Effects of Calcitriol or Calcium on Bone Mineral Density, Bone Turnover, and Fractures in Men with Primary Osteoporosis: A Two-Year Randomized, Double Blind, Double Placebo Study

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Osteoporosis in men is an emerging public health problem. As calcitriol reduces the rate of vertebral fractures in osteoporotic postmenopausal women, we conducted a prospective study of this treatment in men with primary osteoporosis. Our study was a 2-yr, randomized, double masked, double placebo-controlled trial of calcitriol (0.25 μg twice daily) or calcium (500 mg twice daily) in 41 men with primary osteoporosis and at least 1 baseline fragility fracture. Thirty-three men (85%) completed the study.

There were no differences in baseline characteristics. Spinal and femoral neck bone mineral densities at 2 yr were unchanged in both groups. Serum osteocalcin decreased in both groups by 30% (P < 0.05), whereas urine N-telopeptide cross-links decreased only in the calcium group by 30% (P < 0.05). After 2 yr, fractional calcium absorption increased by 34% (P < 0.01) in the calcitriol group. Nineteen incident fragility fractures occurred (14 vertebral and 5 nonvertebral) in 7 men. Over 2 yr, the number of men with vertebral fractures (6 es. 1; P = 0.097) was similar in both groups.

In conclusion, the efficacy of calcitriol remains unproven as a single agent for the treatment of osteoporosis in men. (J Clin Endocrinol Metab 86: 4098–4103, 2001)
Subjects and Methods

The study comprised 41 Caucasian men with primary osteoporosis, aged 27–77 yr, recruited consecutively from hospital clinics and the participating physicians’ private practices. Each patient had at least 1 fragility fracture; 39 had low trauma vertebral fractures, and 2 young men had low trauma proximal femoral fractures. One of the men with a prior hip fracture sustained a vertebral fracture during the study. In 4 men (3 in the calcium group and 1 in the calcitriol group), all evaluable lumbar vertebrae were fractured, and their LS-BMD data were excluded from the spinal BMD analysis (Table 1). The presence of a low trauma fracture was the main criterion for entry. Although low BMD was not required, the majority of men had a baseline spinal or hip T score of less than –2.5. No men had disease known to affect bone or mineral metabolism, and all had normal baseline 25-hydroxyvitamin D (25OHD) and T concentrations.

The 2-yr prospective study was double masked with a double placebo. Patients were randomized to receive either calcitriol (0.25 µg twice daily) and placebo calcium tablets or calcium (500 mg twice daily) and placebo calcitriol capsules. BMD and BMC were measured at baseline and every 6 months; biochemical measurements of bone turnover were measured at baseline and every 3 months; thoracicolumbar spine x-rays were performed at baseline and annually, and FCA was measured at baseline and at study completion. All patients gave informed consent, and the human research and ethics advisory committees of The Royal Melbourne Hospital Research Foundation and Geelong Hospital approved the research protocol.

Bone densitometry and biochemical markers of bone turnover

BMDs of the spine (second to fourth lumbar vertebrae) and the femoral neck, and total body BMC were measured by dual x-ray absorptiometry using QDR-2000 (Hologic, Inc., San Francisco, CA; Royal Melbourne Hospital; n = 35) and DFX-L (Lunar Corp., Madison, WI; Geelong Hospital; n = 6) densitometers. The in vitro and in vivo coefficients of variation were 0.38% and 1% at the lumbar spine and 0.38% and 1.7% at the femoral neck, respectively (22). Standardized BMD was determined by comparison of the individual BMD with the appropriate North American reference data and was expressed as number of sd (z-score) different from the age- and sex-specific mean BMD. For measurement of biochemical bone turnover markers, blood samples were taken, and 2-h urine specimens were collected between 0700–0900 h after an overnight fast. All samples were stored at −70 C until analysis. The urine total pyridinium cross-links, pyridinium and deoxypyridinium were measured by monitoring fluorescence of eluates from HPLC (23). All pyridinium cross-link values were corrected for the individual measured recovery of the internal standard, isodesmosine, and urinary creatinine concentrations. Intra- and interassay coefficients of variation were each 8% and 10% for pyridinium and deoxypyridinium, respectively. Urinary N-telopeptide (NTx) cross-links were measured by duplicate ELISAs (Osteomark, Seattle, WA). The intra- and interassay coefficients of variation were 8% and 9%, respectively.

Serum alkaline phosphatase was measured by duplicate immunoradiometric assays (24) using two monoclonal antibodies directed toward the bone isoenzyme of alkaline phosphatase (Metrabiosystems, Mountain View, CA). The intraassay coefficient of variation was 8%, and cross-reaction with other alkaline phosphatases was 6%. Serum osteocalcin (OC) was measured by duplicate immunoradiometric assays using antibodies raised against human OC (Immutopics, Palo Alto, CA). The intra- and interassay coefficients of variation were 7% and 9%, respectively.

Assessment of FCA

Active, or vitamin D-dependent, intestinal calcium absorption was assessed by a modification of the method described by Nilsson et al. (16). Radiocalcium (45Ca) was purchased from the Australian Atomic Energy Commission (Lucas Heights, Australia) and was administered orally with 20 mg calcium carrier (as CaCl2) in 200 ml deminorized water. Heparinized blood samples were obtained at baseline, 30 and 60 min after treatment, instead of at 60 min alone, and FCA was calculated as the fraction absorbed per h. FCA was not corrected for age or dietary calcium intake. Dietary calcium intakes were calculated from 4-d dietaries at baseline and 2 yr.

Thoracicolumbar spine radiographs

Roentgenograms of the thoracic and lumbar spine were obtained using two x-ray machines. The heights of the anterior, mid, and posterior margins of each vertebral body were measured to the nearest 0.1 mm; all spinal measurements were made with a pair of calipers by two observers, masked to the treatment assignment (P.R.E. and M.A.K.). One of the observers (P.R.E.) remeasured vertebral heights measured at the second site. A vertebral fracture was defined as a decrease of 20% in the anterior, mid, or posterior height of the body of any vertebra from T4 to L4. The changes in vertebral heights at yr 1 and 2 were compared with baseline to detect new vertebral. All incident vertebral fractures represented changes from a normal vertebra, and the majority of fractures

TABLE 1. Baseline variables (mean ± sd) relating to age, bone density (BMD), total body bone mineral content (TBBMC), prevalent vertebral fractures, fractional calcium absorption (FCA), dietary calcium intake (diet Ca), biochemical bone turnover markers (osteocalcin; bone alkaline phosphatase (BAP); deoxypyridinoline (D-Pyr); and N-telopeptide (NTx)), serum hormone concentrations, creatinine clearance, and urinary calcium excretion for 39 men with primary osteoporosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Calcium (n = 19)</th>
<th>Calcitriol (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60.5 ± 12.4</td>
<td>57.5 ± 11.3</td>
<td>0.43</td>
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</tr>
<tr>
<td>LS-BMD (g/cm²)</td>
<td>0.840 ± 0.176</td>
<td>0.868 ± 0.191</td>
<td>0.66</td>
</tr>
<tr>
<td>(n = 16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FN-BMD (g/cm²)</td>
<td>0.636 ± 0.121</td>
<td>0.688 ± 0.103</td>
<td>0.16</td>
</tr>
<tr>
<td>TBBMC (g)</td>
<td>2148 ± 576</td>
<td>2375 ± 408</td>
<td>0.08</td>
</tr>
<tr>
<td>FCA [fraction]</td>
<td>4.5 ± 3.6</td>
<td>3.9 ± 2.3</td>
<td>0.16</td>
</tr>
<tr>
<td>(0.26–0.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet Ca [mg/d (800 mg/d)]</td>
<td>697 ± 287</td>
<td>675 ± 375</td>
<td>0.84</td>
</tr>
<tr>
<td>Osteocalcin [ng/mL (12.1–18.9)]</td>
<td>6.2 ± 2.6</td>
<td>5.2 ± 1.7</td>
<td>0.15</td>
</tr>
<tr>
<td>BAP [IU/L (15–41.3)]</td>
<td>12.1 ± 3.0</td>
<td>11.9 ± 2.7</td>
<td>0.82</td>
</tr>
<tr>
<td>D-Pyr [nmol/mmol creatinine (8–14)]</td>
<td>12.0 ± 5.0</td>
<td>10.5 ± 3.6</td>
<td>0.29</td>
</tr>
<tr>
<td>NTx [pmol BCE/mmol Cr (19.6–62.6)]</td>
<td>62 ± 24</td>
<td>50 ± 24</td>
<td>0.60</td>
</tr>
<tr>
<td>T [nmol/m (7–28)]</td>
<td>19.3 ± 8.1</td>
<td>16.9 ± 5.7</td>
<td>0.27</td>
</tr>
<tr>
<td>PTH [pmol/liter (1–6.5)]</td>
<td>3.5 ± 1.2</td>
<td>4.3 ± 2.0</td>
<td>0.15</td>
</tr>
<tr>
<td>25OHD [nmol/liter (25–108)]</td>
<td>86 ± 27</td>
<td>91 ± 42</td>
<td>0.69</td>
</tr>
<tr>
<td>1,25-(OH)₂D₃ [pmol/liter (34–134)]</td>
<td>75 ± 26</td>
<td>83 ± 17</td>
<td>0.27</td>
</tr>
<tr>
<td>Creatinine clearance, ml/sec (1.5–2.5)</td>
<td>1.9 ± 0.9</td>
<td>1.9 ± 0.6</td>
<td>0.99</td>
</tr>
<tr>
<td>Urinary Calcium [mmol/d (2.5–6.2)]</td>
<td>4.7 ± 2.6</td>
<td>4.5 ± 2.6</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Normal ranges are in parentheses where indicated.
were also clinically apparent. Clinical non vertebral fractures were ascertained by questioning the patient, and incident worsening of prevalent baseline vertebral fractures was also noted.

**Statistical analysis**

Preliminary power calculations showed that we had 88% power (α = 0.05) to detect a difference of 3% in spinal BMD between groups at 2 yr, assuming an sd of 3% in the percent change in BMD. Two-sample t tests or their nonparametric equivalent, e.g. the Wilcoxon rank sum test if data were found not to be normally distributed, were performed to test for baseline differences and to compare differences between treatment groups in responses of bone density, biochemical bone turnover markers, and FCA. Changes from baseline were defined as the study time point value minus the baseline value, expressed as a percentage. To assess these changes, a one-sample t test and or its nonparametric equivalent, e.g. Wilcoxon sign test, was performed for each treatment group. The differences between groups were compared using two-sample t tests or their nonparametric equivalent. Repeated measures ANOVA was also used to test for differences between treatment groups and changes over time within treatment groups for the BMD parameters and the biochemical bone marker data. The differences in incident vertebral fractures were tested by Fisher’s exact test. The analysis was by intention to treat (ITT), and where there were missing data, the last value entered was carried forward to each visit up to month 24 for analysis of BMD data and repeated measures analyses. All analyses were performed with the SAS software program (25).

**Results**

Of the 41 men enrolled, 39 men were evaluable for ITT analysis. Thirty-seven men (17 in the calcium group and 20 in the calcitriol group) completed 12 months, and 33 men (16 in the calcium group and 17 in the calcitriol group) completed 24 months. The overall study retention rate was 85%.

Baseline variables for the 39 men evaluable for ITT analysis are shown in Table 1. There were no differences in baseline characteristics. The men had an overall mean of 3.8 prevalent baseline vertebral fractures (range, 0–12). Regarding baseline bone turnover, mean serum OC and urinary bone resorption markers were in the upper part of the normal range for men. The mean baseline FCA was decreased by more than 1 sd in 18% compared with controls (16). Baseline serum T, 25OHD, and 1,25-(OH)₂D concentrations were all within the normal range in both groups.

**Changes in BMD, biochemical bone turnover markers, and FCA**

The changes in regional BMDs and total body BMC are shown in Table 2 and Fig. 1. Although there was a transient increase in femoral neck BMD in the calcium-treated group, by 2 yr there were no significant changes in BMD in either group relative to baseline or relative to each other. If spinal BMD data of the men with four lumbar vertebral fractures were included, BMD appeared to increase by 8.8% and 7.8% at 1 and 2 yr, respectively, in the calcium group. There were also nonsignificant increases of 1.4% and 1.6%, respectively, in the calcitriol group.

There were no differences between treatment groups in bone turnover markers (Table 2 and Fig. 2). Mean serum bone alkaline phosphatase concentrations decreased during the first 6 months of treatment in both groups and then increased above baseline at 24 months; however, the percent increases in each group were not significant. Urinary NTx/creatinine decreased significantly at 6 months in both groups; however, at 24 months it had decreased by 30% (P < 0.05) in the calcium group and by 6% (P = 0.75) in the calcitriol group. The decrease in NTx/creatinine after calcium treatment is greater than the decrease seen with calcium (500 mg) and vitamin D (400–450 IU) in men with osteoporosis, where NTx decreased by 9% (12). However, it is less than the 59% decrease seen in men treated with alendronate in addition to calcium and vitamin D in the same study. Serum osteocalcin decreased by 35% in the calcium group and by 25% in the calcitriol group (P < 0.01 and P < 0.05, respectively) at 12 months, remained below baseline in both groups, and was significant in the calcium group (P < 0.05) at 24 months.

The mean daily dietary calcium increased by 24% to 729

<table>
<thead>
<tr>
<th>Variable</th>
<th>Calcium</th>
<th>Calcium</th>
<th>p₁²</th>
<th>p₂₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS-BMD (g/cm²)</td>
<td>12 months (n = 17)</td>
<td>24 months (n = 16)</td>
<td>12 months (n = 20)</td>
<td>24 months (n = 19)</td>
</tr>
<tr>
<td>FN-BMD (g/cm²)</td>
<td>2.7 ± 5.3</td>
<td>2.0 ± 6.0</td>
<td>0.2 ± 4.0</td>
<td>−0.05 ± 4.3</td>
</tr>
<tr>
<td>TBBMC (g)</td>
<td>1.3 ± 4.0</td>
<td>−0.9 ± 5.7</td>
<td>0.6 ± 2.7</td>
<td>−0.9 ± 4.8</td>
</tr>
<tr>
<td>FCA (fraction/h)</td>
<td>14 ± 48</td>
<td>34 ± 55</td>
<td>0.47 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>Dietary Ca (mg/d)</td>
<td>24 ± 71</td>
<td>40 ± 97</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Osteocalcin (ng/ml)</td>
<td>−35 ± 22</td>
<td>−18 ± 26</td>
<td>−25 ± 33</td>
<td>−6.9 ± 39</td>
</tr>
<tr>
<td>BAP (IU/liter)</td>
<td>−5.5 ± 21</td>
<td>23 ± 26</td>
<td>−4.0 ± 28</td>
<td>41 ± 46</td>
</tr>
<tr>
<td>D-Pyr (nmol/pmol creatinine)</td>
<td>−17 ± 44</td>
<td>8 ± 56</td>
<td>0.4 ± 54</td>
<td>42 ± 112</td>
</tr>
<tr>
<td>NTx (nmol BCE/pmol creatinine)</td>
<td>−19 ± 47</td>
<td>−30 ± 55</td>
<td>−16 ± 28</td>
<td>−6 ± 83</td>
</tr>
<tr>
<td>T (ng/ml)</td>
<td>−2.0 ± 21</td>
<td>2.9 ± 32</td>
<td>0.81 ± 0.33</td>
<td></td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>−13 ± 55</td>
<td>−26 ± 44</td>
<td>−23 ± 41</td>
<td>−26 ± 42</td>
</tr>
<tr>
<td>25(OH)D (nmol/liter)</td>
<td>−3 ± 48</td>
<td>−11 ± 27</td>
<td>0.53 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>1,25(OH)₂D (nmol/liter)</td>
<td>−9.2 ± 12</td>
<td>3.3 ± 19.3</td>
<td>0.009 ± 0.003</td>
<td></td>
</tr>
<tr>
<td>Ca (cor) (mmol/liter)</td>
<td>2.0 ± 4.4</td>
<td>1.6 ± 5.1</td>
<td>2.7 ± 3.6</td>
<td>4.6 ± 5.3</td>
</tr>
<tr>
<td>24-h urinary Ca (mmol/d)</td>
<td>6.2 ± 45</td>
<td>0.7 ± 44</td>
<td>115 ± 285</td>
<td>140 ± 231</td>
</tr>
<tr>
<td>Creatinine clearance (ml/sec)</td>
<td>−10 ± 31</td>
<td>−6 ± 26</td>
<td>−0.1 ± 19</td>
<td>−0.3 ± 25</td>
</tr>
</tbody>
</table>

For differences from baseline: d, P < 0.05; c, P < 0.01, differences between groups at 12 and 24 months, respectively: P₁² and P₂₄. Numbers evaluable by ITT analysis: a, n = 16; b, n = 19; c, n = 20 at all time points for calcium and calcitriol groups, respectively, and c, n = 18 for calcitriol group at 24 months.
mg/d ($P = 0.19$), and by 40% to 757 mg/d ($P = 0.08$) in the calcium and calcitriol groups, respectively (Table 2). At 2 yr, the total daily calcium intake in the calcium group was 1729 mg. FCA increased by 34% ($P = 0.01$) at 2 yr in the calcitriol group, but did not change significantly in the calcium group (14%). Sixteen men (10 in the calcium group and 6 in the calcitriol group) had low baseline fractional calcium absorption ($<0.55/h$). They did not have greater increases in spinal, femoral neck, or total hip BMDs with either calcitriol or calcium therapy than men with normal baseline FCA.

Fractures

A total of 19 new fragility fractures (14 vertebral and 5 nonvertebral) occurred in 7 men over 2 yr. Three incident vertebral fractures occurred in 3 men, and 10 incident vertebral fractures occurred in 5 men in the calcitriol group during the first and second years of the study, respectively. Two men in the calcitriol group had incident vertebral fractures in both years of the study. Only 1 incident vertebral fracture occurred in the calcium group in the first year of the study. Thus, over 2 yr, 1 of 16 patients (6%) in the calcium group and 6 of 19 patients (32%) in the calcitriol group had at least 1 new fracture. There was a nonsignificant trend for more men in the calcitriol group to sustain vertebral fractures (6 vs. 1; $P = 0.097$) over 2 yr. All 5 nonvertebral fractures (2 ribs, distal radius, and superior and inferior pubic rami) occurred in the calcitriol group. The fractured pubic rami were sustained after a fall down steps, whereas all other fractures were low trauma fractures. Incident worsening of a prevalent vertebral fracture occurred only in 1 patient in the calcium group, who also sustained an incident new vertebral fracture.

Changes in calciotropic hormone and $T$ concentrations

Neither serum 25OHD nor total T concentrations differed significantly from baseline (Table 2). Serum 1,25-(OH)$_2$D$_3$ decreased by 9% in the calcium group ($P = 0.01$), but increased slightly ($P = 0.89$) in the calcitriol group, with a significant difference between treatment groups ($P = 0.03$). Venous sampling was performed at inconstant times after the calcitriol treatment and may have been too late to detect increases in serum 1,25-(OH)$_2$D$_3$ concentrations related to calcitriol therapy. Serum PTH concentrations in the calcitriol group decreased by 23% and 26% at 1 and 2 yr ($P = 0.01$ and $P = 0.12$, respectively), but did not change significantly in the calcium group.

Safety

Two patients, one in each treatment group, were included in the safety population, although they were excluded from the ITT population, one because a repeat serum T concentration was below the normal range, and the second because
of 0.62

Gallagher and Goldgar (18), using an average calcitriol dose
hypercalciuria and hypercalcemia in the calcitriol group.
in the placebo group, and there was a high incidence of
used or differing habitual dietary calcium intakes. Aloia
BMD may be related to either differing doses of calcitriol
uncontrolled (21).

produced by calcitriol therapy; the latter 2 yr of this study were
of another 3-yr study, vertebral fracture rates were also re-
in the first year

3-fold increase in the vertebral fracture rate over the last 2 yr
In men with osteoporosis. In a 3-yr study of postmenopausal

Serum calcium levels rose within the normal range, and
urinary calcium excretion increased by 140% from baseline
during calcitriol therapy. Although urinary calcium excre-
tion was increased above 10 mmol/d in 2 of the patients
taking calcitriol, it was asymptomatic. However, there were
22 of 35 patients (63%) with urinary calcium that increased
by more than 0.1 mmol/d above baseline. No man com-
plained of passing urinary gravel or of renal colic. In 1 of
these patients, a decreased creatinine clearance did not re-
turn to normal. Serum calcium (corrected for the serum al-
bumin concentration) increased above normal to 2.67 mmol/
liter in only 1 man in the calcium group. No hypercalcemia
occurred in the calcitriol group.

Discussion

We found that men with primary osteoporosis treated
with calcitriol and calcium therapy had transient increases in
spinal and femoral neck BMDs; however, in both groups
BMD returned to baseline at both sites by 2 yr. No lasting
in the total body calcium with calcitriol or calcium treatment. FCA was increased by calcitriol, whereas serum PTH concentrations were decreased.

There are no previous data on the use of calcitriol therapy
in men with osteoporosis. In a 3-yr study of postmenopausal
women with osteoporosis, calcitriol therapy resulted in sta-
bilization of the vertebral fracture rate compared with a
3-fold increase in the vertebral fracture rate over the last 2 yr
of the study in women receiving calcium (20). In the first year
of another 3-yr study, vertebral fracture rates were also re-
duced by calcitriol therapy; the latter 2 yr of this study were
uncontrolled (21).

Differences between studies in the effects of calcitriol on
BMD may be related to either differing doses of calcitriol
used or differing habitual dietary calcium intakes. Aloia et al.
(17) showed significant increases in spinal and distal radius
BMDs and total body calcium with calcitriol at an average
dose of 0.8 μg/d. Vertebral fracture rates tended to be higher
in the placebo group, and there was a high incidence of
 hypercalcuria and hypercalcemia in the calcitriol group.

Gallagher and Goldgar (18), using an average calcitriol dose
of 0.62 μg/d, showed an increase in spinal BMD and stable
total body calcium compared with decreases in subjects tak-
ing placebo, without an adverse effect on serum calcium
concentrations. However, there were no differences in frac-
ture rates.

Ott and Chestnut (26) used the lowest final average cal-
itriol dose (0.43 μg/d), and the dietary calcium intake of
their placebo group was 400 mg/d higher. Changes in BMD
at most sites were similar in each group. The incidence of
vertebral fractures was 10% higher in the calcitriol group, but
this difference was not significant. When subjects in this
study were subdivided according to average daily calcitriol
doses, those receiving more than 0.6 μg/d had the greatest
increases in BMD (27). Only one study using low average
daily calcitriol doses (0.42 μg/d) has shown vertebral height
loss (28), which was not seen in women receiving hormone
replacement therapy alone or placebo.

The goal of osteoporosis treatment is to prevent further
fragility fractures. Although fractures were a secondary end
point of our study, and we had limited power to detect
differences between groups, we detected a trend for an
increased number of new fractures in men receiving calcitriol.

Only one man receiving calcium had a new vertebral frac-
ture. Neither treatment group showed a decrease in BMD
after 2 yr of treatment.

Although the men receiving calcitriol had an average di-
etary calcium intake below the recommended daily allow-
ance, dietary calcium intakes were similar in men with and
without fractures in the calcitriol group (857 ± 359 and 711 ±
402 mg/d; P = 0.45). An elevated bone resorption rate is an
independent risk factor for fracture (29). However, there was
no evidence of increased bone resorption in the calcitriol
group in our study. It is also possible that there is a narrow
therapeutic window for calcitriol, and the response to a fixed
dose in a population is heterogeneous (30), or that there are
gender differences in its effects on bone and mineral metab-
olism, including bone turnover. In women treated with cal-
citriol, bone turnover is decreased, and this may partially
result from suppression of the activation of bone turnover by
PTH. However, high doses of calcitriol (2 μg/d) given to
normal men over 7 d increased bone formation markers
without increasing bone resorption (31).

The incident fracture rate in our study is high, with a 32%
2-yr incidence of fractures in the calcitriol group. However,
the main limitation of our study is its small sample size and
limited power to detect differences in fracture rates. Al-
though our study had only 38% probability to detect a dif-
fERENCE IN fracture rates, a 26% difference in fracture rates
between treatment groups is of biological concern. Never-
theless, we cannot confidently distinguish fracture rates be-
tween groups. However, a larger study adequately powered
to examine differences in fracture rates, would be unwise
given that our study may indicate a safety problem with the
use of calcitriol alone in men with severe osteoporosis. By
comparison, our power to detect differences in BMD based
on our current data were even more limited.

In conclusion, there were no differences between calcitriol
and calcium with respect to their effects on BMD and bone
turnover, but there was a trend for calcitriol therapy to be
associated with an increased number of vertebral fractures.
The latter raises concern, but our study had limited power to
detect a difference in fracture rates. In conclusion, the efficacy
of calcitriol remains unproven as a single agent for the treat-
ment of osteoporosis in men.

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References


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