Original Article

Comparison of the Treatment Effects of Ossein-Hydroxyapatite Compound and Calcium Carbonate in Osteoporotic Females

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Abstract. The aim of the study was to evaluate whether ossein-hydroxyapatite (OHC) is more effective than calcium carbonate (CC) in preventing further bone loss in postmenopausal osteoporosis. Forty osteoporotic patients were monitored for 20 months. The patients were randomly assigned to one of two groups and treated in a double-masked manner with 1400 mg calcium per day, in the form of either OHC or CC. OHC consists of hydroxyapatite, collagens and non-collagenous proteins/peptides containing insulin-like growth factor I (IGF-I; 1341 ng), insulin-like growth factor II (IGF-II; 670 ng), transforming growth factor beta (TGF-β; 166 ng) and osteocalcin (47 μg). The bone densities were evaluated at intervals of 4 months with high-precision peripheral quantitative computed tomography. After 20 months of treatment the loss of trabecular bone was 0.8 ± 0.5% in the OHC group and 1.8 ± 0.7% in the CC group. The difference between the OHC and CC groups was statistically significant. This study shows that OHC is more effective than CC in slowing peripheral trabecular bone loss in patients with manifest osteoporosis.

Keywords: Bone densitometry; Computed tomography; Ossein-hydroxyapatite compound; Postmenopausal osteoporosis

Introduction

Calcium intake throughout life appears to be a key factor determining whether or not osteoporosis may develop. Women who consumed milk with every meal during childhood and adolescence are reported to have a higher bone density than women drinking milk less frequently [1]. Adequate calcium intake until adulthood may also be helpful in achieving a high peak bone mass [2]. In the menopausal age range data are sparse, however, and bone loss might be influenced by other factors such as ovulatory disturbances [3]. In the first 5 years after menopause, bone loss and calcium intake are probably no longer directly related [4], whereas healthy older postmenopausal women may again profit from calcium supplementation, especially if their daily calcium intake is less than 400 mg/day [5]. A review of 36 papers on calcium intake and bone mass [6] concluded that a calcium supplement of around 1000 mg/day in postmenopausal women can prevent the loss of approximately 1% of bone mass per year. It has been suggested that the relationship between calcium intake and bone mass displays a threshold effect, so that beyond a certain intake additional calcium has no effect [7]. This threshold is assumed to be below 800 mg/day.

Whilst the therapeutic effect of calcium supplementation in older women with a low daily calcium intake is no longer a controversial issue, the efficiency of various calcium sources is. In general calcium citrate malate is said to be better than calcium carbonate [8,9], but others [10] state that all forms of calcium supplementation have approximately the same bioavailability.

In a pilot study we evaluated the effect of OHC (ossein-hydroxyapatite compound) on manifest osteoporosis using high-precision, low-dose peripheral
quantitative computed tomography (pQCT). The results indicated a positive effect of OHC treatment [11]. The aim of the present study was to discover whether OHC is superior to calcium carbonate (CC) in preventing bone loss in postmenopausal osteoporosis. To this end a double-masked, comparative study was performed.

Methods

Experimental Subjects

Forty postmenopausal patients in the age range 58–78 years were treated for 20 months. Osteoporosis was diagnosed on the basis of at least one crush fracture of the spine without adequate trauma. No treatment with estrogens, calcium, vitamin D, or any other drug that could have influenced bone had been given prior to therapy. No history of an event known to influence bone metabolism, such as alcoholism, nicotine abuse, steroid administration or antiepileptic drugs, diabetes mellitus, thyroid disease or hyperparathyroidism, was present.

The patients were randomly assigned to one of two groups and treated in a double-masked manner with 8 film-coated tablets per day (breakfast 2, lunch 2, dinner 4). The film-coated tablets contained a total of 1400 mg calcium in the form of either OHC or CC. Five dropouts occurred during the observation period of 20 months: 3 in the OHC group (1 fell ill, 1 refused the drug, 1 changed to estrogens) and 2 in the CC group (1 fractured the radius at the measuring site, 1 changed to estrogens). The complete data on 17 patients in the OHC group (age 67.2 ± 7.0 years) and 18 patients in the CC group (age 65.6 ± 5.4 years) were available for the final analysis.

Medication

Ossein-hydroxyapatite compound (OHC), derived from bone of bovine origin, contains an organic and an inorganic component. The organic component, ossein, consists of collagen and non-collagenous peptides/proteins with growth factors and bone-specific proteins insulin-like growth factors I and II (IGF-I and IGF-II), transforming growth factor beta (TGF-β) and osteocalcin. These factors have been isolated and quantified by Stepn et al. [12]. The inorganic part, hydroxyapatite, supplies calcium and phosphorus in a physiological ratio of 2:1. OHC 6.64 g (1.4 g calcium) corresponds to 3.32 g hydroxyapatite, 1.72 g collagen, 0.6 g non-collagenous peptides/proteins with 1341 ± 90 ng IGF-I, 670 ± 70 ng IGF-II, 166 ± 10 ng TGF-β and 47 ± 4 μg osteocalcin.

Bone Densitometry

Bone density measurements were performed at intervals of 4 months using peripheral quantitative computed tomography (pQCT). Measuring sites were the distal tibia (a weight-bearing bone) and the distal radius (a non-weight-bearing bone) for trabecular bone density (TBD) examinations. The diaphysis of the radius was used for the determination of a parameter describing compact bone. The measuring and evaluation procedure has been described previously [13,14] and can be characterized as follows:

The patient’s arm (or leg) is positioned in a radiolucent cast which enables comfortable immobilization during the measuring process and allows reproducible orientation of the bone axis relative to the measuring plane. The measuring system – a special-purpose CT instrument for low-dose bone densitometry – provides a digital radiogram as a positioning aid for the examination site. The examination site in the ultradistal radius (or tibia) is then covered with a stack of ten tomograms (slice thickness 1 mm, interslice distance 1 mm). During the 20 months of follow-up six such measurements are made. After the sixth measurement the bone volume common to all examinations of a patient is determined. Then the bone density changes in this bone sample are evaluated. This procedure enables a reproducibility in routine patient examinations of 0.3% at a radiation dose of only 0.1 mSv per examination [15].

Statistical Analysis

The mean, SD and SEM for values at visits 1 to 6 were calculated for all variates. The changes in bone densities between the first visit (baseline) and all subsequent visits were determined. Within groups these changes were analyzed with a paired t-test. The differences between the mean bone density over time and the densities measured at the visits 1 to 6 were also calculated for each patient and an analysis of variance performed.

Results

The baseline values are summarized in the Tables 1 and 2. For trabecular bone the baseline values of the two treatment groups are the same (difference not statistically significant). They are approximately 30% below the respective bone densities of healthy women at the age of 50 years [14]. For cortical bone the baseline values are different (p <0.05).

To analyse the effects of the two treatment modalities on the bone densities we followed a two-step approach. First, all bone density changes relative to the respective baseline values were calculated and analyzed with a paired t-test. From month 8 onwards the trabecular bone loss (Table 1) in the CC group was significantly different from baseline. In the OHC group this difference did not reach significance. In contrast, as regards cortical bone loss the values in both groups differed significantly from baseline (Table 2). In addition to the relative values in Tables 1 and 2, absolute values are