Effects of alendronate and hormone replacement therapy, alone or in combination, on bone mass in postmenopausal women with osteoporosis: a prospective, randomized study

M.B.Tiras¹³, V.Noyan¹, A.Yıldız¹, M.Yıldırım¹ and S.Dayaa²

¹Gazi University School of Medicine, Department of Obstetrics and Gynecology, Besevler, Ankara, Turkey and ²Department of Obstetrics and Gynecology, McMaster University, Hamilton, Ontario, Canada

© European Society of Human Reproduction and Embryology

Introduction

Osteoporosis typically affects women within the first 15 years after menopause, and is characterized mostly by loss of trabecular bone (Riggs and Melton, 1990). With increasing life expectancy, up to 30% of postmenopausal women are affected by osteoporosis which has now become a major public health problem. The bone remodelling process, which is characterized by bone resorption and formation, is almost in equilibrium before menopause. However, after the menopause, with the absence of oestrogen, resorption predominates and results in bone loss (Riggs and Melton, 1992).

The maximal bone mass that is gained in the third decade is an indicator of future risk of osteoporosis. Up to 1–3% of cortical bone and 5% of trabecular bone is lost per year after menopause. Women lose up to 50% of trabecular bone and 35% of cortical bone mass in their life time (Riggs et al., 1981). Vertebral crush fractures are seen in 25% of postmenopausal women after 70 years of age. The life-time risk of hip fracture in women is 15% and rises to 35% at the age of 90 years. These fractures are associated with a high level of morbidity and the overall mortality rate has been reported to be 20% (Genant et al., 1989).

Bone mineral density (BMD) measurements reflect bone mass and fracture risk. For a woman whose femoral neck BMD is 1 SD lower than the mean value for her age group, the risk of hip fracture is almost seven times higher compared with a woman whose femoral neck BMD is 1 SD higher than the mean (Cummings et al., 1990).

Since the early 1970s, several studies have proved that hormone replacement therapy (HRT) reduces bone loss. HRT stabilizes bone turnover and has been claimed to decrease hip fractures by nearly 50–60% (Kiel et al., 1987). The major drawback of HRT is discontinuation or complete refusal of the treatment owing to side-effects such as abnormal uterine bleeding, oedema and breast tenderness and a fear of developing cancer. For long-term preservation of BMD, women should take oestrogen for at least 7 years after menopause and even this duration of therapy may have little residual effect on bone density among women 75 years of age and older, who have the highest risk of fracture (Felson et al., 1993).

A variety of agents is now being used for the management of postmenopausal osteoporosis. Vitamin D analogues, sodium fluoride, calcitomin, selective oestrogen receptor modulators (SERM) and bisphosphonates may be used when HRT is contra-indicated or not acceptable by the patient (Meunier et al., 1999) and if proven effective may be alternatives to HRT. But it should be emphasized that they lack the beneficial effects of HRT on the cardiovascular system, genito-urinary tract and mental status. Alendronate; a new bisphosphonate, whose exact mechanism of action is still controversial, has been shown to be beneficial in patients with postmenopausal osteoporosis (Jeal et al., 1997).

The objective of the present study was to identify changes
in BMD and bone turnover markers in patients with postmenopausal osteoporosis, treated with HRT, alendronate or a combination of HRT and alendronate. We wanted to determine whether alendronate can be offered as an alternative when HRT is contra-indicated or refused by the patient and whether alendronate should be added to the treatment regimen when HRT is administered to women with osteoporosis.

Materials and methods

Protocol

Women attending the menopause clinic of Gazi University School of Medicine, Department of Obstetrics and Gynecology between January and November 1997 and who were found to have low BMD values, i.e. at least 2 SD below normal, were eligible for the study.

At the initial visit, general physical and pelvic examinations were performed and a Pap smear was taken. Baseline laboratory tests were performed for measurement of serum FSH, LH, oestradiol concentrations, a complete blood count and liver and renal function tests. Pelvic ultrasonography and bilateral mammography were also performed. To document osteoporosis, lumbar and femoral neck BMD measurements were performed. Serum parathormone, osteocalcin, alkaline phosphatase, calcium, phosphorus and morning urinary calcium excretion were measured for each patient.

The inclusion criteria for the study were: (i) at least 1 year of amenorrhoea, serum FSH concentrations >40 IU/l and serum oestra-
diol concentrations >40 pg/ml (only natural menopausal women with intact ovaries); (ii) lumbar L2-L4 BMD at least 2 SD below the mean peak values for young premenopausal women [measured with dual energy X-ray absorptiometry (DEXA), T score <-2] where T score is the difference between the mean peak bone density values for young premenopausal women and the measured subjects; (iii) not using HRT or any agent affecting bone turnover in the previous year; (iv) no metabolic disease that alters bone metabolism or systemic disease affecting general health status; (v) no evidence of malignancy associated with oestrogen use (e.g. endometrial or breast cancer); (vi) no contra-indications for HRT use, such as undiagnosed uterine bleeding, active liver disease or thrombo-embolic disease; (vii) body mass index (BMI) <30 kg/m²; (viii) no active upper gastro-intestinal disease or calcium urolithiasis; (ix) no vertebral deformity that may affect measurement of BMD.

The study groups were planned as follows: group I (n = 40): micromized 17β-oestradiol 2.0 mg ± norethisterone acetate 1.0 mg/day per os (Kliogest tablet; Novo Nordisk, Bagsvaerd, Denmark); group II (n = 40): alendronate-Na 10 mg/day per os (Fosamax tablet 10 mg; Merck & Co., Inc., Whitehouse Station, NJ, USA); group III (n = 40): micromized 17β-oestradiol 2.0 mg ± norethisterone acetate 1.0 mg/day per os (Kliogest tablet; Novo Nordisk) + alendronate-Na 10 mg/day per os (Fosamax tablet 10 mg; Merck & Co., Inc.).

Elementary calcium 1500 mg/day per os (Ca Sandoz effervescent tablet 1500 mg; Novartis Pharma AG, Basel, Switzerland) was added to each treatment regimen.

The total treatment period was planned to be 12 months and patients were examined every 6 months. At each visit, general physical examination was performed and patients questioned about adverse effects. Lumbar and femoral neck BMD measurements and serum concentrations of parathormone, osteocalcin, alkaline phosphatase, calcium, phosphorus and urinary calcium excretion were planned to be measured.

For patients treated with HRT, the presence of venous thrombo-embolic disease, jaundice, severe headache, uncontrolled hypertension, abnormalities in liver function tests and irregular or heavy uterine bleeding during the study period were reasons to be withdrawn from the study. For those using alendronate, withdrawal criteria included oesophagitis or oesophageal ulceration, severe deterioration in renal function and extensive allergic reactions.

Patients who stopped or irregularly used their medications or who did not come to the follow-up visits would also be withdrawn from the study.

Measurements

Institutional Review Board approval was obtained and patients were informed and written consents were obtained. A total of 120 patients who met the inclusion criteria were randomized into one of three treatment groups using a blocked randomization method with a blocking factor of 5.

BMD measurements were performed with DEXA using a Norland XR-36 Bone Densitometer (Norland Corp., Fort Atkinson, WI, USA). A standard mode setting of 60 mm/s was used. In our laboratory, the coefficient of variation for replicate measurements at the lumbar spine and femoral neck was ~1.5%.

Osteocalcin concentrations were measured with DSL-6900 radioimmunoassay kits from DSL, with a sensitivity of 0.6 ng/ml and intra and interassay coefficients of variation (CV) of 7.4 and 6.7% respectively (Diagnostic Systems Laboratories Inc., Webster, TX, USA). Parathormone concentrations were measured with DSL-8000 radioimmunoassay kits from DSL with a sensitivity of 12 pg/ml and intra- and inter-assay CV of 5.7 and 4.5% respectively. Serum and urinary calcium concentrations were measured spectrophotometrically with DAX Technicon 48 (Bayer Corporation, Tarrytown, New York, USA), using O-cresolphthalein complexone. Serum phosphate concentrations were measured spectrophotometrically with DAX Technicon 48 using ammonium hepta molibdate. Serum alkaline phosphatase concentrations were measured spectrophotometrically with DAX Technicon 48 using American Associated Clinical Chemistry (AACC) and International Federation of Clinical Chemistry (IFCC) methods. Urinary creatinine concentrations were measured spectrophotometrically with DAX Technicon 48 using Taffe reaction.

Statistical analysis

The results are expressed as the mean ± SD for age, BMI, time since menopause, BMD and bone turnover markers. Changes from baseline lumbar and femoral neck BMD measurements are expressed as mean ± SEM. Multiple group comparisons for percentage changes in BMD from baseline were made at 6 and 12 months of follow-up by one-way analysis of variance (ANOVA). Between-group differences were assessed by Bonferroni’s post-hoc test. Changes from baseline in biochemical variables and bone mass measurements were evaluated by paired t-test.

Results

Participant flow and follow-up

Out of the 120 patients who began the study, four were discharged owing to side-effects and 21 were excluded because of non-compliance with the study. Thus, analysis was performed on 95 subjects who completed the follow-up period to the end of the 12th month. Group I (HRT) had 31, group II (alendronate) 32 and group III (HRT + alendronate) 32 subjects (Figure 1).

Analysis

Clinical features of the patients are shown in Table I. There were no significant differences between the groups when age,
Figure 1. Flow chart describing progress of patients through the randomized trial. *Group I: hormone replacement therapy (HRT); group II: alendronate; group III: HRT + alendronate.

Table I. Clinical features of the treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 31)</th>
<th>Group II (n = 32)</th>
<th>Group III (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.7 ± 5.6</td>
<td>53.8 ± 6.8</td>
<td>51.9 ± 6.1</td>
</tr>
<tr>
<td>Time since LMP (years)</td>
<td>4.9 ± 4.6</td>
<td>6.5 ± 5.6</td>
<td>6.4 ± 4.8</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.2 ± 3.6</td>
<td>23.8 ± 4.1</td>
<td>24.6 ± 3.9</td>
</tr>
</tbody>
</table>

Group I: hormone replacement therapy (HRT); group II: alendronate; group III: HRT + alendronate.
Values are mean ± SD.
There were no significant differences between the groups.
LMP = last menstrual period.

time since last menstrual period and BMI were considered (Table I).
There were no differences in baseline vertebral and femoral neck BMD measurements and all were at least 2 SD below the mean peak BMD measurements in young premenopausal subjects (T score <−2).

Both at the 6 and 12 month periods, the mean vertebral and femoral neck BMD measurements were significantly higher compared to baseline. However, no significant differences in mean BMD measurements were seen between the groups at 6 and 12 months (Table II).

When evaluating the percentage changes from baseline L2-L4 vertebral BMD measurements, the highest increase was observed in group III (8.41 ± 0.94%) at the end of the 12th month. This increase was 2.63 ± 0.63% for group I.

Percentage changes from baseline in lumbar BMD measurements were significantly different between the groups both at 6 and 12 months. When analysed with the post-hoc test of Bonferroni, this difference was found to be higher between groups I and II, and I and III. In other words, BMD measurements increased more in patients in groups II and III compared to patients in group I (Figure 2).

Femoral neck BMD measurements increased 4.57 ± 0.97% in group III at the end of the 12th month and this was the highest increase among the groups. There were no significant differences between the groups for the percentage changes in femoral neck BMD measurements (Figure 3).

No significant differences were present between the groups for baseline alkaline phosphatase and osteocalcin concentrations (Table III). Declining alkaline phosphatase measurements were observed in all groups. The decrease in osteocalcin concentrations was significant for all groups both at 6 and 12 months except for group I at the 6 months. Baseline calcium and phosphorus concentrations were not different between the groups. Both calcium and phosphorus measurements revealed a non-significant decrease in group I over the study period but the differences for groups II and III were statistically significant. Phosphorus concentrations were significantly different at 6 months between groups I and III (Bonferroni’s post-hoc test). There were no differences in baseline parathormone concentrations and urinary calcium/creatinine (urinary calcium excretion) ratio between the three groups. Parathormone measurements increased significantly at 6 months for groups II and III. At 12 months there were decreases in parathormone concentrations in these two groups compared with the 6th month but this was only significant in group II (P < 0.005).

Parathormone measures did not change significantly in group I throughout the study period. Urinary calcium/creatinine ratio decreased significantly in all groups at 6 months. At the 12th month urinary calcium excretion was not different compared with the 6th month in groups I, II and III (Table III). These changes in biochemical bone markers all indicated that the three treatment options were effective anti-resorptive agents.

Four patients were excluded from the study owing to side-effects. One patient from each of groups II and III were excluded at the third and fourth months respectively because of severe epigastric pain which in one of them was due to oesophagitis. Another two patients, one each from groups I and III, were withdrawn due to irregular, long-lasting heavy uterine bleeding. Endometrial biopsy demonstrated proliferative endometrium in both of them.

Discussion
There are several alternatives for the prevention and treatment of osteoporosis, HRT being the most commonly used regimen because of its documented effectiveness on bone mass and other beneficial effects during postmenopausal years (Reid., 1999).

In the present study, we found a 2.63 ± 0.63% increase in vertebral BMD and 3.21 ± 0.56% increase in femoral neck BMD at the end of the 12th month in patients managed with HRT. These increases were statistically significant and confirm that HRT not only prevents more bone loss but can also increase BMD. Some authors claim that HRT cannot restore the lost bone mass (Renzo et al., 1994) but others report HRT to increase bone mass regardless of the time that has passed after menopause (Quigley et al., 1987).

HRT been found to increase vertebral BMD by 10% and femoral neck BMD by 5.5% at the end of a 3 year treatment period (Lindsay and Tohme, 1990). HRT was reported to

2089
Table II. Baseline, 6th and 12th month L2-L4 vertebral and femoral neck bone mineral density measurements of the patients

<table>
<thead>
<tr>
<th>Time of measurement (months)</th>
<th>Group I ( (n = 31) )</th>
<th>Group II ( (n = 32) )</th>
<th>Group III ( (n = 32) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>L2-L4 (g/cm²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.798 ± 0.08</td>
<td>0.746 ± 0.07</td>
<td>0.788 ± 0.10</td>
</tr>
<tr>
<td>6</td>
<td>0.813 ± 0.08</td>
<td>0.777 ± 0.06</td>
<td>0.817 ± 0.10</td>
</tr>
<tr>
<td>12</td>
<td>0.822 ± 0.08</td>
<td>0.799 ± 0.06</td>
<td>0.841 ± 0.09</td>
</tr>
<tr>
<td>Femoral neck</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.742 ± 0.07</td>
<td>0.729 ± 0.06</td>
<td>0.739 ± 0.09</td>
</tr>
<tr>
<td>6</td>
<td>0.755 ± 0.07</td>
<td>0.742 ± 0.06</td>
<td>0.765 ± 0.09</td>
</tr>
<tr>
<td>12</td>
<td>0.765 ± 0.07</td>
<td>0.751 ± 0.06</td>
<td>0.771 ± 0.09</td>
</tr>
</tbody>
</table>

Group I: hormone replacement therapy (HRT); group II: alendronate; group III: HRT + alendronate. Values are mean ± SD.

*P < 0.05 change from baseline with paired t-test.

*P < 0.005 change from baseline with paired t-test.

There were no significant differences between the groups by analysis of variance.

decrease hip and distal forearm fractures by 50–60% and vertebral fractures by 70–80% after long-term treatment (Weiss et al., 1980; Ettinger et al., 1985; Genant et al., 1989).

The combination of 17β-oestradiol 2.0 mg + norethisterone acetate 1.0 mg/day used in this study has been documented to be effective in osteoporotic patients. Of 63 osteoporotic patients included in a clinical trial using this HRT regimen or placebo, vertebral BMD after 1 year of treatment was found to increase 2.5% in the HRT group and to decrease 4.9% in those receiving placebo (Ettinger et al., 1992).

Alendronate is a new bisphosphonate that has been used in managing postmenopausal osteoporosis and has been found to have a beneficial effect on BMD, reducing the risk of fractures (Jeal et al., 1997). In the present study, 7.23 ± 0.67% increase in vertebral and 3.02 ± 0.44% increase in femoral neck BMD measurements at the end of the 12th month were consistent with the findings in the literature. An important point is that alendronate increased vertebral BMD significantly more than did HRT at 6 and 12 months after commencing treatment. The increases in femoral neck BMD measures did not differ, probably because of the low bone turnover rate in cortical bone.

In a study including 478 postmenopausal patients treated with different doses of alendronate for 3 years, a 10 mg/day dose increased vertebral and femoral neck BMD measurements 9.6 and 4.7% respectively and these increases were not different in the group treated with 20 mg/day (Tucci et al., 1996). We have also used alendronate at a dose of 10 mg/day.

It has been reported that the increases in BMD were highest in the first year of the treatment period in patients using alendronate. This accelerated increase is thought to be due to decrease in bone turnover and mineralization of the present bone remodelling units (Heaney, 1994). Although maximal effects of alendronate are seen in the first 6–12 months, increases in BMD have also been reported in the second or third years (Jeal et al., 1997). At the end of 3 years, Devogelaer and co-workers found that alendronate had increased vertebral and hip BMD measurements 7.4 and 5.5% respectively (Devogelaer et al., 1996).

It has also been reported that the incidence of new fracture risk was 3.2% in patients treated with alendronate compared to 6.2% in those taking placebo at the end of the 3 years. They concluded that alendronate decreases fractures by 48% (Liberman et al., 1995).

Furthermore, women with increases of ≥3% in BMD during the first 1 or 2 years of alendronate treatment were found to have the lowest incidence of new vertebral fractures, suggesting that, among women taking anti-resorptive agents, greater...
In conclusion, alendronate was found to be more effective than HRT. The increases in BMD are associated with lower risk of new vertebral fractures (Hochberg et al., 1999).

In a decision analytical Markov model to compare the effects of alendronate, raloxifene and HRT, it was found that HRT, alendronate therapy and raloxifene therapy had similar predicted efficacies in preventing hip fractures (estimated relative risk, 0.57, 0.54 and 0.58 respectively) (Col et al., 1999).

There have been only a few clinical trials in which alendronate has been compared with or used in combination with other agents. In 1995 a study was performed on rats in which alendronate and HRT were used in combination (Shea et al., 1996; Jeal et al., 1997). They concluded that BMD measurements increased more in the group managed with alendronate and HRT in combination compared to the groups which used these agents separately. In a recent report (Lindsay et al., 1999), 428 postmenopausal women with osteoporosis, who had been receiving HRT for at least 1 year were, randomized to receive either alendronate or placebo. HRT was continued in both groups. Compared with HRT alone, at 12 months alendronate plus HRT produced significantly greater increases in BMD of the lumbar spine (3.6 versus 1.0%, P < 0.001) and hip trochanter (2.7 versus 0.5%, P < 0.001).

In the present study, maximal increases in vertebral BMD measurements were observed in the group treated with alendronate plus HRT, yielding a 8.41 ± 0.94% change. This increase was significantly higher when compared with the group using HRT alone. Although not statistically significant, this increase was also higher when compared with the alendronate-only group. At the end of the 12th month, femoral neck BMD percentage changes did not differ significantly between the groups, but the 4.57 ± 0.97% increase observed in the group using alendronate and HRT in combination was still higher than the 3.02 ± 0.44 and 3.21 ± 0.56% increases found in the groups using only alendronate or HRT respectively. More studies are needed to clarify the issue of whether these two anti-resorptive agents have an additive effect on bone mass measurements when used in combination.

Probably the most important point to be emphasized is that the increases in spinal BMD measurements are significantly higher in patients using alendronate alone and alendronate plus HRT compared with those managed with HRT alone. Alendronate seems to be more effective than HRT with respect to changes in BMD, and combining HRT with alendronate might produce a synergistic effect in patients with postmenopausal osteoporosis, especially in the first 2–3 years of the treatment period.

The changes in biochemical bone markers in all groups all indicated that the three treatment options were effective anti-resorptive agents, consistent with the literature (Garnero et al., 1996; Jeal et al., 1997).

Table III. Baseline, 6th and 12th month alkaline phosphatase (ALP), osteocalcin, calcium, phosphorus, parathormone (PTH) and urinary calcium/creatinine (Ca/CR) measurements of the patients

<table>
<thead>
<tr>
<th>Time of measurement (months)</th>
<th>Group I (n = 31)</th>
<th>Group II (n = 32)</th>
<th>Group III (n = 32)</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP (U/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>94.4 ± 22.2b</td>
<td>94.8 ± 32.6b</td>
<td>90.8 ± 24.1b</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>84.6 ± 18.2b</td>
<td>73.1 ± 19.1b</td>
<td>74.2 ± 24.8b</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>72.7 ± 17.0b</td>
<td>68.5 ± 18.6b</td>
<td>64.5 ± 23.5b</td>
<td>NS</td>
</tr>
<tr>
<td>Osteocalcin (ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7.0 ± 2.2b</td>
<td>8.0 ± 2.5</td>
<td>8.2 ± 2.6</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>6.7 ± 1.7b</td>
<td>7.0 ± 2.0b</td>
<td>6.9 ± 2.1b</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>6.5 ± 2.0b</td>
<td>7.0 ± 1.9b</td>
<td>6.9 ± 2.1b</td>
<td>NS</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>9.6 ± 0.7</td>
<td>9.7 ± 0.5</td>
<td>9.7 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>9.6 ± 0.7</td>
<td>9.4 ± 0.4b</td>
<td>9.5 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>9.4 ± 0.5</td>
<td>9.3 ± 0.4b</td>
<td>9.3 ± 0.4b</td>
<td>NS</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>3.7 ± 0.5</td>
<td>3.6 ± 0.6</td>
<td>3.6 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>3.7 ± 0.5</td>
<td>3.4 ± 0.5b</td>
<td>3.3 ± 0.7b</td>
<td>0.024</td>
</tr>
<tr>
<td>12</td>
<td>3.6 ± 0.5</td>
<td>3.4 ± 0.4b</td>
<td>3.2 ± 0.4b</td>
<td>NS</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>30.2 ± 10.4</td>
<td>30.6 ± 9.0</td>
<td>32.9 ± 9.9</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>31.5 ± 8.8</td>
<td>34.4 ± 8.9b</td>
<td>36.0 ± 7.7b</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>30.5 ± 9.0</td>
<td>32.6 ± 8.9b</td>
<td>33.4 ± 8.5</td>
<td>NS</td>
</tr>
<tr>
<td>Ca/CR (mg/mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.16 ± 0.07b</td>
<td>0.17 ± 0.09b</td>
<td>0.18 ± 0.07b</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>0.12 ± 0.04b</td>
<td>0.12 ± 0.03b</td>
<td>0.12 ± 0.04b</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>0.12 ± 0.04b</td>
<td>0.12 ± 0.03b</td>
<td>0.11 ± 0.03b</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group I: hormone replacement therapy (HRT); Group II: alendronate; Group III: HRT + alendronate.
Values are mean ± SD.
aAnalysis of variance.
bP < 0.005 change from baseline with paired t-test.
cP < 0.05 change from baseline with paired t-test.
osteoporosis. Alendronate may also be used in postmenopausal patients with osteoporosis when HRT is contra-indicated or when the patient is reluctant to use any hormonal treatment.

References


Received on March 31, 2000; accepted on July 11, 2000