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Treatment of Vitamin D Deficiency Increases Lower Limb Muscle Strength in Institutionalized Older People Independently of Regular Physical Activity: A Randomized Double-Blind Controlled Trial

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Key Words
Cholecalciferol · 25-Hydroxyvitamin D · Institutionalized elderly · Muscle strength · Vitamin D

Abstract
Aims: To investigate the effects of a 6-month supplementation with calcium and cholecalciferol on biochemical parameters and muscle strength of institutionalized elderly. ***Methods:*** This prospective, double-blind, placebo-controlled, randomized trial included Brazilian institutionalized people ≥60 years of age receiving a 6-month supplementation (December to May) of daily calcium plus monthly placebo (calcium/placebo group) or daily calcium plus oral cholecalciferol (150,000 IU once a month during the first 2 months, followed by 90,000 IU once a month for the last 4 months; calcium/vitamin D group). Fasting blood samples for 25-(OH)D, PTH and calcium determination were collected (n = 56) and muscle tests were performed (n = 46) to measure the strength of hip flexors (SHF) and knee extensors (SKE) before (baseline) and after the 6-month intervention (6 months). ***Results:*** Due to seasonal variations, serum 25(OH)D significantly enhanced in both groups after treatment, but the calcium/vitamin D group had significantly higher 25-(OH)D levels than the calcium/placebo group (84 vs. 33%, respectively; $p < 0.0001$). No cases of hypercalcemia were observed. While the calcium/placebo group showed no improvement in SHF and SKE at 6 months ($p = 0.93$ and $p = 0.61$, respectively), SHF was increased in the calcium/vitamin D group by 16.4% ($p = 0.0001$) and SKE by 24.6% ($p = 0.0007$). ***Conclusions:*** The suggested cholecalciferol supplementation was safe and efficient in enhancing 25(OH)D levels and lower limb muscle strength in the elderly, in the absence of any regular physical exercise practice.

Introduction

Reductions in muscle mass and strength, even in healthy people, accompany the physiological aging process. Some studies [1–4] report that, associated with the loss of muscle strength, low levels of serum 25-hydroxyvitamin D [25(OH)D] can be observed in older subjects, especially in the institutionalized ones. This population is at risk for vitamin D deficiency due to decreased sunlight exposure, reduced dietary intake, reduced dermal ability to synthesize the prohormone cholecalciferol, im-

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paired intestinal absorption as well as impaired kidney or liver function [5].

Researches showed that older adults with a higher level of vitamin D in their blood scored better in muscle strength and mobility tests [6, 7], such as walking and getting up from a seated position. It seems that along with other factors, deficiency in both 25(OH)D and 1,25-hydroxyvitamin D contributes to the age-related decline in muscle strength [8].

Studies on seniors' muscle strength [9–12] indicate that vitamin D plays an important role in the improvement of this neuromuscular function. On the other hand, some authors have found no relation between vitamin D serum levels and muscle strength in similar populations [13, 14]. There is still some controversy concerning this topic, and other questions remain unclear, such as if the supplementation with vitamin D is more effective in individuals showing a more severe deficiency and if muscle strength of older people can be improved only by the natural enhancement of 25(OH)D levels due to seasonal variations.

As the first controlled trial focused on Brazilian institutionalized elderly people, the present study aims to evaluate the 25(OH)D levels in different seasons and to compare the effects of seasonal and therapeutic increments in 25(OH)D levels on muscle strength in this population.

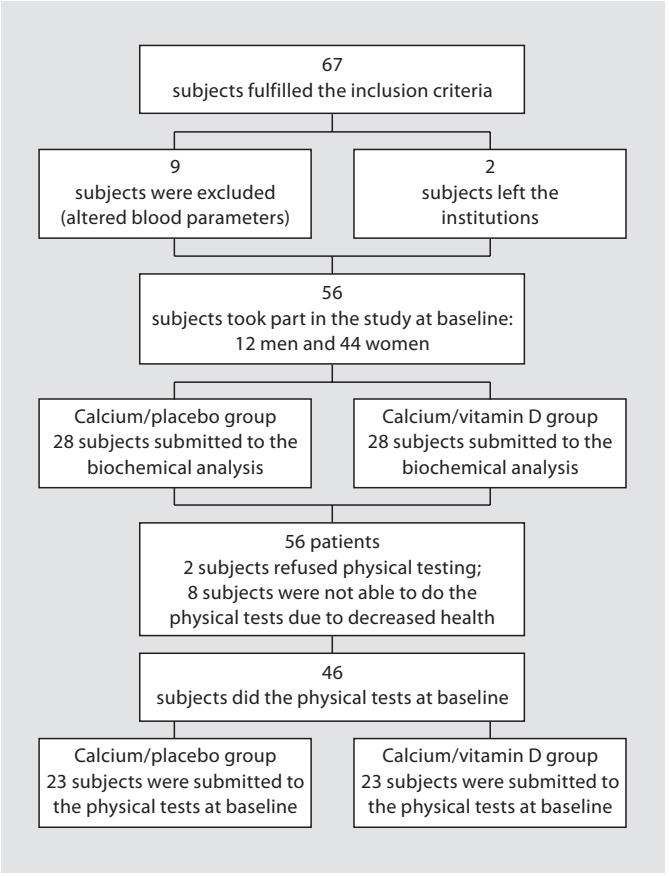

Fig. 1. Study design of the present intervention in the elderly.

Subjects and Methods

Subjects

This study evaluated both men and women aged 60 and older (median 77.6; range 62–94 years) living in two different long-stay geriatric care (LSGC) units in the city of São Paulo, Brazil. The study was approved by the Ethics Committee of the Federal University of São Paulo and the committees of the LSGC units. Before study entry, all subjects signed a written consent.

For a better understanding of the design and results of this trial, it is relevant to point out that the profile of institutionalized elderly Brazilians is somehow different from that of many other countries. Not only because of economic reasons but also due to cultural aspects, elderly Brazilians usually live with their family until they die, with those living in LSGC units frequently being the more frail ones, which explains why in 11 subjects health status deteriorated during the 6-month period of this research, and therefore they could not perform the physical tests at the end of the trial.

Subjects were included when their cognition status allowed them to understand and respond to the authors' questions and commands during the questionnaire and physical tests. Participants meeting the following exclusion criteria were excluded: hypercalcemia; primary hyperparathyroidism; chronic kidney disease (serum creatinine >2 mg/dl); history of recent hip fracture (in the last 2 years); dependency on alcohol or illicit drugs; therapy with bisphosphonates, calcitonin, calcium, vitamin D and its metabolites; estrogen, selective estrogen receptor modulators and fluoride in the previous 6 months; any physical conditions that might affect the performance in the physical tests (severe osteoarthritis, rheumatic arthritis, edema or ulcer in the lower limb); use of any medications that might interfere with vitamin D metabolism; systolic blood pressure ≥200 mm Hg and/or diastolic blood pressure ≥100 mm Hg.

Daily calcium intake was estimated considering the nutrition table prepared by the nutritionists of each LSGC unit. Both institutions had very similar alimentary routines and none of them supplied >500 mg calcium/day. Vitamin D diet sources were irrelevant.

None of the subjects were engaged in any regular physical activity program, performing only the natural activities of daily life. Subjects' sunlight exposure was comparable in both institutions, and sunscreen lotion was not part of their habits according to reports of the nurses responsible for them in each LSGC unit. Their daily exposure to sunlight improved significantly during summer and hot days, whereas in winter and on cold days it decreased considerably.

Table 1. Characteristics of the study groups at baseline

Variables	Calcium/placebo (n = 28)	Calcium/vitamin D (n = 28)	p
Age, years	78 (63–92)	78.5 (62–94)	0.532
Gender, males/females	6/22	6/22	
Ethnicity			0.673
White	17	19	
Black	7	4	
Asian	0	1	
Mixed	4	4	
25(OH)D, nmol/l			
RV: >100 nmol/l	39.5 (20.3–68.8)	45.9 (20.3–84.8)	0.298
Ca^{2+}, nmol/l			
RV: 1.18–1.42 nmol/l	1.3 (1.2–1.4)	1.3 (1.2–1.4)	0.237
Total calcium, mg/dl			
RV: 8.5–10.5 mg/dl	9.0 (7.4–9.4)	8.9 (7.9–9.9)	0.300
Albumin, g/l			
RV: 3.2–5.6 g/l	4.2 (3.2–4.9)	4.2 (3.5–5.0)	0.569
Alkaline phosphatase, U/l			
RV: 50–250 U/l	153 (83–366)	191 (87–280)[a]	0.123
Phosphorus, mg/dl			
RV: 2.5–4.5 mg/dl	3.5 (2.3–4.5)	3.5 (2.6–4.7)	0.736
Creatinine, mg/dl			
RV: 0.2–1.4 mg/dl	1.1 (0.8–1.8)	1.2 (0.7–1.5)	0.708
iPTH, pg/ml			
RV: 15–65 pg/ml	45 (20.7–162.7)	48.5 (42.3–158.1)	0.857
SHF, kg	11.7 (5.5–16.9)[b]	10.2 (5.7–17.3)[b]	0.482
SKE, kg	11.9 (3.7–22.0)[b]	11.3 (6.7–21.4)[b]	0.733

Medians (ranges) are shown. RV = Reference values. [a] n = 27; [b] n = 23.

Design

In this prospective, randomized, double-blind, placebo-controlled trial, at the first recruitment 67 subjects of the two LSGC units fulfilled the inclusion criteria. They had their first 8-hour fasting morning blood samples collected between 6 and 8 a.m. for the biochemical analyses (August, September and October 2005). Ionized calcium was measured immediately, while the remainder of the blood samples was centrifuged for subsequent serum separation and storage at –20°C until analysis. After the biochemical examinations (November 2005), 9 subjects were excluded because of altered blood parameters and 2 others left the institution. Thus, of the initial 67 patients, 56 were considered for the biochemical analysis of this trial, and only 46 of them agreed to be submitted to a physical evaluation followed by the muscle strength tests. The study design is depicted in figure 1.

Patients were then randomized (block randomization) to one of two groups: the calcium/placebo group and the calcium/vitamin D group. Treatments with placebo or cholecalciferol were carried out from December 2005 to May 2006. At the end of the 6-month treatment, the second fasting morning blood samples were collected and analyzed followed by the final muscle strength tests.

Laboratory Analysis

Blood levels of 25(OH)D, ionized calcium (Ca^{2+}), total calcium (Ca), albumin, total alkaline phosphatase, phosphorus, creatinine and intact parathyroid hormone (iPTH) were measured before (baseline) and after (6 months) treatment. Chemiluminescence commercial assays (Elecsys 1010; Roche Diagnostics, Indianapolis, Ind., USA) were used to quantify iPTH. Ca^{2+} was measured by a specific ion electrode method (AVL 9180 Electrolyte Analyzer; AVL Scientific, Roswell, Ga., USA). Phosphorus and creatinine were measured by ultraviolet detection and alkaline picrate assay, respectively (ADVIA 1650; Bayer, Tokyo, Japan). The enzymatic colorimetric assay (ADVIA 1650; Bayer) was used to measure total calcium, albumin and alkaline phosphatase. Serum 25(OH)D was determined by means of a immunoradiometric assay (Diasorin, Stillwater, Minn., USA) presenting the following coefficients of variation: intra-assay = 5.6% and interassay coefficients of variation = 10.8%. All reference values are presented in table 1.

Questionnaire and Physical Evaluation

The examiners interviewed all the subjects using a questionnaire including the following items: clinical history, family history, dietary habits, consumption of alcohol and cigarettes, phys-

ical activity habits, limitations in activities of daily life and medications administered.

Before the beginning of the physical evaluation, parameters such as blood pressure, height, weight and condition of the lower limb skin were verified.

Muscle Strength Tests

Forty-six subjects (77.6 ± 8.2 years; 11 males and 35 females) did the physical tests at baseline, which were repeated in 35 of them (77.8 ± 8.2; 7 males and 28 females) at the end of the study. The dropouts were similar in both groups (at 6 months, there were 18 subjects in the calcium/placebo group and 17 in the calcium/vitamin D group) due to the following reasons: 2 patients died of stroke, 1 died of diabetes complications, 1 died of intestinal cancer, 1 left the institution and 6 had a deterioration in their general health state.

Subjects were tested for their maximum isometric strength of hip flexors (SHF) and knee extensors (SKE), measured by a portable mechanical dynamometer (model 01163; Manual Lafayette Muscle Test System, Ind., USA), which is easy to carry and handle and provides reliable measures when assessing elderly muscle strength.

The intraclass correlation coefficient was used for the analysis of the reliability of the muscle strength tests using the Lafayette dynamometer. After 15 days, 9 of the 47 subjects (75.4 ± 5.3 years) were retested, and the intraclass correlation coefficients were 0.94 for SHF and 0.97 for SKE.

The muscles of hip flexors and knee extensors of the dominant limb were assessed through a test in which the main examiner held the dynamometer perpendicularly over the tested muscle and then the subject exerted the maximum strength against the examiner's resistance. Before the beginning of the test, the movement was explained and demonstrated by the examiner to the patient that had to repeat it before the test started. Maximum isometric strength was estimated as a mean of three measures in each muscle group.

Hip Flexors. The subject remained seated in a chair supported on the back (hip and knees flexed at 90°) with both arms crossed over the chest to prevent him/her from using the hands on the chair and thus enhance the strength applied against the dynamometer. Patients were instructed to relax all parts of the body and make the effort only in the tested limb. The main examiner positioned the dynamometer perpendicularly on the subject's thigh 5 cm above the superior edge of the patella. An assistant examiner stood behind the patient with the hands holding his/her shoulders to stabilize the movement. After the command of the main examiner, the patient had to elevate the knee being tested, thus the maximum isometric muscle strength was applied against the dynamometer for 5 s.

Knee Extensors. The test for the knee muscles was very similar to the one described above, except that in the starting position the subject had the tested knee flexed at 80°. After the examiner's command to start the test, the patient had to try to extend the knee against the resistance applied by the examiner with the dynamometer placed 5 cm above the medial point between the lateral and medial malleolus.

Intervention

After randomization, calcium/placebo or calcium/cholecalciferol treatment was started in a double-blind manner. Participants of both groups received 1,000 mg of elementary calcium (oral) per day throughout the 6-month intervention. Vitamin D (cholecalciferol) drops (Magister Handling Pharmacy, São Paulo, Brazil), 10,000 IU/drop, were directly administered into the subjects mouths by the authors, once a month. Subjects in the calcium/vitamin D group were given 150,000 IU cholecalciferol/month for 2 months, and then, 90,000 IU/month in the following 4 months.

In this study, serum levels of 25(OH)D were set as follows: deficiency ≤25 nmol/l; insufficiency 26–50 nmol/l; sufficiency 51–100 nmol/l, and ideal level >100 nmol/l [15]. The dietary routine of all participants was left unchanged throughout the study to prevent them from obtaining calcium or vitamin D from any other sources.

Statistical Analysis

For all statistical tests, results were considered significant when $p < 0.05$. The Kolmogorov-Smirnov test was used to test the hypothesis of normality of the variables. Among all the biochemical parameters, only iPTH, 25(OH)D and serum calcium levels did not present a normal distribution, thus these variables were analyzed using the Wilcoxon signed-rank test. The other quantitative biochemical and muscle strength parameters were normally distributed, so they were compared in two different ways: (a) between paired groups, using Student's t test for dependent variables, and (b) between two independent groups using Student's t test for independent samples. Since 25(OH)D and iPTH were nonparametric variables, their correlation between each other and SHF and SKE was determined using Spearman's coefficient (ρ). The generalized estimation equations were used for the analysis of the correlation between initial 25(OH)D serum levels and the development of muscle strength in subjects.

Results

The subjects' characteristics at baseline are presented in table 1. The groups were similar in all parameters: age, gender, body mass index, ethnicity, and biochemical and hormonal serum values. There was also no statistical difference between groups at baseline concerning the SHF and SKE tests. At the beginning of the study, 10.7% of the subjects in the calcium/placebo group and 3.6% in the calcium/vitamin D group presented deficient levels in 25(OH)D (<25 nmol/l), while 53.65% of the subjects in the calcium/placebo group and 67.9% in the calcium/vitamin D group had insufficient levels (<50 nmol/l).

At 6 months, the effect of seasonality on serum 25(OH)D levels could be seen in the calcium/placebo group, with 33% increases in 25(OH)D ($p = 0.0002$). Nevertheless, the supplementation of vitamin D produced a greater increase in serum 25(OH)D in the calcium/vitamin D group, enhancing their initial levels by 84% ($p < 0.0001$; fig. 2).

According to the 25(OH)D blood concentrations at the end of the study, 40% of the subjects in the calcium/

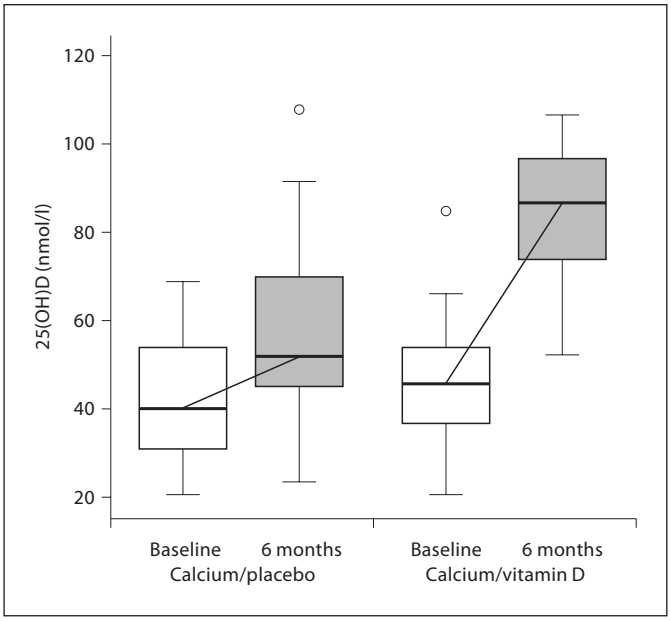

Fig. 2. Serum levels of 25(OH)D in both groups before (baseline) and after (6 months) the treatment.

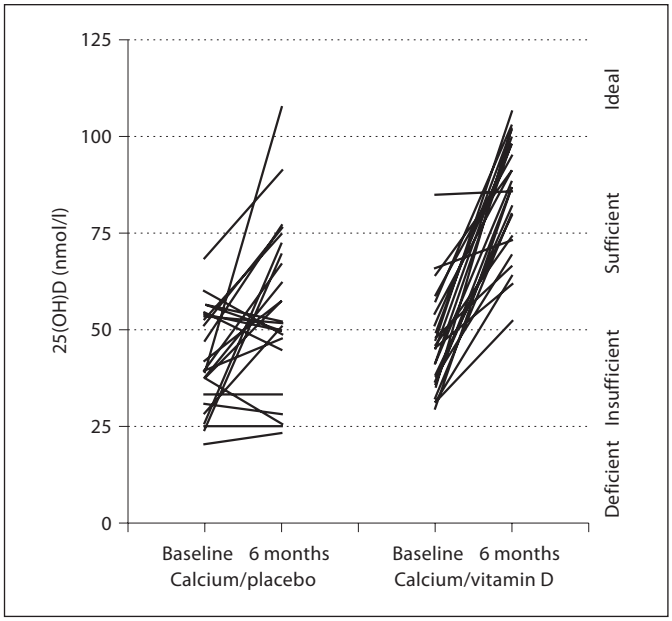

Fig. 3. Subjects of the calcium/placebo group and the calcium/vitamin D group divided by serum levels of 25(OH)D at baseline and 6 months after the supplementation with calcium-placebo or calcium-cholecalciferol.

placebo group still presented deficient/insufficient levels (<50 nmol/l), whereas no subject in the calcium/vitamin D group had insufficient or deficient levels. Also, in the calcium/vitamin D group, sufficient levels (51–100 nmol/l) were achieved by 80.8% of the subjects, and 19.2% reached ideal levels (>100 nmol/l; fig. 3).

In both groups, there were no differences in iPTH levels between baseline and 6 months ($p = 0.73$). At baseline, there was a significant negative correlation between 25(OH)D and iPTH serum levels in all patients ($r = -0.34$; $p = 0.01$), and at 6 months the negative correlation was lower and did not reach significance ($r = -0.26$; $p = 0.07$). Although prevalence of secondary hyperparathyroidism increased by 10% (from 17.9 to 28%) in the calcium/placebo group and decreased by 5.4% in the calcium/vitamin D group (from 21.4 to 16%), these results were not statistically significant ($p = 0.259$).

In both groups, total calcium levels did not significantly differ between baseline and 6 months ($p = 0.759$). In both study groups, serum levels of total calcium were increased by 2% at the end of the intervention compared to baseline ($p = 0.009$), but no subject developed hypercalcemia (>10.5 mg/dl) after cholecalciferol supplementation. The biochemical parameters of both groups at 6 months are presented in table 2.

There was a positive correlation between SHF and SKE at baseline ($r = 0.6$; $p < 0.001$) and 6 months ($r = 0.7$; $p < 0.001$).

Subjects of both groups scored the same values during lower limb muscle strength tests at baseline (table 1), but showed different results at the end of the trial. While SHF and SKE were not statistically different between baseline and 6 months in the calcium/placebo group, SHF had increased by 16.4% (fig. 4) and SKE by 24.7% in the calcium/vitamin D group at study completion (fig. 5).

When subjects were grouped according to their baseline 25(OH)D levels, significant improvements in SHF were particularly noticeable in those with low baseline levels (<50 nmol/l; odds ratio = 1.10; 95% confidence interval = 1.03–1.17; $p = 0.003$; fig. 6).

Discussion

It is already known that institutionalized elderly people often present with low or very low levels of serum vitamin D [16, 17]. However, researchers have not established a consensual threshold for optimal 25(OH)D serum levels, mostly because it can vary depending on the physiologic effect expected after treatment. In this study,

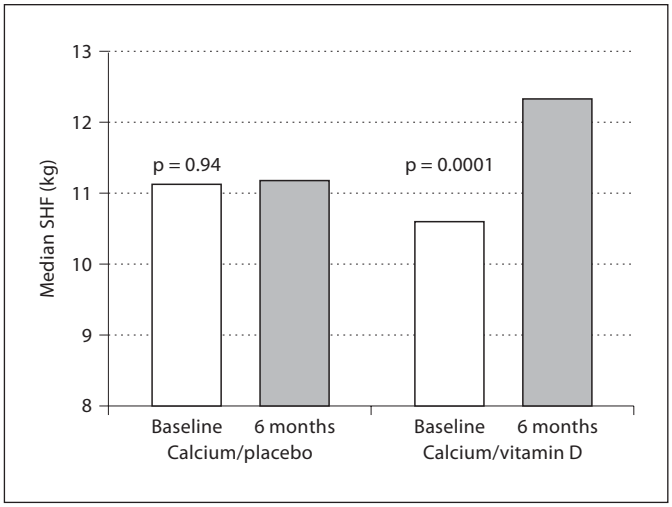

Fig. 4. Progression of muscle strength of hip flexors in the calcium/placebo group and the calcium/vitamin D group at baseline and at 6 months.

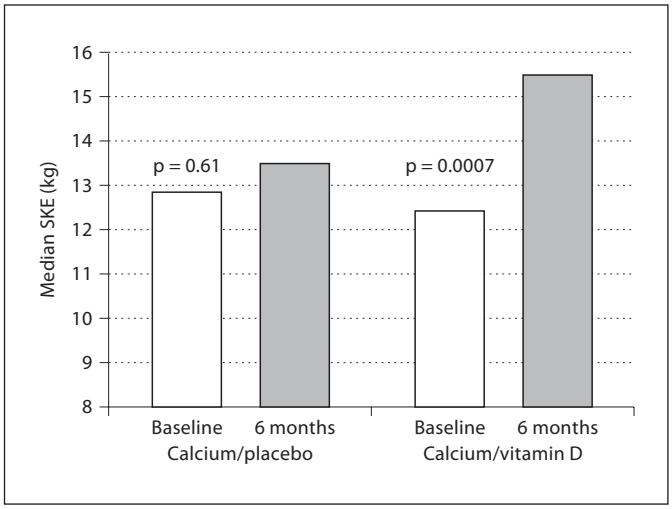

Fig. 5. Progression of muscle strength of knee extensors in the calcium/placebo group and the calcium/vitamin D group at baseline and at 6 months.

Table 2. Biochemical parameters of the study groups at the end of the study (6 months)

	Calcium/placebo (n = 25)	Calcium/vitamin D (n = 26)	p value
25(OH)D, nmol/l			
RV: >100 nmol/l	51.8 (23.5–107.8)	86.6 (52.3–106.5)	<0.0001
Ca^{2+}, mmol/l			
RV: 1.18–1.42 nmol/l	1.27 (1.17–1.41)	1.25 (1.17–1.36)	0.032
Total calcium, mg/dl			
RV: 8.5–10.5 mg/dl	8.9 (7.3–10.0)	9.10 (8.3–9.8)[a]	0.008
Phosphorus, mg/dl			
RV: 2.5–4.5 mg/dl	3.4 (2.7–4.8)	3.4 (2.7–4.4)[a]	0.023
iPTH, pg/ml			
RV: 15–65 pg/ml	47.5 (6.6–101.5)	41.4 (21.6–151.6)[a]	0.574

Results are expressed as medians (ranges). RV = Reference values. [a] n = 25.

as the main outcome expected was an improvement in lower-extremity function, ideal 25(OH)D levels were defined as levels >100 nmol/l, based on the research of Bischoff-Ferrari et al. [18], which suggests that serum 25(OH)D concentrations of 40 nmol/l are desirable, but levels of 90–100 nmol/l are better for the preservation of lower-extremity muscle strength.

As a major fraction of vitamin D is synthesized in the skin via sunlight exposure, it would be reasonable to imagine that in tropical countries like Brazil, with hot and sunny days during the whole year, the incidence of vitamin D deficiency/insufficiency is low. However, a recent study focusing on elderly Brazilians indicated the contrary [19]. Blood samples of 177 institutionalized elderly (125 women and 52 men; 76.6 ± 9 years of age) were analyzed, and a very high prevalence of inappropriate 25(OH)D levels was detected. Deficiency (<25 nmol/l) was found in 40.7%, insufficiency (<50 nmol/l) in 30.5%, and an association with secondary hyperparathyroidism in 61.7% of the subjects.

The importance of vitamin D supplementation for the health of the elderly has already been recognized. How-

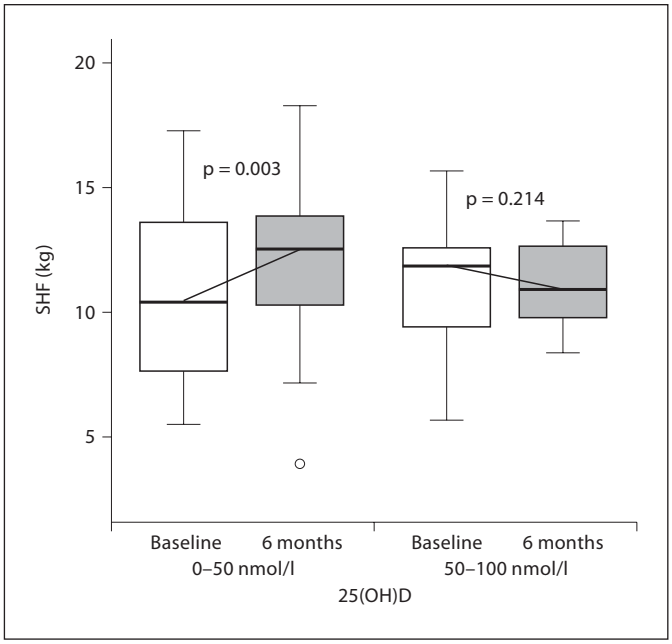

Fig. 6. SHF at baseline and at 6 months according to initial 25(OH)D serum levels of all subjects, showing that only in those with initial 25(OH)D serum levels <50 nmol/l SHF significantly increased.

ever, so far, the amount of vitamin supplementation has not been defined for elderly patients with vitamin D deficiency. Some clinical trials found that in order to maintain satisfactory serum 25(OH)D levels, 500–1,000 IU of vitamin D should be ingested daily [20, 21]. Nevertheless, other researchers recommend higher doses of vitamin D to treat deficient patients [22, 23]. Bischoff-Ferrari et al. [18] stated that to reach the desirable range of 90–100 nmol/l, vitamin D doses of >1,000 IU would be needed. According to studies in adults, intakes as high as 4,000–10,000 IU/day are safe, and those of 4,000 IU/day may increase 25(OH)D concentrations to 75 nmol/l in 88% of adults [24, 25]. Holick [26] affirms that giving 50,000 IU vitamin D_2 orally once a week for 8 weeks to patients with serious 25(OH)D deficiency is a reasonable treatment strategy.

Our subjects had very low 25(OH)D levels before the intervention, therefore a higher initial dosage of oral cholecalciferol was given: 150,000 IU once a month in the first 2 months, and 90,000 IU once a month for the following 4 months. As no cases of hypercalcemia were found, this dosage was considered safe. Some other trials administered levels of 4,000 IU/day and concluded that this dosage is safe for up to 6 months [25, 27, 28].

In a recent study conducted at the Division of Endocrinology in the Federal University of São Paulo [29], treatment of geriatric institutionalized patients with 1,000 IU of cholecalciferol/day for 12 weeks did not result in 25(OH)D levels exceeding 75 nmol/l in most patients, and therefore, higher cholecalciferol dosages were suggested to treat this population.

The intervention implemented in the present trial seemed to be efficient in correcting 25(OH)D deficiency, considering that 64.3% of the calcium/placebo patients had vitamin D deficiency/insufficiency (<50 nmol/l) at baseline and that in 40% insufficiency was still present at 6 months, despite the increase in serum 25(OH)D due to enhanced sunlight exposure (summer). However, while 71.5% of the patients in the calcium/vitamin D group presented with vitamin D insufficiency in the beginning, at the end of the study all of them presented serum levels >50 nmol/l: in 80.8% levels were sufficient (50–100 nmol/l) and in 19.2% ideal (>100 nmol/l).

A negative correlation between iPTH and serum 25(OH)D was seen at baseline, but at the end of the intervention it lost its significance, demonstrating that iPTH correlates with vitamin D mainly in the presence of low serum 25(OH)D.

Vitamin D acts directly on skeletal muscle function and is important to maintain skeletal muscle mass, strength and speed of muscle contraction [30]. Some researchers have found associations between low blood levels of 1,25-hydroxyvitamin D and 25(OH)D in elderly populations with impaired neuromuscular function, such as body sway, muscle strength, risk of falls and general disability for activities of daily life [31–34], although these were not observed by others [35, 36].

In the current study, a striking correlation was found between SKE and SHF at 6 months in all patients (r = 0.65), indicating a high reliability of the instrument (hand-held dynamometer) used for measuring muscle strength in older people [37].

A wide range of variables affects muscle strength, e.g. general health, a previous history of physical activity and genetic potential (number and quality of muscle fibers), and such aspects could not be controlled in this trial. Nevertheless, our results demonstrated that cholecalciferol supplementation efficiently increased lower limb muscle strength in the treated group. While the calcium/vitamin D group presented a 16.4% improvement in SHF and a 24.6% increase in SKE at 6 months, the calcium/placebo group showed no improvement at all. Our findings agree with others that also evidenced an increase in lower limb muscle strength in older people after an inter-

vention with different vitamin D metabolites [6, 38, 39]. Glerup et al. [10], in a 3-month treatment with 0.5 μg/day of α-calcidol combined with 400 IU of ergocalciferol and 1,000 mg of calcium, found a 24.8% increase in lower limb strength in a vitamin D-deficient elderly population, findings very similar to the ones observed in the present study.

Vitamin D nuclear receptors were identified on muscle cells and their number decreases with advancing age [40]. Vitamin D deficiency may lead to loss of type II muscle fibers and thus to atrophy of proximal muscles with an increased risk of falling and fractures [41]. Although our study did not evaluate the risk of falling and fractures, the improvement in lower limb muscle strength in the treated group led us to suppose that our intervention could further attenuate such negative events.

In this trial, we observed that vitamin D supplementation significantly enhanced SHF only in patients with lower initial serum levels of 25(OH)D. Janssen et al. [42] had already suggested that the improvement in neuromuscular function following vitamin D supplementation occurs mainly in subjects with low 25(OH)D serum levels, i.e., levels <40 nmol/l. If this is correct, it could explain some negative results found by others, e.g. Grady et al. [43], who did not find any increase in muscle strength in elderly women >69 years after calcitriol treatment, probably because initial serum 25(OH)D levels exceeded 60 nmol/l. Kenny et al. [44] also reported that vitamin D supplementation in healthy older community-dwelling men showing average serum 25(OH)D levels of 65 nmol/l did not improve their functional abilities.

In spite of the increase in 25(OH)D levels in the calcium/placebo group due to seasonal variation, 40% of subjects (and 0% in the calcium/vitamin D group) still had deficient/insufficient vitamin D levels (<50 nmol/l) and only 1 patient reached the ideal level (>100 nmol/l). Even with a 33% improvement in 25(OH)D levels at 6 months, the subjects in the calcium/placebo group did not show any enhancement in lower limb muscle strength. These results indicate that in an elderly institutionalized population with such low levels of serum 25(OH)D, the increase in sunlight exposure does not suffice either to normalize vitamin D levels in blood or to increase the muscle strength of lower limbs satisfactorily. It has been recommended that older people at high risk, such as the frail, housebound or institutionalized ones and those with restricted mobility, should receive routine supplementation of vitamin D [45, 46] in order to preserve muscle strength and functional ability [9, 11, 42, 47].

Two of the various reasons why older people cannot synthesize enough vitamin D in skin via sunlight exposure are the reduction in skin thickness combined with a decrease in the 7-dehydrocholesterol (vitamin D precursor) content of the skin. It has been estimated that the vitamin D production capacity of the skin at the age of 70 is reduced to only 30% of the capacity of a 20-year-old person [48–51]. Thus, after exposing their bodies to sunlight, it is possible that older people will not produce the amount of vitamin D required to maintain optimum serum 25(OH)D levels and to preserve muscle function. Oral vitamin D supplementation should be recommended in these cases.

This trial presented some limitations with respect to the relatively small sample size and the fact that very few men took part in the study, which could lead to a possible misinterpretation of the results regarding gender.

One striking point of the present study is that frail older subjects deficient in vitamin D and treated with cholecalciferol could significantly improve their lower limb muscle strength without any extra physical activity program. Although scientific evidence confirms the numerous benefits of the regular practice of physical exercise to children, adults and older persons [52], in some cases, e.g. the institutionalized elderly reported in this trial, patients are so frail initially that their engagement in a fitness program could be more harmful than beneficial. In these cases, vitamin D supplementation may enhance general muscle strength of frail people with low 25(OH)D level, thus restoring their basic muscle function and enabling them to participate in a progressive physical exercise program.

In conclusion, vitamin D deficiency is a common condition among institutionalized elderly people living in Sao Paulo, Brazil, and the 6-month cholecalciferol intervention with an average dose of 3,600 IU/day efficiently and safely increased serum levels of 25(OH)D and improved muscle strength in lower limbs. These results reinforce the idea that supplementation with calcium and vitamin D is an efficient, easy and cheap therapy that can be administered to frail geriatric patients to enhance their muscle strength and, consequently, improve their quality of life.

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