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

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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.[1] Further, postural instability has been identified as a risk factor for Colles'fracture.[2] 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.[3,4] 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.[1] 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.

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Supplementation with vitamin D and calcium reduces the risk of hip fractures and other nonvertebral fractures among elderly people.[10,11] This effect could be caused by an increase in bone mineral density (BMD) at the femoral neck.[10–12] 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.[13] Recent studies have shown a high incidence of secondary hyperparathyroidism (sHPT).[14,15] 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.[16]

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).[17] 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.[18] 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

TABLE 1. BASE-LINE CLINICAL CHARACTERISTICS OF THE 148 SUBJECTS

Characteristic	*Value*	
	Calcium mono (n = 74)	*Calcium-vitamin D (n = 74)*
Age (years)	74.7 ± 0.5	74.8 ± 0.5
Range (years)	70–86	70–86
Height (cm)	162.8 ± 0.6	162.0 ± 0.7
Weight (kg)	65.1 ± 1.1	65.2 ± 1.1
Physical activity		
Daily/weekly/monthly/sporadic (%)	19/31/0/50	16/27/1/55
Concomitant diseases—no. (%)		
Cardiovascular	27 (18)	31 (21)
Central nervous, neurological	8 (5)	11 (7)
Psychiatric	1 (<1)	0
Musculoskeletal system	17 (11)	16 (11)
Concomitant medication—no. (%)		
Benzodiazepine use	2 (1.4)	2 (1.4)
Thyroidotherapy	10 (6.8)	10 (6.8)
Cardiovascular drugs	47 (32)	53 (36)

Values for age, height, and weight are the mean ± SD.

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 saggital direction were recorded. In addition, the sway area was calculated by multiplying the frontal diameter with the saggital diameter. The coefficients of variation for the measurements were 1.7% (frontal diameter), 1.5% (saggital 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 pyridinolines and deoxypyridinolines by high pressure liquid chromatography, serum ionized calcium and urinary calcium by kresolphtalein method, and urinary creatinine by the Jaffé 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 saggital diameter, an increase was seen in the calcium mono group, whereas a decrease was

TABLE 2. INITIAL LABORATORY VALUES AND CHANGES AT 8 WEEKS IN 148 STUDY SUBJECTS, ACCORDING TO STUDY GROUP (INTENTION-TO-TREAT)

Index and study group	*Initial value*	*Change*	P *value*
Serum ionized calcium (mmol/ml) [2.1–2.7]			
Calcium mono	2.40 ± 0.11	+0.08 ± 0.13*	
Calcium-vitamin D	2.43 ± 0.11	+0.09 ± 0.13*	
Serum 25-hydroxyvitamin D (nmol/ml) [25–75]			
Calcium mono	24.63 ± 12.14	+18.30 ± 20.94*	
Calcium-vitamin D	25.65 ± 13.63	+40.46 ± 27.01*	$P = 0.0001^{\dagger}$
Serum 1,25-dihydroxyvitamin D (ng/liter) [16–43]			
Calcium mono	36.78 ± 15.69	+11.65 ± 26.29*	
Calcium-vitamin D	36.35 ± 16.52	+14.53 ± 24.19*	
Serum parathyroid hormone (pmol/liter) [1.1–6.9]			
Calcium mono	6.14 ± 2.60	−0.90 ± 2.48*	
Calcium-vitamin D	6.11 ± 2.34	−1.70 ± 1.87*	$P = 0.0432^{\dagger}$
Serum osteocalcin (μg/liter) [2.4–10.0]			
Calcium mono	8.68 ± 6.74	−0.38 ± 6.44	
Calcium-vitamin D	8.33 ± 2.89	+0.15 ± 1.88	
Serum bone alkaline phosphatase (μg/liter) [3.4–19.8]			
Calcium mono	13.92 ± 5.75	−1.47 ± 4.38*	
Calcium-vitamin D	14.34 ± 7.23	−2.34 ± 6.39*	
Urinary *N*-telopeptide:creatinine ratio (nmol/g) [44–575]			
Calcium mono	683.9 ± 500.9	−197.6 ± 502.0*	
Calcium-vitamin D	702.7 ± 471.8	−281.4 ± 426.3*	
Urinary pyridinoline:creatinine ratio (μg/g) [120–260]			
Calcium mono	512.8 ± 282.8	−157.9 ± 261.1*	
Calcium-vitamin D	494.6 ± 267.6	−137.2 ± 309.7*	
Urinary deoxypyridinoline:creatinine ratio (μg/g) [20–52]			
Calcium mono	81.6 ± 56.3	−24.8 ± 46.6*	
Calcium-vitamin D	79.3 ± 55.1	−22.0 ± 55.9*	
Urinary calcium:creatinine ratio (nmol/liter)			
Calcium mono	1.84 ± 1.52	+1.58 ± 2.57*	
Calcium-vitamin D	1.60 ± 1.15	+1.73 ± 2.32*	

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)

Index and study group	*Initial value*	*Change*	P-*value*
Body sway frontal diameter (mm)			
Calcium mono	12.8 ± 9.3	−1.7 ± 11.0*	
Calcium-vitamin D	13.3 ± 9.2	−3.2 ± 8.7*	
Body sway saggital diameter (mm)			
Calcium mono	17.0 ± 6.8	+0.4 ± 8.0	
Calcium-vitamin D	17.0 ± 6.2	−1.1 ± 7.6	$P = 0.0435^{\dagger}$
Body sway area (mm^2)			
Calcium mono	148.5 ± 157.9	−24.3 ± 163.2*	
Calcium-vitamin D	149.6 ± 151.1	−47.1 ± 135.4*	

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.

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 saggital 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 4. NUMBER OF FALLS AND NONVERTEBRAL FRACTURES AMONG 137 SUBJECTS AFTER 1 YEAR OF FOLLOW-UP

	Calcium mono (n = *67*)	*Calcium-vitamin D* (n = *70*)
History of falls		
Number of subjects who fell—no. (%)	19 (28)	11 (16) $P = 0.0373$*
Number of falls—no. (%)	30 (45)	17 (24) $P = 0.0346$*
Site of fracture		
Radius or ulna	3	2
Pelvis	1	0
Hip	1	0
Ankle or foot	1	1
Total—no. (%)	6 (9)	3 (4) $P = 0.1367$

* *P* Values represent the probability of the difference between the two treatments.

The number of falls and nonvertebral fractures after 1 year of follow-up are documented in Table 4. In the calcium mono group 28% of the subjects experienced at least one fall, whereas only 16% in the vitamin D calcium group had at least one fall during the follow-up period ($p = 0.0373$). The mean number of falls was 0.45 in the calcium mono and 0.24 in the vitamin D calcium group ($p = 0.0346$). There also was a reduction in the rate of nonvertebral fractures, which, however, did not reach statistical significance. However, a seasonal variation in the frequency of falls was not observed.

DISCUSSION

In this study, short-term supplementation with calcium and vitamin D reduced body sway in women 70 years of age or older who were living in the community. So far, there is only little evidence from the literature concerning hormonal regulation of postural stability. Gloth et al. reported a functional improvement with vitamin D supplementation in a cohort of older people assessed by questionnaire.[19] Receptors for vitamin D on muscle tissue have been identified more than 10 years ago.[20] The clinical relevance of these receptors is still unclear. Grady et al. found no effect of three dosages of calcitriol on muscle strength in healthy elderly women.[21] However, myopathy and neuropathy are well-known features in osteomalacia.[22] Deficiencies in vitamin D lead to myopathies and to disturbances of balance and neuromuscular coordination.[23,24] An improvement in neuromuscular coordination defects is readily conceivable in the light of the induction of nerve growth factor synthesis by vitamin D derivatives as shown in vitro in fibroblasts and astrocytes and in vivo in rat brain.[25] This supports the concept that vitamin D deficiency affects more coordinative muscle function more so than strength.

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.[26] 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,[26] 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 calcium 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.[27,28] PTH secretion leads to an increased bone turnover and bone loss, particularly in cortical bone,[17] 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.[10] In our study we found a decrease in serum PTH of 26% and an increase in serum 25-hydroxyvitamin D of 158% after short-term therapy with the same therapeutic regimen. Our results are in agreement with Brazier et al.[29] 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.

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REFERENCES

1. Nguyen T, Sambrook P, Kelly P, Jones G, Lord S, Freund J, Eisman J 1993 Prediction of osteoporotic fractures by postural instability and bone density. Br Med J **307:**1111–1115.
2. Crilly RG 1987 Postural stability and Colles' fracture. Age Ageing **16:**133–138.
3. Cummings SR, Nevitt MC 1989 A hypothesis: The causes of hip fractures. J Gerontol **44:**107–111.
4. Gaerdsell P, Johnell O, Nilsson BE, Nilsson JA 1989 The predictive value of fracture, disease, and falling tendency for fragility fractures in women. Calcif Tissue Int **45:**327–330.
5. Fernie GR, Gryfe CI, Holliday PJ, Llewellyn A 1982 The relationship of postural sway in standing to the incidence of falls in geriatric subjects. Age Ageing **11:**11–16.
6. Lord SR, McLean D, Stathers G 1992 Physiological factors associated with injurious falls in older people living in the community. Gerontology **38:**338–346.
7. Lord SR, Sambrook P, Gilbert C, Kelly PJ, Nguyen T, Webster IW, Eisman J 1994 Postural stability, falls and fractures in the elderly: results from the dubbo osteoporosis epidemiology study. Med J Aust **160:**688–691.
8. Maki BE 1994 A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. J Gerontol **49:**72–84.
9. Jones G 1995 Osteoarthritis, bone density, postural stability, and osteoporotic fractures: A population based study. J Rheumatol **22:**921–925.
10. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ 1992 Vitamin D_3 and calcium to prevent hip fractures in elderly women. N Engl J Med **327:** 1637–1642.
11. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE 1997 Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. N Engl J Med **337:**670–676.
12. Ooms ME, Roos JC, Bezemer PD, van der Vijgh WJF, Boutier LM, Lips P 1995 Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind study. J Clin Endocrinol Metab **80:**1052–1058.
13. Lips P, Netelenbos C, Jongen MJM, van Ginkel FC, Althuis AL, Schaik CL 1982 Histomorphometric profile and vitamin D status in patients with femoral neck fracture. Metab Bone Dis Res **4:**85–93.
14. Chapuy MC, Schott AM, Garnero P, Hans D, Delmas PD, Meunier PJ 1996 Healthy elderly french women living at home have secondary hyperparathyroidism and high bone turnover in winter. J Clin Endocrinol Metab **81:**1129–1133.
15. Fardellone P, Sebert JL, Garabedian M 1995 Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. Rev Rhum Engl Ed **62:**576–581.
16. Chapuy MC, Arlot ME, Delmas PD, Meunier PJ 1994 Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. Br Med J **308:**1081–1082.
17. Anatomical Therapeutic Chemical (ATC) classification index. WHO Collaborating Centre for Drug Statistics Methodology, Oslo, January 1993, updated January 1994.
18. Lord SR, Clark RD, Webster IW 1991 Postural stability and associated physiological factors in a population of aged persons. J Gerontol **46:**M69–M76.
19. Gloth FM, Smith CE, Hollis BW, Tobin JD 1995 Functional improvement with vitamin D replenishment in a cohort of frail, vitamin D deficient older people. J Am Geriatr Soc **43:**1269–1271.
20. Simpson RU, Thomas GA, Arnold AJ 1985 Identification of 1,25-dihydroxyvitamin D_3 receptors and activites on muscle. J Biol Chem **260:**8882–8891.
21. Grady D, Halloran B, Cummings S, Leveille S, Wells L, Black D, Byl N 1991 1,25-dihydroxyvitamin D and muscle strength in the elderly: A randomized controlled trial. J Clin Endocrinol Metab **73:**1111–1117.
22. Skaria J, Katiyar BC, Srivastava TP, et al. 1975 Myopathy and neuropathy associated with osteomalacia. Acta Neurol Scand **51:**37–40.
23. Boland R 1986 Role of vitamin D in skeletal muscle function. Endocr Rev **7:**434–448.
24. Schott GD, Wills MR 1976 Muscle weakness in osteomalacia. Lancet **20:**62662–9.
25. Neveu I, Naveilhan P, Jehan F, et al. 1994 Rat brain glial cells synthesize and respond to 1,25-dihydroxy-vitamin D_3 by an increased production of nerve growth factor. In: Norman AW, Bouillon R, Thomasset M (eds.) Vitamin D. A Pluripotent Steroid Hormone: Structural Studies, Molecular Endocrinology and Clinical Applications. Proceedings of the Ninth Workshop on Vitamin D, Orlando, FL, U.S.A., pp. 621–628.
26. Heikinheimo RJ, Inkovaara JA, Harju EJ, Haavisto MV, Kaarela RH, Kataja JM 1992 Annual injection of vitamin D and fractures of aged bones. Calcif Tissue Int **51:**105–110.
27. Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg C, Meunier PJ Prevalence of vitamin D insufficiency in an adult normal population. Osteoporos Int **7:**439–443.
28. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS 1998 Hypovitaminosis D in medical inpatients. N Engl J Med **338:**777–783.
29. Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M 1995 Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. J Bone Miner Res **10:**1753–1761.

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