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Vitamin D supplementation: position Statement of the Iberoamerican Society of Osteoporosis and Mineral Metabolism (SIBOMM)

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ABSTRACT

Background: Vitamin D (VD) deficiency is a global pandemic that affects more than a third of the population worldwide. The population of Latin America and the Caribbean exceeds 620 million inhabitants with diverse ethnic origins and different latitudes and altitudes, which make comparisons and generalizations difficult.

Aim and method: We sought to establish an expert consensus regarding the recommendations for VD supplementation in Latin America by means of the Delphi methodology.

Results: The prophylactic dosage of VD in the general population should be individualized according to age, race, body weight, sun exposure of an individual, altitude, and dietary and exercise habits, without ruling out existing chronic diseases.

Conclusion: The importance of VD has been widely documented and its deficiency is a pandemic. Many individuals have difficulty meeting daily VD requirements through food and the sun. The population of Latin America and the Caribbean has diverse ethnics, cultures, in addition to living in different latitudes and altitudes. Therefore, it is important to make a position on VD supplementation, given the different characteristics, ages and serum levels of 25(OH)D.

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Introduction

Since the beginning of this century, vitamin D (VD) has been included in what has been called the VD hormone complex [1]. In fact, it is not really a vitamin because it meets all the criteria to be named a hormone, circulating throughout the bloodstream and acting *via* specific receptors. Currently, VD deficiency is a global pandemic that affects more than a third of the population worldwide. To date, the population of Latin America and the Caribbean exceeds 620 million inhabitants with diverse ethnic origins and different latitudes and altitudes, which make comparisons and generalizations difficult. In this region, the prevalence of individuals with insufficient VD levels (<30 ng/mL) fluctuates between 40.2% and 96.8% with average ages observed between 58 and 79 years [2–7]. A systematic review reported that in Latin America and the Caribbean the prevalence of VD deficiency (≤ 20 ng/L) among healthy individuals of all ages, ranged from 20–40%. Nevertheless, the extent of its magnitude is unknown [8].

Only 10% of the VD content in our body is ingested through the diet, the remaining is obtained through its synthesis at the skin, as a consequence of the action of ultraviolet B (UVB) rays. Despite this, there are various factors in many of our Latin American countries that make VD synthesis difficult, such as the existence of solar filters (i.e. ozone layer and clouds, pollution, crystals, oblique incidence of solar rays depending on latitude, dark color of skin, sun protection factors, etc.). All these make oral VD supplementation necessary to maintain adequate blood levels [4,9].

There is considerable controversy within the scientific community regarding the optimal 25-hydroxyvitamin vitamin D (25(OH)D) levels for human health. There is an international consensus [10–13] that the optimal VD requirements are those that allow 25(OH)D reach serum levels higher than 30 ng/L (75 nmol/L). Values between 21 and 29 ng/mL are considered insufficient, levels below 20 ng/mL considered deficiency and severe deficiency those below 10 ng/mL.

In recent years, there has been a notable interest in VD beyond its crucial role over bone mineral metabolism, basically

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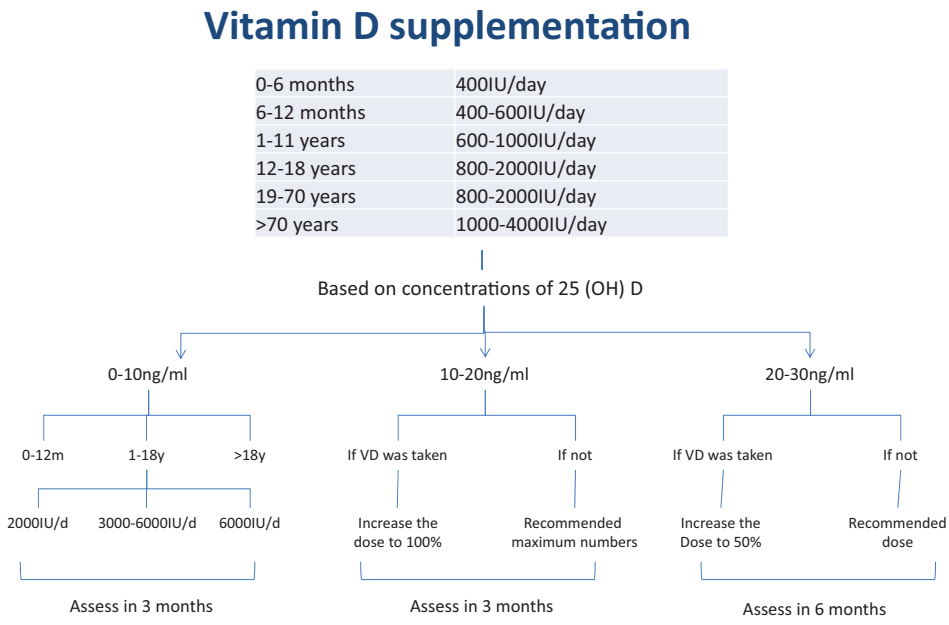

Figure 1. Vitamin D supplementation.

due to the characterization of its extra-osseous effects that have a relevant impact on all stages of life [8–14].

During adolescence, adequate levels of VD are positively correlated with cardiovascular health, with less frequency of depressive states and better physical activity. Thus, an inverse relationship with adiposity and a direct relationship with serum ferritin levels has been demonstrated [10,15].

Regarding fertility, VD is involved in various reproductive physiological functions, highlighting endometrial receptivity and the implantation process, and in cases of polycystic ovary syndrome (PCOS) it improves follicular development [8,14].

Maternal VD serum levels decrease throughout pregnancy, which has been associated to maternal obstetrical adverse outcome such as pre-eclampsia, preterm delivery, an increased risk of cesarean section, bacterial vaginosis, gestational anemia and a higher risk of gestational diabetes. In addition, fetal-neonatal complications have also been observed such as low birth weight, intrauterine growth restriction, respiratory tract infections, greater number of allergies and the presence of autistic features and neural tube defects [7,11,16].

Due to various factors aging is clearly related to the risk of suffering VD deficiency, reaching an incidence of 70% of the elder population. During the aging process, VD deficiency is directly related to osteoporosis, sarcopenia and the risk of falls and fractures. In addition, VD deficiency also increases the risk of suffering chronic conditions such as obesity, cardiovascular diseases (coronary heart disease and strokes), high blood pressure, type 2 diabetes and the development of neoplastic processes such as breast cancer and colon cancer [12].

It is a fact that many individuals have difficulty to obtain greater amounts of VD of natural sources, namely from food and sunlight [8]. Few foods are good sources of VD and therefore recommended (i.e. fortified dairy products, salmon, tuna, and the plant called horsetail). One cup of fortified milk offers about 100 IU of VD. Salmon (100 gr) offers about 650 IU of VD. Most people do not eat enough of these foods each day in order to reach the recommended daily allowance, and that is the reason for supplementation.

Given the recent recommendations of International Societies regarding VD, and the diversity of the Latin American and Caribbean population, the Iberoamerican Society of Osteoporosis and Mineral Metabolism (SIBOMM) has decided to give its position regarding VD supplementation.

Method

The modified Delphi methodology was used for this position statement [17]. This method is a structured methodology that is used to systematically collect judgments from a panel of experts in order to solve a complex problem and make decisions when the evidence is controversial. The purpose of this technique is to build a consensus or general group agreement from the statistical processing of the differences and coincidences between the individual assessments and their modifications, through the different rounds of realizations and reviews. We sought to establish an expert consensus regarding the recommendations for VD supplementation. For this purpose, a systematic review of the literature was carried out, limiting it to the analysis of studies and reviews in humans, published in English, Spanish and Portuguese from electronic databases: Science Direct, Medline, Scopus, Embase, The Cochrane Library, searched until September 30th, 2020. We used the following key words: Vitamin D (mesh) and supplements and regimens and dosage and time and monitoring, Vitamin D supplementation and recommendations, and severe deficiency, and deficiency and suboptimal concentration and optimal concentration.

All authors independently screened the tittles of the papers obtained by search strategy. The text of each potentially relevant study was considered for inclusion when 4 or more authors recommended it. The result was analyzed and discussed and finally resolved by consensus.

After reading the different Latin American and International recommendations and some selective papers [8–27], and based on the experience of the different experts, each one gave their opinion on VD supplementation. All the recommendations were subsequently agreed upon by all the experts, with the freedom of adding or including any updated article that was considered important.

Vitamin D supplements (regimens and dosage, time, monitoring)

The majority of studies report that lower levels of VD are related to worst outcomes for various chronic diseases. The balanced choice of recommendations to follow depends on individual health outcomes, age, race, body weight, latitude of residence, and dietary and cultural habits.

Recommendations on VD supplementation have changed over the years and have followed the results of recent clinical data. However, even current doses recommended by scientific societies differ significantly from each other, ranging from 400/600 to 2,000 IU/day [18,19]. This is mainly due to discrepancies regarding the definition of normal minimal 25(OH)D serum concentrations, which was defined by very wide ranges, between 10 and 40 ng/mL, and depend on how different groups of experts perceive the action of the VD [20–23]. Most endocrine societies, including the Endocrine Society (USA), as well as those dealing with bone health, such as the International Osteoporosis Foundation [24,25] and recent Latin American positionings [26,27], consider that a 25(OH)D serum concentration above 30 ng/mL is necessary to achieve health benefits and these are the recommendations on which we should base ourselves.

General recommendations [9–12,15,18–20,26,27]

1. The prophylactic dosage of VD in the general population should be individualized according to age, race, body weight, sun exposure of an individual, altitude, and dietary and exercise habits, without ruling out existing chronic diseases.
2. In the general population, in the case of analytically determined VD deficiency, VD administration should be based on doses dependent on the serum 25(OH)D concentration, in addition to the individual characteristics discussed above.
3. Prophylactic VD dosing in VD deficiency risk groups should be implemented according to the recommendations for the general population.
4. It is not necessary measuring 25(OH)D levels before three months after starting supplementation and/or treatment unless the patient has manifestations that suggest intoxication.

Recommendations for the supplementation of vitamin D in the general population (Figure 1) [10–12,15,16,18–20,26,27]

Term newborns and infants up to 12 months

0–6 months: 400 IU/day from the beginning of life, regardless of the form of feeding.

6–12 months: 400–600 IU/day, the dose is adapted to the type of diet.

Children (1–11 years)

Supplementation is not necessary in healthy children who sunbath with their forearms and legs uncovered for at least 15–20 min between 09:00 and 15:00 h, without sunscreen; although supplementation can be recommended and is safe. If the above sun exposure guidelines are not met, supplementation with 600–1,000 IU/day is recommended, based on lifestyle, body weight and dietary VD intake.

Adolescents aged 12–18

Supplementation is not necessary in healthy adolescents with good lifestyle, sun exposure and diet; although supplementation can be recommended and is safe. If the above guidelines are not met, supplementation of 800–2,000 IU/day is recommended.

Adults aged 19–70

Supplementation is not necessary in healthy adults who have a good lifestyle, including sun exposure and a balanced diet; although supplementation can also be recommended and it is safe in the above guideline.

At these ages we can recommend supplementation, due to the decrease in VD synthesis by the skin, its supplementation is recommended at a dose of 800–2,000 IU/day, depending on body weight and VD dietary intake.

Elder > 70 years

The supplementation is recommended at a dose of 1,000–4,000 IU/day, depending on body weight and VD dietary intake.

Pregnant women

Both, women who want to become pregnant and when they are pregnant, could receive VD supplementation under the control of 25(OH)D serum levels in order to maintain optimal concentrations within the ranges of > 30–60 ng/mL.

Supplementation in VD deficiency risk groups

Obese individuals comprise a special risk group who require higher VD dosages than the recommended for their non-obese counterparts of similar age. Among VD deficiency risk groups, supplementation should be implemented and monitored under the control of 25(OH)D concentrations in order to maintain optimal concentrations of > 30–60 ng/mL. If measuring 25(OH)D concentrations is not possible, dosing should be performed according to the guidelines for the general population and at the maximum doses for a given age group.

Recommendations for the supplementation of vitamin D based on serum 25(OH)D concentrations (Figure 1) [10–12,14–16,18–23,26,27]

Severe deficiency: 0–10 ng/mL

- If they were already taking VD supplementation, it should be ensured if it was complying with the recommendations given. The need to comply with the necessary doses adapted to current results should be pointed out.
- The therapeutic doses should be implemented according to individual characteristics ranging from lifestyle, race, altitude and body weight; control 25(OH)D concentration testing should be performed 3 months after therapy.

From birth to 12 months of age: 2,000 IU/day.

1–18 years: 3,000–6,000 IU/day.

18 years: 30,000 IU/day or 60,000 IU/week.

Treatment of severe deficiency should be carried out for 3 months or until a 25(OH)D concentration of > 30–60 ng/mL is reached. Then a consecutive maintenance dose is recommended,

that is, a prophylactic dose that is recommended for the general population, in accordance to age and body weight. Take into account that obese individuals, those who have malabsorption syndrome or those receiving concomitant medications that alter VD metabolism require doses greater than 6,000 IU/day, until normal 25(OH)D levels be reached. Also the maintenance doses should be higher (3,000–4,000 IU/day).

Deficiency: > 10–20 ng/mL

- If they were already taking VD supplementation, it should be ensured if it was complying with the recommendations given. The need to comply with the necessary doses adapted to current results should be pointed out.
- If VD supplementation was appropriate, it is recommended to increase the dose by 100% and evaluate 25(OH)D serum concentration in a period of 3 months.
- If VD was not previously supplemented, it is recommended to start VD intake at the maximum recommended dose as for the general population in relation with the age and body weight and evaluate 25(OH)D serum concentration in a period of 3 months.

Suboptimal concentration: 20–30 ng/mL

- If they were already taking VD supplementation, it should be ensured if it was complying with the recommendations given. The need to comply with the necessary doses adapted to current results should be pointed out.
- If VD supplementation was appropriate, it is recommended to increase the dose by 50% and evaluate 25(OH)D serum concentration in a period of 6 months.
- If VD was not previously supplemented, it is recommended to start VD intake at the dose as for the general population in relation with the age and body weight.

Optimal concentration: 30–60 ng/mL

Given that they are optimal concentrations, lifestyle and VD supplementation should be continued.

High concentrations > 60–100 ng/mL

- If VD supplementation was appropriate, it is recommended to reduce the dose by 50% and consider evaluating 25(OH)D serum concentration in a period of 3 months.
- If VD was supplemented with doses higher than those recommended, VD supplementation should be interrupted for 1 month, and then initiate at the doses recommended for the general population.

Higher than 100 ng/mL

VD intoxication is defined as the state in which a serum 25(OH)D concentration > 100 ng/mL could be accompanied by hypercalcemia, hypercalciuria, and apparent parathyroid hormone suppression. In cases that 25(OH)D levels are above 100 IU, which can be considered toxic, VD supplementation should be stopped immediately. Calcemia and calciuria should be evaluated, and 25(OH)D concentration should be monitored at 1 month intervals until 25(OH)D concentrations of ≤ 60 ng/mL are reached.

Frequency and duration of VD supplementation

In addition to the dose, there are two other aspects VD supplementation (frequency and duration) that are independently associated with blood 25(OH)D levels. There is concern about the dosage regimen: Is it the same to use VD daily, than to use it weekly or even monthly or quarterly? Several studies have evaluated and confirmed the similarity of the efficacy and safety of a dose equivalent to 1,000 IU daily, administered in a single dose of 1,000 IU/day, 7,000 IU/weekly or 30,000 IU/monthly for 3 months or even 1,00,000 IU monthly or quarterly [23,28].

The duration of treatment will depend on the severity of the deficiency, and is generally administered for 3 months. After the patient reaches serum 25(OH)D levels between 30 and 60 ng/mL, a maintenance dose should be established, and it is recommended to evaluate serum levels again in 3–4 months after and then 2 times a year [28].

Final remarks

The importance of VD has been widely documented and its deficiency is a pandemic. Many individuals have difficulty meeting daily VD requirements through food and the sun. The population of Latin America and the Caribbean has diverse ethnics, cultures, in addition to living in different latitudes and altitudes; all this makes it difficult to give general recommendations. Therefore, it is important to make a position on VD supplementation, given the different characteristics, ages and serum levels of 25(OH)D.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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