Vitamin D Deficiency in Children Despite Correctly Applied Rickets Prophylaxis

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Vitamin D is essential for calcium absorption and for maintaining bone health in the pediatric population. We conducted a retrospective study to establish the profile of a child aged under 3 years old with vitamin D deficiency in the context of correct prophylaxis, on a cohort of 49 children from two general practitioner offices. From the study group 30.6% of children (15 cases) had low vitamin D levels. The mean serum 25(OH)D level was 41.5±16.6 ng/ml. Regarding nutrition in the first year of life, breastfeeding predominated (83.7% of patients), and only 8.16% of patients had clinical signs of rickets. So, low serum levels of vitamin D can also be found in children who have successfully received correct prophylaxis with vitamin D.

Keywords: vitamin D, children, rickets

Current epidemiological data shows that vitamin D deficiency is a real public health problem and occurs in different age groups, from different geographical areas, from rural or urban areas, with varied socio-economic status [1,2]. The EMAS guide showed that in Europe the suboptimal level of vitamin D is found in about 70% of the population, distributed as follows: 35% - insufficiency, 25% - mild and moderate deficiency and 10% - severe deficit [3].

Despite its name, vitamin D is a steroid hormone, classically known for its important role in regulation of calcium and phosphate metabolism. Nowadays, it is well known that the vitamin D has a broad range of actions in the human body: cardiovascular homeostasis, nervous function, immunomodulatory and antiproliferative role [4-6]. The main causes that lead to vitamin D deficiency are insufficient exposure to sunlight, consumption of low vitamin D foods, absence of prophylaxis in risk groups, absorption disorders, increased needs or increased losses of vitamin D [7].

The objectives of the study were to establish the profile of a child aged under 3 years old with vitamin D deficiency in the context of correct rickets prophylaxis.

Experimental part

Material and methods

The authors presented the results of a retrospective study realized between January 2018 - September 2019 in two general practitioner offices from Iași. In this study, the authors evaluated the serum levels of vitamin D (25-hydroxyvitamin D or 25(OH)D) of 49 infants and toddlers between 3-36 months old. Only children who received correctly rickets prophylaxis were included in the study: the vitamin D dose ranging from 400 to 1600 IU/day was administered daily for children from birth to 18 months and only in the cold season (September-April) in children between 18 and 36 months. Children with chronic conditions (malabsorption syndromes, who received chronic treatment) were excluded from the study. The following parameters were evaluated: nutrition in the first months of life (breastfeeding or milk formula), the season of birth (sun exposure), family eating habits (vegetarian or vegan diet). The complete physical examination was performed on all children to assess the rate of growth (weight, waist), weight index or body mass index, muscle tone and anterior fontanel

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size, as well as the presence of clinical signs of rickets. 25(OH)D level and phospho-calcium metabolism (alkaline phosphatase, phosphorus, and total and ionized calcium) were evaluated in all children. Vitamin D status according to 25(OH)D concentration was defined as: deficiency < 30 ng/ml, sufficiency between 30-100 ng/ml, toxicity >100 ng/ml. All chlidren received only supplements containing vitamin D_3.

Continuous variables were presented as mean±standard deviation and categorical variables as frequency and percentage. Kruskal-Wallis and the Mann–Whitney U test for variables without normal distribution. The association between the analyzed variables was performed with the Pearson correlation test, based on the correlation coefficient value and the significance level. The level of statistical significance was defined as P<0.05. Data was analyzed with the SPSS Software Version 24.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results and discussions

The demographic and anamnesic data of the patients are shown in table I. We observed an equal distribution of patients by gender. Regarding nutrition in the first year of life, breastfeeding predominated (83.7% of patients), and only 8.16% of patients had clinical signs of rickets.

Table 1
THE DESCRIPTIVE CHARACTERISTICS OF THE STUDY LOT

	n (%)
Gender (F/M)	24 (48.98 %)25 (51.02%)
Distribution by age groups 0-12 months 13-24 months 24-36 months	 10(20.4%) 20 (40.8% 19 (38.7%)
Nutrition in the first year of life Breastfeeding / milk formula	 41 (83.7 %)/8 (16.3 %)
Anterior fontanel Open/closed	 21/28 (42.9% / 57.1%)
25(OH)D (ng/ml)	41.5±16.6* 95%CI for mean:36.7-46.2
Alkaline phosphatase (mg%)	335.3±174.4* 95%CI for mean: 270.2-400.5
Clinical signs of rickets (absent / present)	45/4 (91.84% / 8.16%)
Vit. D dose: 400/800/1200/1600	12/22/11/4 (24.5%/44.8%/22.5%/8.2%)

**mean±standard deviation*

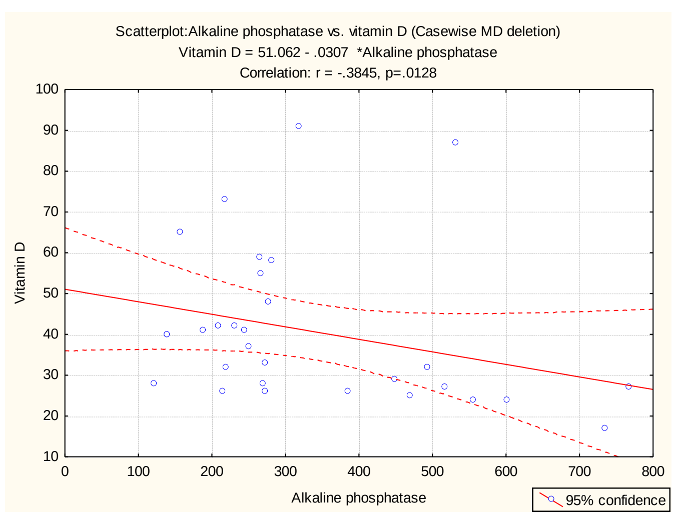

Fig.1. The correlation between alkaline phosphatase and 25(OH)D

Assessing the circulating status of vitamin D and phospho-calcium metabolism, it is found that for high values of alkaline phosphatase there were low values of vitamin D. Between these parameters there is a significant inverse correlation (r = -0.384, p = .0128) (Fig.1)

Regarding the dose of vitamin D administered, 12 patients (24.5%) received a dose of 400 IU daily, 22 patients (44.8%) received a daily dose of 800 IU, 11 patients (22.5%) received 1200 IU and only 4 patients (8.2%) received 1600 IU daily. Under the conditions of correct prophylaxis, however, 30.6% of children (15 cases) had low vitamin D levels.

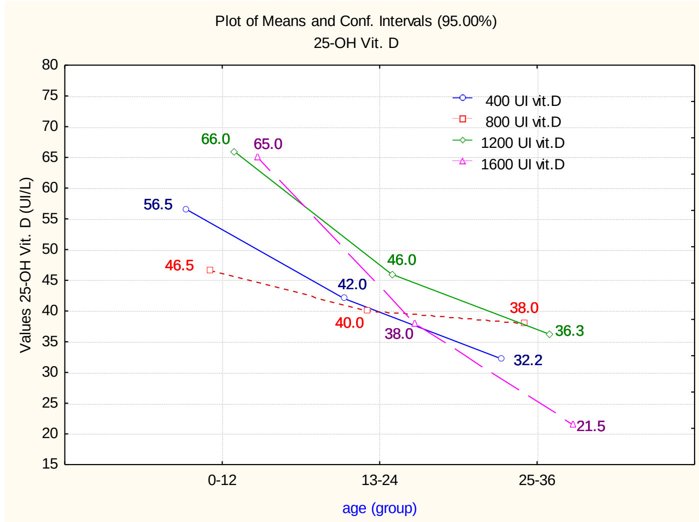

Fig. 2. Serum levels of vitamin D (ng/ml) depending on the vitamin D dose administered by age group

Serum levels of 25(OH)D (ng/ml) depending on the doses administered and the age group are shown in Figure 2. The distribution of 25(OH)D values indicates that most children with deficiency received doses of 400 - 800 IU vitamin D, although there are 2 cases that received 1200 and 1600 IU daily. Also, the cases of vitamin D deficiency increased with age, possibly due to the administration of foods poor in vitamin D and the intermittent administration of vitamin D supplements.

Regarding the season in which the children were born, it was not possible to establish a correlation between the cold season and the vitamin D deficiency. The pollution, the use of creams with high sun protection factor and the lack of sun exposure of the children can explain this fact.

Vitamin D, a fat-soluble vitamin, found in two forms, vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol) (figure 3), is naturally present in very few foods (fish, eggs, mushrooms), added in others fods (milk, fortified cereals) or available as a dietary supplement. Cod liver oil has vitamin D3 in it. Vitamin D is also an endogenous product synthesized in the skin after UV irradiation [8-10].

The standard supplement is vitamin D_3 which tends to be better absorbed than other forms of vitamin D. In the liver, D3 is transformed into 25 (OH) D (25-hydroxycholecalciferol) via the enzyme cholecalciferol 25-hydroxylase and then sent out to the kidneys to get hydroxylated into 1,25 (OH) D (1,25-dihydroxycalciferol). 1,25 (OH) D or calcitriol is the active hormone that is the final result of vitamin D3 ingestion [11,12].

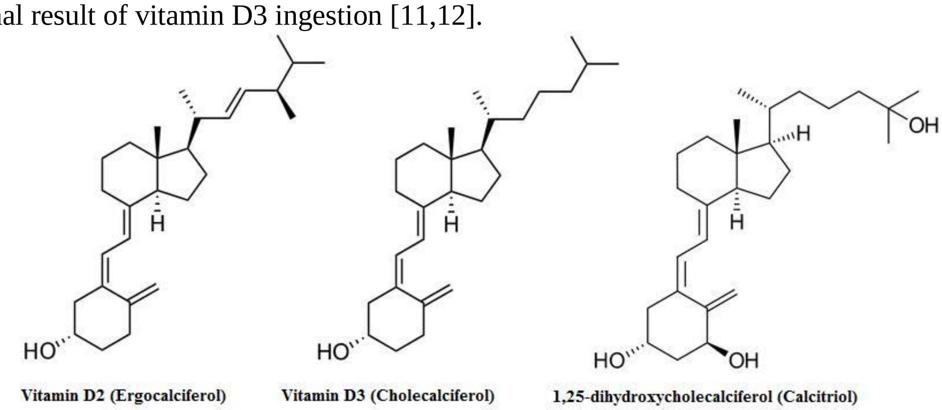

Fig. 3. Forms of vitamin D

The circulating half-life of 25 (OH) D is 15 days. Serum concentrations of 25 (OH) D most accurately reflect the amount of vitamin D produced endogenously and assimilated from foods and supplements, but does not indicate the amount of vitamin D stored in tissues. Circulating 1,25 (OH) D has a circulating half-life of 15 hours, and serum concentrations are influenced by parathormone, calcium and phosphatemia values, thus not being an indicator of vitamin D status [13].

The absorption efficiency or bioavailability depends on lipid composition and food supplement vehicle. Oil-soluble vehicles produce a greater increase of 25 (OH) D in blood serum when compared to powder - and ethanol-based supplements. Studies have shown that vitamin D_3 absorption efficiency varies between 55% to 99% (14-16 weeks), also depending on long chain fatty acids interferences or molecular form of vitamin D - insertion into micelles, microcapsules, or liposomes increased absorption efficiency). Moreover, the baseline of 25 (OH) D levels may be another possible contributor to the variations in the bioavailability of vitamin D different vehicles (14). It is difficult to compare vitamin D intake from different dietary supplements, sun exposure affecting vitamin D status in every individual. According to this, we can think that the defiency in our children that received 1200 U and 1600 U of vitamin D could have appeared as a consequence of a low serum value of vitamin D that decreased bioavailability or a reduced exposure to the sun.

In Romania, the Ministry of Health recommends preventing rickets by administering vitamin D to all infants and young children up to the age of 18 months, in a dose of 400-800 U.I. daily. However, statistics in Romania show that 29% of children present deficiency and insufficiency vitamin D level (15). The factors which contribute to the occurrence of deficient rickets are considered to be: incorrect application of vitamin D prophylaxis schemes and failure to adjust vitamin D doses to the specific needs of each child. Under a correct prophylaxis, our case study registered only 3 children under the age of 18 months who had vitamin D deficiency. Most cases of such a deficiency have been identified in children over 18 months of age, due to the consumption of poor vitamin D foods, inadequate vitamin D administration and inadequate sun exposure.

Conclusions

Low serum levels of vitamin D can also be found in children who have successfully received correct prophylaxis with vitamin D. Among the incriminating factors we mention inadequate exposure to ultraviolet radiation, atmospheric pollution that filters ultraviolet radiation and reduces cutaneous synthesis of vitamin D, altered intestinal absorption, renal dysfunction, polymorphism of the enzymes involved in hydroxylation, which may explain the varying levels of vitamin D in different subjects under the same exogenous doses, the vitamin D transporter globulin polymorphism and the errors in the administration process. Dosing 25 OH cholecalciferol in children undergoing prophylactic treatment with vitamin D proves to be useful for establishing optimal doses and preventing rahitism, as some children in the urban area may require higher doses than those recommended by guides.

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