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Influence of Risk Factors and Food Habits on Serum Levels of Vitamin D

Luís Henrique Cerqueira Vila Verde*
Western Paraná State University Department of Dentistry MSc Program in Dentistry with emphasis on Applied Pathology to Dental Clinics Cascavel, PR, Brazil

Adriano Piccolotto
Western Paraná State University Department of Dentistry MSc Program in Dentistry with emphasis on Applied Pathology to Dental Clinics Cascavel, PR, Brazil

Adriane Yaeko Togashi
Western Paraná State University Department of Dentistry PhD, Professor, Associate, Stricto Sensu Graduate Program in Dentistry, Cascavel, PR, Brazi

Abstract

Vitamin D (VD) plays an important role in the formation, development, maintenance and repair of bone tissue. Due to the physiological importance of VD, this study aimed to observe the rate of hypovitaminosis D (hD) in a population and the factors that may influence the incidence of hD. All participants of the groups were submitted to a Semi-Quantitative Food Frequency Questionnaire (SQFFQ) on the intake of dietary calcium, in order to assess the risk factors. The patients were submitted to laboratory examinations of serum 25-hydroxyvitamin D; those who presented serum VD levels below 30 ng/mL were allocated to the abnormal group (insufficient or deficient) and participants with levels equal to or above 30 ng/mL were allocated to the normal group (sufficient). Patients who were allocated to the abnormal group were submitted to VD supplementation. 35% of subjects in the study population presented hD. Regarding the food questionnaire, a lower amount of milk-derived intake, such as yogurt, and a lower frequency of physical activities presented a higher risk for hD development. One can conclude that less than half of the sample had hD and calcium-rich foods may contribute to normal serum levels of VD.
Keywords: Hypovitaminosis D; Bone density; Clinical study; Vitamin D.

1. Introduction

VD has a proven involvement in the development and maintenance of bone tissue, playing a fundamental role in the homeostasis of calcium and phosphorus [1]. The physiological process consists in the production of organic bone matrix or osteoid mineralization by osteoblasts followed by precipitation of calcium and phosphorus on the organic matrix. For a normal mineralization of this matrix to occur, adequate systemic levels of calcium and phosphorus are required. After the synthesis of Vitamin D3 (VD3) in the skin, it is hydroxylated in the liver to 25-hydroxyvitamin D3 (25D) and, subsequently, to 1,25-di-hydroxyvitamin D3 (1,25D) in the kidney, thus forming the active vitamin metabolite that will act in the intestine in the absorption of calcium [2, 3]. This process occurs through the binding of the active metabolite to the nuclear VD receptor (VDR) present in the cells of the small intestine. An established presentation of hD may lead to a decrease in the absorption of calcium in the intestine, leading to hypocalcemia [4, 5]. In these cases a correction mechanism may occur through compensatory hyperparathyroidism that will arise, with the production of parathyroid hormone (PTH) in order to mobilize bone calcium and decrease the excretion of calcium by the kidneys.

The active biological form of VD is known as a regulator of bone formation, mediated by osteoblasts, as well as a regulator of bone resorption mediated by osteoclasts [6, 7]. Experimental studies performed by Dekel, *et al.* [8] and Lidor, *et al.* [9] demonstrated that the active forms 25(OH) D3 and 24-25(OH) D3 are incorporated into bone callus of recent fractures in children. There is a decrease in blood levels of 25(OH) D3 and 24-25(OH) D3 in patients with bone fractures of delayed healing, as well as in cases of multiple fractures with excessive formation of bone callus. The decrease in the levels of VD metabolites in the blood is suggested to be due to participation in the healing process of fractures [10].

Other functions performed by VD include effects on the pancreas, the vascular system of the smooth muscle cells and monocytes. This active metabolite also has antiproliferative activity and decreases inflammation markers. Its deficiency can influence the pathogenesis of autoimmune diseases, such as multiple sclerosis, diabetes type 1, some types of cancer, premature birth and fetal malformation [11].

VD3 is obtained from the diet from foods such as fish, fruits and also by the skin through exposure to ultraviolet light where it is synthesized [12]. The prevalence of hD has increased after the industrial revolution, and in the 1930s, it was discovered that exposure to sunlight or artificial ultraviolet formed VD3 [13, 14]. The main factors that contribute to the onset of hD are age, pigmented skin, excessive use of sunscreen and clothing in addition to lack of physical activity. In case of diagnosed insufficiency or deficiency of VD it can be restored through supplementation.

*Corresponding Author

Sociocultural factors and schooling can contribute to a more balanced intake of foods beneficial for the balance of VD in the body, as well as of physical activity [4, 14].

In the 1970s, the first laboratory tests to assess serum VD levels began to appear [4]. Currently it is estimated that approximately 1 billion people in the world have VD insufficiency or deficiency [1, 15]. Saraiva, *et al.* [16], showed that the hD in institutionalized elderly reaches 71.2% and in elderly outpatients reached 43.8%. Silva, *et al.* [17], found VD insufficiency in 42.4% of a group studied in Belo Horizonte.

The protocol of the Endocrine Society establishes that the levels of VD are deficient when below 20 ng/mL, insufficient between 21-29 ng/mL and sufficient when above 30 ng/mL [18].

Given the importance of the VD and the number of people who have altered serum VD levels, this study aimed to assess the prevalence of hD in the population, and the factors that influence the incidence of this presentation.

2. Methodology

The clinical study performed was a controlled, transverse and interventional study. The project was approved by the Ethics and Research Committee of UNIOESTE (Opinion 121.462). Patients were recruited from the Institute of Dental Clinics of the Western Paraná State University (UNIOESTE), in Cascavel, Paraná, where a convenience sample was obtained. Recruitment and data collection took place between March 2013 and December 2016.

2.1. Inclusion Criteria

1) Age range of 18 to 60 years;
2) Gender: men and women;
3) Condition of proper oral hygiene; bleeding and index less than 5%;
4) Absence of periodontal diseases and controlled systemic condition.

The minimum age of 18 years was defined since bone mass is already formed. The maximum age of 60 years was defined to reduce the chances of recruiting individuals with osteoporosis.

2.2. Exclusion Criteria

1) Age less than 18 years and higher than 60 years;
2) Osteoporosis diagnosed in treatment;
3) Previous diseases: Primary hypogonadism, primary hyperparathyroidism, current hyperthyroidism, Cushing's syndrome, hyperprolactinoma, anorexia nervosa, osteomalacia, rheumatoid arthritis, chronic obstructive pulmonary disease, neoplasms, Marfan syndrome, Ehlers-Danlos syndrome, homocystinuria, diabetes and osteopenia.
4) Continuous use of the following medications: corticosteroids, excess thyroxine, anticonvulsants, lithium, alendronate, methotrexate;
5) Pregnancy.

Patient triage was performed through the verification of medical records at the Institute of Dental Clinics of UNIOESTE. The individuals were then evaluated clinically and physically and selected according to the inclusion and exclusion criteria, they were invited to participate, and received clarifications about the project, its risks and benefits; and finally signed the informed consent form (ICF). Only patients who adequately filled the ICF were included in the study.

Patients were subjected to laboratory tests of 25-hydroxyvitamin D dosing. Participants who had a serum VD level of less than 30 ng/mL were allocated to the abnormal group (deficient or insufficient) and participants with levels equal to and above 30 ng/mL were allocated to the normal (sufficient) group.

After the distribution of the participants in the groups, they were submitted to a Semi-Quantitative Food Frequency Questionnaire (SQFFQ), assessment of smoking habits, alcoholic intake and practice of physical activity [19].

The tests used for the statistical analysis were the Chi-square test (two-sided with Yates correction) with Kat approximation, with Wolf approximation.

3. Results

After the analysis, 155 patient files were separated, of which 88 were called for the initial evaluation, the remainder had outdated phone numbers, had moved out of the city, were incapacitated to appear at the university or chose not to attend. After screening, the patients were selected according to the inclusion criteria of the study, and after signing the consent form and completing the questionnaire, the laboratory tests were requested, of which 20 were not performed. This left 68 patients with complete laboratory tests.

After analysis of complementary exams, 24 patients were allocated to the abnormal group (insufficient and deficient), and 44 to the normal group (sufficient) with VD levels equal to and above 30 ng/mL. Thus, 64.7% of the patients had sufficient blood levels of VD while 35.2% has hVD.

The following shows the comparative tables of the groups and the relationship with the variables collected in the SQFFQ, smoking habit, alcohol consumption and physical activity [19].

It should be noted that of the 36 participants who drank at least one glass of milk a day, 25 patients belonged to the normal group, which corresponds to 36.8% of the total number of patients, while 11 (16.2%) belonged to the abnormal group. Of those who did not consume milk 19 patients (27.9%) belonged to the normal group, while 13 (19.1%) belonged to the abnormal group (Table 1).

Table-1. Daily consumption of milk - Groups of vitamin D and their relation with daily intake of milk

	Yes		No	
Normal	25	36.8%	19	27.9%
Abnormal	11	16.2%	13	19.1%
Total = 68	36		32	

In the assessment of physical activity, 27 patients who perform at least 3 hours of exercise per week (40 patients), i.e., 39.7%, belong to the normal group, while 13 (19.1%) belong to the abnormal group. Among those who did not exercise or exercised less than 3 hours per week (28 patients), 17 of them (25%) belonged to the normal group and 11 (16.2%) belonged to the abnormal group (Table 2).

Table-2. Physical activity - Groups of vitamin D and their relation with daily physical activity

Vitamin D	Yes		No	
Normal	27	39.7%	17	25.0%
Abnormal	13	19.1%	11	16.2%
Total = 68	40		28	

Most of the 67 patients (53 patients) who answered the questionnaire regarding the number of daily meals claimed to have 2 to 3 meals per day, of which 35 (52.2%) belonged to the control group and 18 (26.9%) to the abnormal group. 12 of them had from 4 to 5 meals per day, of which 8 (11.9%) were from the normal group and 4 (6%) from the abnormal group. The remaining participants had 6 or more meals per day, with a total of 2 patients, of which 1 (1.5%) belonged to the normal group and the other to the abnormal group (Table 3).

Table-3. Groups of vitamin D and their relation with the number of daily meals

			Number of meals			
Vitamin D	**2 to 3**		**4 to 5**		**6 or more**	
Normal	35	52.2%	8	11.9%	1	1.5%
Abnormal	18	26.9%	4	6.0%	1	1.5%
Total = 67	53		12		2	

Of all patients, 51 stated eating at least one slice of cheese per day, of which 33 (48.5%) belonged to the normal group and only 18 (26.5%) to the abnormal group.

The remainder, 17 of them, did not consume cheese daily; of these, 11 (16.2%) belonged to the normal group and 6 (8.8%) to the abnormal group (Table 4).

Table-4. Cheese - Groups of vitamin D and their relation with the consumption of cheese

	Yes		No	
Normal	33	48.5%	11	16.2%
Abnormal	18	26.5%	6	8.8%
Total = 68	51		17	

Regarding yogurt intake, of the 68 interviewees, only 38 ate yogurt daily, of which 28 (41.2%) were from the normal group and 10 (14.7%) from the abnormal group. The remainder had no habit of daily intake of yogurt, of which 16 (23.5%) belonged to the normal group and 14 (20.6%) to the abnormal group (Table 5).

Table-5. Yogurt - Groups of vitamin D and their relation with the consumption of yogurt

Vitamin D	Yes		No	
Normal	28	41.148%	16	23.5%
Abnormal	10	14.7%	14	20.6%
Total = 68	38		30	

A daily intake of vegetables was observed in 57 of 68 patients, of these 36 (52.9%) were normal while 21 (30.9%) belonged to the abnormal group. Of the 11 who did not have the habit of eating vegetables, 8 were from the normal group (11.8%) and 3 (4.4%) from the abnormal (Table 6).

Table-6. Vegetables - Groups of vitamin D and their relation with the consumption of vegetables

Vitamin D	Yes		No	
Normal	36	52.9%	8	11.8%
Abnormal	21	30.9%	3	4.4%
Total = 68	57		11	

Fifty-six patients ate at least one fruit daily, of which 36 (52.9%) were from the normal group and 20 (29.4%) were from the abnormal group. 12 patients did not eat fruits, of which 8 (14.4%) belonged to the normal group and only 4 (7.2%) belonged to the abnormal group (Table 7).

Table-7. Fruit- Groups of vitamin D and their relation with the consumption of fruit

	Yes		No	
Normal	36	52.9%	8	14.4%
Abnormal	20	29.4%	4	7.2%
Total = 68	56		12	

No statistical difference was observed among the studied variables with normal and abnormal groups. However, with the exception of vegetables, smoking and drinking, all other (milk, physical activity, cheese, yogurt and fruit) were risk factors for hD in the population studied, in particular the absence of yogurt consumption which can lead to a two-fold risk of the emergence of hD (Table 8).

Table-8. Likelihood of the interaction of normal levels of vitamin D with factors analyzed, relative risk and Odds-ratio

Daily consumption factors	p-value[1]	Relative[2] Risk	Odds-ratio[3]
Milk	0.5398 ns	1.24	1.56
Physical activity	0.7501 ns	1.13	1.34
Number of meals	0.8930 ns	Na	na
Cheese	1.0000 ns	1.00	1.00
Yogurt	0.1367 ns	1.53	2.45
Vegetables	0.7922 ns	0.94	0.64
Fruit	0.7376 ns	1.03	1.25
Tobacco	0.5035 ns	0.00	0.82
Alcohol	0.5035 ns	0.00	0.82

[1] χ^2, 5%- Two-sided; [2] with Kat approximation; [3] with Wolf approximation. ns: not significant at 5%; na: not applicable for 2 x 3 contingency tables. Chi-square statistic (two-tailed, with Yates correction)

4. Discussion

A 35.2% prevalence of hD was found in the present study, values similar to those of Silva, *et al.* [17], which was 42.4%. These figures indicate that a significant portion of the population in Brazil and in the world presents a decrease of serum VD levels, possibly due to changes in life habits such as the use of sunscreens, sedentary lifestyle, and even some types of clothing [16, 20].

Given the importance of the VD and the increasing number of people with hD, more studies should be carried out in order to inform health professionals, be they doctors or dentists, in the elaboration of clinical and therapeutic procedures in order to re-establish the normal levels of this vitamin.

The protocol of the Endocrine Society establishes that the level of 25 (OH) vitamin D is considered deficient if the laboratory testing is below 20 ng/mL, insufficient between 21-29 ng/mL and sufficient when above 30 ng/mL. A re-establishment, in cases of deficiency in adults, is 50,000 IU per week for 8 weeks. The Italian protocol in turn, recommends, in cases of VD deficiency, a cumulative dose of 300,000 to 1,000,000 IU in 4 weeks [18]. The supplementation dose of VD is 600-800 IU per day according to the protocol of the Endocrine Society and 800-2000 IU per day, according to the protocol of the Italian consensus [18, 21].

Although this study does not present the results of VD supplementation, it is important to maintain adequate VD levels, as can be observed in the study carried out in humans with kidney disease, in which Barros, *et al.* [22] found that after VD supplementation there was reestablishment of levels as well as the elimination of compensatory hyperparathyroidism. Bhalla, *et al.* [23], reports the inhibition of cytokine production and antigen-induced T cell proliferation as the anti-inflammatory effects of VD3. The study by Dietrich, *et al.* [24], reports that VD can reduce susceptibility to gingivitis through its anti-inflammatory effects.

The ingestion of milk did not show a statistically significant influence on the groups (p=0.5398), however the relative risk (1.24) as well as the Odds ratio (1.56), indicated the importance of milk as it can decrease the likelihood of the individual acquiring systemic diseases. The same applies for the intake of fruits (relative risk 1.03; Odds-ratio 1.25), which in this study was taken as at least one daily unit or portion, but is more important according to the increase in intake [21].

The intake of yogurt was an important variable with a relative risk of 1.53 and an Odds- ratio of 2.45, with the highest impacts in the evaluated population, in agreement with Araujo [25], who demonstrated that yogurt only has a lower concentration of VD than fresh sardines. In contrast, the ingestion of vegetables presented a lower relative risk and odds-ratio, 0.94 and 0.64 respectively, in agreement with the literature in which vegetables are not the main sources of VD3, despite several benefits. Mushrooms are the only component with a significant concentration of VD (0.62 µg per 100 g), however this food is not usually part of the dietary habits of the population studied [26].

Eating habits such as fruit intake contribute to a better quality of life as well as a decrease in respiratory diseases, cardiovascular disease, diabetes, obesity and are sources of VD, which at low levels can contribute to the appearance of rickets, osteomalacia and osteoporosis [13, 27, 28].

Rickettsia is characterized by abnormalities in epiphyseal growth plate formation, with non-mineralized areas, disorganization of cellular architecture and delay in bone maturation. Osteomalacia is characterized by deficient mineralization of the osteoid matrix of cortical and trabecular bone with accumulation of osteoid tissue. These processes, in general, are associated. After the end of growth, with the ossification of epiphyseal cartilage, only osteomalacia remains [27].

Osteoporosis is defined as a systemic skeletal disorder characterized by the impairment in bone strength, which predisposes to an increased risk of fractures, because it affects the trabecular and cortical bone microstructure. Bone resistance reflects the integration of two main aspects, which are, bone mineral density and bone quality [28].

Individuals with osteoporosis display a reduction in the number and thickness of the trabecular plate. The interior of the maxillary bone is the most sensitive to distinguish patients with osteoporosis due to enlargement of the medullary bone trabeculae and smaller thickness of the cortical bone. During radiographic evaluation, individuals with osteoporosis have more erosion on the bottom edge of the mandible [28].

Physical activity is an important factor in obtaining VD3 as well as in the maintenance of calcium [13, 28].

In the present study, there was a significant risk (relative risk 1.13 and odds ratio 1.34) of VD deficiency within this population regarding physical activity, however it was considered only above 3 hours per week. Note that in addition to the importance of performing physical activities, the duration is a relevant variable. Individuals with low rates of sunlight exposure are at a risk for developing hD, demonstrating the importance of sun exposure. According to the Brazilian Society of Endocrinology and Metabolism (SBEM), at least 2 hours of weekly physical activity outdoors is recommended [29].

Although the present study did not find statistical difference between the normal and abnormal groups and their habits, continuous studies are required to discover new influences and benefits of VD3, as well as within dentistry and its relation with clinical aspects.

5. Conclusion

This study revealed that 35% of the population presented hD. Physical activity was important in the prevention of hD, together with a diet rich in calcium, in which the milk and yogurt can be rich sources of VD.

Further studies should be carried out with the aim of better understanding the relationship of hD with systemic and buccal changes.

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