Eldecalcitol Reduces Serum Undercarboxylated Osteocalcin Levels Along with a Decreased Bone Metabolic Turnover in Patients with Osteoporosis

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Abstract

Undercarboxylated osteocalcin (ucOC) is a marker of vitamin K deficiency. In addition, ucOC reflects bone metabolic turnover besides vitamin K sufficiency status. Increased ucOC level is considered a predictor of proximal femoral fracture. Eldecalcitol has been reported to strongly influence bone metabolism as compared with the conventional vitamin D supplementation. In this study, we examined the effects of eldecalcitol supplementation on ucOC levels.

We evaluated 25 patients with osteoporosis who had no history of treatment for osteoporosis. After the first examination, we administered eldecalcitol 0.75 μg/day and reexamined the patients 6 months later.

ucOC was correlative with the N-telopeptide of type 1 collagen (NTX) and bone-specific alkaline phosphatase (BAP). The serum ucOC level was reduced in 88.0% of the patients who received additional eldecalcitol treatment. NTX and BAP also decreased significantly.

In this study, it was concluded that eldecalcitol supplementation reduced serum ucOC levels along with a decreased bone metabolic turnover in patients with osteoporosis.

Keywords: Undercarboxylated Osteocalcin (ucOC); Eldecalcitol; Osteoporosis

Introduction

Osteocalcin (OC) is a bone-specific protein that is synthesized by osteoblasts, and widely used as a marker of bone formation. OC is characterized by the presence of γ-carboxyglutamic acid residues. Fully carboxylated OC has a high ability to bind hydroxyapatite. Vitamin K is a necessary factor for the posttranslational γ-carboxylation of glutamic acid. The synthesis of OC depends on vitamin K level. In vitamin K deficiency, undercarboxylated OC (ucOC) is released from osteoclasts into the blood circulation. ucOC has no ability to bind hydroxyapatite. Thus, vitamin K is thought to maintain bone strength via the γ-carboxylation of OC [1]. Moreover, vitamin K deficiency has been reported to be a risk factor of proximal femoral fracture [2,3].

Consequently, vitamin K treatment is currently considered as the therapy of choice to control high ucOC levels [4,5]. However, vitamin K supplementation is limited in patients receiving warfarin for a preexisting condition. In addition, ucOC reflects bone metabolic turnover besides vitamin K sufficiency status. Bisphosphonate supplementation is useful for reducing bone metabolic turnover [6]. However, bisphosphonate supplementation has been reported to obstruct a process in vitamin K metabolism [7,8]. Hence, patients receiving bisphosphonate supplementation should be carefully monitored even if ucOC levels decrease [9].

In the recent past, eldecalcitol has been developed as an active vitamin D derivative. Eldecalcitol has been reported to strongly influence bone metabolism as compared with the conventional vitamin D supplementation [10-13]. However, reports on the effects of eldecalcitol on ucOC levels are few.

Hence, we examined the effects of eldecalcitol supplementation on ucOC levels.

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Patients and Methods

We evaluated 25 patients with osteoporosis who had no history of treatment for osteoporosis (mean age, 78.6 years). We analyzed ucOC, the N-telopeptide of type I collagen (NTX; a marker of bone resorption), and bone-specific alkaline phosphatase (BAP; a marker of bone formation). Bone Mineral Density (BMD) was measured at the lumbar spine and proximal femoral levels by using dual-energy X-ray absorptiometry. After the first examination, we administered eldecalcitol 0.75 μg/day and reexamined the patients 6 months later.

Values are shown as mean ± S.E. Comparisons were conducted by using the paired Student t-test. Correlations between two independent measurements were assessed by using Pearson correlation coefficient. Differences were considered statistically significant at p values of < 0.05. All statistical analyses were performed by using SPSS version 21.0 (IBM).

Results

The mean ucOC level was 9.19 ± 12.46 ng/mL. The ucOC levels in 18 patients (72.0%) were higher than the standard value (< 4.49 ng/mL). ucOC was correlated with NTX (r = 0.562, p < 0.01) and BAP (r = 0.469, p < 0.05) (Figure 1).

After 6 months, serum ucOC level decreased significantly, and the mean ucOC was 5.46 ± 7.06 ng/mL. The serum ucOC level was reduced in 88.0% of the patients who received additional eldecalcitol treatment. NTX and BAP also decreased significantly. However, additional eldecalcitol treatment showed no significant effect on BMD (Table 1).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre medication</th>
<th>After medication</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ucOC (ng/mL)</td>
<td>9.19 ± 12.46</td>
<td>5.46 ± 7.06</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>NTX (nM BCE/mM • Cr)</td>
<td>60.72 ± 34.67</td>
<td>38.80 ± 24.88</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>BAP (U/L)</td>
<td>19.82 ± 8.31</td>
<td>16.03 ± 6.03</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Lumbar BMD (YAM %)</td>
<td>79.36 ± 16.68</td>
<td>79.68 ± 18.00</td>
<td>P = 0.73</td>
</tr>
<tr>
<td>Proximal Femoral BMD (YAM %)</td>
<td>70.40 ± 11.14</td>
<td>69.96 ± 10.31</td>
<td>P = 0.57</td>
</tr>
</tbody>
</table>

Table 1: Biochemical measurements and bone mineral density.

YAM: Young Adult Mean

Discussion

Eldecalcitol controls bone resorption by inhibiting the differentiation of previous osteoclasts. It has a mechanism of action that to promotes the differentiation of previous osteoblasts, and activates bone formation [14,15]. Clinical trials have reported that eldecalcitol suppresses an important bone resorption marker and increases the BMD of the lumbar vertebrae and proximal femur.

We examined the effects of eldecalcitol supplementation on ucOC levels. Eldecalcitol supplementation reduced ucOC levels along with a decreased bone metabolic turnover.

In this study, the supplementation period was short (6 months), hence, a significant increase in BMD could not be confirmed. However, we observed decreases in ucOC levels and other bone metabolism markers. Thus, future long-term follow-up studies should evaluate if eldecalcitol supplementation has a protective effect against proximal femoral fracture by reducing ucOC levels.

Conclusion

In this study, it was concluded that eldecalcitol supplementation reduced serum ucOC levels along with a decreased bone metabolic turnover in patients with osteoporosis.

Bibliography


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