Effects of a Short-Term Vitamin D and Calcium Supplementation on Body Sway and Secondary Hyperparathyroidism in Elderly Women

MICHAEL PFEIFER,1 BETTINA BEGEROW,1 HELMUT W. MINNE,1 CHRISTINE ABRAMS,2 DETLEF NACHTIGALL,3 and CORINNA HANSEN3

ABSTRACT

Long-term vitamin D and calcium supplementation is effective in reducing nonvertebral fractures in elderly people. Increased bone fragility caused by secondary hyperparathyroidism (sHPT) and impaired balance are known risk factors for hip fractures. The hypothesis is that short-term therapy with calcium and vitamin D may improve body sway as well as sHPT more effectively than calcium monotherapy. The effects of 8 weeks of supplementation with vitamin D (cholecalciferol) and calcium on body sway and biochemical measures of bone metabolism were measured. The sample consisted of 148 women (mean ±SD age, 74 ± 1 years) with a 25-hydroxycholecalciferol level below 50 nmol/liter. They received either 1200 mg of calcium plus 800 IU of vitamin D or 1200 mg of calcium per day. We measured intact parathyroid hormone (PTH), markers of bone turnover, and body sway before and after treatment. Falls and fractures among the participants were followed over a 1-year period. Compared with calcium mono, supplementation with vitamin D and calcium resulted in an increase in serum 25-hydroxyvitamin D of 72% (p < 0.0001), a decrease in the serum PTH of 18% (p = 0.0432), and a decrease in body sway of 9% (p = 0.0435). The mean number of falls per subject during a 1-year follow-up period was 0.45 for the calcium mono group and 0.24 for the calcium and vitamin D group (p = 0.0346). Short-term supplementation with vitamin D and calcium improves sHPT and body sway and therefore may prevent falls and subsequent nonvertebral fractures in elderly women. (J Bone Miner Res 2000; 15:1113–1118)

Key words: vitamin D, body sway, falls, secondary hyperparathyroidism, hip fractures

INTRODUCTION

Increased bone fragility and increased number of falls caused by impaired muscle function are known risk factors for hip fractures.13 Further, postural instability has been identified as a risk factor for Colles' fracture.25 The percentage of elderly people who fall increases steeply in those older than 70 years of age, and over 90% of hip fractures in elderly people occur as a result of a fall.13,26 Impaired balance and increased body sway are important causes of falls.5-8 Nguyen et al. (1993) showed that besides bone density at the femoral neck, the main predictive factors for nonvertebral fractures were body sway and quadriceps strength.14 This is confirmed by Jones et al. (1995) in a population-based study.9 We hypothesized that inadequate vitamin D intake has an impact on body sway and that therefore vitamin D supplementation is beneficial to elderly people.
Supplementation with vitamin D and calcium reduces the risk of hip fractures and other nonvertebral fractures among elderly people. This effect could be caused by an increase in bone mineral density (BMD) at the femoral neck. However, these small changes in BMD suggest that vitamin D and calcium have an additional effect on bone quality, which explains the reduced fracture rate.

Furthermore, inadequate intake of calcium and vitamin D leads to reduced calcium absorption and increased serum concentrations of parathyroid hormone (PTH). Elevated PTH levels lead to an increased bone turnover and bone loss, particularly in cortical bone. Recent studies have shown a high incidence of secondary hyperparathyroidism (sHPT). sHPT contributes to bone fragility and even mild forms should be treated. Long-term treatment with calcium and vitamin D is successful in reducing sHPT.

The aim of this study was to evaluate the effect of a short-term treatment with calcium and vitamin D in comparison with calcium monotherapy with regard to sHPT and body sway in the elderly. Patients’ treatment started at the end of winter allowing the comparison of the effect of naturally synthesized vitamin D in the calcium mono group to the effect of vitamin D supplementation in the calcium and vitamin D group.

MATERIALS AND METHODS

Subjects

We studied healthy ambulatory women 70 years of age or older who were recruited through newspaper advertisements in the community. The inclusion criterion was a 25-hydroxycholecalciferol serum level below 50 nmol/liter while the exclusion criteria included hypercalcemia or primary HPT; fractures of the extremities caused by osteoporosis; therapy with a bisphosphonate, calcitonin, vitamin D and vitamin D metabolites, estrogen, tamoxifen in the past 6 months, or fluoride in the past 2 years; known intolerance to study medication; chronic renal failure (serum creatinine above 20% of the upper limit of the reference range); history of drug or alcohol abuse; nicotine abuse (more than 20 cigarettes per day); more than seven cups of coffee daily; scheduled holiday along the geographic longitude during the study period; diabetes mellitus and other diseases; and medications possibly interfering with postural stability and balance. Specifically, anticonvulsant users were excluded because of interference with vitamin D metabolism.

Two hundred eight subjects were prescreened by a standardized telephone interview. One hundred sixty-five subjects (79%) were invited for screening of which 148 (71%) were finally enrolled. The protocol was approved by the responsible Ethics Committee, and written informed consent was obtained from each subject.

Study design and supplements

During an 8-week, double-blind, controlled trial, subjects were randomly assigned to either the calcium mono or the calcium–vitamin D group. At study entry, a complete physical examination and assessment of the subjects’ medical history, diet, and physical activity were performed. In addition, blood and urine were analyzed and body sway was measured. The subjects were advised to maintain their usual diets and to avoid taking supplemental calcium and vitamin D on their own. The subjects took either one tablet containing 600 mg of elemental calcium in the form of calcium carbonate or one tablet with 600 mg of elemental calcium and 400 IU of cholecalciferol at breakfast and dinner together with the meals.

The study took place in Bad Pyrmont and Hameln, two neighborhood cities in Lower Saxony, Germany (latitude, 52°N) and commenced in March 1997, when vitamin D levels are known to be at their lowest level, and terminated in May 1997. At that time point, supplementation with vitamin D and calcium as well as calcium alone was discontinued.

Status of subjects and compliance

During the trial, one subject in the calcium mono group was excluded from the study because of noncompliance. She refused to undergo the measurements. One subject in the vitamin D–calcium group and another in the calcium mono group discontinued for personal reasons (loss of interest and decision to go on holidays). One hundred forty-five subjects were examined at the final visit and included in the intention-to-treat analyses.

The mean (±SD) rate of compliance with treatment, assessed on the basis of pill counts, was 95 ± 12% for the calcium mono tablets and 96 ± 10% for the vitamin D–calcium tablets.

The number of falls was recorded by questionnaires. A fall was defined as falling onto the floor or ground or hitting an object like a chair or stair. Not included as falls were controlled or intentional movements toward a chair or bed or a near fall in which the participant caught herself before falling onto the floor or ground.

All fractures were the result of falls and were verified by X-ray and medical reports. After 1 year of follow-up the response rates were 91% for the calcium mono group and 95% for the vitamin D–calcium group.

Measurements

The calcium and vitamin D intake of the subjects was assessed semiquantitatively by a food-frequency questionnaire. Physical activity, as well as consumption of alcohol and nicotine, also was determined by questionnaire. Height was measured with a stadiometer, and weight was measured with a digital scale. Concomitant medication was classified according to anatomical therapeutic chemical (ATC) groups and anatomic regions depending on the active compound and the indication (ATC classification index 1994). These parameters were assessed at baseline at the end of the 8-week trial and the 1-year period of follow-up.

Body sway was measured by using a sway meter that measured displacements of the body at the level of the waist in 30-s periods. The device consists of a rod attached to the subject at waist level by a firm belt. The rod is 40 cm in length and extends behind the subject. A digitizing tableau...
is fixed on an adjustable height table located behind the subject. The height of the table is adjusted so that the rod is in a horizontal plane and the tip of a pen can record the movements of the subject via digitizing tableau to a computerized system. Displacements of the body in frontal and sagittal direction were recorded. In addition, the sway area was calculated by multiplying the frontal diameter with the sagittal diameter. The coefficients of variation for the measurements were 1.7% (frontal diameter), 1.5% (sagittal diameter), and 2.5% (area).

Laboratory analyses

Blood was drawn between 8:00 and 9:30 a.m. after the subjects had fasted for at least 8 h. Urine measurements were made in overnight collections, taken between 12:00 p.m. and 7:00 a.m. Serum 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, and bone-specific alkaline phosphatase were measured by radioimmunoassay (Nichols Institute, CA, U.S.A.), serum PTH and serum osteocalcin by immunometric assay (Nichols Institute, San Juan Capistrano, CA, U.S.A.), urinary N-telopeptide cross-links by enzyme-linked immunosorbent assay (Ostex International, Seattle, WA U.S.A.), urinary pyridinoline and deoxypyridinoline by high pressure liquid chromatography, serum ionized calcium and urinary calcium by kresolphtalein method, and urinary creatinine by the Jaffe method. The coefficients of variation for these assays ranged from 5.5% to 7.9%. All samples, except for the screening samples were frozen at −80°C and analyzed at the same time.

Statistical analyses

The biostatistical evaluation was carried out using the statistical software package SAS for Windows, version 6.10, and NCSS, version 6.0.21 (CCDRD, Berlin, Germany). For determination of the sample size the software package NCSS-PASS 1.0 was used. The expected difference between both therapy groups was estimated at 40–60% of the standard deviation. To prove a difference of 50% of the standard deviation with a power of 80%, 74 subjects per group were needed. A normal distribution could be assumed to the pre-postdifferences. A two-sided t-test for independent samples could be applied. If a significant deviation from normality was found, the Mann-Whitney U test had been used.

RESULTS

Of the 165 subjects who underwent screening, 151 (91%) had a 25-hydroxycholecalciferol level below 50 nmol/liter. The baseline characteristics of the 148 subjects enrolled in this trial are shown in Table 1. Compared with baseline, significant increases in serum ionized calcium, urinary calcium, serum 25-hydroxyvitamin D, and serum 1,25-dihydroxyvitamin D were found in both treatment groups. Significant decreases were found for serum PTH, bone-specific alkaline phosphatase, urinary pyridinolines and deoxypyridinolines, and urinary excretion of N-telopeptide. Serum osteocalcin concentrations did not differ significantly in both groups (Table 2).

As compared with calcium mono, a significant increase in serum 25-hydroxyvitamin D and a significant decrease in serum PTH were observed in the vitamin D–calcium group. The decline in urinary excretion of N-telopeptide was more pronounced in the vitamin D and calcium group, but this did not reach statistical significance.

The changes of the body sway parameters are presented in Table 3. As compared with baseline, significant decreases were found for frontal diameter and area in both treatment groups. Concerning the sagittal diameter, an increase was seen in the calcium mono group, whereas a decrease was
observed in the vitamin D–calcium group. However, these differences were not statistically significant. As compared with calcium mono, treatment with calcium and vitamin D led to a significant reduction in body sway, as measured by the sagittal diameter ($p = 0.0435$). The reduction in frontal diameter and area also was more marked under treatment with vitamin D and calcium but did not reach statistical significance.

### Table 2. Initial Laboratory Values and Changes at 8 Weeks in 148 Study Subjects, According to Study Group (Intention-to-Treat)

<table>
<thead>
<tr>
<th>Index and study group</th>
<th>Initial value</th>
<th>Change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum ionized calcium (mmol/ml) [2.1–2.7]</td>
<td>Calcium mono 2.40 ± 0.11</td>
<td>+0.08 ± 0.13*</td>
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<tr>
<td>Calcium-vitamin D 2.43 ± 0.11</td>
<td>+0.09 ± 0.13*</td>
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<tr>
<td>Serum 25-hydroxyvitamin D (nmol/ml) [25–75]</td>
<td>Calcium mono 24.63 ± 12.14</td>
<td>+18.30 ± 20.94*</td>
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<tr>
<td>Calcium-vitamin D 25.65 ± 13.63</td>
<td>+40.46 ± 27.01*</td>
<td>$P = 0.0001$†</td>
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<tr>
<td>Serum 1,25-dihydroxyvitamin D (ng/liter) [16–43]</td>
<td>Calcium mono 36.78 ± 15.69</td>
<td>+11.65 ± 26.29*</td>
<td></td>
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<tr>
<td>Calcium-vitamin D 36.35 ± 16.52</td>
<td>+14.53 ± 24.19*</td>
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<tr>
<td>Serum parathyroid hormone (pmol/liter) [1.1–6.9]</td>
<td>Calcium mono 6.14 ± 2.60</td>
<td>−0.90 ± 2.48*</td>
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<tr>
<td>Calcium-vitamin D 6.11 ± 2.34</td>
<td>−1.70 ± 1.87*</td>
<td>$P = 0.0432$†</td>
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<tr>
<td>Serum osteocalcin (mg/liter) [2.4–10.0]</td>
<td>Calcium mono 8.68 ± 6.74</td>
<td>−0.38 ± 6.44</td>
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<tr>
<td>Calcium-vitamin D 8.33 ± 2.89</td>
<td>+0.15 ± 1.88</td>
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<tr>
<td>Serum bone alkaline phosphatase (mg/liter) [3.4–19.8]</td>
<td>Calcium mono 13.92 ± 5.75</td>
<td>−1.47 ± 4.38*</td>
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<tr>
<td>Calcium-vitamin D 14.34 ± 5.75</td>
<td>−2.34 ± 6.39*</td>
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<td></td>
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<tr>
<td>Urinary N-telopeptide:creatinine ratio (nmol/g) [44–575]</td>
<td>Calcium mono 683.9 ± 500.9</td>
<td>−197.6 ± 502.0*</td>
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<tr>
<td>Calcium-vitamin D 702.7 ± 471.8</td>
<td>−281.4 ± 426.3*</td>
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<tr>
<td>Urinary pyridinoline:creatinine ratio (mg/g) [120–260]</td>
<td>Calcium mono 512.8 ± 282.8</td>
<td>−157.9 ± 261.1*</td>
<td></td>
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<tr>
<td>Calcium-vitamin D 494.6 ± 267.6</td>
<td>−137.2 ± 309.7*</td>
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<tr>
<td>Urinary deoxypyridinoline:creatinine ratio (mg/g) [20–52]</td>
<td>Calcium mono 81.6 ± 56.3</td>
<td>−24.8 ± 46.6*</td>
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<tr>
<td>Calcium-vitamin D 79.3 ± 55.1</td>
<td>−22.0 ± 55.9*</td>
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<tr>
<td>Urinary calcium:creatinine ratio (nmol/liter)</td>
<td>Calcium mono 1.84 ± 1.52</td>
<td>+1.58 ± 2.57*</td>
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<tr>
<td>Calcium-vitamin D 1.60 ± 1.15</td>
<td>+1.73 ± 2.32*</td>
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</table>

Values are the mean ± SD; [reference range].

* $P < 0.001$ (probability for a population mean of 0 by the Wilcoxon test by chance alone).

† $P$-values represent the probability of the difference between the two treatments.

### Table 3. Initial Body Sway Parameters and Changes at 8 Weeks in 148 Study Subjects, According to Study Group (Intention-to-Treat)

<table>
<thead>
<tr>
<th>Index and study group</th>
<th>Initial value</th>
<th>Change</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body sway frontal diameter (mm)</td>
<td>Calcium mono 12.8 ± 9.3</td>
<td>−1.7 ± 11.0*</td>
<td></td>
</tr>
<tr>
<td>Calcium-vitamin D 13.3 ± 9.2</td>
<td>−3.2 ± 8.7*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body sway sagittal diameter (mm)</td>
<td>Calcium mono 17.0 ± 6.8</td>
<td>+0.4 ± 8.0</td>
<td></td>
</tr>
<tr>
<td>Calcium-vitamin D 17.0 ± 6.2</td>
<td>−1.1 ± 7.6</td>
<td>$P = 0.0435$†</td>
<td></td>
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<tr>
<td>Body sway area (mm²)</td>
<td>Calcium mono 148.5 ± 157.9</td>
<td>−24.3 ± 163.2*</td>
<td></td>
</tr>
<tr>
<td>Calcium-vitamin D 149.6 ± 151.1</td>
<td>−47.1 ± 135.4*</td>
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</tbody>
</table>

Values are the mean ± SD.

* $P < 0.001$ (probability for a population mean of 0 by the Wilcoxon test by chance alone).

† $P$-Value represents the probability of the difference between the two treatments.
Heikinheimo et al. found that a single annual injection of vitamin D can prevent fractures of the upper limbs and ribs but not other fractures. This surprising and so far unexplained result could be explained by our findings that a short-term supplementation with vitamin D and calcium reduces body sway and the mean number of falls during a 1-year period of follow-up. However, we were unable to detect a significant reduction in fracture rates, which may be in part caused by our smaller sample size and the lower dosage of vitamin D. The short-term supplementation with vitamin D and calcium was not repeated over several years. Therefore, a cumulative effect on fracture rates could not be expected. Heikinheimo et al. injected 150,000–300,000 IU of vitamin D intramuscularly, whereas the mean cumulative dosage in our study was 44,800 IU of orally administered vitamin D. However, this dosage helped to prevent vitamin D deficiency over a 1-year period and therefore had a prolonged effect on tendency to fall.

sHPT was reduced in both treatment groups. Although this study was started at the end of winter, there was a significant advantage for the vitamin D and calcium group in comparison with vitamin monotherapy. This indicates that, even in spring, naturally synthesized vitamin D in the skin is not able to compensate for the loss in winter. Hypovitaminosis D and sHPT leading to increased bone fragility are common findings in northern latitudes, and represents a potential risk factor in senile osteoporosis. Chapuy et al. described a decrease in serum PTH of 46% and an increase in serum 25-hydroxyvitamin D of 160% after long-term therapy with 800 IU of vitamin D and 1200 mg calcium per day. In our study we found a decrease in serum PTH of 26% and an increase in serum 25-hydroxyvitamin D of 158% after long-term therapy with the same therapeutic regimen. Our results are in agreement with Brazier et al. They reported a decrease of serum PTH of 50% in 72 elderly subjects after 6 months therapy with 800 IU of vitamin D and 1000 mg calcium.

We conclude that a short-term supplementation with vitamin D and calcium improves body sway and sHPT and therefore may prevent falls and subsequent nonvertebral fractures in elderly women.

**ACKNOWLEDGMENTS**

We are grateful to Dr. H.A. Griesser, editor-in-chief of our local newspaper ("DEWEZET," Hameln) for his help in recruiting the participants of this study. Strathmann AG Hamburg, which markets vitamin D and calcium, provided the drugs and funding for the study. We therefore would like to express our gratitude especially to Dr. D. Strathmann, the founder of the company. Scientists from Strathmann Co. (C.H. and D.N.) were directly involved in the design, monitoring, and data management of the study and agreed to be listed as authors. However, Strathmann Co. had no control over the decision to approve or submit the manuscript for publication. Parts of this work were presented as oral presentations at the meeting of the International Osteoporosis...
REFERENCES