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Original Article

The Effects of Calcium Supplementation and Exercise on Bone Density in Elderly Chinese Women

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Abstract. A randomized controlled trial was carried out to determine whether calcium supplementation and load-bearing exercise can increase or maintain bone mass in the elderly. Fifty Chinese women, aged 62–92 years, living in a hostel for the elderly in Hong Kong were randomized to enter one of four treatment groups: (I) calcium supplementation of 800 mg (as calcium lactate gluconate) daily; (II) load-bearing exercise four times a week plus a daily placebo tablet; (III) calcium supplementation daily and load-bearing exercise four times a week; (IV) a placebo tablet daily. The interventions went on for 10 months. The bone mineral density (BMD) was measured at three sites in the hip (femoral neck, Ward's triangle and intertrochanteric area) and the L2–4 level of the spine. The percentage change in BMD in 10 months was used as the main outcome measurement. The parathyroid hormone level and indices of bone metabolism were also measured before and after 10 months of intervention.

The BMD at Ward's triangle and the intertrochanteric area increased significantly in subjects on calcium supplement ($p<0.05$), but there was no significant change at the spine and femoral neck. Exercise had no effect on bone loss at any site. However, the results of two-way analysis of variance showed a significant joint effect of calcium supplements and exercise at the femoral neck ($p<0.05$), but not at the other sites. The parathyroid hormone levels fell significantly in subjects on calcium supplements ($p<0.01$).

Calcium supplement in the form of calcium lactate gluconate was adequately absorbed in elderly Chinese women with a calcium intake of less than 300 mg per day. It was effective in reducing bone loss at the hip, and there may be interaction effects with exercise in maintaining bone density.

Keywords: Bone loss; Bone mass; Calcium supplement; Elderly; Load-bearing exercise; Randomized controlled trial

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Introduction

The effectiveness of calcium supplements in preventing bone loss is controversial [1–3]. In a recent controlled trial, calcium supplementation was found to retard the rate of bone loss in post-menopausal women whose dietary calcium intake was less than 400 mg per day [4]. Calcium supplements were effective in reducing bone loss in some previous studies [5–8], but the results were negative in others [9–11].

The effects of exercise in retarding bone loss in perimenopausal women have been consistently demonstrated. In these studies bone density was measured at the forearm [12–14] and for the total body [15]. The ability of load-bearing exercise to reduce bone loss at the hip and spine of elderly subjects has not been studied and the interaction between exercise and calcium supplements has not been investigated.

Osteoporosis and hip fracture are important public health problems in Hong Kong Chinese [16]. The dietary calcium intake of the local elderly population is extremely low (less than 400 mg per day) [17]; this low calcium intake and lack of load-bearing activity were found to be important risk factors for hip fracture in

Hong Kong [18]. We have demonstrated previously that a single dose of calcium taken orally suppressed bone resorption in elderly Chinese [19], and we report here a study on the effectiveness of calcium supplements and load-bearing activities in retarding bone loss at the hip and spine in elderly Chinese women.

Subjects and Methods

Study Subjects

The study subjects were female residents of a hostel for the elderly. Women with metabolic bone disease, diabetes mellitus, a previous history of hip fracture or a blood creatinine level higher than 125 μmol/l (laboratory normal value) were excluded from the study. Mental function was assessed by the Hodkinson Scale [20], and only subjects who scored 6 or more were recruited. Sixty subjects met these criteria and were included in the study. The average calcium intake was assessed by the food diary method over 3 consecutive days, and was then calculated from the calcium contents of food items in the South East Asia food composition table [21]. Informed consent was obtained from all subjects.

Bone Mineral Density (BMD) Measurements

BMD values at the hip and spine were measured by dual X-ray densitometry (Norland model NR26). The BMD at the three sites at the hip and at the L2–4 level of the spine was measured at the beginning of the study and after 10 months. Serial BMD measurements were largely a computerized and automatic procedure with the Norland dual X-ray densitometer. In order to ensure correct placement of the cursor for the anatomical markings, the operator referred to copies of the first scan images in subsequent measurements.

Randomization Methods and Treatment Groups

The study subjects were randomized into four treatment groups. The method of restricted randomization was used to ensure that all groups were of equal size. The subjects were divided into 16 random permuted blocks. Hence each block contained 4 patients, who were assigned randomly into one of the four treatment groups. The assignment list was prepared before the subjects entered the trial, and was independent of the sequence of their arrival.

The four treatment groups were:

I: Calcium supplementation group. The subjects took 800 mg of calcium in the form of calcium lactate gluconate (two Sandocal (Sandoz) tablets) 2 h after breakfast every day.

II: Exercise group. In the exercise programme the subjects stepped up and down a block (9 inches (23 cm) in height) 100 times and then exercised for 15 min. This involved moving the upper trunk while standing. Exercise was performed four times a week. The exercise was submaximal and the heart rate was not monitored during exercise.

III: Calcium supplementation and exercise group. The subjects were given a calcium supplement every day and exercised four times a week.

IV: Placebo group. The subjects took a placebo tablet every day.

The taking of calcium supplements and the exercise were supervised by a research nurse throughout the study.

Duration of Study

The interventions went on for 10 months. The BMD and biochemical measurements were done at the beginning of the study and after 10 months.

Biochemical Methods

Before the subjects were started on their treatments a calcium absorption test was done using the method of Marshall and Nordin [22]. After an overnight fast all subjects ingested an oral dose of 5 $\mu Ci^{45}Ca$ in a solution of 20 mg calcium carrier in distilled water. One hour later blood samples were taken for the measurement of radioactivity. The fraction of the dose of ^{45}Ca in the extracellular fluid at 1 h was calculated by multiplying the fraction of the dose per litre of plasma by 15% of total body weight to allow for the extracellular calcium. The fractional rate of radiocalcium absorption (α) was derived from this by reference to a calibration curve as described by Marshall and Nordin [22].

Fasting blood and urine samples were collected before and after treatment. Plasma calcium, alkaline phosphatase, albumin, phosphate and creatinine levels were measured by automated methods on a parallel analyzer (American Monitor Corp., IN, USA). The inter-assay coefficients of variation for calcium estimation were 1.57% and 1.72% at 1.91 mmol/l and 2.90 mmol/l respectively; those for phosphate were 3.13% and 1.23% at 0.64 mmol/l and 1.63 mmol/l respectively; those for alkaline phosphatase were 5.31% and 1.72% at 61.4 IU/l and 236.8 IU/l respectively.

Plasma calcium concentration was corrected for variation in plasma albumin concentration by the following formula [23].

$$\text{Albumin-adjusted calcium concentration} = \text{measured calcium concentration} + 0.025\,(40 - \text{albumin concentration})$$

Urine hydroxyproline was measured in acid conditions by a colorimetric reaction with dimethylaminobenzaldehyde after choloramine T oxidation on a centrifugal analyser (Cobas Bio, Roche Diagnostic, Basle, Switzerland). Analytical recovery was 89%. The intra-assay coefficient of variation was 2.0% at 79.0 μmol/l, and 1.8% at 159.7 mmol/l. The inter-assay coefficient of variation was 4.3% at 80.4 μmol/l, and 2.4% at 158.7 μmol/l.

Plasma was stored at −70°C for analysis of 25-hydroxyvitamin D (25-OHD) by competitive protein binding assay. Plasma was extracted with acetonitrile and 25-OHD was separated on a Sep Pak C18 cartridge (Waters Associated, USA) and assayed by a competitive protein binding method using plasma from vitamin D deficient pigs at a dilution of 1 in 4000. Recovery of extraction was monitored by each specimen by adding a small amount of labelled 25-OHD to the sample, and ranged from 60% to 80%. All values were separately corrected for losses throughout the whole procedure. The precision of the assay at 28 μg/l was 6.9%.

Plasma parathyroid hormone (PTH) was measured using an immunochemiluminometric assay (Ciba Corning Diagnostics, Medfield, MA, USA). The assay is specific for the whole molecule of PTH and the detection level was 1.4 ng/l. The intra-assay coefficient of variation of PTH is 2.64% at 38.08 ng/l of PTH.

Statistical Methods

The baseline BMD measurements, calcium intake, 25-hydroxyvitamin D and calcium absorption rates were compared by the one-way analysis of variance. For each subject the percentage change in BMD at each site over 10 months was calculated. The separate effects of calcium supplements and exercise and their joint effects on the biochemical and BMD measurements were analysed by the two-way analysis of variance. In all statistical tests in the study a p value smaller than 0.05 was considered to be of statistical significance.

Results

A total of 60 subjects were recruited into the trial. Ten subjects did not complete the trial for the following reasons: one developed cervical cord compression, one suffered a stroke, one developed epigastric discomfort from the calcium tablets, one developed diarrhoea after taking the calcium tablets, and six were transferred to Care and Attention Homes during the trial.

The demographic and other characteristics of the 50 subjects who completed the trial are presented in Table 1. There were no significant differences in the mean age, calcium intake, bone density, calcium absorption rates and 25-hydroxyvitamin D levels between the subjects in the four groups.

The precision of the BMD measurements was not studied in our laboratory. However, published data showed the following precision obtained by 5 scans on 7 normal subjects: lumbar spine, 2.3%; femoral neck, 2.1%; Ward's triangle, 4.4%. The corresponding figures were 2.3%, 4.2% and 8.4% respectively for 5 scans on 7 osteoporotic subjects [24].

The individual changes at the spine and hip are shown in Fig. 1. There was a wide scatter of percentage changes at Ward's triangle and the intertrochanteric area. Subjects with extreme changes were not excluded from the final analysis. The mean and 95% confidence interval of the original BMD measurements are shown in Table 1 and the percentage changes in bone density at the hip and the spine are presented in Table 2. The BMD at Ward's triangle and the intertrochanteric area increased significantly in subjects on calcium supplements ($p<0.05$), but there was no significant change at the spine and femoral neck. Exercise did not have any significant effect on the rate of bone loss at any site. However, the results of two-way analysis of variance showed significant interaction of calcium supplements and exercise at the femoral neck ($p<0.01$), but not at the other sites.

The mean and 95% confidence interval of the original

Table 1. Demographic and baseline characteristics of the subjects in the four groups (mean and 95% confidence interval)

	Group I: calcium supplements (n = 12)	Group II: exercise and placebo (n = 11)	Group III: calcium supplements and exercise (n = 15)	Group IV: placebo (n = 12)
Mean age (range)	75 (72–79)	79 (76–81)	76 (73–80)	75 (71–78)
Calcium intake (mg/day)	275 (220–330)	259 (241–277)	248 (232–263)	253 (212–294)
Bone mineral density				
Spine (L2–4)	0.70 (0.63–0.78)	0.68 (0.57–0.78)	0.70 (0.65–0.75)	0.63 (0.56–0.69)
Femoral neck	0.54 (0.47–0.60)	0.53 (0.48–0.58)	0.53 (0.48–0.59)	0.50 (0.45–0.55)
Ward's triangle	0.51 (0.44–0.58)	0.51 (0.41–0.61)	0.46 (0.40–0.53)	0.47 (0.41–0.53)
Intertrochanteric area	0.46 (0.39–0.53)	0.45 (0.38–0.52)	0.43 (0.38–0.48)	0.43 (0.38–0.47)
25–hydroxyvitamin D (μg/l)	20.6 (14.9–26.3)	24.9 (19.2–30.6)	20.8 (17.9–23.8)	28.1 (25.4–30.8)
Fractional calcium absorption rate	0.63 (0.50–0.76)	0.56 (0.42–0.69)	0.61 (0.40–0.82)	0.62 (0.42–0.82)

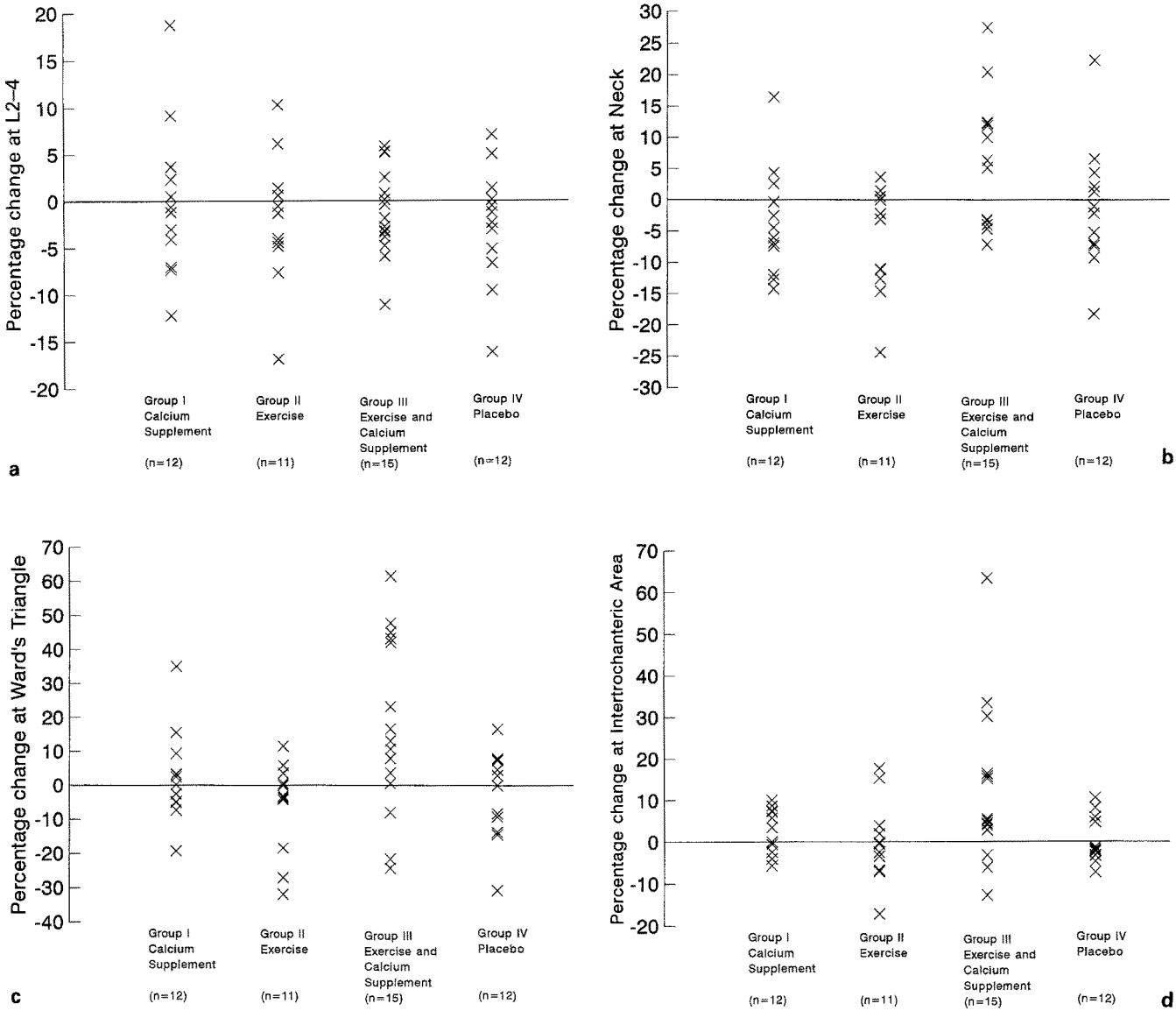

Fig. 1. Percentage changes in BMD for individual subjects: **a** L2–4; **b** femoral neck; **c** Ward's triangle; **d** intertrochanteric area.

Table 2. Percentage changes in bone mineral density for the four groups (mean and 95% confidence interval)

	Group I: calcium supplements (n = 12)	Group II: exercise and placebo (n = 11)	Group III: calcium supplements and exercise (n = 15)	Group IV: placebo (n = 12)
Spine (L2–4)	−0.08 (−5.2–5.1)	−1.9 (−6.7–2.8)	−1.1 (−3.7–1.4)	−2.5 (−6.5–1.4)
Femoral neck	−3.5 (−9–1.8)	−6.6 (−12–0.8)	5.0 (−0.77–10)	−1.1 (−7.4–5.3)
Ward's triangle	2.5 (−5.9–11)	−6.0 (−15–3.2)	17 (3–31)	−2.4 (−10–5.9)
Intertrochanteric area	2 (−1.6–5.7)	0.1 (−6.5–6.7)	11 (1.3–22)	0.25 (−3.3–3.8)

The percentage changes at Ward's triangle and the intertrochanteric area for the calcium supplements group were statistically significant ($p<0.05$) by two-way analysis of variance. The interaction between calcium supplements and exercise were significant ($p<0.05$) at the femoral neck by two-way analysis of variance.

Table 3. Biochemical measurements before and after intervention for 10 months (mean and 95% confidence interval)

	Group I: calcium supplements (n = 12)	Group II: exercise and placebo (n = 11)	Group III: calcium supplements and exercise (n = 15)	Group IV: placebo (n = 12)
Parathyroid hormone (pg/l)				
Baseline	30.1 (19.1–41.1)	25.7 (16.6–34.7)	34.0 (29.2–38.7)	28.6 (23.5–33.6)
After 10 months	21.5 (14.5–28.4)	26.6 (19.0–34.2)	26.6 (20.2–33.1)	28.2 (23.1–33.4)
Albumin-adjusted calcium (mmol/l)				
Baseline	2.24 (2.19–2.28)	2.23 (2.21–2.26)	2.27 (2.23–2.30)	2.20 (2.15–2.24)
After 10 months	2.33 (2.26–2.40)	2.22 (2.20–2.24)	2.34 (2.21–2.47)	2.18 (2.15–2.20)
Alkaline phosphatase (IU/l)				
Baseline	63.0 (46.7–79.9)	82.0 (67.1–96.8)	75.5 (61.7–89.2)	70.0 (59.6–80.3)
After 10 months	74.9 (59.1–90.6)	101.2 (75.0–127.4)	85.7 (60.8–110.7)	84.4 (68.6–100.2)
Urine hydroxyproline/creatinine ratio (μmol/mmol)				
Baseline	22.5 (14.8–30.2)	20.8 (16.3–25.2)	24.1 (18.5–29.7)	26.5 (20.4–32.6)
After 10 months	26.8 (14.5–39.1)	22.7 (18.7–26.6)	24.3 (16.6–32.1)	23.0 (18.7–27.3)
Urine calcium/creatinine ratio (mmol/mmol)				
Baseline	0.37 (0.25–0.49)	0.29 (0.19–0.39)	0.38 (0.24–0.51)	0.49 (0.34–0.64)
After 10 months	0.46 (0.31–0.60)	0.45 (0.28–0.61)	0.55 (0.38–0.72)	0.63 (0.47–0.79)

For the subjects on calcium supplement the parathyroid hormone level was significantly lower ($p<0.01$) and the albumin-adjusted calcium was significantly higher ($p<0.01$) after 10 months by two-way analysis of variance.

and final biochemical measurements are shown in Table 3. There was no significant difference in parathyroid hormone, albumin-adjusted calcium, alkaline phosphates, urine calcium/creatinine ratio and urine hydroxyproline/creatinine ratios between the four groups before treatment. The parathyroid hormone level decreased significantly in the subjects on calcium supplements ($p<0.01$), but no interaction of calcium supplements and exercise was demonstrated. The albumin-adjusted calcium levels increased significantly in the subjects on calcium supplements ($p<0.01$), but no significant changes in urinary calcium/creatinine and hydroxyproline/creatinine levels were demonstrated. There was no significant change in the biochemical measurements for subjects who exercised.

Discussion

Oral calcium supplements in the form of calcium lactate gluconate were well-tolerated by elderly Chinese. In our study only two subjects developed gastrointestinal symptoms after taking the calcium supplements. Calcium lactate gluconate was adequately absorbed by elderly women, resulting in a suppression of parathyroid hormone secretion and a decrease in the rate of bone loss at the hip. It was also demonstrated that moderate load-bearing exercise *per se* was not effective in maintaining bone density in elderly Chinese women. However, there may be significant interaction between load-bearing exercise and calcium supplements in decreasing bone loss at the femoral neck.

The results of epidemiological studies on the effects of dietary calcium intake on the rates of hip fracture [25–27] and bone loss [28–29] were mixed. All of these studies were conducted in Caucasians with calcium intakes higher than 400 mg. Studies of the effects of calcium intake and calcium supplements on bone density are particularly important in populations such as the Hong Kong Chinese where the calcium intake is extremely low. We have already demonstrated previously that a low calcium intake is an important risk factor for hip fracture in Chinese [18]. Dawson-Hughes et al. [4] have recently demonstrated that healthy older postmenopausal women with a daily calcium intake of less than 400 mg could significantly reduce bone loss by increasing their calcium intake to 800 mg per day. Our study population is much older and had a calcium intake similar to that of the low calcium intake group in their study. Calcium supplements were shown to prevent bone loss at the hip in both studies, but in our study we failed to demonstrate any effects on the spine. The results of earlier studies on calcium supplements in retarding bone loss were controversial. Calcium supplements were found to be effective in reducing the rate of bone loss in some studies [5–8] but not in others [9–11]. A possible explanation is the existence of a threshold effect for calcium supplements: it may be beneficial in populations with low calcium intake. Our results indicated clearly that calcium supplements were effective in preventing bone loss in our elderly population on a very low calcium diet, but the effects were limited to the hip.

We have also shown that moderate load-bearing exercise per se could not retard bone loss in elderly Chinese women. This was contrary to our expectations, though in most of the past studies with positive results the study subjects were younger and the exercise more strenuous. According to Lanyon [30], bone responds in proportion to the amount of stress placed on it. Abramson and Delagi [31] showed that weight-bearing and

muscle contractions generate the stress necessary to prevent bone loss. The function of load-bearing exercise in maintaining bone loss in this group may have been offset by the extremely low calcium intake – i.e. in subjects without calcium supplements, the increased calcium requirement generated by exercise could not be met. The positive interaction between calcium supplements and exercise in maintaining bone density at the femoral neck supported this hypothesis. Although exercise was not shown to reduce bone loss, it is potentially important in improving muscle strength and coordination, and hence in preventing falls and fracture in the elderly.

We conclude that a calcium supplement of 800 mg per day was effective in reducing bone loss at the hip in elderly Chinese women on a low calcium diet. Moderate load-bearing activities per se were not effective in preventing bone loss, but might accentuate the benefits of a calcium supplement. Calcium supplementation is an important measure for preventing osteoporosis in the Hong Kong Chinese population.

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