Low BMD Tied to Risk of Less-Severe Hip Fractures

**Bisphosphonate**

PHILADELPHIA — The increased risk of hip fracture in women with lower bone mineral density mainly reflects an increased risk of nonsevere fracture rather than severe fracture, Jane A. Cauley, Dr.P.H., reported at the annual meeting of the American Society for Bone and Mineral Research.

Dr. Cauley, a professor of epidemiology at the University of Pittsburgh, looked for differences in risk factors for severe and nonsevere hip fractures using data from the longitudinal Study of Osteoporotic Fractures, involving 9,704 women aged 65 years and older.

The women were contacted every 4 months by postcard to determine if a hip fracture had occurred. The average follow-up period was 10.5 years.

Preoperative hip radiographs were obtained for 462 women—249 with femoral neck fractures and 213 with intertrochanteric fractures.

The fractures were rated by a single radiologist using the Garden and Kyle systems.

Most hip fractures were classified as severe. Of the femoral neck fractures, 70% were displaced. Of the intertrochanteric fractures, 72% were unstable.

For femoral neck hip fracture, women who went on to have stable fractures had an intertrochanteric BMD about 7% lower than did women who had a displaced fracture. Among women in the lowest tertile for intertrochanteric BMD, 62% had unstable intertrochanteric fractures compared with about 80% of women with higher BMD, said Dr. Cauley.

Again, while low intertrochanteric BMD was associated with an increased risk of both types of intertrochanteric fractures, women with lower BMD had a threefold increase in the risk of having a stable intertrochanteric fracture, compared with an almost twofold increased risk of having an unstable fracture.

One standard deviation decrease in walking speed was a risk factor for femoral neck displaced and undisplaced fractures. A greater height at the age of 25 and steroid and alcohol use were associated with an increased risk for a femoral neck displaced fracture.

Dr. Cauley disclosed that she has received consulting fees from Novartis.

Increased BMD

The trial was funded by Novartis; Dr. Black disclosed a significant financial relationship with Novartis.

In the women, randomized to the treatment group received an annual infusion of zoledronic acid (5 mg). All women received calcium (1,000 mg-1,500 mg/day) and vitamin D (400 IU-1,200 IU/day).

Women were included in the trial if they were aged 65-89 years (mean age, 73 years) with either a femoral neck T score of ≤ -2.5 or less or prevalent vertebral fracture and a femoral neck T score of ≤ -1.5 or less.

Women were recruited into two groups based on their osteoporosis treatment history. A total of 6,084 women were not currently taking an osteoporosis drug and had minimal prior therapy; 1,652 women were currently taking a selective estrogen-receptor modulator, calcitonin, or hormone therapy for osteoporosis at baseline.

Primary end points included new morphologic vertebral fractures in women not currently taking an osteoporosis drug and hip fractures in both those undergoing and those not undergoing treatment at baseline. Secondary end points included nonvertebral fractures, change in bone mineral density (BMD) measured by dual-energy x-ray absorptiometry, changes in biochemical markers of bone metabolism, and changes in bone density and size determined by quantitative CT.

Safety end points included evaluation of adverse events, assessment of bone histology by histomorphometry, and postdose monitoring for acute changes in renal laboratory values.

A total of 3,875 women were randomized to zoledronic acid (3.045 mg in stratum I and 830 mg in stratum II), while 3,861 were randomized to placebo (1,039 mg in stratum I and 822 mg in stratum II). Dr. Black presented data from the trial start-up to March 31, 2006 (the study was scheduled to end in June 2006).

Additional sampling was performed just after the third infusion at 24 months to determine in more detail how B-CTX levels responded to zoledronic acid infusion. "There is an immediate decline in B-CTX values at 1 year, compared with 4% and 14% in treated women, compared with those on placebo. Lumbar spine BMD was increased by 7% and total hip BMD was increased by 6% in treated women, compared with those on placebo.

In addition, bone markers were measured in a subsample of 405 women (300 on zoledronic acid and 105 on placebo). There was a decline in beta C-telopeptide of type 1 collagen (β-CTX), a bone resorption marker, following the first infusion. The values remain relatively constant over the 36 months of the study," said Dr. Black.

The mean β-CTX values for women on zoledronic acid remained within the premenopausal reference range. There was no progressive decline in β-CTX levels over 3 years.

Dr. Black disclosed that she has received consulting fees from Pfizer Inc., Novartis Pharmaceuticals Corp., Merck & Co, and Eli Lilly & Co. She also has received consulting fees from Novartis.

Annual Zoledronic Acid Reduces Fractures

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<th>Vertebral</th>
<th>Hip</th>
<th>Nonvertebral</th>
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Note: Based on a 3-year study of 7,736 postmenopausal women with osteoporosis. Source: Dr. Black