деревьев, эпителия животных, клещей бытовой пыли, пищевым и грибковым аллергенам. У больных БА в сочетании с МС и показателями уровня витамина D_3 ниже 20 нг/мл показатели $ОФВ_1$ и ФЖЕЛ оказались достоверно ниже по сравнению с больными с уровнем витамина D_3 более 20 нг/мл ($p = 0,002$). Установлена обратная взаимосвязь наиболее значимых параметров функции внешнего дыхания с избыточной массой тела: ЖЕЛ ($r_{xy} = -0,45$, $p = 0,002$), ФЖЕЛ ($r_{xy} = -0,52$, $p = 0,001$), $ОФВ_1$ ($r_{xy} = -0,78$, $p = 0,001$).

Выводы. Тяжесть и контролируемость БА у больных с различными фенотипами зависит как от наличия МС, так и от уровня витамина D_3, дефицит витамина D_3, соответственно, может выступать одним из факторов риска развития БА и МС, а также влиять на тяжесть течения БА и МС. Дефицит витамина D_3 и наличие МС существенно влияют на показатели $ОФВ_1$, ФЖЕЛ, ПСВ, снижая показатели внешнего дыхания у детей, приводят к более выраженным обструктивным изменениям.

Bronchial asthma (BA) is currently the most prevalent chronic disease in pediatric patients. For more than a century, clinicians have attempted to subdivide asthma into different phenotypes based on triggers that cause asthma attacks, the course of the disease, or the prognosis. Asthma is a heterogenous disorder that can be classified into several different phenotypes. The first phenotypes that were described included allergic asthma, nonallergic asthma or infectious asthma, and aspirin-exacerbated asthma. Asthma phenotypes were initially focused on combinations of clinical characteristics [1].

Allergic asthma is the most common asthma phenotype. Allergen-induced (allergic asthma): this is the asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. The average age of onset of allergic asthma is younger than that of nonallergic asthma. Although the spectrum of allergic asthma may vary from mild to severe, studies have reported that allergic versus nonallergic asthma is less severe. Total IgE levels usually are higher in allergic versus nonallergic asthma, but levels substantially overlap between the 2 groups. Virus-induced (non-allergic) asthma: this is the asthma phenotype which is not associated with allergy. Virus-induced asthma is a phenotype which is characterized by a sudden onset and sometimes a severe clinical course. Each viral infection may alter the course of preexisting asthma, or can affect the immune system and subsequently modify the susceptibility to allergen sensitization and asthma in childhood.

Recent cluster analyses have identified an “obese-asthma” phenotype which is characterized by late onset and lack of atopy. In addition, obesity among early-onset asthmatics clearly exists and heightens the clinical presentation. Observational studies have demonstrated that asthma among the obese has a clinical presentation that is more severe, harder to control, and is not as responsive to standard controller therapies [2].

Along with such classic risk factors for BA development as sex, age, family allergic anamnesis, atopy manifestations, eosinophilia, increased body mass index (BMI), there are several factors which can influence the severity of BA, vitamin D_3 deficiency being one of them. The study of potential effect of vitamin D_3 deficiency on BA course is of great significance because of its ability to influence the cellular and humoral immunity, thus decreasing the inflammatory process [3], as well as due to the predisposition to frequent respiratory diseases in

case of its deficiency. This mechanism is caused by gene expression and cytokine synthesis. A great number of scientific studies demonstrate the relationship between vitamin D_3 level and frequency and severity of viral, bacterial and fungal infection course. Besides, negative correlation was found between infectious process activity, the number of complications and vitamin D_3 level. The major mechanism of vitamin D_3 anti-infectious action is its ability to induce the formation of β-defensin-2 and cathelicidin in macrophages, neutrophils, natural killers (NK-cells) and epithelial cells, destroying microorganisms and being active to bacteria, viruses and fungi. Sufficient level of $25(OH)D_3$ supply is associated with increased number of circulating Th1-cells which induce the secretion of anti-inflammatory cytokines (γ-interferon, IL-2, IL-12, TNF-α), while decreased serum $25(OH)D_3$ level is followed by activation of Th2-immune response, i.e. by the increase in IL-4, IL-5, IL-13 populations, promoting atopic reactivity of the body. Besides, overweight and obesity were recently found to be caused by low vitamin D_3 level [4], in part, due to high similarity of calcitriol and vitamin D_3 receptor. Vitamin D_3 receptors and vitamin D metabolic enzymes were found in many cells: T- and B-lymphocytes, macrophages, including lung alveolocytes and bronchial smooth muscles [5]. Asthma-related morbidity is higher among children with vitamin D_3 deficiency and obesity, morbidities that frequently co-exist among minority children. However, the effect of co-existent obesity and vitamin D_3 deficiency on pulmonary function is poorly understood [6].

Though many reports on the problem discussed have already been published, the molecular mechanisms of non-classic action of vitamin D_3 are still unstudied. This can be explained by insufficient number of randomized studies to assess the impact of vitamin D_3 on metabolic processes and BA course.

Objective

To establish specific features of BA course in children with various phenotypes on the background of metabolic syndrome, depending on serum vitamin D_3 level.

Materials and methods

106 children with BA (age – 15.8 ± 1.8 years, BMI = 10.2 ± 0.57 kg/m^2) participated in the study. By the phenotype 61 (57,5%) of patients had allergen-induced (allergic) asthma and 45 (42,5 %) – virus-induced (non-allergic) BA. 42 patients had BA associated with metabolic syndrome (MS), and 64 had BA with no MS. The control group consisted of 44 children (the patients with MS and those without MS and BA), average age 15.5 ± 1.3 years. BA severity, the phenotype, the level of BA control were evaluated by GINA 2011 criteria and "Protocol of diagnosis and treatment of bronchial asthma in children", approved by the Order of the Ministry of Health of Ukraine of October 8, 2013".

All the patients underwent a unified complex of diagnostic investigations: general physical examination, measurement of waist circumference and body mass index (BMI), clinical blood test, spirometry, lipid profile. Weight categories (normal weight, excess weight and obesity) were determined by percentiles (P) of BMI variation series with regard to age, as indicated in WHO recommendations ("Classification of BMI in children and adolescents"). In accordance with this classification, the children with BMI corresponding to P5 of variation series, were referred to under-normal weight category; those with BMI corresponding to P5-P84 – to normal weight group; P85-P94 – to excess weight group, and over P94 – to obesity group. Serum $25(OH)D_3$ levels were determined by enzyme immunoassay. Blood sampling was done in winter period. In accordance with the recommendations of the US Institute of Medicine, vitamin D_3 level ≥20 ng/ml was considered sufficient, 11–20 ng/ml – insufficient, ≤10 ng/ml – deficient. General and specific serum IgE levels were determined by enzyme immunoassay. All the analysis were done from 9 to 11 a.m.

Statistical data processing was done with Statistical package for Windows v. 8.0 (№ AXXR910A374605FA) using parametric methods. The normal distribution was evaluated according to Shapiro–Wilk test. Digital information of all clinical investigations was processed by variance statistical method calculating the mean value (M) and its error (m). The comparison of quality indicators was performed using the χ^2 criterion. The conjugacy coefficient (φ) was determined to estimate the strength of the relationship between the features. Odds ratios (OR) and the corresponding 95 % confidence intervals (CI) were used to compare the quantitative indices of the two characteristics. The significance of difference between two means was calculated by Student's t-test (t). Correlation analysis with calculation of Pearson's correlation (r_{xy}) was used to establish the relationship between the studied indices. Differences were considered significant if significance value was 95 % ($P < 0.05$).

Results and discussion

Intermittent, mild, moderate and severe BA were diagnosed in 13 %, 39 %, 39 % and 9 % of patients, respectively, by physical and instrumental examination. By etiology 39 % of patients had allergic, 26 % – mixed and 35 % – non-allergic BA. In 50 % of patients BA was controlled and in 50 % – uncontrolled. All the patients were divided into three weight categories by BMI: those with normal weight (NW) – 34.1 %, overweight (OW) – 34.6 % and obesity – 31.3 % of children.

Having grouped all the children according to their weight and age, we found an increased number of children with obesity in pubertal age (OR = 3.6; 95 % CI: 1.14–11.35; P = 0.003; OR = 9.0; 95 % CI: 1.56–51.87; P = 0.008 and OR = 3.71; 95 % CI: 1.06–12.98; P = 0.04, respectively). And the number of obese children decreased together with the increase of age (OR = 0.28; 95 % CI: 0.09–0.88; P = 0.003; OR = 0.11; 95 % CI: 0.02–0.63; P = 0.008; OR = 0.27; 95 % CI: 0.08–0.94; P = 0.04, respectively). No relationship between obesity and sex in BA children were found, but a tendency to increased obesity in males as compared to females (P = 0.059) was observed. Besides, the relationship between body weight and clinical manifestations of allergy was found. Among the children suffering from atopic BA, 37.4 % had excess weight, 34.3 % – obesity , 28.3 % – normal weight, while

among those with mixed BA overweight was found in 25 %, obesity – in 20.8 %, and normal weight – in 54.2 % of patients. More than a half of the patients with non-atopic BA (58.7 %) had normal body weight. The children with atopic BA were found to have overweight (OR = 2.86; 95 % CI: 1.31–6.25; P = 0,005) and obesity (OR = 3.15; 95 % CI: 1.38–7.20 P = 0.007) significantly more often as compared to the patients with non-atopic BA.

In the group of patients with BA associated with MS as well as those with BA with no MS there were 32 % of children with vitamin D_3 deficiency, 42 % – with vitamin D_3 insufficiency, and 26 % – with sufficient level of Vitamin D_3. In the control group there were 33 % of patients with vitamin D_3 deficiency, 9 % – with vitamin D_3 insufficiency, and 58 % – with sufficient vitamin D_3 level. Vitamin D_3 level was largely influenced by the severity of BA. It was 19.8 ± 5.0 ng/ml in intermittent, 17.3 ± 5.9 ng/ml – in mild; 14.9 ± 4.2 ng/ml – in moderate; 12.8 ± 4.6 ng/ml – in severe BA; P < 0.05.

The level of BA control and comorbidity were influenced by the level of vitamin D_3 as well. In the group of patients with BA associated with MS as well as in those with BA and no MS vitamin D_3 level was significantly lower in the children with uncontrolled BA (P = 0.005). It was 18.9 ± 4.9 ng/ml in the group of patients with controlled BA and 12.6 ± 2.7 ng/ml – in those with uncontrolled BA (t = 3.2, P = 0.005).

The patients with vitamin D_3 deficiency were found to have uncontrolled BA four times as often as the children with normal levels of vitamin D_3. In the group of patients with vitamin D_3 level below 20 ng/ml, 19.5 % had controlled BA and 41.3 % – uncontrolled BA, while among the children with vitamin D_3 level over 20 ng/ml, 30.4 % had controlled BA and 8.6 % – uncontrolled BA (χ^2 = 9.12, P < 0.05). Mean value of vitamin D_3 concentration in the control group was significantly higher than in the patients with BA associated with MS and BA without MS (P < 0.05). BMI in the patients with vitamin D_3 level below 20 ng/ml was found to be significantly higher than among the children with vitamin D_3 level over 20 ng/ml. Mean value of BMI in the patients with vitamin D_3 level below 20 ng/ml was 32.8 ± 3.4 while among the children with vitamin D_3 level over 20 ng/ml it was 29.01 ± 5.1 (t = 2.49, P = 0.01), respectively. E. Forno, J. C. Celedón [7] found it was obesity increases the risk of asthma – and worsens asthma severity or control – via multiple mechanisms. “Obese asthma” is a complex, multifactorial phenotype in children.

Significant increase in triglycerides and cholesterol levels was revealed in the patients with BA together with the decrease of vitamin D_3 level (P < 0.05). There was negative correlation between the level of low density lipoproteins and vitamin D_3 level (r_{xy} = -0.58, P = 0.008), while the level of high density lipoproteins increased together with the increase of vitamin D_3 level (P = 0.06). No statistically significant differences between the levels of vitamin D_3 and total IgE were found (P > 0.05). Having analyzed immunologic indices, high level of total IgE was revealed practically in all the children with allergic and mixed BA, ranging from 300 to 600 IU/ml, and reaching 1500–2000 IU/ml in some patients. Statistical analysis showed obese children to have higher total IgE level (2.7; 95 % CI: 2.64–2.84) as compared to those with OW (2.46; 95 % CI: 2.40–2.60) and NW (2.37; 95 % CI: 2.30–2.50). Study of the relationship between IgE level and body weight demonstrated that the children with OW not always had high total IgE level (OR = 1.86; 95 % CI: 0.70–5.09, P = 0.21) as compared to the children with NW, while obese children appeared to have higher total IgE level (OR = 4.20; 95 % CI: 1.13–15.60, P = 0.02) than those with normal weight. With high probability (P = 0.02) of correlation (χ^2 = 4.56) between body weight and total IgE level, strong degree of this association (φ = 0.59) was found as well. The relationship between OW, obesity and atopy was confirmed by high serum level of sIgE antibodies in those weight categories. High sIgE levels to allergens from the pollen of meadow grass, weeds and trees, animal epithelium, household dust mite, food and fungal allergens were determined much more frequenty in the children with OW and obesity than in those with NW. The proportion of patients with NW, OW and obesity having sIgE to meadow grass pollen was 51.7 %, 60.2 % and 84.9 % respectively; to weeds – 50.3 %, 78.6 %, 85.7 %, respectively; to trees – 25.8 %, 43.7 %, 70.8 %, respectively; to epidermal allergens – 56.5 %, 72.8 %, 82.3 %, respectively; and to food allergens – 50.6 %, 55.7 %, 59.8 %, respectively. Besides, obesity in BA children was associated with sensitization to considerably greater number of allergens, namely: to allergens from the pollen of meadow grass (OR = 6.10; 95 % CI: 1.78–3.57; P = 0.0001), weeds (OR = 5.0; 95 % CI: 1.43–8.53; P = 0.006), trees (OR = 4.56; 95 % CI: 1.72–10.0; P = 0.004), animal epithelium allergens (OR = 4.58; 95 % CI: 1.34–7.25; P = 0.003), food (OR = 4.00; 95 % CI: 1.02–6.86; P = 0.004), household dust mite allergens (OR = 3.68; 95 % CI: 1.18–7.08; P = 0.001) and fungus (OR = 2.15; 95 % CI: 1.39–5.39; P = 0.002).

Significant decrease of forced expiratory volume in 1 second (FEV_1) and forced vital lung capacity (FVLC), peak expiratory flow rate (PEF) were detected in BA patients as compared to normal values (P = 0.01 and P < 0.001, respectively). FEV1 decrease by 0.49 % (95 % CI: 0.69–0.15), FVLC – by 0.38 % (95 % CI: 0.56–0.14), and PEF – by 0.42 % (95 % CI: 0.42–0.17) with every unit of BMI increase were revealed in the patients with BA associated with MS. Besides, significant decrease of FEV_1 values was demonstrated to be influenced by vitamin D_3 level. In the patients with BA associated with MS and vitamin D_3 level below 20 ng/ml, FEV_1 and FVLC values appeared to be significantly lower as compared to those with vitamin D_3 level over 20 ng/ml (P = 0.002). Mean value of vitamin D_3 concentration in the control group was significantly higher than in the patients with BA associated with MS and BA without MS (P = 0.003). Inverse relationship between the most important parameters of external respiration function and BMI was established: VLC (r_{xy} = -0.45, P = 0.002), FVLC (r_{xy} = -0.52, P = 0.001), FEV1 (r_{xy} = -0.78, P = 0.001), respectively.

L. A. Lautenbacher et al. [6] found that vitamin D_3 deficiency was associated with pulmonary function deficits among obese children, but not among normal-weight children with asthma, an association that was independent of Th1 and Th2 serum inflammatory measures. Vitamin D_3 deficiency may be one potential mechanism underlying the obese-asthma phenotype.

Conclusions

1. The severity of BA as well as the degree of its control in the patients with different phenotypes was found to be influenced by both the presence of MS and vitamin D_3 level. Therefore, vitamin D_3 deficiency can be one of the risk factors of BA and MS development, and can affect the severity of both BA and MS course.

2. Vitamin D_3 deficiency and the presence of MS greatly influence FEV1, FVLC, PEF values, decreasing the indices of external respiration in children and leading to more severe obstruction.

The perspectives of further scientific research in this direction are to study the best ways of pharmacological therapy and rehabilitation in patients with BA.

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