Ada Borowiec[1], Monika Milczarek[1], Katarzyna Wyborska[1], Agata Cichal[1], *Anna M. Kucharska[2]

Assessment of vitamin D supplementation in the Warsaw's children after infancy – a preliminary study

Ocena suplementacji witaminą D u dzieci warszawskich po okresie niemowlęcym – badanie pilotażowe

[1]Student's Scientific Group of the Department of Pediatrics and Endocrinology, Medical University of Warsaw
Student's scientific group supervisor: Anna M. Kucharska, MD, PhD
[2]Department of Pediatrics and Endocrinology, Medical University of Warsaw
Head of Department: Beata Pyrżak, MD, PhD

Key words

vitamin D, supplementation, children, 25-hydroxyvitamin D level

Słowa kluczowe

witamina D, suplementacja, dzieci, poziom 25-hydroksywitaminy D

Summary

Introduction. An adequate concentration of blood 25-hydroxyvitamin D promotes pleiotropic actions of vitamin D.

Aim. The aim of the study was to assess the vitamin D status in the Warsaw's children after infancy. Study data were collected from records of children hospitalized in the Department of Pediatrics and Endocrinology in the period August-December 2012.

Material and methods. Study group included 257 children: 132 girls and 125 boys, mean age 10.44 ± 4.25 years. Serum 25-hydroxyvitamin D – 25(OH)D – concentrations were measured at hospitalization with Microparticles Chemiluminescence (Abbott, Wiesbaden, Germany). The study analysis included the correlations between 25(OH)D concentration and selected variables.

Results. Mean 25(OH)D concentration was estimated at 23.86 ± 7.96 ng/ml. Only 21.40% of children approximated values higher than 30 ng/ml. Prior vitamin D supplementation was provided to 38.13% of children. 159 children had no supplementation whatsoever, 64 children were supplemented at a dose of 500 IU and 34 children at a dose of 1000 IU. 25(OH)D concentration in children supplemented with vitamin D was significantly higher than in patients without supplementation ($p < 0.005$). A statistically significant difference was observed between mean 25(OH)D level in pubertal and pre-pubertal children ($p = 0.002$). The mean 25(OH)D concentration was significantly lower in obese children than in other patients ($p = 0.00001$).

Conclusions. According to our study data vitamin D dose of 500-1000 IU/d is required to maintain the current level in the blood. Few children receive vitamin D supplementation which favors the maintenance of adequate 25(OH)D concentration. During puberty as well as in obese children the requirement for vitamin D is higher.

Streszczenie

Wstęp. Zapewnienie optymalnego stężenia 25-hydroksywitaminy D w surowicy krwi jest niezbędne, aby ujawniło się plejotropowe działanie witaminy D.

Cel pracy. Celem pracy była ocena zaopatrzenia w witaminę D dzieci warszawskich, na podstawie analizy dzieci hospitalizowanych w Klinice Pediatrii i Endokrynologii w okresie od sierpnia do grudnia 2012 roku.

Materiał i metody. Grupę badaną stanowiło 257 dzieci: 132 dziewczynki i 125 chłopców, średni wiek wynosił 10,44 ± 4,25 roku. Do badania włączono dzieci, które w trakcie hospitalizacji miały oznaczony poziom 25-hydroksywitaminy D – 25(OH)D. Stężenie oznaczano metodą chemiluminescencji z użyciem mikrocząstek (Abbott, Wiesbaden, Niemcy). Na podstawie analizy dokumentacji pacjentów oceniano korelacje między stężeniem 25(OH)D a wybranymi parametrami.

Wyniki. Średnie stężenie 25(OH)D w surowicy w grupie badanej wynosiło 23,86 ± 7,96 ng/ml. Zaledwie 21,40% dzieci osiągnęło zalecane wartości referencyjne powyżej 30 ng/ml. Wcześniejszą suplementację otrzymywało 38,13% dzieci. Grupę badaną podzielono na trzy podgrupy według suplementacji witaminą D: 159 dzieci bez suplementacji, 64 dzieci przyjmujących 500 IU/d, 34 dzieci otrzymujących 1000 IU/d. Dzieci otrzymujące suplementację miały istotnie statystycznie wyższe stężenia 25(OH)D niż pacjenci

Address/adres:

*Anna M. Kucharska
Department of Pediatrics and Endocrinology
Medical University of Warsaw
ul. Marszałkowska 24, 00-576 Warszawa
tel./fax +48 (22) 621-46-17
anna.kucharska@litewska.edu.pl

bez suplementacji ($p < 0,005$). Wykazano różnicę istotnie statystyczną między średnim stężeniem 25(OH)D u dzieci przed dojrzewaniem oraz dojrzewających ($p = 0,002$). U dzieci z otyłością stężenie 25(OH)D było istotnie niższe w porównaniu do pozostałych pacjentów ($p = 0,00001$).

Wnioski. U większości dzieci grupy badanej poziom 25(OH)D w surowicy jest poniżej zalecanych wartości referencyjnych. Nieliczne dzieci mają suplementację witaminą D, pozwalającą na utrzymanie odpowiedniego stężenia 25(OH)D. Zapotrzebowanie na witaminę D jest wyższe w okresie dojrzewania oraz u dzieci otyłych.

INTRODUCTION

Numerous research studies of the last decades have revolutionized our perception of the role vitamin D in the human body. Apart from its well-known classic actions on musculoskeletal health, vitamin D has other pleiotropic effects (1): affects the immune system by reducing the number of respiratory infections (2, 3) minimizes the development of autoimmune diseases such as multiple sclerosis (4), diabetes type 1 (5), Crohn's disease (6), rheumatoid arthritis (7), systemic lupus erythematosus (8), asthma (9). Vitamin D also has a positive influence on the cardio-vascular system and endocrine system (10). Vitamin D deficiency impacts the prevalence of numerous common diseases such as hypertension, cardiovascular disease (11), diabetes (12) and several types of malignancies (13).

The main natural source of vitamin D is the skin (14). The most effective vitamin D synthesis is achieved when 35% of skin is exposed to summer sun at a daily dose of 90 minutes between 10 am and 3 pm local time (15). Vitamin D is also provided in food. The diet most rich in vitamin D consists of oily fish such as wild salmon, sardines, mackerel, as well as cod liver oil. In developed countries however changes of eating habits and rhythm of daily activity in school children have led to vitamin D deficiencies (16). School-age children spend most of their time indoors in classrooms and on indoor activities. Effective vitamin D cutaneous synthesis is therefore possible only during holidays. Moreover, in most countries regular vitamin D supplementation is provided only during infancy.

AIM

The aim of the study was to assess the vitamin D status in the Warsaw's children after infancy. Study data was collected from records of children hospitalized in the Department of Pediatrics and Endocrinology of the Medical University of Warsaw in the period August-December 2012.

MATERIAL AND METHODS

The study included 257 children: 132 girls (51.4%) and 125 boys (48.6%), mean age 10.44 ± 4.25 years. The study group comprised 63 pre-pubertal children (25 girls and 38 boys) and 186 children at puberty (102 girls and 84 boys). 3 boys with congenital adrenal hyperplasia and 5 girls with precocious puberty were not included to this analysis.

Children were hospitalized for infectious diseases (2.3%) and endocrine disorders: growth hormone deficiency (27.2%), short stature (23.4%), thyroid disease (12.8%), obesity (12.8%), precocious puberty (7.8%), type 1 diabetes (5.0%), multiple pituitary hormone deficiency (3.5%), Turner's syndrome (3.50%). Other grounds for hospitalization (8.2%) included individual characteristics/ailments such as headaches, stomach aches and syncope. Patients on steroid therapy were excluded from the study.

This retrospective analysis included records of patients hospitalized in the clinic in the period 1st August-31st December 2012 with determined serum 25-hydroxyvitamin D (25(OH)D) levels. Serum 25-hydroxyvitamin D concentration was measured by Chemiluminescence Microparticle Immunoassay (Abbott, Wiesbaden, Germany). Subsequent assessment of vitamin D status was performed according to the classification guidelines for Central Europe 2013, which define the sufficient 25-hydroxyvitamin D concentration as higher than 30 ng/ml, insufficient as 20-30 ng/ml and deficient as below 20 ng/ml (15).

Statistical analysis was performed to determine the relationship of 25(OH)D concentration to age, sex, vitamin D supplementation, puberty status, type of diagnosis, and the month when blood tests was made. Inter-group differences were compared with the T-Student test. A two-tailed 0.05 significance level was considered. Evaluation of correlation was performed using the Spearman test.

RESULTS

Mean 25(OH)D serum concentration for the study group was estimated at 23.86 ± 7.96 ng/ml. Only 21.40% ($n = 55$) of children reached the > 30 ng/ml level which is optimal for 25(OH)D. 43.97% of children had insufficient concentration levels of 25(OH)D and for 34.63% ($n = 89$) the level was deficient (tab. 1). Only 38.13% of children had prior vitamin D supplementation. The study group was divided into three subgroups according to vitamin D supplementation. Subgroup 1 included 159 (61.87%) children with no supplementation, subgroup 2 included 64 (24.90%) children with vitamin D supplementation at a daily dose of 500 IU and subgroup 3 included 34 (13.23%) children with supplementation at a daily dose of 1000 IU (tab. 2). Mean 25(OH)D level in subgroup 1 was 22.48 ± 8.13 ng/ml, in subgroup 2 it was 25.30 ± 5.99 ng/ml and in subgroup 3 it was 27.61 ± 8.91 ng/ml. We observed statistically significant differences between subgroup 2 and subgroup 1 as well as between subgroup 3

and subgroup 1. The highest percentage of children (44.65%, n = 71) with vitamin D deficiency was in subgroup 1, a considerably lower percentage was observed in subgroup 2 (20.31%) and subgroup 3 (14.71%). The highest number of results approximating optimal 25(OH)D level (> 30 ng/ml) were reported for subgroup 3 (32.35%) and there was only a slight difference between subgroup 2 and subgroup 1 (20.31 and 19.50% respectively) (fig. 1).

Table 1. The percentage of children with deficient, insufficient and sufficient 25(OH)D serum concentration.

Serum 25(OH)D concentration	Deficient: < 20 ng/ml	Insufficient: 20-30 ng/ml	Sufficient: ≥ 30 ng/ml
Percentage of children	34.63%	43.97%	21.40%

Table 2. The percentage of children with additional vitamin D supplementation.

Supplementation	Without	500 IU/day	1000 IU/day
Percent of children	61.87%	24.9%	13.23%

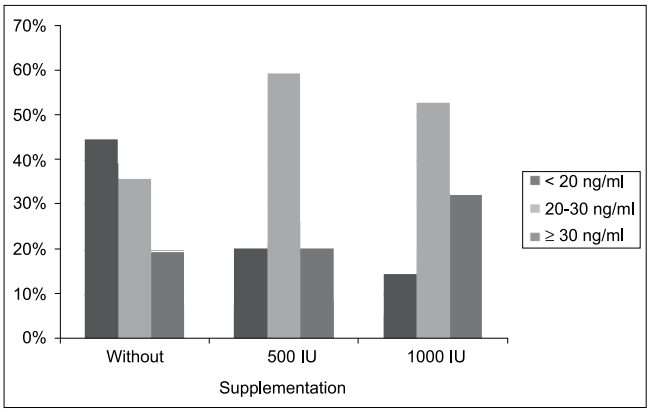

Fig. 1. Vitamin D status in subgroups: without supplementation, at a dose of 500 IU and at a dose of 1000 IU per day.

Mean 25(OH)D concentration was similar among girls (23.36 ± 8.12 ng/ml) and boys (24.39 ± 7.8 ng/ml). The 25(OH)D concentration was significantly lower for pubertal age children than for children at pre-pubertal age: 22.99 ± 7.84 ng/ml vs 26.68 ± 7.99 ng/ml respectively (p = 0.002). In subgroup 2 the 25(OH)D concentration was negatively correlated with age (r = -0.47, p < 0.05). Significantly lower 25(OH)D concentration values were observed in children with obesity than in children with other diagnoses: 18.96 ± 5.94 ng/ml vs 24.58 ± 7.98 ng/ml, respectively (p = 0.00001).

During the study period the mean 25(OH)D concentration values did not exceed 30 ng/ml regardless of the month. The lowest mean 25(OH)D level was noted in December 19.50 ± 7.00 ng/ml, it was slightly higher in October (21.50 ± 6.42 ng/ml) and November (21.12 ± 7.08 ng/ml). Markedly higher mean 25(OH)D levels were observed for September 28.86 ± 7.93 ng/ml and August 28.06 ± 6.93 ng/ml (fig. 2). The differences in mean 25(OH)D values for individual months were not statistically significant.

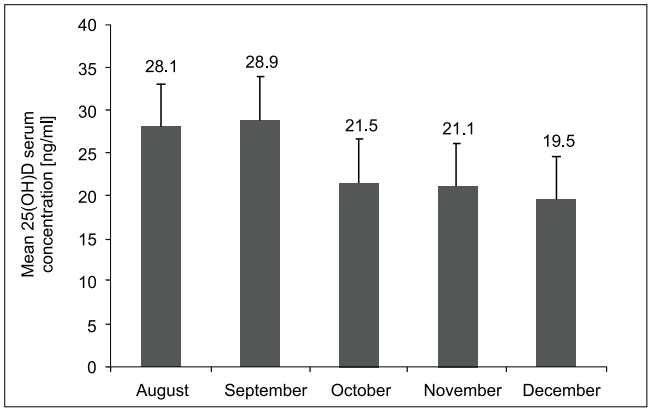

Fig. 2. Mean serum 25-hydroxyvitamin D concentrations by months.

DISCUSSION

The results demonstrated that most children of our study children had either vitamin D deficiency or an insufficient level of vitamin D. This may prove that a typical urban habitat negatively affects the natural production of vitamin D. What is responsible for this phenomenon? The main source of vitamin D is skin synthesis under UVB radiation (wavelength of 290-315 nm) which usually occurs in the first 30 minutes of exposure. Unfortunately, to reduce the risk of skin damage and skin cancer, it is necessary to use protection against UV radiation. When the amount of UVB radiation is reduced by sunscreen use, the skin blocks the main source of vitamin D synthesis. Moreover, nowadays the lifestyle of children does not favor exposure to sun-light in the most beneficial time of the day (from 10 am and 3 pm). At the time children are usually indoors watching television or spending their free time in front of the computer screen. The use of computer for more than 3-4 hours a day is a significant predictor of vitamin D deficiency (11). Several papers describe the effect of widespread use of sunscreen on vitamin D synthesis. In a study performed by Matsuoka et al. (17), the authors observed that whole-body coverage with sunscreen prevents vitamin D synthesis, while higher levels of vitamin D_3 were detected when more than 19% of the total body surface was left with no sunscreen. In a different study, Holick et al. demonstrated a 90% reduction in cutaneous vitamin D production, measured as serum 25(OH)D levels following daily application of sunscreen with SPF 8 on sun-exposed areas (18, 19). Similar results were described by Faurschou et al. (20). On the other hand there are studies which demonstrate that frequent use of sunscreen does not reduce vitamin D production dependent on sufficient amount of exposure to sunlight. In a 1995 study with 113 Australian subjects who used either SPF 17 sunscreen or placebo cream Marks et al. (21) observed a similar increase in 25(OH)D level in both groups. However, when all the aforementioned studies

are considered we may arrive at a conclusion that sunscreens do affect natural skin production of vitamin D, the inhibition of which is related to the area of skin covered with SPF and the value of SPF.

Contemporary diet cannot be considered a rich source of vitamin D. Daily intake of cheese (20 IU/100 g) (22), eggs (20 IU/yolk) (14) and cereal (40 IU/serving) is no substitute for oily fish, the consumption of which is still low. It is therefore recommended to rely on pharmaceutical supplementation. We should however be aware that unconditional supplementation all the year long is recommended only for infants (15). For older children pharmaceutical supplementation is recommended September to April provided cutaneous synthesis of vitamin D during summertime is sufficient. Our study demonstrates that prophylaxis of vitamin D deficiency in older children is not continued on regular basis, as almost 2/3 of children were left with no supplementation whatsoever. Post infancy changes that involve lower intake of fortified milk also contribute to decreased supply of vitamin D (11). An important issue considered by Au et al. (23) is the dependence on the use of vitamin D supplements. In a randomized trial, the authors demonstrated that parents and patients adherence was negatively associated with parents' belief that vitamin D is important for strength or energy (23).

As vitamin D is responsible for many pleiotropic actions in the human body, its deficiency may provoke susceptibility to infections (24) as well as other diseases (25, 26). In our study, we found that only obesity was associated with the deficient state of vitamin D. The differences in 25(OH)D concentrations between obese children and those with other diagnosis were not significant.

As vitamin D is fat-soluble its higher uptake by adipose tissue in obese patients increases the requirement for this vitamin. The obese patients may also avoid exposition to sun which limits photosynthesis of vitamin D. The study by Wortsman et al. included 19 healthy normal-weight subjects (BMI = < 25 kg/m^2) and 19 healthy obese subjects (BMI > 30 kg/m^2). Each group was treated with the same dose of UVB radiation (wavelength 290-320 nm). Blood samples were taken before and 24 hours after exposure. The body surface of obese subjects was larger so they were expected to have higher serum levels of vitamin D_3. The study demonstrated however similar basal concentration of vitamin D, significant increase in both groups and also significant difference between the responses of each group. It is likely that subcutaneous fat stores vitamin D_3, and the obese persons have better developed adipose tissue. Another study focused on the response to an oral challenge with vitamin D_2 (50 000 IU of ergocalciferol). Samples were taken 6, 10 and 24 hours after the intake of vitamin D_2. 25(OH)D levels were significantly lower in the obese than in the control subjects. Moreover, the higher BMI, the lower blood peak of vitamin D concentration. This may justify the conclusion that oral intake of vitamin D can correct vitamin D deficiency in obese patients but the doses must be larger than usual (27).

The vitamin D intake of at least 600 IU/d in children aged 1 to 18 years (28) as recommended by guidelines is sufficient to maximize bone health. However, to maintain the 25(OH)D blood level of > 30 ng/ml and provide all potential non-calcemic actions of vitamin D higher doses of 1000 IU/d may be required (29). In our study the difference between mean 25(OH)D concentration in subgroup 2 and 3 was not statistically significant so no superiority of higher supplementation was demonstrated in maintaining stable 25(OH)D level. Vitamin D intake should be also adjusted to phase of puberty. Studies describe a high prevalence of vitamin D insufficiency among healthy adolescents (30, 31) and in our analysis we observed considerably lower 25(OH)D concentrations in pubertal-age children. The results suggest that during pubertal growth spurt higher supplementation doses should be considered.

CONCLUSIONS

According to our study data vitamin D dose of 500-1000 IU/d is required to maintain the current level in the blood. Few children receive vitamin D supplementation which favors the maintenance of adequate 25(OH)D concentration. During puberty as well as in obese children the requirement for vitamin D is higher.

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