

Original Article

The efficacy and safety of calcitriol and/or Caltrate D in elderly Chinese women with low bone mass

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Aim: To observe the efficacy and safety of Rocaltrol (calcitriol) and/or Caltrate D (calcium carbonate plus vitamin D) in elderly Chinese women with osteopenia or osteoporosis.

Methods: One hundred fifty Chinese women aged over 65 years with osteopenia or osteoporosis from three centers were randomly divided into two groups. Seventy-six participants received Caltrate D as one pill daily; the other 74 participants received 0.25 µg Caltrate D plus Rocaltrol daily. The changes in bone mineral density (BMD) served as primary end-points. Height changes, the presence of new vertebral fractures, muscle strength and balance were evaluated.

Results: The following are the mean percentage changes (and SD) in BMD over 12 months: at L2–L4, 0.83±3.88 in the Caltrate D group and 2.84±4.04 in the Rocaltrol+Caltrate D group ($P=0.003$, by ANCOVA); at the femoral neck, 0.04±3.94 in the Caltrate D group and 2.01±5.45 in the Rocaltrol+Caltrate D group ($P=0.085$, by ANCOVA); and in the trochanter, 1.59±4.57 in the Caltrate D group and 3.76±6.25 in the Rocaltrol+Caltrate D group ($P=0.053$, by ANCOVA). The stand and maximal forward reach test (SMFRT) was significantly enhanced in both groups during the 12 months of treatment, but no significant differences were found between these two groups. No severe adverse event related to these medications occurred throughout the study.

Conclusion: Treatment with Rocaltrol plus Caltrate D or Caltrate D for 12 months in elderly Chinese postmenopausal women effectively increased BMD at the lumbar spine. Rocaltrol plus Caltrate D was more effective at the lumbar spine than Caltrate D alone.

Keywords: osteoporosis; elderly Chinese women; calcitriol; vitamin D; bone mass

Acta Pharmacologica Sinica advance (2009) 30: 372–378; doi: 10.1038/aps.2009.12

Introduction

Osteoporosis, a common disease among aging people, is characterized by decreased bone mass and microarchitecture deterioration of bone tissue, leading to increased bone fragility and fracture^[1]. Many age-related factors contribute to osteoporosis, such as a decline of gonadal function, a reduction in intestinal calcium absorption, vitamin D insufficiency, decreased production of 1,25(OH)₂D₃ and secondary hyperparathyroidism^[2].

Vitamin D insufficiency is common in older people^[3]. If untreated, it leads to bone loss and consequently to an increased risk of fracture. Vitamin D insufficiency may progress to a clinical deficiency, which is associated with severe muscle weakness in elderly adults and often results in a marked disability^[4, 5] that can be ameliorated within several weeks of vitamin D supplementation. Metabolites of vitamin D not only can increase the intestinal absorption of calcium but also possess other cellular effects^[6]. Calcitriol [1,25 (OH)₂ vitamin D, the most active metabolite] has been thought to play an important role in promoting bone formation, since it increases osteocalcin production by osteoblasts^[7]. Calcitriol has been advocated for treatment of osteoporosis, but its effects in such use are inconsistent^[8, 9].

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Received 2008-08-03 Accepted 2009-01-23

In this randomized, multi-center, open-label, placebo-controlled clinical trial, the effects of 12 months of treatment with Rocaltrol plus Caltrate D or Caltrate D alone on bone mass, muscle function and balance have been investigated in elderly Chinese women.

Materials and methods

Subjects and methods This was a multi-center, randomized, open-label, controlled clinical trial, conducted by the Endocrinology Department of Peking Union Medical College Hospital, the Department of Gynaecology and Obstetrics of the Chinese PLA General Hospital and the Radiology Institute of Medical Research of Shanghai Fudan University. The study protocol was approved by the institutional review boards at each study site. All subjects gave signed informed consent.

Subjects and study design Volunteers were recruited through notices posted in the communities surrounding the three centers. Postmenopausal women aged over 65 years were eligible for the study when both of the following criteria were met: a) a bone mineral density (BMD) T score of -1.0 or less at the lumbar spine (meaning that fractures did not involve more than two lumbar vertebrae) and the anatomical structures were suitable for DXA scanning or femoral neck, and b) body mass index (BMI) between 18 and 30 kg/m². Exclusion criteria included the use of bisphosphonates within the previous 12 months or fluoride within the previous 24 months; tibolone, parathyroid hormone or any derivative, or systemic glucocorticoids (more than 5 mg of prednisone equivalent daily for more than 10 days); inhaled glucocorticoids (more than 2000 µg daily for more than 10 days); anabolic steroids or testosterone within 6 months; and estrogens, selective estrogen receptor modulators, calcitonin, or calcitriol within 3 months of enrollment. Other causes of secondary osteoporosis were excluded, including hyperparathyroidism or hypoparathyroidism, hyperthyroidism or hypothyroidism, hypocalcemia, rheumatoid arthritis, Paget's disease, osteomalacia, and serum creatinine greater than 1.7 mg/dL.

There were 150 subjects enrolled in the study, and 142 of them completed the 12 months of treatment. The study subjects were assigned to either the Caltrate D group or the Rocaltrol+Caltrate D group using randomized permuted blocks. Seventy-six subjects were allocated to the Caltrate D group and received oral treatment of 1 pill/day Caltrate D (containing 600 mg calcium and 125 IU vitamin D, Wyeth Pharmaceuticals, Health Care Products, Suzhou, China). Seventy-four subjects were placed in the

Rocaltrol+Caltrate D group, receiving 0.25 µg/day Rocaltrol (Calcitriol, Roche Pharmaceuticals Co, Shanghai, China) and 1 pill/day Caltrate D. At the end of the study 72 women were available for statistical processing in the Caltrate D group and 70 patients in the Rocaltrol+Caltrate D group.

The primary efficacy end points were the percent changes in bone mineral density at the lumbar spine (lumbar vertebrae 2 to 4) and hip after 12 months of treatment. Secondary efficacy end points were changes in height, new vertebral and nonvertebral fractures, grip strength of both hands, the time to perform the five-times-sit-to-stand test (FTSST) and the stand maximal forward reach test (SMFRT).

Measurement of bone mineral density The BMD of the lumbar spine (L2–L4), right femoral neck (Neck) and trochanter (Troch) was measured at baseline and at 6- and 12-month follow-up using dual-energy X-ray absorptiometry (DXA) (Mode GE Lunar Prodigy, Madison, WI). Scanner software version 5.0 was used for acquisition and analysis. The coefficients of variation (CV) for the DXA measurements were 1.7% (L2–L4), 0.9% (femoral neck) and 1.1% (trochanter). Bone mineral density was expressed as milligrams per square centimeter.

Radiographic analysis Radiography of the lateral lumbar and thoracic spine was performed at baseline, at 12 months and whenever study subjects presented with new back pain. All radiographs were centrally assessed in a blinded fashion by two trained observers — a radiologist and an independent reader — according to the method of Genant *et al*^[10]. This method consists of visual inspection of the spine from thoracic vertebra 4 through lumbar vertebra 5, comparing each vertebra with those below and above. If an abnormally shaped vertebra is identified, the anterior, middle, and posterior heights of this vertebra are measured with a ruler and scored as follows: grade 0, normal; grade 1, a decrease in the height of 20 to 25 percent; grade 2, a decrease of 25 to 40 percent; and grade 3, a decrease of 40 percent or more. A new fracture was defined as a decrease in height of at least 15 percent on vertebra graded 0 at baseline and with a grade on the semiquantitative scale of 1, 2, or 3. A new vertebral deformity on a radiograph obtained consequent to new back pain was defined as a symptomatic vertebral fracture.

Nonvertebral fractures were confirmed by radiologic evaluation or by a hospital report. Standing height was measured with a stadiometer at baseline and every six months. The measurement was made three times at each visit, and the mean value of the three measurements was recorded.

Evaluation of muscle function and balance Hand-grip strength was measured with the WCS-100 digital Hand Dynamometer (Jianming, XinDongHuaDeng Sports Instru-

ment Co, Beijing, China) according to the manufacturer's instruction. Briefly, the participants stood upright, put their arms straight down and gripped the dynamometer. Three trials with brief pauses were allowed for each hand alternately. Subjects were encouraged to exert their maximal grip. The best result from each side was chosen for the analyses^[11]. The CV for the hand dynamometer was 2.8%.

The FTSST^[12] was administered as follows. Using a chair of standard height (40–45 cm), subjects stood up and sat down five times, as rapidly as possible. Their arms were folded across their chests. Timing with a digital stopwatch began with the command “go” and ceased when subjects stood up for the final time. Two trials were allowed, and subjects were allowed sufficient time between trials to fully recover. The CV for the FTSST was 5.0%.

In the SMFRT^[13], subjects stood with their arms extended forward along a yardstick. They were instructed to reach forward as far as possible while keeping their feet flat on the floor and without letting their hand touch the yardstick. The location of the middle finger (in cm) was recorded. The trial distance (in cm) was obtained by recording the distance between the tip of the middle finger and the starting position. One practice trial was performed to ensure that patients understood the instructions, and the next trial was recorded. The CV for the SMFRT was 3.6%.

All three tests were performed initially to establish a baseline and again after 6 and 12 months of treatment.

Biochemical measurement Measurements of biochemical parameters, including calcium, phosphorus, creatinine, albumin, alanine aminotransferase (ALT), alkaline phosphatase (ALP) and glucose in serum collected at baseline and 6 and 12 months were analyzed using routine assays available at the center laboratory.

Safety criteria and adverse events At each visit, all adverse events were recorded. The degree of association between each event and the study drugs was scored as “no relation,” “possible,” “probable,” or “definite.” The biochemical parameters of liver and renal function, complete blood count (CBC), urine analysis, and kidney ultrasound were also employed as safety indexes.

Statistical analysis Quantitative values are expressed as mean±SD with 95% confidence intervals. The analysis was based on the intention-to-treat (ITT) principle. With 70 subjects per treatment group, assuming a 20 percent dropout rate, a sample size of 56 subjects in each group was needed to provide 90 percent power to detect a mean difference of 2 percent at a significance level of 0.05. A common standard deviation of 3.6 percent for each percentage change in BMD was assumed. The two independent-samples *t* test

or Wilcoxon test (if data were found not to be normally distributed) were used to compare baseline measurements between the Caltrate D group and the Rocaltrol+Caltrate D group. Comparison between the two groups was made using analysis of co-variance (ANCOVA), adjusting for baseline measurements. Changes in BMD (expressed as percentage changes from baseline) between groups were compared using ANCOVA, adjusting for baseline BMD. Paired-sample *t* tests were performed to compare the differences between 6- and 12-month and baseline measurements for each treatment group. For all tests, a *P* value ≤0.05 was considered to indicate statistical significance. All analyses were performed with the SPSS 13.0 software package.

Results

Baseline characteristics, bone mineral density and the parameters of muscle strength and balance for the two groups are shown in Table 1. There were no significant differences in baseline parameters between the two groups except in the BMD at the femoral neck.

Changes in BMD The BMD measurements before and after treatment are shown in Table 2. After 12 months of treatment, the BMD values at L2–L4, the femoral neck and the trochanter were significantly higher than baseline in the Rocaltrol+Caltrate D group; the BMD values at L2–L4 and the trochanter were significantly higher than baseline in the Caltrate D group. The mean percentage changes of BMD from baseline are reported in Table 3. The BMD at the lumbar spine (L2–L4) significantly increased from baseline by 2.8% (*P*<0.01 compared with baseline) in the Rocaltrol+Caltrate D group and 0.8% (*P*<0.05, compared with baseline) in the Caltrate D group at 12 months, respectively. The percentage changes from baseline of BMD at L2–L4 in the Rocaltrol+Caltrate D group were significantly higher than that in the Caltrate D group (*P*<0.05). Femoral neck BMD increased by 2.0% (*P*<0.01) and 0.04% from baseline after 12 months of treatment in the Rocaltrol+Caltrate D group and the Caltrate D group, respectively. No significant difference was found in the percentage changes from the baseline BMD at the neck after adjusting for baseline differences (*P*>0.05). After 12 months of treatment, the BMD at the trochanter had increased by 3.8% (*P*<0.01 compared with baseline) and 1.6% (*P*<0.01 compared with baseline) from baseline in the Rocaltrol+Caltrate D group and the Caltrate D group, respectively. The differences in the percentage changes of BMD at the trochanter between these two groups was not significant after adjusting for baseline BMD (*P*>0.05).

Changes in muscle strength and balance The grip

Table 1. Baseline characteristics, BMD and the parameters of muscle strength and balance of the two groups.

	Caltrate D	Rocaltrol+ Caltrate D	P value
Num	76	74	
Age (year)	70.4±3.6	70.4±3.9	0.951
Time of menopause (year)	21.7±7.4	20.9±6.1	0.463
Age of Menarche (year)	15.0±2.6	15.3±2.0	0.332
Height (cm)	153.4±5.7 (152.1–154.7)	154.0±5.5 (152.8–155.3)	0.500
Body weight (kg)	58.9±10.3	58.7±11.0	0.948
BMI (kg/cm ²)	25.0±3.0	24.7±3.4	0.659
BMD (mg/cm ²)			
L2-L4	930±126 (901–995)	916±132 (886–947)	0.509
NECK	731±96 ^a (710–754)	688±94 (666–710)	0.005
TROCH	635±94 ^a (614–657)	607±90 (686–628)	0.06
FTSST(s)	9.3±2.6 ^b (8.7–9.9)	9.7±3.5 ^c (8.9–10.6)	0.793
Grip strength of left hand (kg)	20.4±4.5 ^b (19.4–21.6)	20.7±5.0 ^c (19.5–21.8)	0.792
Grip strength of right hand (kg)	20.7±4.7 ^b (19.6–21.8)	20.6±4.7 ^c (19.5–21.8)	0.899
SMFRT(cm)	23.0±4.8 ^b (21.9–24.2)	23.8±4.8 ^c (22.7–25.0)	0.308

Notes: FTSST denotes five times sit-to-stand test, SMFRT denotes stand maximal forward reach tests. Values were expressed as mean±SD and number in parentheses are 95% confidence intervals. P value denotes the comparison between these two groups. There were no significant differences between the two groups except BMD of femoral neck. Subjects number a=75, b=73, c=72.

strength of the left hand was significantly decreased in both groups after 6 months of treatment, but this change was not found after 12 months of treatment. There was no significant change in the grip strength of the right hand in either group during the 12 months of treatment. The FTSST time decreased significantly from baseline in the Caltrate D group ($P<0.01$) but not in the Rocaltrol+Caltrate D group. The SMFRT time significantly increased in both two groups after 12 months of treatment (Table 4).

Vertebral fractures, body height, and nonvertebral fractures During the 12 months of treatment, 2 and 1 new vertebral fractures occurred in the Caltrate D group and Rocaltrol+Caltrate D group, respectively. All of these vertebral fractures were asymptomatic. At baseline, the mean height measurements were comparable between these two

groups [153.4 ± 5.7 cm (Caltrate D group) vs 154.0 ± 5.5 cm (Rocaltrol+Caltrate D group), $P>0.05$]. The height changes were not statistically different between the two groups after 12 months of treatment [153.4 ± 5.8 cm (Caltrate D group) vs 153.8 ± 5.4 cm (Rocaltrol+Caltrate D group), $P>0.05$]. Nonvertebral fractures occurred in two patients in the Rocaltrol+Caltrate D group over the study: one patient with a right femoral neck fracture and another with a clavicular fracture. There were no nonvertebral fractures in the Caltrate D group during the 12 months of treatment.

Withdrawal from the study and adverse events A total of eight participants (four in each group) withdrew from the study. In the Caltrate D group, one patient withdrew owing to lung cancer. In the Rocaltrol group, one patient withdrew because a fracture was attributable to a severe adverse event but not to the use of study medication, according to clinical judgment. The other six patients withdrew for reasons independent of study medication. There were no clinically relevant changes from baseline in blood pressure, pulse rate, or other physical signs during the study. No significant differences in markers of hepatic and renal function were recorded. The concentration of serum calcium and phosphorus concentrations and the total alkaline phosphatase activities in the two groups remained within normal ranges throughout the study. No renal lithiasis or calcification was detected by ultra-sound examination at the end of the 12 months of treatment.

Discussion

The incidence of osteoporotic fractures increases with age. It is projected that by the year 2050 there will be 900 million men and women who are 65 years of age and older in. As a result, while only 30% of all hip fractures in the world occurred in Asia in 1990, more than 50% of all hip fractures will occur in this continent by the year 2050. By then, the total number of individuals with hip fractures in Asia will be approximately 3.2 million per year^[14]. Prevention of osteoporotic fractures in Asia is therefore of paramount importance.

Two major kinds of drugs are used to prevent or treat osteoporosis; one inhibits bone resorption, the other increases bone formation. The antiresorptive treatments have been used most widely; these include calcium, estrogen, calcitonin, bisphosphonate and vitamin D^[15]. Calcium and standard vitamin D are considered secondary treatment for osteoporosis^[15], but they have been reported to increase BMD in healthy postmenopausal women^[16]. Our results showed that after 12 months of treatment with Caltrate D

Table 2. The BMD in lumbar spin, femoral neck, and trochanter of two groups before and after treatment.

	Caltrate D			Rocaltrol+Caltrate D		
	Pre-treat 76	6M 73	12M 72	Pre-treat 74	6M 73	12M 70
BMD (mg/cm ²)						
L2–L4	930±126 (901–959)	946±126 ^c (916–975)	935±137 ^b (902–967)	916±132 (886–947)	935±130 ^c (906–966)	945±130 ^{cd} (914–956)
NECK	731±96 (n=75, 710–754)	729±90 (n=72, 708–750)	730±95 (n=71, 708–753)	688±94 (666–710)	693±95 (671–715)	703±92 ^c (681–725)
TROCH	635±94 (n=75, 614–657)	637±93 (n=72, 615–659)	640±91 ^b (n=71, 619–659)	607±90 (586–628)	616±91 ^c (595–637)	628±90 ^c (607–651)

Note: 6M and 12M denote 6 and 12 months after treatment, respectively. Values were expressed as mean±SD and number in parentheses are 95% confidence intervals. ^bP<0.05, ^cP<0.01 by paired *t* test compared with baseline. ^fP<0.01 compared between two groups by ANCOVA adjusted for baseline BMD.

Table 3. The percentage changes in BMD in women who completed the study over 12 months.

	<i>n</i>	Caltrate D	<i>n</i>	Rocaltrol+Caltrate D	<i>F</i>	<i>P</i> value
L2–L4	6M 73	2.03±4.02 (1.11–2.95)	73	2.29±3.60 (1.46–3.12)	0.06	0.079
	12M 72	0.83±3.88 (-0.07–1.73)	70	2.84±4.04 (1.90–3.79)	9.00	0.003
Neck	6M 72	-0.13±3.59 (-0.97–0.69)	73	0.91±4.80 (-0.19–2.01)	0.64	0.422
	12M 71	0.04±3.94 (-0.88–0.96)	70	2.01±5.45 (0.73–3.29)	3.02	0.085
Troch	6M 72	0.75±3.77 (-0.13–1.62)	73	1.61±4.93 (0.5–2.7)	0.82	0.367
	12M 71	1.59±4.75 (0.48–2.69)	70	3.76±6.25 (2.29–5.23)	3.82	0.053

Note: 6M and 12 M denote 6 and 12 months after treatment respectively. Values were expressed as mean±SD and number in parentheses are 95% confidence intervals. *P* value is compared between two groups by ANCOVA adjusted for baseline BMD.

Table 4. Muscle strength and balance ability of two groups before and after treatment.

	Caltrate D			Rocaltrol+Caltrate D		
	Pre-treat 73	6M 71	12M 70	Pre-treat 72	6M 70	12M 70
Grip strength (Left, kg)	20.4±4.5 (19.4–21.6)	19.5±4.1 ^c (18.6–20.5)	20.1±4.1 (19.2–21.1)	20.7±5.0 (19.5–21.9)	19.5±4.3 ^b (18.5–20.6)	19.6±4.2 (18.6–20.6)
Grip strength (Right, kg)	20.7±4.7 (19.7–21.9)	20.7±4.5 (19.7–21.8)	21.1±4.3 (20.1–22.2)	20.6±4.7 (19.5–21.8)	21.3±4.6 (20.2–22.4)	21±4.8 (19.8–22.2)
FTSST (s)	9.3±2.6 (8.7–10.0)	8.5±2.3 ^c (8.0–9.0)	9.0±2.0 ^c (8.0–9.0)	9.7±3.5 (8.9–10.6)	9.0±4.1 (8.1–10.0)	9.0±3.7 (8.2–9.9)
SMFRT (cm)	23.0±4.8 (21.9–24.2)	24.9±5.2 ^c (23.7–26.2)	24.6±4.4 ^b (23.7–25.7)	23.8±4.8 (22.7–25.0)	24.5±5.5 (23.2–25.8)	25.8±4.5 ^c (24.8–26.9)

Note: FTSST denotes five times sit-to-stand test, SMFRT denotes stand maximal forward reach tests. 6M and 12M denote 6 and 12 months after treatment respectively. Values were expressed as mean±SD and number in parentheses are 95% confidence intervals. ^bP<0.05, ^cP<0.01 compared with base line (Pre-treatment).

(600 mg calcium plus 125 IU vitamin D per day), BMD was significantly increased in L2–L4 and the trochanter in elderly women with low bone mass. These results suggest that calcium and vitamin D are effective at preventing bone

loss among elderly Chinese women. A 2005 survey of Chinese nutrition indicated that the average daily calcium intake was 486 mg^[17]. The dietary reference intakes (DRIs) for people over 50 years are lower than 1000 mg. With a 600

mg calcium supplement, calcium intake can reach a DRI of 1000 mg, which should be sufficient to maintain body calcium homeostasis. Although the serum 25(OH)D levels of the subjects were not measured before and after treatment, vitamin D insufficiency is known to be common in older people^[3]. Our previous study showed that the average 25(OH) vitamin D level was 18.9 ng/mL in the Beijing area during the summer^[18], lower than the recommended optimal concentration of 30 ng/mL. The 125 IU of vitamin D in Caltrate D might be helpful in preserving bone mass and muscle.

Many studies with long-term vitamin D treatment have indicated that hydroxylated form (active vitamin D) has a consistently larger impact on bone density than does standard vitamin D^[8]. The active vitamin D analogs, including 1,25(OH)₂D (calcitriol) and 1 α (OH)D (alphacalcidol), have been used as a remedy for osteoporosis for many years in developed countries^[19]. The long-term effect of calcitriol treatment on bone mineral density was evaluated in previous studies^[20, 21]. During our 12-month trial, the treatment with calcitriol (Rocaltrol) plus Caltrate D increased the BMD of the lumbar spine, femoral neck and femoral trochanter. The BMD of the femoral neck at baseline in the Rocaltrol+Caltrate D group was significantly lower than in the Caltrate D group, but the difference could no longer be found after 12 months of treatment. There was no significant difference in the percentage changes from the baseline BMD at the neck between the two groups after adjusting for baseline BMD ($P>0.05$). Papadimitropoulos *et al*^[8] concluded that at the lumbar spine and forearm sites, hydroxylated vitamin D doses above 0.5 μ g yielded a larger effect than lower doses. The dosage in our study of Calcitriol was smaller — 0.25 μ g/d — but the changes of BMD in the lumbar spine were still significant. This suggests that low-dose calcitriol also had a beneficial effect on bone metabolism in elderly Chinese women.

In addition to low bone mineral density, falls are important in the pathogenesis of osteoporotic fractures. Any condition that can increase the risk of falling can also increase the risk of fractures. More than one-third of people aged over 65 years fall each year; one of the most important risk factors is muscle weakness, which may be associated with vitamin D deficiency. A significant correlation between serum 25-hydroxyvitamin D concentration and the occurrence of falls in elderly people was reported in 1999^[22]. There is more evidence that supplementation of vitamin D can reduce the incidence of falls. A STOP/IT (Sites Testing Osteoporosis Prevention and Intervention Treatments) trial showed that subjects in the calcitriol group experienced fewer fractures from falls than did the subjects in the

estrogen group (odds ratio: 0.78 and 0.94, respectively)^[23]. Interestingly, the FTSSST time was significantly shortened in the Caltrate D group but was not significantly different in the Rocaltrol+Caltrate D group. The reason was not clear, but we think it may be related to individual differences. No significant changes in the grip strengths of either hand was found at the end of 12 months. The SMFRT times were markedly lengthened in both the Caltrate D group and the Rocaltrol+Caltrate D group at the end of 12 months of treatment. These data indicate that treatment with either Caltrate D alone or Rocaltrol+Caltrate D may exert beneficial effects on muscle strength and balance in elderly Chinese women.

In Tilyard's study^[24], patients were treated with 0.25 μ g Calcitriol twice a day for three years. The quantity of new vertebral fractures were significantly reduced during the second and third year compared with people receiving calcium alone. Two and one new vertebral fractures, respectively, occurred in the Caltrate D and Rocaltrol D+Caltrate D groups. Two nonvertebral fractures occurred in the Rocaltrol+Caltrate D group, but none occurred in the Caltrate D group.

In several reports, some patients treated with 0.5 μ g/d Rocaltrol developed hypercalcaemia, which rarely happened in patients treated with 0.25 μ g/d Rocaltrol. In our study, we used 0.25 μ g/d Rocaltrol, and no hypercalcaemia or renal lithiasis was observed throughout the 12-month treatment. This is consistent with the previous conclusions. Compliance and tolerability of treatments were good; no participant withdrew because of events related to either treatment throughout our 12-month trial.

The main limitations of our study include the small sample size, inadequate power to detect differences in fracture rates, and the limited treatment period. Further studies with larger samples should be done to detect the efficacy of both treatments in fracture reduction. Because this is an open-label, controlled study, but not a double blinded one, the results may have some bias. Some studies showed that calcium or vitamin D may have positive effects on bone mass only within a 1- to 2-year treatment period; the effects may blunt after 2 years. Our study lasted for only 12 months of treatment. The long-term effects and safety of Caltrate D and Rocaltrol plus Caltrate D in elderly Chinese postmenopausal women need to be confirmed by further study.

In conclusion, treatment with Rocaltrol plus Caltrate D or Caltrate D alone for 12 months in elderly Chinese postmenopausal women was found to be effective at increasing BMD in the lumbar spine. Compliance and tolerability of the treatments were good. Rocaltrol plus Caltrate D or Cal-

trate D is effective and safe for the management of elderly Chinese women with low bone mass.

Acknowledgments

This work was supported by the Key Technologies R & D Program under grant No 2006BAI02B03 and the National Natural Science Foundation of China (NSFC) under grant No 30370781.

Author contribution

Wei-bo XIA (designed research, performed research, analyzed data and wrote the paper), Zhong-lan ZHANG (performed research), Hong-fu WANG (designed research and performed research), Xun-wu MENG (designed research and performed research), Ying ZHANG (performed research), Guo-ying ZHU (performed research), Xiao-ping XING (performed research), Jian-li LIU (designed research and performed research), Li-hua WANG (performed research), Yan JIANG (performed research), Shi-fang WENG (performed research), Tao XU (statistical analysis), Ying-ying HU (sample collection), Wei YU (performed research), Jun-ping TIAN (BMD measurement).

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