The 10th Anniversary
FUKUOKA ACTIVE AGING CONFERENCE
IN ASIA PACIFIC 2016

Constructing an Age- friendly Collaboration
among Academic, Industrial, Governmental
and Civic Circles

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Appraisers

- Dr. Kathryn Braun
- Dr. Christopher Conybear
- Dr. Tri Budi W. Rahardjo
- Dr. Siti Setiati
- Dr. Sungkook Lee
- Dr. Yoshiko Someya
- Dr. Takeo Ogawa
Osteoporosis Risk Factors of Elderly Indonesian Females

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Abstract
Background: Osteoporosis, a disease characterized by reduced bone mineral density (BMD) and elevated risk of fracture particularly in postmenopausal women, has multifactorial etiology with environmental and genetic roots. While estrogen therapy is an important countermeasure, prevention through complementing alternative or parallel options remains attractive. The increasing life expectancy is expected to exacerbate the challenge, while at present about 50% of females will develop osteoporosis by the time they are 80 years old. The related threat to public health calls for improved methods of prevention and treatment.

Objectives: The present study aimed to assess the association of environmental factors in comparison with polymorphisms of selected regulatory genes on the risk of osteoporosis in postmenopausal Indonesian women.

Materials and methods: The study and applied methods were approved by the ethical committee of the Faculty of Dentistry, University of Indonesia. After obtaining written consent, 206 postmenopausal Indonesian women with a mean age of 55.6 years (ranging from 42 to 80 years) were included in the study, and measured or calculated quantities were obtained such as body mass index (BMI), bone mineral density (BMD) to differentiate between subjects with osteoporosis, osteopenia and normal bone, and blood estrogen, cholesterol and sugar levels and blood pressure. In addition, the levels of daily physical activity, calcium intake and exposure to sunlight were recorded. Genotype patterns were determined for selected genes such as those for the estrogen receptors ESR1 and ESR2, calcitonin receptor CTR, vitamin D receptor VDR by using the PCR-RFLP techniques.

Results: The results confirmed a significant association and positive correlation of BMD with daily calcium uptake and mean time of sunlight exposure. In comparison, the evaluated polymorphic variants of the selected genes were relatively weak indicators of the osteoporosis risk.

Conclusions: Hereditary polymorphic variants of key regulatory genes of bone maintenance may affect the risk of osteoporosis. However, BMD of elderly Indonesian females was more significantly enhanced by calcium uptake and exposure to sunlight. Hence the risk appears to be less dependent on genetic susceptibility than on diet and lifestyle to prevent osteoporosis.

Keywords: Risk factors, Bone mineral density, osteoporosis, ESR, CTR, VDR variants
Osteoporosis Risk Factors of Elderly Indonesian Females

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Introduction

Postmenopausal women require estrogen replacement therapy, as about 50% of women will have osteoporosis by the age of 80. There are two known estrogen receptors, ERa and ERβ. ERα (or ESRI) has eight exons about 140 kilobases long, is located at the chromosomal site 6q26 and ERβ (ESR2) is at the location 14q22-24.1, consists of eight exons spanning about 40 kilobases. ERα is a nuclear receptor protein mediating the action of estrogen in bone including regulation of bone turnover. Calcium is a hormone that decreases bone resorption and acts through specific calcitonin receptors (CTR) in osteoclasts. The vitamin D receptor (VDR) is involved in biological processes metabolism of calcium and phosphorus in the bone turnover. Mutations in the functional areas of the VDR gene have an impact on BMD, and of the several known polymorphisms the 2753C>T (FokI) polymorphism in exon 2 has been reported to modify the

Objectives

Examine the associations between the polymorphisms in the receptor genes ERα, ERβ, CTR and VDR as factors potentially related to bone turnover and osteoporosis in postmenopausal Indonesian women.

Materials and Methods

205 postmenopausal women without estrogen with a mean age of 55.6 years (42 to 89 years). Measurements were taken for body mass index (BMI), blood estrogen, cholesterol, sugar levels, and blood pressure. Bone mineral density (BMD) was measured for the left with dual photon absorptiometry, were used to differentiate between osteoporosis, osteopenia and normal bone. For assessing the frequencies of polymorphic genes, selected restriction enzymes were used to cut DNA of the estrogen receptor genes ERα and ERβ, calcitonin receptor CTR, vitamin D receptor VDR, using samples from peripheral blood. The resulting fragments were subjected to PCR-RFLP, and the number

Results

The subjects and the results from the initial measurements are summarised in Table 1. Regarding bone mineral density (T-score), only one subject of 185 was within the normal range, 30 subjects (18.5%) were in the range of osteopenia and 73 (70.2%) in the range of osteoporosis. The results concerning the observed polymorphisms are summarised in Table 2. Examples of results from the PCR-RFLP experiments are shown in Fig. 1 for Pro1 II and Xba I. Comparison of mean BMD for selected grouping of observed polymorphisms are shown in Table 3.

Discussion

The ERα expression status after cutting with the restriction enzyme PvuII. The normal genotype (F) appears to be associated with higher BMD. The combined normal and heterozygotic groups showed a significantly (though marginally, p < 0.05) lower BMD than the homozygotic group. No combination of the ERβ genotypes showed clear differences in BMD after cutting with AluI, and the same was true for VDR genotypes after cutting with FokI. The normal and heterozygotic genotypes of CTR after cutting with AluI were associated with higher BMD than the homozygotic genotype, but the differences were not statistic.

Conclusion

Polymorphic variation regulatory genes of bone turnover may affect the risk of osteoporosis, bone mineral density of postmenopausal Indonesian women. This suggests that regardless of variation in genetic susceptibility, prudent diet and lifestyle may provide important and effective preventive ways against osteo-

References

Table 1. Summary of selected patient data; estrogen from serum (pg/mL), calcitonin (ng/mL)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>T-score</th>
</tr>
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<tr>
<td>Normal</td>
<td>65.7</td>
<td>4.8</td>
<td>57.2</td>
<td>73.7</td>
<td>-0.79</td>
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<tr>
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<td>63.6</td>
<td>4.5</td>
<td>54.1</td>
<td>74.2</td>
<td>-2.48</td>
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Table 2. Genotype frequencies for observed polymorphisms

<table>
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<tr>
<th>Genotype</th>
<th>Sample</th>
<th>Sample</th>
<th>Sample</th>
<th>Sample</th>
<th>Sample</th>
<th>Significance</th>
</tr>
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<tbody>
<tr>
<td>Pro1 I</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>p &lt; 0.001</td>
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<tr>
<td>Pro1 II</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>p &lt; 0.001</td>
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<tr>
<td>AluI</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>FokI</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>p &lt; 0.001</td>
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