Hypovitaminosis D in Costa Rica: initial report on a case control study

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Abstract

Aim: To describe for the first time clinical characteristics of patients with vitamin D insufficiency in Costa Rica.

Materials and methods: 17 patients with low levels of 25(OH)VD (<75 nmol/L) were selected from the laboratory reports at the Hospital San Juan de Dios. 15 controls were selected with normal 25(OH)VD levels and the same age and gender.

Results: There was no difference in age (52.76±20.88 years in cases vs 46.33±12.50 in control), gender (58.85% cases were females vs 80% in controls) or ethnic background (almost all patients were Hispanic). Mean 25(OH)VD levels in cases were 59.2±10.37 nmol/L. PTH levels were higher in cases (146.86±103.76 vs 47.82±13.77 ng/ml, p=0.004). There was no difference in calcium levels (8.98 cases vs 9.38 mg/dl controls p=.352), phosphorus (4.09 cases vs 2.99 mg/dl control p=.104). BMD at hip and lumbar spine were comparable. There were no differences in the prevalence of nephrotic syndrome, chronic liver failure, chronic renal disease and sun blockers use between both groups. There were no patients in nursing homes in either group. Subjects on the cases group received an average of 0.6 hours of sun exposure per week compared with 1.46 in the control group (p=0.297). In the cases group, we observed a higher prevalence of falls (23.5% vs 6.7% p=0.039), fractures (17.6% vs 0%, p=0.024), diabetes (17.6% vs 6.7% p=0.158), fatigue (26.7% vs 13.3% p=0.012), weakness (40% vs 33% p=0.010), and use of inducers of cytochrome P450 pathway (29.3% vs 0% p=0.009). Body weight was lower in cases (26.6% with overweight or obesity vs 66.7% p=0.009).

Conclusions: Vitamin D insufficiency may present even in tropical countries such as Costa Rica. It is characterized by higher levels of PTH, a lower body weight, use of inducers of liver enzymatic activity, a higher for falls and fractures, fatigue, weakness and diabetes. Both groups had a low sun exposure.

Key words: vitamina D deficiency, vitamina D, hyperparathyroidism

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VD insufficiency provokes rickets in children and osteopenia and osteoporosis in adults. However, in the last years have been described more often the correlation of this deficit with extra skeletal effects, like increase risks of various cancer, diabetes mellitus type 1, multiple sclerosis, Rheumatoid arthritis, acute myocardial infarction and arterial hypertension. American NHANES III results, show an increase of total mortality when the 25(OH) VD is less than 75 nmol/L.6

Prevalence of insufficient and deficient of 25(OH) VD have also been found in populations apparently healthy, in all ages and in different geographic latitudes, that predisposes to future pathologies compromising their quality of life.7,8

Costa Rica is a tropical country in Central America, which geographical position is as follows (external points): latitudes (north: 11°13´12´´ and south: 08°02´26´´ longitudes (east: 82°33´48´´ y west: 85°57´57´´).9 The solar exposure of its habitants is abundant throughout the year. However, this has been decreased considerably in the recent years due to protective measures against various pathologies of the skin.

The Ultraviolet index (UVI) is a diary forecast, calculated and divulgated with anticipation of 24 hours, the amount of ultraviolet radiation received by the Earth’s surface for most solar lighting, usually located around afternoon. It is a measure of guidance aimed at promoting healthy sun exposure, skin photo type adjusted in each person. It’s indicated the ultraviolet radiation levels on a scale of 1 (low) to >11 (dangerously high).10 In Costa Rica, the UVI varies throughout the year, with average of 6, during summer months, in Central Valley (moderated category risk), until 11 and 12 in the rest of the country (high category risk).11

From the different VD molecules that are found in the human body, the 25(OH)VD in plasma is considered VD status “mirror image” of a person, because it reflex the sum of the VD absorbed in the intestine and the level produced in the dermal. If well this molecule is biologically inactive, many research have found that the determination of serum levels constitute an important determinant of multiple biological functions, including the bone and muscular mineralization.12-14

Several studies have evaluated 25(OH) VD different concentrations relative to bone density, lower extremity function, dental health, as well as high fall risks, fractures and colon cancer. The most accepted definition of optimal concentration of this hormone is advocated that the PTH levels above which the latter exerts deleterious effects on the body, mainly in the bone metabolism, is about 75 nmol/L.15

Hypovitaminosis D is the condition that occurs when the 25 (OH) VD levels are lower than 75 nmol/L (30 ng/ml), and its subdivided in two groups: insufficiency (levels between 51 nmol/L to 74 nmol/L; 21-29 ng/ml) and deficiency (lower levels of 50 nmol/L; <20 ng/ml).16-18

In 2007 began measuring levels of 25(OH) VD at the Hormonal Laboratory at San Juan de Dios Hospital, only center in Costa Rican social security leading of that determination.

The object of this study is to describe, for the first time in Costa Rica, clinical characteristics of Hypovitaminosis D patients.

Methods and Materials

Retrospective study of 1 year (January to December, 2008). The Hypovitaminosis D was defined as levels less than 75 nmol/L (30 ng/ml). Was selected 17 patients under those levels and 15 normal controls. Was analyzed the clinical Files of a 32 persons sample, and was recollected demographic and clinical characteristics, like fractures, diabetes mellitus, history of cardiovascular diseases and previous use of medication. The sample was contacted to find out the sun exposure (hours per week), previous use of sunblock and associated symptoms. The vitamin D levels were requested by the attending physician as part of their studies in clinical evaluation for various conditions.

The 25(OH) VD was measured at the Hormonal Laboratory of San Juan de Dios Hospital, by mean of ELISA test, using the reactive kit IDS Octeia. The sample has been taken in fasting. The statistical analysis that were held using the SPSS 15 package; the continues variables were analyzed using the T-student prove and the chi-square categories.

The study was approved by the Local Bioethics Committee of the San Juan de Dios Hospital.

Results

Was identify 17 carriers cases of Hypovitaminosis D and 15 controls were chosen. The average age of the cases group were 52, 76 ± 20,88 years and the group control 46,33 ± 12,50(p=0,307). Females were predominant in both groups, with 58, 8% for cases and 80% for controls (p=0,265).

The laboratory findings, the 25 (OH) VD average level was 59, 2 ± 10,37 nmol/L (23,71 ng/ml) was between insufficient; the PTH was found high between Hypovitaminosis D carriers (average 146,86 pg/mL vs. 47,82 pg/mL controls, p 0,001). Over the other biochemical parameters, there were no significant differences (Table 1).
On risk factors and comorbidities, the 25(OH)VD insufficient showed more weakness (41.2% vs. 33% of controls; p=NS), osteoporosis (35.3% vs. 7% of controls, p<0.001), fatigue (29.4% vs. 13% of controls; p=0.098), falls (23.5% vs. 7% of controls; p=0.039), fractures (17% vs. 0% of controls; p=0.024), diabetes mellitus type 2 (17% vs. 6.7% of controls; p=0.158), and used sunscreens (11.8% vs. 7% of controls) (table 2).

## Discussion

The 1,25 (OH)2 Vitamin D is the active form of this hormone. Contrary to logical thinking, the Hypovitaminosis D is not defined by low levels of this active form of the vitamin, but the 25 (OH) Vitamin D. This is because when the 1,25(OH)2 Vitamin D levels decreases, secondary hyperparathyroidism occurs. The increased activity of PTH stimulates the action of the 1-α-hydroxylase, which catalyzes the 25(OH) Vitamin D conversion to 1,25(OH)2 Vitamin D. In these circumstances, it would have a “normal” false level of 1,25 (OH)2 vitamin D, at the expense of secondary hyperparathyroidism. Measure 25 OH Vitamine D obvious these considerations.19

Despite the abundant solar exposure, the prevalence of Hypovitaminosis D is high among populations of regions with much sun exposure, like Hindus and South Asians, in which can reach the 97% of prevalence.20 The lack of adequate sun exposure is a risk factor to present Hypovitaminosis D. The study identified a trend to low amounts of this hormone, although not statistically significant.

It is to emphasize the value obtained from one exposure of 0.6 hours per week of sunlight, equivalent to only 5
minutes a day. That value is low, despite being a tropical country with abundant sunshine during the all year. Some lifestyle changes explain this finding. Today it was increased awareness about prevention of skin cancer, so people tend to receive less direct sunlight. Furthermore, the type of work has affected the population, a high percentage, if covered for most of the day. All this contributes to that the sun exposure is on average much lower than recommended, at least 15 minutes per day.\textsuperscript{21-23}

Another factor not identified until recently, which may help to explain the high Hypovitaminosis D, is the contribution of genetic factors. Different genes Polymorphisms involved in the VD synthesis, transport and action, are associated with relative risks 2.5 times more likely to have Hypovitaminosis D.\textsuperscript{24}

Females are another risk factor for Hypovitaminosis D, and in this study, 80\% of the women affected. Furthermore, their carriers of both genders have more history of fatigue, osteoporosis, falls, fractures, diabetes mellitus and liver enzyme inducing drugs.

The liver and renal diseases, institutionalized persons, the elderly, mal absorption syndromes, pregnancy, lactation and use of anticonvulsant drugs, are considered risk factor for Hypovitaminosis D.\textsuperscript{25} In the presence of renal insufficiency; the 1-hydroxylase activity is less, so there is a lower activation of Vitamin D, leading to secondary hyperparathyroidism. In this research, the only statistically significant risk factor was the use of hepatic-enzyme induce drugs.

It was also found high prevalence of musculoskeletal symptoms and signs, like fatigue, weakness, osteoporosis and fractures. A quarter of the patients have fall history, which increases fractures risk. No differences were found between the case and the control groups with respect of the use of sunscreen and weakness. The VD has genomics and no genomics effects to muscle fiber. It has been shown that deficiency states, there is muscular fiber atrophy type II, which are rapid response and the first to be recruited to prevent falls. Some studies have shown reductions of up to 20\% on risk of falls when correcting the VD deficiency, which may contribute to anti fracture efficacy has been determinate.\textsuperscript{26}

Although not assessed in this study, the extra skeletal effects of VD are multiples. Different bibliographic sources correlate VD levels to cancer prevalence,\textsuperscript{27} worsening insulin resistant getting and glycemic control,\textsuperscript{28} more prevalence of autoimmune diseases like diabetes mellitus type I and multiple sclerosis. Even some early studies have shown that supplementation before the first year of live is associated to a low risk to developed diabetes mellitus type I during childhood.\textsuperscript{29}

This study has several limitations. The first one is that the sample is small, which may explain why the differences not reach statistical significance in many international risk factors associated to VD deficiency. However, is the first Hypovitaminosis D report in Costa Rica. The second limitation relates to the fact that is a descriptive study and is not known whether replacement therapy of Vitamin D may reverse some of the symptoms studied.

More research is required to know the real prevalence of this condition in Costa Rica, once it is more accessible to determinate. In first place, it can recognize that Hypovitaminosis D occurs in tropical countries, including this one. Second place, to be involved this Hypovitaminosis in multiples diseases, VD correction, being inexpensive, may have implications in preventing falls, fractures, cancer, diabetes improved control and insulin resistance and immunologic diseases, although not features such randomized studies that show dose benefits.

References

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