SHORT REPORT

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Taking Vitamin D With the Largest Meal Improves Absorption and Results in Higher Serum Levels of 25-Hydroxyvitamin D

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ABSTRACT

Many patients treated for vitamin D deficiency fail to achieve an adequate serum level of 25-hydroxyvitamin D [25(OH)D] despite high doses of ergo- or cholecalciferol. The objective of this study was to determine whether administration of vitamin D supplement with the largest meal of the day would improve absorption and increase serum levels of 25(OH)D. This was a prospective cohort study in an ambulatory tertiary-care referral center. Patients seen at the Cleveland Clinic Foundation Bone Clinic for the treatment of vitamin D deficiency who were not responding to treatment make up the stugy group. Subjects were instructed to take their usual vitamin D supplement with the largest meal of the day. The main outcome measure was the serum 259(OH)D level after 2 to 3 months. Seventeen patients were analyzed. The mean age (±SD) and sex (F/M) ratio were 64.5 ± 11.0 years and 13 females and 4 males, respectively. The dose of 25(OH)D ranged from 1000 to 50,000 IU daily. The mean baseline serum 25(OH)D level (±SD) was 30.5 ± 4.7 ng/mL (range 21.6 to 38.8 ng/mL). The mean serum 25(OH)D level after diet modification (±SD) was 47.2 ± 10.9 ng/mL (range 34.7 to 74.0 ng/mL, $p < .01$). Overall, the average serum 25(OH)D level increased by 56.7% ± 36.7%. A subgroup analysis based on the weekly dose of vitamin D was performed, and a similar trend was observed.

Thus it is concluded that taking vitamin D with the largest meal improves absorption and results in about a 50% increase in serum levels of 25(OH)D levels achieved. Similar increases were observed in a wide range of vitamin D doses taken for a variety of medical conditions. © 2010 American Society for Bone and Mineral Research.

KEY WORDS: VITAMIN D; DEFICIENCY; ABSORPTION; ADMINISTRATION; DIET

Introduction

There is an increased awareness of vitamin D insufficiency and deficiency in our society.[1] Traditionally, vitamin D has been associated with disorders of bone and mineral metabolism, but research now suggests that it plays a role in cardiovascular disease, immune system dysfunction, and cancer.[2–5] As a result, many health care providers are testing for and treating vitamin D deficiency, with a goal to normalize serum levels of 25-hydroxyvitamin D [25(OH)D]. In many instances, adequate serum levels are not achieved despite high doses of ergo- or cholecalciferol.

A recent letter indicated that problems with measurement of serum 25(OH)D may be a cause for inaccurate or variable levels when monitoring patients on vitamin D supplements.[6] We have found that administration relative to meal intake can be an additional factor that results in unpredictable serum 25(OH)D levels even when a proper assay is used. We commonly find that patients take the medication on an empty stomach or with a light meal. Because vitamin D is fat soluble, we hypothesized that absorption would be improved if patients were instructed to take their supplement (same dose, same preparation) with their largest meal of the day.[7]

Materials and Methods

We performed an IRB-approved prospective cohort study of patients seen at the Cleveland Clinic Foundation Bone Clinic for treatment of vitamin D deficiency. Patients who were taking a vitamin D supplement (either ergo- or cholecalciferol) who did not achieve an adequate rise in their serum 25(OH)D levels were included. These patients were taking the supplement on an

Received in original form October 30, 2009; revised form December 14, 2009; accepted February 4, 2010. Published online February 8, 2010.
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Journal of Bone and Mineral Research, Vol. 25, No. 4, April 2010, pp 928–930
DOI: 10.1002/jbmr.67

empty stomach or with a small meal, usually breakfast or lunch. They were advised to continue the same vitamin D supplement and take it with the largest meal of the day, usually supper. The subsequent total 25(OH)D level was analyzed 2 to 3 months later to determine the effect of this intervention. The chemiluminescence immunoassay was employed to measure total 25(OH)D (reference range 31 to 80 ng/mL). A paired *t* test statistic was used to analyze data. Results are expressed as mean ± SD; ranges are also provided.

Results

Seventeen patients were analyzed in this study. The mean age (±SD) and sex (F/M) ratio were 64.5 ± 11.0 years and 13 females and 4 males, respectively. Coexisting medical conditions are shown in Table 1. The dose of vitamin D (D_2 or D_3) ranged from 1000 to 50,000 IU daily. The mean baseline serum 25(OH)D level (±SD) was 30.5 ± 4.7 ng/mL (range 21.6 to 38.8 ng/mL). The mean serum 25(OH)D after diet modification (±SD) was 47.2 ± 10.9 ng/mL (range 34.7 to 74.0 ng/mL, $p < .01$; Fig. 1). Overall, the average serum 25(OH)D level increased by 56.7% ± 36.7%.

We performed a subgroup analysis based on the weekly dose of vitamin D: less than 50,000 IU ($n = 7$), 50,000 IU ($n = 7$), or more than 50,000 IU ($n = 3$). The mean age (±SD) and sex (F/M) ratio in the group receiving less than 50,000 IU were 63.6 ± 11.2 years and 6 females and 1 male, respectively. The average weekly dose of vitamin D_3 was 9800 ± 5300 IU. The 25(OH)D levels at baseline and after diet modification were 28.9 ± 4.6 ng/mL (range 21.6 to 34.6 ng/mL) and 45.4 ± 13.0 ng/mL (range 35.8 to 74.0 ng/mL), respectively ($p = .02$). The average serum 25(OH)D level increased by 59.6% ± 47.3%. The subgroup receiving 50,000 IU of vitamin D_2 per week had a mean age (±SD) and sex (F/M) ratio of 68.0 ± 12.8 years and 5 females and 2 males, respectively. The 25(OH)D levels at baseline and after diet modification were 31.3 ± 5.5 ng/mL (range 23.7 to 38.8 ng/mL) and 48.3 ± 11.5 ng/mL (range 34.7 to 69.0 ng/mL), respectively ($p = .01$). The average serum 25(OH)D level increased by 56.5% ± 35.5%. Finally, the 3 patients who received more than 50,000 IU of vitamin D_2 per week had a mean age (±SD) and sex (F/M) ratio of 58.7 ± 3.1 years and 2 females and 1 male, respectively. The average weekly dose of 25(OH)D was 183,333 ± 144,337 IU. The 25(OH)D levels at baseline and after diet modification were 32.4 ± 2.1 ng/mL (range 30.0 to 34.0 ng/mL) and 48.7 ± 5.5 ng/mL (range 45.0 to 55.0 ng/mL), respectively ($p = .03$). The average serum 25(OH)D level increased by 50.2% ± 13.4%.

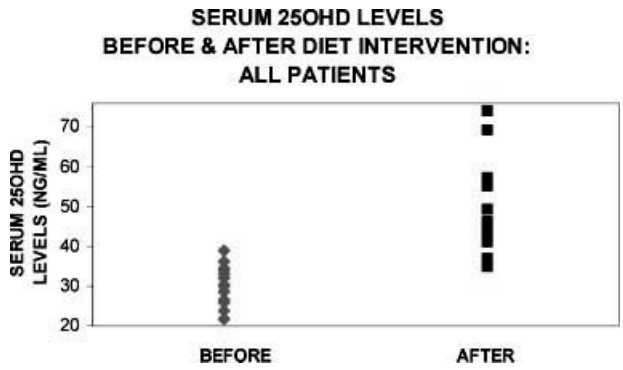

Fig. 1. Change in serum 25(OH)D levels before and after diet intervention observed in all patients.

Table 1. Coexisting Medical Conditions Observed in Patients Treated for Vitamin D Deficiency

Patients receiving <50,000 IU of vitamin D per week
Patient 1: Osteoporosis
Patient 2: Liver transplant, hepatitis C, hepatocellular carcinoma
Patient 3: Osteoporosis
Patient 4: Osteoporosis
Patient 5: Hyperparathyroidism, s/p parathyroidectomy, hypocalcemia
Patient 6: Hyperparathyroidism, s/p parathyroidectomy
Patient 7: Osteoporosis, short-bowel syndrome (malabsorption)
Patients receiving 50,000 IU of vitamin D per week
Patient 1: Osteopenia
Patient 2: Osteoporosis
Patient 3: Hyperparathyroidism secondary to vitamin D deficiency
Patient 4: Osteoporosis, celiac disease (malabsorption)
Patient 5: Osteoporosis
Patient 6: Osteopenia, celiac disease (malabsorption)
Patient 7: Renal osteodystrophy, secondary hyperparathyroidism
Patients receiving >50,000 IU of vitamin D per week
Patient 1: Liver transplant, malabsorption, secondary hyperparathyroidism
Patient 2: Osteoporosis, malabsorption
Patient 3: Osteoporosis

Discussion

In our practice, it is common to see patients treated with vitamin D supplements who do not achieve an appreciable rise in their serum 25(OH)D level after therapy despite large prescribed doses. A consistent increase of 50% or greater was seen in the serum 25(OH)D concentration when patients consumed the vitamin with the largest daily meal. It was not possible to decipher the fat, carbohydrate, and protein components of meals. Therefore, we focused on the meal size. Notably, the type of vitamin D preparation (oil or solid) did not seem to make a difference. Patients in the subgroups taking 50,000 or more than 50,000 IU of vitamin D_2 per week used an oil-based preparation, whereas the patients taking less than 50,000 IU per week of vitamin D_3 took either an oil-based or a solid preparation. Again, the mean rise in all three subgroups was similar, around 50%.

It was clear that some patients required very large doses of supplement to achieve a mid-normal-range value. The use of such large doses concerns many clinicians because of a fear of toxicity. However, it is not the dose prescribed alone that should be considered, but rather how much is actually absorbed. Some

patients require very large doses to achieve mid-normal levels. Monitoring the serum level is critical. A recent study indicates that serum concentration of 25(OH)D only in the high-normal reference interval prevents nonvertebral fractures.[8] Hence, striving to achieve this level (i.e., approximately 50 ng/mL) may be optimal, rather than a level at the low end of the normal range.

At present, there are few studies that provide convincing evidence for the optimal method for taking vitamin D supplements.[9] Admittedly, there are several limits to our study, including the small sample size, lack of a control group, and an inability to know exactly how the patients took their supplements. Despite these limitations, the results are striking and consistent across a rather heterogeneous group of patients (i.e., different disease states and different preparations and doses of vitamin D). It therefore seems reasonable to ask patients to take vitamin D supplements with their largest meal because it may be a cost-effective strategy that could very well help patients to achieve optimal serum levels of 25(OH)D.

Disclosures

Both the authors state that they have no conflicts of interest.

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