Antiretrovirals May Contribute to Bone Loss

BY SHERRY BOSCHERT

FROM A MEETING ON HIV MANAGEMENT

SAN FRANCISCO — People with HIV infection tend to have more risk factors for bone loss than do people without HIV, and antiretroviral medications may be adding to that risk.

The specific role of antiretroviral therapy in bone loss has been controversial: Some studies say there is no association, but others suggest that the drugs do contribute to bone loss. Results of two small but well-conducted studies recently tipped the emphasis toward concern about the differential effects of antiretrovirals on bone mineral density, Dr. Dolores Shoback said.

"I think it's very provocative. We certainly need more data, and this needs to be confirmed," she said at the meeting, which was sponsored by the University of California, San Francisco.

One randomized, controlled trial of 71 HIV-infected patients suggested that antiretroviral regimens that contain a protease inhibitor booster have a greater negative impact on spinal bone density than do regimens without a boosted protease inhibitor, said Dr. Shoback, professor of medicine at UCSF.

At baseline, 31% of the patients were osteopenic and 3% were osteoporotic. Bone densities were retested after 48 weeks of combination HIV therapy with a nonnucleoside reverse transcriptase inhibitor (NNRTI) and nucleoside reverse transcriptase inhibitors (NRTIs), or an NNRTI and a boosted protease inhibitor, or two NRTIs and a boosted protease inhibitor. On average, the cohort as a whole lost 4% of lumbar spine bone mineral density and 3% of hip bone density during those 48 weeks (AIDS 2009; 23:817-24). The groups treated with boosted protease inhibitors lost significantly more spinal density—4.4% when combined with an NNRTI and 5.8% when combined with NRTIs—compared with the NNRTI-plus-NRTI arm (1.5%). Changes in hip bone density did not differ significantly by treatment group.

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DR. SHOBACK

The second study randomized 50 HIV-infected patients to treatment with lopinavir/ritonavir plus zidovudine/lamivudine (ZDV/3TC) or lopinavir/ritonavir plus nevirapine, with bone densities compared at baseline and 2 years. At the start, up to 31% were osteopenic and up to 4% were osteoporotic. The ZDV/3TC group lost 6.3% of bone mineral density in the hip and 5.1% in the spine, compared with smaller losses of 2.3% in the hip and 2.6% in the spine in the nevirapine group. Spinal density decreased mainly in the first year and then stabilized, but hip density continued to fall in the second year (AIDS 2009;23: 1367-76).

The investigators speculated that ZDV/3TC increased osteoclastic activity.

There are not enough data yet to support changing antiretroviral regimens if bone mineral density is low, she added, but physicians should pay attention to nutrition (especially calcium and vitamin D), lifestyle factors, and weight-bearing exercise in patients with HIV.

Ongoing immune activation in HIV infection leads to high levels of cytokines. "There pretty much isn't a cytokine that doesn't have a negative effect on bone," she said.

Many other risk factors for bone loss and fractures are more common in the setting of HIV. Five of six cross-sectional studies found low levels of hydroxyvitamin D in patients with HIV. Compared with the HIV-negative population, people with HIV have higher rates of smoking and alcohol use, are more likely to be treated with steroids, and are more likely to have periods of immobilization and illness, bouts of weight loss, hypogonadism (in men), and amenorrhea (in women). ■

Disclosures: *Dr. Shoback has been a speaker for Novartis.*