Comparison of the efficacy of three once-weekly bisphosphonates on bone mineral density gains in Korean women

Ji Hyun Lee¹, Byung Chul Jee¹,², Chang Suk Suh¹,², Seok Hyun Kim²,³, Young Min Choi²,³, Jung Gu Kim²,³, Shin Yong Moon⁴,³

Department of Obstetrics and Gynecology, ¹Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam; ²Seoul National University College of Medicine, Seoul; ³Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Objective
To assess the efficacies of once-weekly bisphosphonates on bone mineral density (BMD) gains in Korean women aged 50 years or more.

Methods
We selected 166 patients who received: alendronate 70 mg (n=48), alendronate 70 mg + cholecalciferol 2,800 IU (n=31) or risedronate 35 mg (n=87) for one year. The baseline BMD and the % changes of BMD at one-year were compared among the three medication groups.

Results
The menopausal status and number of women with osteoporosis was not different among the three groups, but mean age of women was significantly lower in alendronate group. Baseline BMD at L1-4 and femur neck (FN) was similar, but baseline BMD at femur total (FT) was significantly lower in alendronate group. After one-year use, the median % changes of BMD at three sites were similar among the three groups; however, the median values were highest in alendronate + cholecalciferol group (L1-4: 4.48%, 6.74%, and 4.50%; FT: 2.09%, 3.70%, and 2.31%; FN: 3.05%, 3.79%, and 2.03%).

Conclusion
Among three once-weekly bisphosphonates, BMD gains were highest after one-year use of alendronate+cholecalciferol, although statistically not significant.

Keywords: Alendronate; Bisphosphonate; Bone mineral density; Cholecalciferol; Risedronate

Introduction
Osteoporosis is an increased bone turnover and bone resorption leading to decreased bone mineral density (BMD) and strength and increased fracture risk [1]. The most common consequences of osteoporosis are fractures of the hip, wrist and vertebrae. The bisphosphonate classes of drugs are commonly used for the prevention and treatment for osteoporosis. These include alendronate, risedronate and ibandronate, which act to inhibit bone resorption by interfering with the activity of osteoclasts. During treatment of anti-resorptive
agents, degree of bone turnover markers or BMD changes has been known to be closely associated with risk reduction of fractures [2].

Alendronate and risedronate were commonly used anti-resorptive agents. Alendronate at 10 mg/day for three years of treatment has been shown to increase BMD by 9% in the lumbar spine and 6% in the hip [3,4]. According to long term follow-up, alendronate increased BMD at the lumbar spine and maintained the bone turnover markers to level of the premenopausal women at least 10 years [5]. By using alendronate, the risk reduction was 48% for vertebral fracture and 37% to 55% for non-vertebral fracture and the effects were observed from 6 to 18 months after the treatment [6]. Also, Risedronate 5 mg/day for three years of treatment has been shown to increase BMD by 5% in the lumbar spine, 2% in the femur neck, and 3% in the femur trochanter in postmenopausal women with history of vertebral fracture [7]. The bone turnover marker reduction effect also observed but was smaller than alendronate. Reduction of fracture risk was 36% for vertebral fracture and 19% to 27% for non-vertebral fracture [8]. Unlike alendronate, reduction of fracture risk was observed in the first year of the administration of risedronate.

In order to compare the efficacy of different drugs, direct head-to-head study was required, but such studies are impractical in aspects of the cost or resources. Thus, measurement of BMD or bone turnover marker is commonly used instead of end-point of fracture. Currently, four kinds comparative studies exist, in which alendronate has been consistently reported to be superior to risedronate in terms of BMD or bone turnover marker [9-12].

Materials and methods

The medical records of women who started once-weekly bisphosphonates between 2005 and 2007 at the Seoul National University Bundang Hospital were reviewed. The Institutional Review Board of the Seoul National University Bundang Hospital approved this retrospective study. We selected 166 women who received one of three drugs for one year: alendronate 70 mg (n=48), alendronate 70 mg plus cholecalciferol 2,800 IU (n=31) and risedronate 35 mg (n=87). The inclusion criteria were 1) Korean women aged 50 years or more at initiation of the medications, and 2) who never been used medications for their low BMD. The women who received any treatments for osteoporosis/osteopenia before the time of selection were entirely excluded. Menopause was defined as no natural menses for at least 1 year, or a serum follicle stimulating hormone (FSH) level >40 IU/L with a reported hysterectomy. Osteoporosis was diagnosed that patient had a BMD t-score of ≤-2.5 at the mean lumbar spine (L1-4), femoral neck or total, or a t-score of ≤-1.0 with radiological evidence of at least one vertebral fracture. Their menopausal state, other systemic illness, and co-medications such as calcium, estrogen or glucocorticoids were recorded.

BMD at baseline and one-year was recorded. BMD of the spine and hip was measured by Dual Energy X-ray absorptiometry (Lunar Prodigy whole-body scanner, GE Medical Systems, Madison, WI, USA). In the present study, we used BMD at three sites; L1-4, femur total and femur neck. The fracture event during medications was also recorded by reviewing medical records or contacting personally.

Age of women, baseline BMD, and % changes of BMD at one-year were calculated and presented as median (25th percentile, 75th percentile). The Kruskal-Wallis test was performed to compare median values among three medication groups because data from each group did not show a normal distribution. A P-value of <0.05 was considered statistically significant.

Results

The baseline characteristics of the study subjects were presented in Table 1. The mean age of women was significantly lower in risedronate group. However, menopausal status and number of women with preexisting osteoporosis was not