Clinical Study

Effect of High- versus Low-Fat Meal on Serum 25-Hydroxyvitamin D Levels after a Single Oral Dose of Vitamin D: A Single-Blind, Parallel, Randomized Trial

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Background/Aims. Vitamin D3 is liposoluble, so dietary fat could increase its oral absorption. Our aim was to compare serum 25-hydroxyvitamin D [25(OH)D] after the oral intake of cholecalciferol with a high- or low-fat meal.

Methods. In a single-blind, parallel clinical trial, 32 healthy physicians were divided into two groups. In the same day, they ingested 50,000 IU (1.25 mg) of vitamin D3 with food: group 1 (G1): lipids: 25.6 g and group 2 (G2) lipids: 1.7 g. Serum 25(OH)D (0, 7, and 14 days), and parathyroid hormone (PTH), and calcium (0 and 14 days) were measured.

Results. Baseline mean serum 25(OH)D levels were 42.7 ± 19.0 nmol/L in G1 and 36.4 ± 19.0 nmol/L in G2 (P = 0.38). After cholecalciferol, mean serum 25(OH)D was higher in G1 (P < 0.001): 7 days: G1 = 46.2 (38.4–53.9) nmol/L and G2 = 33.7 (25.4–40.1) nmol/L; 14 days: G1 = 53.7 (45.2–62.1) nmol/L and G2 = 33.7 (25.2–42.2) nmol/L. Serum PTH and 25(OH)D were negatively correlated before and after the intake of vitamin D3, respectively, r = −0.42 (P = 0.02) and r = −0.52 (P = 0.003).

Conclusions. A high-fat meal increased the absorption of vitamin D3, as measured by serum 25(OH)D.

1. Introduction

Vitamin D is important for human health [1], and lower serum 25-hydroxyvitamin D [25(OH)D] has been associated with increased mortality [2]. Moreover, a high prevalence of vitamin D deficiency has been identified worldwide in recent years [3]. Dietary supplements are useful to prevent and treat this deficiency [4].

As vitamin D is liposoluble, its oral absorption could increase if ingested with a fat-rich meal. Although there are several studies about the effect of different ways to supply vitamin D in its serum levels [5–9] or in serum 25(OH)D levels [10–14], only a few of these studies describe the amount of fat ingested with vitamin D [7, 9, 11]. Therefore, the aim of this study was to compare serum 25(OH)D levels after the oral intake of cholecalciferol with a high- or low-fat meal in young adults.

2. Materials and Methods

This single-blind parallel randomized trial included 32 healthy resident physicians in Porto Alegre, latitude 30°, Brazil. Height and weight were measured to calculate body mass index (BMI: weight (kg)/height^2 (m)). Two different groups were formed with 16 individuals, each according to sex and BMI, and randomly assigned to a high-(Group 1: G1) or low-fat meal (Group 2: G2). The exclusion criteria were not drinking milk; BMI ≥30 kg/m^2 or <18.5 kg/m^2; known liver, kidney or endocrine disease; use of supplements of calcium and/or vitamin D; use of anticonvulsants, barbiturates, or glucocorticoids, and travel outside the Brazilian South region during the previous 120 days. Skin phototype was evaluated according to Fitzpatrick [15].

The low-fat meal contained skim milk, white bread with fruit jelly, and fruit salad. The high-fat meal contained...
was kept at measurement of 25(OH)D, PTH, and total calcium. Serum was collected to measure 25(OH)D, parathyroid hormone (PTH), total calcium, albumin, magnesium, and creatinine, and a urine sample was collected to measure creatinine, 25(OH)D, and PTH. Then, 50,000 IU of cholecalciferol in powder (Taizhou Hisound Chemical Co. Ltd, Taizhou, Zhejiang, China) was provided by DEG Ativando Princípios Company, São Paulo, SP, Brazil, which evaluated its content through HPLC (99.9%). The content of vitamin D₃ in the capsules ranged from 48,170–52,777 IU. The number of subjects, calculated to detect a 30% difference in mean serum 25(OH)D levels between groups, with a standard deviation of 7.7 ng/mL [17], power of 80%, and $P < 0.05$, was 15 per group. One additional subject was included in each group to allow for losses.

Repeated measures ANOVA was used to compare mean serum 25(OH)D levels. Correlations were analyzed by the Pearson correlation coefficient. All data were analyzed with SPSSv.16.0, and differences were considered significant when $P < 0.05$.

Cholecalciferol in powder (Taizhou Hisound Chemical Co. Ltd, Taizhou, Zhejiang, China) was provided by DEG Ativando Princípios Company, São Paulo, SP, Brazil, which evaluated its content through HPLC (99.9%). The content of vitamin D₃ in the capsules ranged from 48,170–52,777 IU. All of the vitamin D capsules contained lactose (82 mg) and crystalline micro cellulose (18 mg). One International Unit (1 IU) of vitamin D is equal to 0.025 micrograms.

The study was approved by the Ethics Committee of HCPA, and participants were included after written informed consent.

### 3. Results

Forty resident physicians were invited to participate, and all agreed. Seven were excluded because they had traveled to regions with high UVB incidence in the last 120 days, and one was excluded for having BMI $>30$ kg/m². Two participants, one from each group, did not enter the protocol, for missing the first appointment: one forgot and the other was acutely ill. All others were included in the analyses (Figure 1). The study was conducted in October 2009.

### Table 1: Nutritional composition of meals.

| Nutrients² | Group 1 | Group 2 |
|------------|---------|---------|
| Lipids (%) | 25.6 g (48.7) | 1.7 g (3.3) |
| Carbohydrates (%) | 43.3 g (36.6) | 95.5 g (82.2) |
| Proteins (%) | 17.2 g (14.5) | 16.8 g (14.4) |
| Fiber | 1.5 g | 3.5 g |
| Energy | 473 kcal | 465 kcal |

²According to the Brazilian Table of Food Composition [16].

³Percentage of total calories in the meal.

Figure 1: Flow diagram of the participants. Abbreviation: BMI-Weight (kg)/Height (m)².
The baseline characteristics are shown in Table 2. Photo-
types ranged from I to II. Serum 25(OH)D was <75 nmol/L in 28 subjects, <50 nmol/L in 21 subjects, and <25 nmol/L in 5 subjects. After cholecalciferol, mean serum 25(OH)D levels and mean variation of serum 25(OH)D levels were higher in G1 (P < 0.001), and the differences were significant at day 14 (Figures 2(a) and 2(b)).

At day 14, no one had hypercalcemia, and mean serum total calcium (G1: 2.3 ± 0.1 mmol/L and G2: 2.2 ± 0.1 mmol/L; P = 0.11) and PTH (G1: 33.1 ± 11.0 ng/L; G2: 36.4 ± 9.0 ng/L, P = 0.37) were similar in both groups; the mean change in serum PTH was negative in G1 (−1.8 ± 7.2 ng/L) and positive (5.5 ± 7.1 ng/L) in G2 (P < 0.01). In all participants, serum PTH and 25(OH)D levels were negatively correlated at baseline and 14 days after the intake of vitamin D, as shown in Figure 3.

4. Discussion

The intake of 50,000 IU of cholecalciferol with a fat-rich meal increased mean serum 25(OH)D levels, in young adults. A change in mean serum 25(OH)D levels was not observed in
vitamin D in ethanol could have made its absorption easier. than the one in the present study, and the total amount of fat at baseline (a), and 14 days after the oral intake of 50,000 IU of vitamin D3 (b).

In conclusion, the results of this small randomized controlled trial showed that vitamin D supplementation is more effective when given with fat-containing food. These findings can have important implications to define the adequate dietary intake of vitamin D.

Conflict of Interests

The authors declare no conflict of interests.
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