Age May Alter Bisphosphonate Effect on Stenosis

BY HEIDI SPLETE

WASHINGTON — Nitrogen-containing bisphosphonates were associated with a significantly decreased prevalence of cardiovascular calcification in women older than 65 years, based on data from 3,710 women who are part of a large, ongoing study.

VITALS

Major Finding: The prevalence of aortic valve ring stenosis was 38% in women aged 65 years and older who took nitrogen-containing bisphosphonates, vs. 59% in women who didn't take bisphosphonates.

Data Source: A cross-sectional study of 3,710 women aged 45-84 years.

Disclosures: Dr. Elmariah has received grant support from the New York Academy of Medicine; the National Heart, Lung, and Blood Institute; and GlaxoSmithKline.

"Early on in the analysis, we came across a very unexpected finding," said Dr. Sammy Elmariah of Mount Sinai School of Medicine in New York. "The association with bisphosphonate use was dependent on the patient's age."

The data were taken from the Multi-Ethnic Study of Atherosclerosis (MESA), a longitudinal cohort study of 6,814 asymptomatic men and women aged 45-84 years.

Overall, the bisphosphonate users were more likely to be older and white. In the current study, Dr. Elmariah and his colleagues examined the impact of bisphosphonates on cardiovascular calcification in women.

Clinical studies have shown that bisphosphonates have an effect on serum lipids, Dr. Elmariah said. Some experimental data, including data from animal models and dialysis patients, suggest that nitrogen-containing bisphosphonates (NCBPs) may limit cardiovascular calcification. In addition, the results of one recent study showed that patients on bisphosphonates for osteoporosis had a slower progression of aortic stenosis, he noted.

The prevalence of aortic valve ring stenosis was 38% in women aged 65 years and older who used NCBPs, which was significantly lower than in non-NCBP users of the same age (59%). Aortic valve ring stenosis prevalence also was 38% in women younger than 65 years who used NCBPs; it was significantly lower at 17% among similarly aged non-NCBP users.

Significant patterns also were seen for stenosis of the thoracic aorta and mitral annulus. The relationship between bisphosphonate use and the decrease in cardiovascular calcification in the 65-years-and-older group did not reach statistical significance for the prevalence of aortic valve stenosis and coronary artery stenosis, but the trends were similar.

COURTESY DR. SAMMY ELMARIAH

NCBPs significantly cut cardiovascular calcification in women over 65, said Dr. Sammy Elmariah.

This study is the first evaluation of the relationship between bisphosphonate use and the prevalence of cardiovascular calcification in a healthy patient population, Dr. Elmariah said.

Cardiovascular calcification was measured using cardiac CT. Bisphosphate use was defined as use of either oral or intravenous bisphosphonates at the time of the cardiac CT. The average age of the NCBP users was 67 years, and the average age of the nonusers was 62 years. Approximately 60% of the women were white.

After adjustment for variables including age, body mass index, diabetes, hypertension, smoking, race, insurance status, education, and income level, the significance remained, Dr. Elmariah said.

"We get a fairly dramatic reduction in the prevalence of cardiovascular calcification in bisphosphonate users over the age of 65," he added.

When the researchers divided the study population into 10-year age groups, they saw a gradual reduction in cardiovascular calcification with increasing age, he noted.

The study was limited by its cross-sectional design and by the lack of data on the duration of bisphosphonate use. "It's unclear whether this finding is due to true age-related differences in the pathogenesis of cardiovascular calcification or in the effect of bisphosphonates," said Dr. Elmariah. But the results merit additional studies to tease out the reason for the age-related impact of bisphosphonates on cardiovascular calcification in women, he said. ■

Bone Loss in Adolescents on DMPA Tied to Vitamin D

BY ROBERT FINN

LAS VEGAS — Abnormally low levels of vitamin D were seen in a subset of 15 adolescent girls who had substantial losses in bone mineral density while using depot medroxyprogesterone acetate for contraception, according to preliminary results from a prospective study presented at the annual meeting of the North American Society for Pediatric and Adolescent Gynecology.

The girls were among 181 adolescents using depot medroxyprogesterone acetate (Depo-Provera, Pfizer) in a prospective study. Bone mineral density (BMD) losses of 5% or more were seen at the lumbar spine in 25% and at the hip in 50% of the study participants.

The relative estrogen deficiency associated with depot medroxyprogesterone acetate (DMPA) did not correlate with the magnitude of BMD loss, according to Dr. Zeev Harel of Brown University in Providence, R.I.

Moreover, serum estradiol remained above 40-50 pg/mL in almost all participants, Dr. Harel said. This level is considered to be sufficient to conserve bone in elderly women.

Dr. Harel and his colleagues examined a subset of 15 young women who lost at least 5% of BMD from baseline. Their average age was 17 years, and they were an average of 61 months post menarche. Body mass index was within the normal range, and none of the women was obese. Their ethnicity was diverse and they resided in various U.S. locations.

Investigators noted BMD losses in the majority of the 15 girls after two or three DMPA injections, but some participants did not exhibit BMD losses until after their 10th or 13th injection.

Serum 25-hydroxyvitamin D (25[OH]D) levels were available for 14 of the 15 girls, and all but 1 had low levels of vitamin D. Levels above 30 ng/mL are considered sufficient, levels between 20 and 30 ng/mL are referred to as "insufficient," and levels below 20 ng/mL are referred to as "deficient." Seven of the 14 participants (50%) were vitamin D insufficient, 6 (43%) were vitamin D deficient, and 1 (7%) had normal levels of vitamin D.

The results were surprising, given that the cohort comprised mostly white, nonobese women who had sun exposure.

DR. HAREL

The mean serum 25(OH)D level among the participants was about 25 ng/mL, in the insufficient range. Mean levels of parathyroid hormone, on the other hand, were in the normal range.

In an interview, Dr. Harel expressed surprise at these results. "I was expecting probably less than 30% [of the participants would have low levels of vitamin D]," he said "We were surprised specifically because when we drew the blood we did it at the end of the summer. Typically we absorb vitamin D from the sun. Also, most of the patients were [white]. We know that vitamin D deficiency is common in African Americans and Hispanics. Also, they were not extremely obese. We know we can find vitamin D deficiency in obesity. And we also had representatives from states that were really sunny, California for example."

Dr. Harel emphasized that the results were preliminary. Additional studies would require a comparison group of young women on depot medroxyprogesterone acetate who did not experience declines in BMD. And he said that it would be important to study whether vitamin D supplementation would reverse the decline in BMD.

VITALS

Major Finding: In a substudy of 15 adolescent girls with significant bone loss while using depot medroxyprogesterone acetate, only 1 participant had a "sufficient" serum vitamin D level of greater than 30 ng/mL.

Data Source: Subset of a prospective study of 181 adolescent girls on depot medroxyprogesterone acetate.

Disclosures: The study was sponsored by Pfizer/Pharmacia, and one of the investigators was employed by that company. Dr. Harel disclosed financial relationships with Merck, Teva/Duramed, Ortho-McNeil, GlaxoSmithKline, Novartis, and Warner Chilcott.

Still, Dr. Harel found results sufficiently worrisome to recommend close monitoring of young women on depot medroxyprogesterone acetate. "We know in the adult elderly population that many are aware of their vitamin D status. In adolescents still we are in the beginning," he said.

He recommended that total 25(OH)D status be measured in all adolescent girls using depot medroxyprogesterone acetate.

"And if it's low—deficient or insufficient—treat it accordingly. The current recommendation if we have a patient with vitamin D deficiency is to take 50,000 IU once a week for 8 weeks and then repeat the total 25(OH)D. Those who have insufficient vitamin D, we typically treat with 800 IU of vitamin D a day and we do it for 3 months, and then again we repeat the total 25(OH)D," he said. ■