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Vitamin D supplementation in theory and daily practice – implementation of new updated Polish recommendations on the example of one pediatric centre

Suplementacja witaminy D w teorii i codziennej praktyce – wprowadzanie nowych, zaktualizowanych polskich zaleceń na przykładzie jednego ośrodka pediatrycznego

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Abstract

Introduction: According to updated evidence-based national recommendations which have been published recently vitamin D deficiency remains still highly prevalent in Poland and requires supplementation.

Aim of the study was to evaluate the effectiveness of implementation of the new national recommendations into daily practice.

Material and methods: An analysis of medical records of 100 children aged from 6 months to 14 years admitted to the Department of Pediatrics, Hospital in Brzesko, Lesser Poland, from 1st July 2018 to 31st August 2018.

Results: 41% patients declared vitamin D supplementation. Among patients under 1 year of age 3 (60%) received recommended supplementation of 400-600 IU daily, in the group of 1-11 years old 15 (19.5%) used a 600-1000 IU dose daily, 13 (17%) < 600 IU/daily, and 2 (2.5%) > 1000 IU daily, 1 patient did not remember the dose. In the group >11 years of age 6 (37.5%) supplemented 800-2000 IU/day, 1 (6.3%) less than 800 IU, no one overdosed supplementation. In the group without supplementation, there were 3 patients with a decreased 25(OH)D blood serum level (< 20 ng/ml). Mean 25(OH)D serum level was significantly higher in the group with vitamin D supplementation (42 vs. 33.9 ng/ml; $p = 0.0006$). There was no significant difference between mean 25(OH)D level in patients receiving adequate (40.5 ng/ml), to low (43 ng/ml), or to high vitamin D doses (49 ng/ml). There was no significant correlation between vitamin D dose and the 25(OH)D serum level [R = (–) 0.24, $p > 0.05$)].

Conclusions: There is an urgent need for physicians to provide an education concerning general rules of vitamin D supplementation, because the present guidelines of the vitamin D supplementation are not implemented well enough.

Key words:
vitamin D, children.

Streszczenie

Wprowadzenie: Zgodnie z opublikowanymi ostatnio polskimi, opartymi na dowodach naukowych, zaleceniami niedobór witaminy D występuje powszechnie i konieczna jest jej suplementacja.

Cel pracy: Realizacja nowych polskich zaleceń w codziennej praktyce.

Materia i metody: Analizie poddano dokumentację medyczną 100 pacjentów w wieku od 6 miesięcy do 14 lat hospitalizowanych na Oddziale Dziecięcym Szpitala w Brzesku w Małopolsce w okresie od 1 lipca 2018 r. do 31 sierpnia 2018 r.

Wyniki: Suplementację witaminy D zadeklarowało 41% pacjentów. Wśród pacjentów poniżej 1. roku życia 3 (60%) otrzymywało rekomendowaną dawkę suplementacyjną, tj. 400–600 IU dziennie. W grupie 1–11 lat 15 pacjentów (19,5%) stosowało rekomendowaną dawkę 600–1000 IU dziennie, 13 (17%) < 600 IU dziennie i 2 (2,5%) > 1000 IU dziennie, w przypadku 1 pacjenta nie udało się ustalić dawki. W grupie > 11 lat 6 pacjentów (37,5%) stosowało dawkę 800–2000 IU dziennie, 1 (6,3%) mniej niż 800 IU, nikt nie stosował dawki większej niż rekomendowana. U 3 osób spośród niestosujących suplementacji stwierdzono zmniejszone stężenie 25(OH)D w surowicy krwi (< 20 ng/ml). Średnie stężenie 25(OH)D w surowicy był istotnie większe w grupie stosującej suplementację (42 *vs* 33,9 ng/ml; $p = 0,0006$). Nie stwierdzono natomiast istotnej różnicy między średnim stężeniem 25(OH)D u pacjentów otrzymujących dawkę rekomendowaną (40,5 ng/ml), w porównaniu z przyjmującymi mniejszą (43 ng/ml) lub większą (49 ng/ml) dawkę niż zalecana. Nie stwierdzono istotnej korelacji między dawką witaminy D a stężeniem 25(OH)D w surowicy [R = (–) 0,24; $p > 0,05$)].

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Wnioski: Istnieje pilna potrzeba wprowadzenia właściwej edukacji pacjentów w zakresie zasad suplementacji witaminy D na poziomie podstawowej opieki zdrowotnej, ponieważ obecnie codzienna praktyka znacząco odbiega od zaleceń ekspertów.
Słowa kluczowe:
witamina D, dzieci.

Introduction

The problem of vitamin D deficiency has been one of the most frequently emerging topics in medical literature in recent years. Historically, vitamin D was connected with the recognition of a new childhood bone disease named rickets by Francis Glisson in 1650 [1]. The first report linking rickets with lack of sunlight was published by Śniadecki in 1822, and soon liver cod oil became an antirachitic medication [1]. It seemed to be the first model of vitamin D supplementation, although the process of transformation of 7-dehydrocholesterol via ultra-violet irradiation in the skin was discovered a hundred years later [2]. These discoveries, and subsequent food fortification with vitamin D reduced significantly rickets incidence rate in Europe and North America [1, 3]. In recent years, an active form of vitamin D [calcitriol, 1,25-dihydroxycholecalciferol (1,25(OH)2D)], has proved not only to be an important element of calcium level regulation, but also a hormone with a huge impact on the functioning of the entire body. Calcitriol acts as a transcription factor but it also impacts on many tissues in a "non classical way" using nuclear (VDR) and membrane receptors (MARRS), and regulates cellular proliferation and apoptosis. [2, 4-6]. Many studies showed that vitamin deficiency may be associated with an increased risk of cancer, diabetes, cardio-pulmonary diseases, metabolic and autoimmune disorders and even infections and mental illness [2]. This information became more significant, considering that vitamin D deficiency can affect as many as 70% of adults, children and adolescents in Poland [7, 8] Therefore, vitamin D supplementation has become an important issue in public health. Consequently, many recommendations concerning supplementation have been published over the recent years by the scientific society all over the world. Recently, new and updated guidelines were published in 2018 for the general population in Poland and for groups at risk of vitamin D deficiency. It has been generally recommended that prophylactic dosing of vitamin D in the general population should be individualized depending on age, body weight, isolation (season, time of year), sun exposure of an individual, dietary habits and lifestyle. For healthy neonates and infants (0-6 months): 400 IU/day from the first days of life, regardless of the method of feeding. For infants 6-12 months: 400-600 IU/day, depending on the daily amount of vitamin D taken with food. For children (1-10 years) 600-1000 IU/day, and for adolescents (11-18 years) 800-2000 IU/day based on body weight and the dietary vitamin D intake, except for healthy children and adolescents sunbathing with uncovered forearms and legs for at least 15 min between 10.00 a.m. and 3 p.m., without sunscreen, in the period from May to September. In this last group, supplementation is not necessary, although still recommended and safe [5, 9, 10]. In order to evaluate patients' vitamin D status, the guidelines recommend using the serum 25(OH)D level [11, 12]. According to the present guidelines, the optimal level of 25(OH)D is defined as 30-50 ng/ml. Deficiency is a clinical syndrome defined as a 25(OH)D serum level < 20 ng/ml, and insufficiency as a 21-29 ng/ml. Both of these clinical statuses are recommended for 25(OH)D treatment or supplementation, respectively [4, 5].

The aim of the present study was to evaluate the effectiveness of implementation of these new national recommendations into daily practice on the example of one paediatric centre.

Material and methods

This retrospective analysis included the medical records of 100 children aged from 6 months to 14 years admitted to the Department of Pediatrics, Hospital in Brzesko, Lesser Poland, from 1st July 2018 to 31st August 2018. All analyzed patients were living in the district of Brzesko which, according to the Central Statistical Office data, has 15 325 inhabitants under 14 years old. The analyzed probe contained 0.6% of the total population. No one was admitted due to vitamin D deficiency, nor calcium-phosphorus metabolism disorders. Most of the patients were admitted due to respiratory and gastrointestinal infections or the suspicion of allergy. Calcium, phosphorus and 25(OH)D levels in blood were measured on admission, using the immunochemistry method (ECLIA) with a Cobas e411 machine (Roche Diagnostics GmbH, Mannheim, Germany). Data from the patients' medical history included: date of birth, date of hospital admission, presence of concomitant chronic diseases and medications, 25(OH)D serum level, vitamin D supplementation details: dose and form. Based on reported data, children were classified into two main groups: with and without supplementation of vitamin D. Additional subanalyses considering dosage and the type of preparation used were performed as well. To compare two sets of data, the t-Student test was employed for independent samples, and in case of absence of normal data distribution – a two-sided Mann-Whitney U test. To compare more than two groups, the variance analysis and post hoc tests were used.

Spearman's Rank-Order Correlation was used to measure the strength of association between pairs of variables. Calculations were performed using the STATISTICA 13 software.

Results

Even though the study included summer months (July and August) only, in which according to the guidelines, supplementation is not necessary except the first year of life, 41/100 (41%) of patients received vitamin D. Fourteen of them used medications: 5 used a prescription drug, and 9 an over-the-counter (OTC)

drug; 11 used various diet supplements containing vitamin D only, 7 complex diet supplements, 1 patient used a medication not registered in Poland, 8 did not remember the drug's name and dose (Fig. 1). The group included 3/5 (60%) patients under 1 year with the recommended supplementation of 400-600 IU daily. In the older group of patients between 1-11 years, 15/76 (19.5%) used a dose of 600-1000 IU daily, 13/76 (17%) < 600 IU/daily, and 2/76 (2.5%) > 1000 IU daily, 1/76 patient did not remember the dose. In the adolescents over > 11 years 6/16 (37.5%) supplemented 800-2000IU/day, 1/16 (6.3%) less than 800 IU, no one overdosed supplementation (Fig. 2). In the group of patients with decelerated 25(OH)D supplementation, there was no case of with vitamin D deficiency defined as a 25(OH)D serum level < 20 ng/ml. In the group without supplementation, there were 3 patients with decreased vitamin D blood serum level, but clinically asymptomatic. There was no significant difference between mean 25(OH)D level in patients receiving drugs or medical supplements (41.6 vs. 43.7 ng/ml; $p > 0.05$). There was no significant difference between mean 25(OH)D level in patients receiving drugs and diet supplements (Fig. 3). There was no significant difference between mean 25(OH)D level in patients receiving adequate (40.5 ng/ml), to low (43 ng/ml), or to high vitamin D doses (49 ng/ml) (Fig. 4).

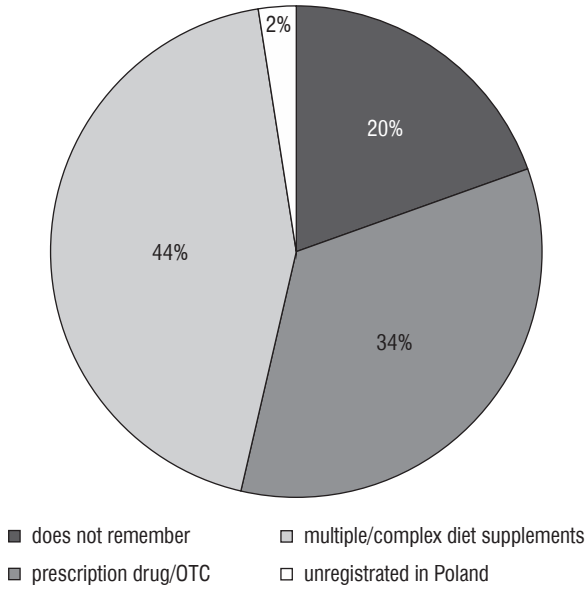

Figure 1. Structure of the types of preparations used containing vitamin D

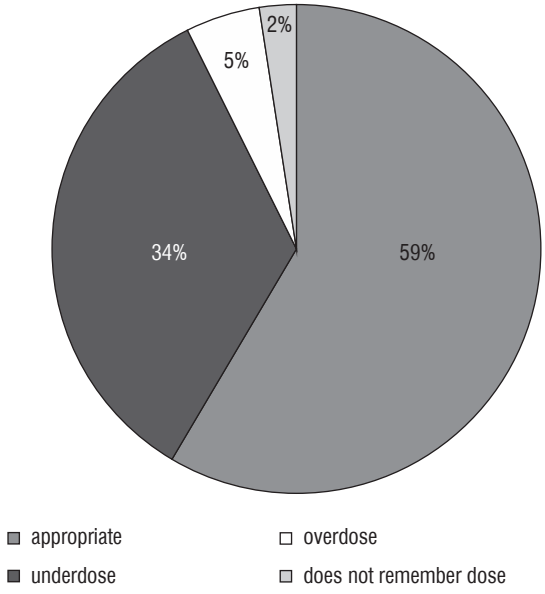

Figure 2. Vitamin D supplementation in the studied group in relation to current recommendations

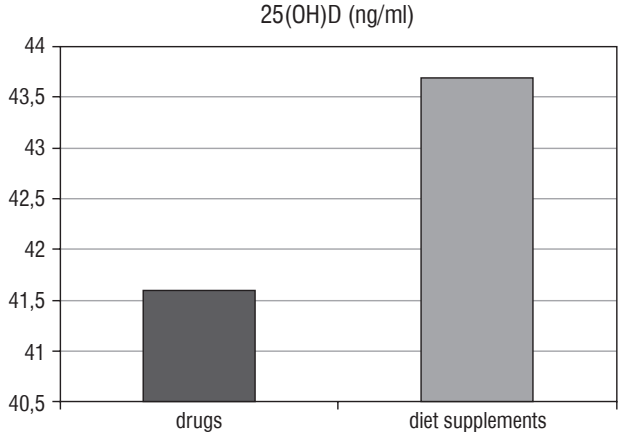

Figure 3. Comparison of the 25(OH)D levels between patients using drugs and diet supplements. The difference was not statistically significant ($p > 0.05$)

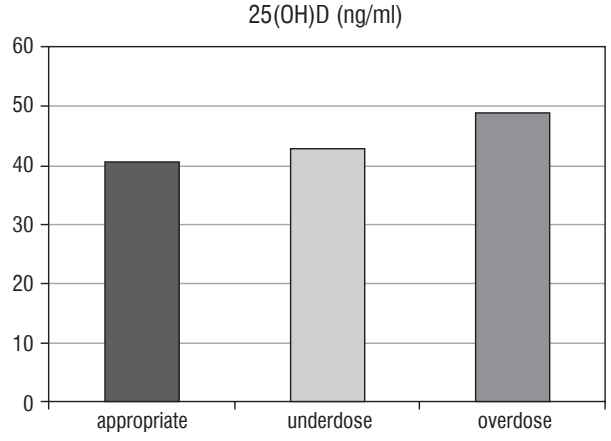

Figure 4. Comparison of the 25(OH)D levels between patients using different doses of vitamin D. The difference was not statistically significant ($p > 0.05$)

There was no significant correlation between the supplemented vitamin D dose, and 25(OH)D serum level [R = (–) 0.24, $p > 0.05$)]. Mean 25(OH)D serum level was significantly higher in the group of children with declared vitamin D supplementation (42 vs. 33.9 ng/ml; $p = 0.0006$) (Fig. 4).

Discussion

Vitamin D is a group of fat-soluble steroids responsible for intestinal absorption and skeletal mobilization of calcium, magnesium, and phosphate. In addition to this classic role, vitamin D and its metabolites also have pleiotropic effects, as evidenced by numerous studies published in recent years [1, 4]. The main two forms of Vitamin D are cholecalciferol (D_3) and the less potent ergocalciferol (D2). Cholecalciferol can be synthesized in the skin through a reaction dependent on UV radiation. This natural skin production in exposure to sunlight remains the major source of 25(OH)D. However, skin synthesis is affected by such factors as: geographic region, season of the year, day time, air pollution, exposed skin area and skin tone [1, 10, 13]. Another important limitation is also the use of sunscreen (SPF over 15) that reduces natural vitamin D skin synthesis to 1-5%. Sedentary life style and limitation of natural physical activity outside is even more problematic. According to the statistics, a quarter of children in the European Union lead a sedentary lifestyle, spend more time indoors and have an unhealthy diet [5, 13]. Both (D_3 and D_2) can be also ingested from the diet and from supplements [7, 8, 10]. Because only few foods naturally contain vitamin D, fish and fish liver oil became the main food 25(OH)D source [4]. It is estimated that a balanced, healthy diet can cover no more than 20% of the daily vitamin D demand. The UK Food Standards Agency assay that daily food vitamin D intake is less effective that sunlight related skin synthesis [14, 15]. Łupińska assessed factors afering serum vitamin D status in schoolchildren from Łodź and noted that food with high vitamin D concentration has no significant influence on serum 25(OH)D level. What is more, according to common vitamin D insufficiency in diet only 5% children had optimal daily vitamin D intake [16]. Therefore, some countries (ex. USA and Canada) already fortify daily food products such as bread, cereals, yogurts and cheese with vitamin D, while in Europe some Scandinavian countries fortify milk [4]. Unfortunately these actions seem to remain insufficient, because as it has been suggested in previously published papers the consumption of milk is decreasing. Furthermore, children now spend less and less time outdoors. Thus, the skin synthesis of vitamin D is reduced [4]. A Scandinavian study assessed food fortification as an alternative for supplements by milk-based vitamin D supplementation dose in order to gain sufficient 25(OH)D concentration in children with fair and dark skin in the southern and northern parts of Sweden. In that study, the daily intake of 6-20 μg/day (fair skin) and 14-28 μg/day (dark skin) was sufficient to maintain concentration 20 ng/ml [17]. Similar studies conducted in Denmark and in Canada emphasized the need for food fortification [18, 19]. Therefore, there is a need of additional vitamin D supplementation at the population level in developed countries [20-22]. In recent years, many guidelines and recommendations of vitamin D supplementation have been published. Recent Polish guidelines by Rusińska *et al*. were published this year [4, 5, 7, 8]. Although recommendations are general and common in their nature, the knowledge and application at the population level seems to be insufficient as yet [11]. Our present study was dedicated to the assessment of the vitamin D supplementation practices in one paediatric centre. We chose a sample of the local population (0.6%) for the analysis. The strength of such selection is the homogenous structure of the investigated group. All of the participants and their parents lived in the same, limited geographic area, and presented a similar socioeconomic status and educational level. Limitation of the duration time to the two summer months only allowed us to eliminate the potential impact of sun exposure on the 25(OH)D levels. The main weakness of the study is the fact that the sample was not random, but selected from the patients admitted to the hospital, although we excluded participants with the presence or suspicion of calcium-phosphorus disorders or treated with medications that may impact on vitamin D metabolism. The results of the present study show that almost half of the participants received vitamin D containing drugs or diet supplements. We did not identify any patient with vitamin D deficiency in the group receiving supplementation, but there were 3 individuals with 25(OH) D level < 20 ng/ml in the group without supplementation. However, patients did not demonstrate any symptoms of vitamin D deficiency this observation confirms that the use of vitamin D may be beneficial also during the summer, which has been clearly articulated in the new national recommendations. The former recommendations of vitamin D supplementation in the summer period not being necessary was based on the fact that exposure to sunlight allows skin synthesis from 7-dehydrocholesterol to previtamin D by a photochemical, non-enzimatic process using UVB lights with wavelengths between 270 and 300 nm, with a peak between 295 and 297 nm. In a few hours, using thermal energy, previtamin D becomes cholecalciferol (vitamin D3), which is transported with proteins to the liver. The liver is the first step of vitamin D activation using 25-hydroxylase from cytochrome 450. The second step is the kidneys, where 25(OH)D under 1α-hydroxylase (CYP27B1) becomes 1,25-dihydroxycholecalciferol – calcitriol. 1,25(OH)D is the only active form of vitamin D [1, 4, 5]. Even though the mean level of 25(OH)D was significantly higher in patients receiving vitamin D supplementation, there was no case of going over the limit of the range. That confirms that oral supplementation of vitamin D is rather safe, even in case of use incompatible with what is recommended. Nevertheless, it is still interesting why patients are failing to comply with recommendations. Is it only a health-care professional issue? Some hint may be found in the analysis of the stricture of used preparations containing vitamin D. Only 5 participants received a prescription drug, but only 1 under 1 year of age. The remaining group of 36 people declaring regular supplementation used OTC drugs (no one < 1 year) or diet supplements, one used a supplement which was not even registered in Poland. These results show clearly that vitamin D supplementation in the investigated group is not only incompatible with the present guidelines, but probably out of control of the physicians. This seems to be a consequence of the fact, that vitamin D deficiency

prevention is not a medical problem any more, but a life style issue as well. The awareness of vitamin D supplementation in parents in Poland seems to be sufficient. Nevertheless, the way it is conducted raises concern, which has been confirmed by the results of the present study. Therefore, it is necessary to put an emphasis on the education provided by physicians. There is a significant role of primary care physician in the implementation of the guidelines in the population [2, 4, 11]. Also it would be worth considering conducting similar study assessing if realization recent guidelines may affect on patients compliance measured by reduction vitamin D deficiency in population in future years.

Conclusions

The present guidelines of the vitamin D supplementation are not implemented well enough. Oral supplementation of vitamin D with the daily dose of 200-2000 IU in children and adolescents even in the summer does not cause an increase of the 25(OH)D level above the upper limit of the range. There is an urgent need for education to be provided by physicians concerning general rules of vitamin D supplementation.

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