Effects of 5-year treatment with elcatonin and alfacalcidol on lumbar bone mineral density and the incidence of vertebral fractures in postmenopausal women with osteoporosis: a retrospective study

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Abstract The purpose of this retrospective study was to compare the effects of long-term treatment (5 years) with elcatonin and alfacalcidol on bone mineral density (BMD) and the incidence of vertebral fractures in postmenopausal women with osteoporosis. Fifty-six osteoporotic women, more than 5 years after menopause and 58–79 years of age, were enrolled in the study and allocated to an elcatonin treatment group (20 units IM, weekly; \( n = 30 \)) or an alfacalcidol treatment group (1\( \mu \)g/day, daily; \( n = 26 \)). BMD of the lumbar spine (L2-L4) was measured by dual energy X-ray absorptiometry at baseline and every year for 5 years. There were no significant differences in age, body mass index, years since menopause, BMD, or number of prevalent vertebral fractures at baseline between the two groups. One-way analysis of variance with repeated measurements showed no significant longitudinal changes in BMD in either group, suggesting that both treatments sustained the BMD over 5 years. Two-way analysis of variance with repeated measurements also showed no significant differences in longitudinal changes in BMD between the two groups, suggesting that the effects of the two treatments on BMD were similar. However, the number of incident vertebral fractures per patient was significantly lower in the alfacalcidol treatment group than in the elcatonin treatment group (0.80 ± 1.19 and 2.08 ± 2.73, respectively; \( P < 0.05 \)). These findings indicate that both treatments appeared to sustain lumbar BMD similarly over a 5-year period in postmenopausal women with osteoporosis, but alfacalcidol treatment may be superior to elcatonin treatment regarding the incidence of vertebral fractures. Further study with prospective observations are needed to confirm the results of the present study.

Key words Elcatonin · Alfacalcidol · Osteoporosis · Bone mineral density (BMD) · Vertebral fracture

Introduction

Osteoporosis, characterized by low bone mass and increased risk of fractures, is a major public health problem. Although age-related bone loss in men is modest, women usually experience marked bone loss after menopause with increased bone turnover.\textsuperscript{9,10,12,26} Because of physiological changes associated with menopause, osteoporosis primarily affects untreated late postmenopausal women. Recently, it has been clearly demonstrated that postmenopausal women, even though elderly, show high bone turnover.\textsuperscript{26} Therefore, the efficacy of antiresorptive agents for osteoporosis in postmenopausal women has been strongly confirmed.\textsuperscript{6,23}

In Japan, calcitonin and vitamin D\(_3\) have been widely used for osteoporosis treatment for many years. Because calcitonin and vitamin D\(_3\) have an antiresorptive effect on bone, they are considered to be efficacious for high-turnover osteoporosis in postmenopausal women.\textsuperscript{16,17} Calcitonin, elcatonin, when given by weekly intramuscular injection, increases lumbar bone mineral density (BMD) over 6 months\textsuperscript{17} and sustains it over 3 years.\textsuperscript{7} However, treatment of osteoporosis with intramuscular injection of elcatonin usually results in a high discontinuation rate, particularly in view of the long treatment duration. Thus, few studies have reported the long-term outcome of elcatonin treatment for osteoporosis. Because there may be a potential for the development of resistance to calcitonin, which may originate from neutralizing antibodies or the “escape phenomenon,”\textsuperscript{19} it is important to examine whether long-term treatment with calcitonin could result in a positive effect on osteoporosis.

On the other hand, it has been accepted that 1\( \alpha \)-hydroxyvitamin D\(_3\), alfacalcidol sustains lumbar BMD for 1 year and reduces the incidence of vertebral fractures in patients with postmenopausal osteoporosis.\textsuperscript{16} A retrospective study has already confirmed the efficacy and safety of long-term treatment (5 years) with...
alfacalcidol for osteoporosis.22 The purpose of the present retrospective study was to compare the effects of long-term treatment (5 years) with elcatonin and alfacalcidol on lumbar BMD and the incidence of vertebral fractures in postmenopausal women with osteoporosis.

Subjects and methods

Subjects
A series of 56 osteoporotic women more than 5 years after menopause (58–79 years of age) who had been treated with either elcatonin (20 units IM, weekly; n = 30) or alfacalcidol (1 µg/day, daily; n = 26) over 5 years at a hospital in Tatebayashi, Gunma, Japan were enrolled in the study. The final data of the subjects were collected during the 6 months between October 2001 and March 2002. All of them had continued treatment of osteoporosis for 5 years without any serious adverse effects. The pre- and posttreatment examinations included a medical history, physical examination, and plain radiographic examination of the thoracic and lumbar spine. Blood samples were obtained, and serum calcium and phosphorus levels were measured with standard laboratory techniques. BMD of the lumbar spine was measured at baseline and each year for 5 years, as described below. None of the subjects suffered from any metabolic bone disease, and none had a history of hormone (estrogen) replacement therapy or had ever taken medication that affects bone metabolism prior to the present study. None of the subjects had participated in sporting activity for at least the past 5 years, and none participated in such activity during the present study. All of the subjects had been instructed to take 600 mg of calcium daily through food intake. Informed consent was obtained from all participants.

Measurement of BMD of lumbar spine
The BMD of the lumbar spine (L2-L4) in the antero-posterior view was measured by dual energy X-ray absorptiometry (DXA) using a Hologic QDR 1500W instrument (Bedford, MA, USA). The coefficient of variation (100 × standard deviation/mean) of five measurements each time with repositioning within 72 h was less than 1.1% in three persons.

Assessment of vertebral fractures
Before treatment, plain radiographic examination of the thoracic and lumbar spine was performed to seek evidence of vertebral fractures. At the end of the 5-year treatment, plain radiographic examination of the tho-

Results

Characteristics of study subjects
Table 1 shows the baseline characteristics of the study subjects. The mean age was 69.0 years (range 60–76 years) in the elcatonin group and 69.1 years (range 58–79 years) in the alfacalcidol group. There were no significant differences in mean age, height, body weight, body mass index, or years since menopause at baseline between the two groups. Serum calcium and phosphorus levels were within normal limits in all subjects, with no significant differences between the two groups. The mean initial BMD of the lumbar spine was 605 mg/cm² (T score 59.9%) in the elcatonin group and 601 mg/cm² (T score 59.6%) in the alfacalcidol group, with no