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25(OH)D LEVEL, DEFICIENCY AND INSUFFICIENCY IN THE KYIV CITY SCHOOLCHILDREN

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The deficiency of vitamin D in children and adolescents in recent years is a topical issue and, according to some authors, it becomes a pandemia. It is commonly known that one of the main functions of vitamin D is to provide phosphorous-calcium metabolism and maintain bone health. The aim of our study was to study the level of 25(OH)D in schoolchildren in Kyiv, to determine the frequency of its deficiency and insufficiency and their correlation with season, obesity and stage of puberty. The level of 25(OH)D was determined in 87 apparently healthy children aged 8–17 using the electrochemiluminescent method. It was found that vitamin D deficiency among schoolchildren in Kyiv was 41%. No age and gender characteristics of the formation of vitamin D deficiency have been established. It has been determined that 25 (OH) D levels in healthy children and adolescents in the winter were 25.3% lower than in the summer period. Relatively lower 25 (OH) D levels were recorded in adolescents in third stage of puberty. Vitamin D deficiency was common among healthy children and required correction, especially in the winter season.

Key words: vitamin D, children, adolescents, sexual maturation.

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РІВЕНЬ 25(OH)D, ДЕФІЦИТ ТА НЕДОСТАТНІСТЬ У ШКОЛЯРІВ МІСТА КИЄВА

Дефіцит вітаміну D у дітей та підлітків є актуальною проблемою охорони здоров'я у зв'язку з широкою розповсюдженістю не лише в Україні, а й у світі. Вітамін D відіграє ключову роль у регулювання кальцій-фосфорного обміну, а його дефіцит порушує формування піку кісткової маси, цим самим підвищуючи ризик розвитку остеопорозу. Метою дослідження було визначення частоти дефіциту і недостатності 25(OH)D та їх зв'язок з порою року, ожирінням і статевим розвитком. Рівень 25(OH)D визначали в сироватці крові 87 практично здорових дітей 8–17 років за допомогою електрохемілюмінесцентного методу. Виявлено, що дефіцит вітаміну D серед школярів міста Києва складає 41%. Не встановлено вікових та гендерних особливостей формування дефіциту вітаміну D. Визначено, що у здорових дітей та підлітків з листопада по квітень рівні 25(OH)D на 25,3% нижчі порівняно з періодом з травня по жовтень. Достовірно нижчий рівень 25(OH)D реєструється у підлітків у 3 стадії статевого розвитку, разом із цим у цей період починається пубертатний стрибок у формуванні піку кісткової маси. Аналіз отриманих результатів продемонстрував, що дефіцит вітаміну D значно поширений серед здорових дітей 8–17 років та потребує корекції, особливо в зимовий сезон.

Ключові слова: вітамін D, діти, підлітки, статевий розвиток

The study is a fragment of the research project "Prerequisites for the formation of somatic pathology in children and adolescents and the improvement of treatment and rehabilitation measures" (state registration No. 0117U002213).

The deficiency of vitamin D (DV D) and its insufficiency (IV D) in children and adolescents is a relevant and socially significant health problem. Data from recent epidemiological studies indicated that it is prevalent among children and adolescents throughout the world. Thus, in Great Britain, DV D was found to be 40 % of the children's population [14]. In 30 % of the world's population, there was vitamin D deficiency and 60% has its insufficiency. Even in countries where nutrition is fortified with vitamin D, 25(OH)D levels are less than 30 ng/ml in 70 % of children [8].

Vitamin D plays a key role in regulating calcium-phosphorus metabolism. Its deficiency interrupts the formation of peak bone mass, increasing the risk of osteoporosis. It has been proved that vitamin D directly or indirectly regulates about 1250 genes, performing so-called "extraskeletal" functions. Thus, vitamin D can affect the state of the musculoskeletal system, as well as a wide range of diseases, in particular, the cardiovascular, immune system, diabetes, obesity, etc. [10].

Vitamin D, or calciferol, is a group of lipid-soluble compounds that are formed of 7-dehydrocholesterol in the dermis of the skin under the influence of ultraviolet radiation with a wavelength of 290–315 nm. Vitamin D_3 or cholecalciferol is synthesized due to the photochemical reaction. The latter satisfies the needs of the body by 80 %. The remaining 20 % comes from food in the form of vitamin D_2 (ergocalciferol). Vitamin D_2 is formed in plants and mushrooms of ergosterol under the influence of sun rays. It is distinguished from the vitamin D_3 by a double bond between C22–C23 and a methyl group at the C24 level in the side chain. These differences reduce the affinity of D_2 to vitamin-D-binding protein (DBP), which leads to an increase in the concentration of free vitamin D [1, 3].

To become biologically active, vitamin D should be metabolized in the body. Regardless of the source, in the first stage, it is formed in the liver, under the influence of the enzyme 25-hydroxylase calcidiol

(25(OH) D) [10]. 85–90 % of calcidiol conjugates to DBP, the remaining 10–15 % to albumin and less than 1% remains free. Unconjugated calcidiol is able to penetrate through the membrane of cells of any organs, due to lipophilic properties. At that time only kidneys, parathyroid glands and placenta are able to absorb vitamin D conjugated to DBP by endocytosis due to the megalin/cubilin complex [3].

The next step is hydroxylation in the proximal sections of the renal tubules under the influence of 1-α-hydroxylase (CYP27B1), which converts 25(OH)D into 1.25 $(OH)_2D$, or calcitriol [5].

Today there are only a few publications on the level of 25(OH)D, as well as the prevalence of vitamin D deficiency and insufficiency among apparently healthy children and adolescents in Ukraine [12]. Also, the most significant risk factors influencing the formation of DV D and IV D have not been studied.

The purpose of the study was to assess the level of 25(OH)D in schoolchildren of Kyiv, to determine the frequency of its deficiency and insufficiency, and their correlation with season, obesity and sexual maturation.

Materials and methods. 87 children aged 8–17 (40 girls and 47 boys) were examined at school No.9 in Kyiv. The mean age of the examined children was 13.1±1.4; mean weight 52.12±12.64 kg; mean height – 1.60±0.14 m.

To determine the correlation of 25(OH)D level to the age, the examined children and adolescents were divided into the following age groups: Group I (n=21) schoolchildren aged 8–11, Group II (n=37) – 12–14 years old and Group III (n=29) – 15–17 years old (fig. 1).

This study did not include children who took vitamin D supplements over the past 6 months. The participants and their parents agreed to participate in the study, as well as the directorate of the educational institution. The protocol of the study was approved by the committees of bioethics of Shupyk National Medical Academy of Postgraduate Education and D.F. Chebotarev State Institute of Gerontology NAMS of Ukraine.

All schoolchildren were provided with a standard clinical examination, measurements of height and body weight. Body mass index (BMI) was determined by the Cattel's formula: body weight in kilograms divided by height in square meters (kg/m^2). BMI indices were accessed based on the tables developed by WHO for children and adolescents aged 5–19, separately for both gender [15]. BMI indices within 10 and 75 percentiles corresponded to the norm, between 75 and 95 – overweight, above 95 percentile – obesity, and indices below 10 percentile was regarded as thinness. The evaluation of sexual maturation was carried out according to Tanner's classification.

Parents of children filled out a questionnaire where they indicated the presence and localization of fractures in children, the cause and nature of their occurrence; the presence of concomitant diseases; medicine administration.

Determination of 25(OH)D level was carried out by electrochemiluminescent method with Elecsys 2010 (Roche Diagnostics, Germany), using cobas® test systems based on the D.F. Chebotarev State Institute of Gerontology NAMS of Ukraine. Venous blood draw for serum was held on an empty stomach in the morning.

The status of vitamin D was determined using the classification adopted by the International Institute of Medicine and the Committee of Endocrinologists for the development of Clinical Practice Guidelines in 2011. Vitamin D deficiency was established at 25(OH) D level in blood serum below 50 nmol/l or 20 ng/ml, and vitamin D deficiency was detected at 25(OH)D levels between 50–75 nmol/l or 21–30 ng/ml. Concentration of 25(OH)D from 75 to 125 nmol/l or 31–50 n/ml was considered as the optimal level of vitamin D.

Statistical analysis was carried out using the program Statistica 6.0. The normality of distribution was estimated according to the criteria of Shapiro-Wilk and Kolmogorov-Smirnov. Intergroup differences were evaluated using a one-way analysis of variance (ANOVA). The relationship between 25(OH)D with BMI and weight was determined using linear regression. Results were considered probable at $p<0.05$.

Results of the study and their discussion. According to the results of the study, the deficiency of 25(OH)D was detected in 41 % of the examined children, insufficiency – in 40 %, and only 19 % of healthy schoolchildren in the city of Kyiv had an optimal level. Their mean level of 25(OH)D was 22.9±9.5 ng/ml.

During the study, there was no significant difference in the 25(OH)D levels between schoolchildren of different age groups ($p=0.32$). Therefore, the age of the examined children and adolescents did not affect the status of vitamin D and was not a risk factor for the formation of its deficiency.

There was also no significant difference between the 25(OH)D level in children and adolescents, depending on gender. The mean level of 25(OH)D in boys was 24.4±1.5 ng/ml, and in girls – 21.4±1.5 ng/ml ($p=0.14$). In fig. 2 the results of the study of the incidence of vitamin D deficiency and insufficiency are presented, based on gender.

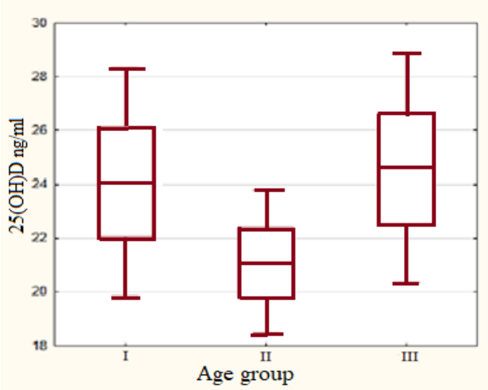

Fig. 1. 25(OH)D level depending on age group: Group I (8–11 years old); Group II (12–14 years old); Group III (15–17 years old)

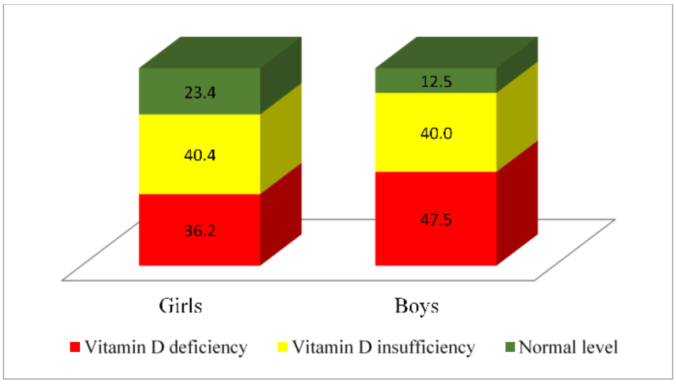

Fig. 2. The incidence of vitamin D deficiency and insufficiency based on gender, %

Today, one of the risk factors for vitamin D deficiency is overweight and obesity. In numerous studies it has been confirmed that the latter is associated with lower concentrations of 25(OH)D in serum [2]. Among the examined children, we found obesity in seven schoolchildren and overweight in nine schoolchildren. In the correlation analysis, there was no significant association between the 25(OH)D level and BMI (p=0.6), which may be due to a small sample and a low percentage of obese children. In determining the relationship between body mass and the level of 25(OH)D, no reliable link was also found (p=0.2).

We found that the lowest levels of 25(OH)D in children were observed at stage 3 of puberty according to the Tanner classification (19.6±8.8 ng/ml). The highest rates were observed in stage 1 of puberty – 26.9±8.7 ng/ml (p=0.02) (fig. 3). Schoolchildren in stage 3 of puberty had significantly lower levels of 25(OH)D not only in comparison with children in stage 1 (p=0.02), but also in stage 5 (p=0.04).

As the geographic latitudes where Ukraine is situated are favorable for the synthesis of vitamin D from the end of April to September, all examined were divided into two groups depending on the season of blood draw.

The period from May 1 to October 31 was defined as the summer season, and from November 1 to April 30 – as winter. In fig. 4 the results of studying the effect of the seasonal factor on the mean values of 25(OH)D level in the blood serum of the examined pupils are presented. It is likely that higher 25(OH)D values were observed in the summer period (27.3±1.8 ng/ml) compared with winter period (20.4±1.1 ng/ml) (F=12.3; p=0.0007).

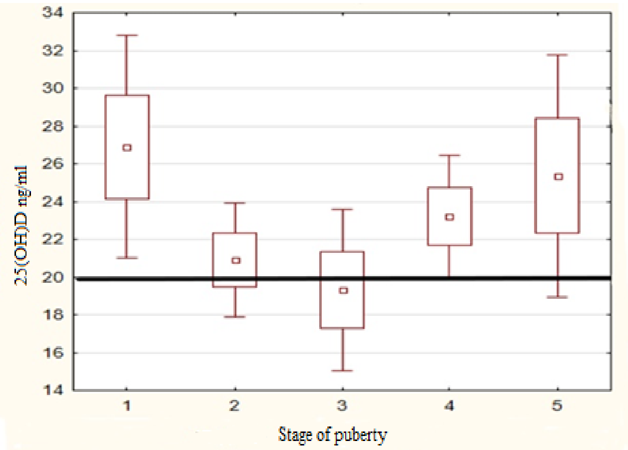

Fig. 3. 25(OH)D level depending on the stage of puberty
Note: The bold line separates a group of children with DV D

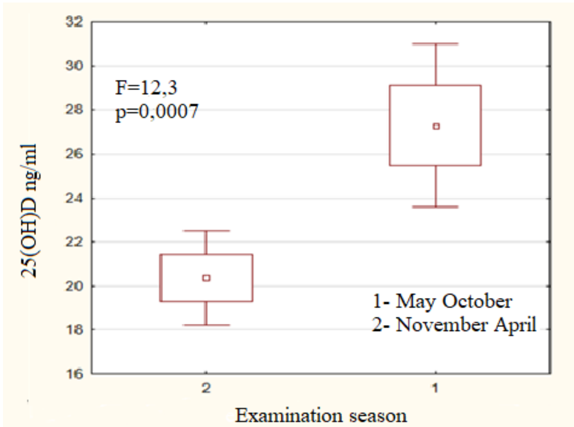

Fig. 4. Distribution of examined children depending on season and 25(OH)D level

In a recent study on the vitamin D status among children, the most vulnerable group from the European countries were adolescents. At the age of 15–18, DV D was found in 12.2–39.6 % of adolescents. For comparison, in other age groups this index ranged from 0.9 to 19.6 % [4]. However, in our study, we have not established the age-specific characteristics of the formation of DV D.

There is an undeniable relationship between obesity and a decrease in the concentration of 25(OH)D. In the study of Spanish children, there was a reciprocal relationship between BMI and 25(OH)D [2]. Also, the higher prevalence of DV25D was recorded in obese children (95.6 % vs. 66.7 % in children with normal body weight). The lack of a reliable link between BMI and vitamin D in our study was due to the small number of examined children with overweight and obesity.

Another significant factor that can affect 25(OH)D level is sexual maturation. Thus, in the study of children from Iran, it was found that the concentration of 25(OH)D decreases with an increase in the stage of puberty. In this case, the most frequently deficiency of vitamin D was found in adolescents with a stage 4–5 of puberty. Similar data were also obtained in obese children, where in the prepubertal period vitamin D deficiency was found to be 46 %, and in the puberty period it increased to 75 % [6].

A number of studies reported a significant effect of the season on the 25(OH)D level. While examining healthy children in Turkey, the prevalence of vitamin D deficiency was 93 % during spring and 71% in autumn period [9]. According to Shakeri H. (2017), only 48.5 % of children who at the end of summer had the optimal status of vitamin D, were able to support it by the end of the winter [13]. In a recent study, in 42 % of Danish children, DV D was detected in the winter, and only in 16% in the summer [7]. Differences in levels of vitamin D in this study may be explained by the fact that 32 % of children in Denmark, according to the study, received vitamin D during the year. In our study, no participant received vitamin D.

Lower levels of vitamin D may be due to lifestyle changes in adolescence. Namely, reducing physical activity and staying outside leads to a reduction in the synthesis of vitamin D in the skin.

Reduction of 25(OH)D in children may be a temporary phenomenon. Researchers from Johannesburg (South Africa) had been assessing the variability of 25(OH)D every 2 years for 10 years in healthy adolescents. They found that levels of 25(OH)D at the age of 11 and 13 did not correlate with its levels at the age of 15 and 17 [11]. However, the decrease of 25(OH)D level in our study coincides with the most distinct accumulation of bone mass. For girls this age is 11–14 years old, for boys – 13–17 years old.

Conclusions

1. Among schoolchildren in Kyiv, vitamin D deficiency was found to be in 41 %, insufficiency – in 40 %, optimal level – in 19 % of the examined.

2. The indices of 25(OH)D level among schoolchildren in Kiev in the winter period were 6.9 ng/ml (25.3 %) lower than in the summer.

3. Relatively lower levels of 25(OH)D are defined in stage 3 of puberty, at the same time in this period a puberty leap in the formation of the peak bone mass begins, which in its turn indicates the need for an active correction of vitamin D deficiency during this period of a child's formation.

4. Risk factors for the formation of vitamin D deficiency among schoolchildren in Kyiv, especially in the winter, require further study and development of appropriate correction.

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