Antiretrovirals May Contribute to Bone Loss in HIV Patients

BY SHERRY BOSCHERT

SAN FRANCISCO — People with HIV infection tend to have more risk factors for bone loss than do those without, 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.

The 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 study to look at that,” she continued.

The heart benefits of short-term control of HIV first became apparent with the Strategies for Management of Antiretroviral Therapy (SMART) study, which compared strategies of viral suppression with drug conservation (repeatedly starting and stopping therapy) in 5,472 patients. Patients in the drug suppression group were 57% more likely to have an MI, coronary intervention, or cardiovascular death, compared with the viral suppression group (N. Engl. J. Med. 2006;355:2283-96).

A separate study found improvements in endothelial function in 82 antiretroviral-naive patients after starting treatment with 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 over the course of 48 weeks (AIDS 2009;23:817-24).

“To put that in perspective, in early menopause, 1%-5% per year is about the rate of change we see at the spine,” she said.

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

Antiretrovirals May Increase Cardiovascular Risk

BY SHERRY BOSCHERT

SAN FRANCISCO — Antiretroviral medications may protect against heart attacks or increase cardiovascular risk, depending on the drug and the duration of use, recent studies suggest.

“This is an extremely complicated issue,” Dr. Priscilla Hsue said at a meeting on HIV management that was sponsored by the University of California, San Francisco.

In general, the risk of MI appears to decrease in patients with HIV after starting most antiretroviral therapies, probably resulting from control of HIV-related inflammation, said Dr. Hsue, a cardiologist at the university.

Two drugs, however, may increase the risk of MI with short-term use—abacavir and didanosine.

Six studies (some not yet published) now have shown increased risk of MI with short-term abacavir, while three studies found no association between short-term abacavir and MI risk.

Other drugs showed increased cardiovascular risk with long-term use of protease inhibitors, she added.

In the six studies showing increased risk of MI with short-term abacavir, patients tended to be older (in their mid-40s) than the patients in the three negative studies (mid-to late 30s), she noted.

Patients in the six positive studies were highly treatment experienced, and most had an undetectable viral load.

In the three negative studies, patients had no previous antiretroviral use and so had higher viral loads.

Some investigators have hypothesized that the negative cardiovascular effects of abacavir appear only in patients who are virologically suppressed. “That’s most of the patients we see,” Dr. Hsue noted.

Prior to viral suppression, any increased cardiovascular risk from abacavir may be outweighed by abacavir’s beneficial effects in reducing HIV-relate inflammation. “That’s speculative. We need a lot more studies to look at that,” she continued.

The heart benefits of short-term control of HIV first became apparent with the Strategies for Management of Antiretroviral Therapy (SMART) study, which compared strategies of viral suppression with drug conservation (repeatedly starting and stopping therapy) in 5,472 patients. Patients in the drug suppression group were 57% more likely to have an MI, coronary intervention, or cardiovascular death, compared with the viral suppression group (N. Engl. J. Med. 2006;355:2283-96).

A separate study found improvements in endothelial function in 82 antiretroviral-naive patients after starting treatment with an NNRTI and a boosted protease inhibitor.

The investigators speculated that zidovudine/lamivudine increased osteoclastic activity. “I think there probably is, in fact, a signal here,” Dr. Shoback said.

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 really isn’t much of 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 immunosuppression and illness, bouts of weight loss, hypogonadism (in men), and amenorrhea (in women).

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

‘We spend millions of dollars talking about which antiretroviral medications increase cardiovascular risk, but smoking cessation is much more important’ for reducing MI risk.

The study was highly controversial, and a surprise to everyone. It has since been confirmed in other studies,” Dr. Hsue said.

An unpublished analysis of SMART study data showed increased risk of cardiovascular disease with continuous use of abacavir, but not with didanosine.

And an unpublished study done using the French Hospital Database found a doubling of MI risk in patients with exposure to abacavir in the past 6 months and cumulative exposure of less than 1 year. Another unpublished DAD study data reported increased MI risk with the use of protease inhibitors, recent use of didanosine, and both recent and cumulative exposure to abacavir, but no increased MI risk with several other antiretrovirals.

Physicians should keep these findings in perspective. More traditional cardiovascular risk factors play a much larger role in MI risk than do antiretrovirals in people with HIV, Dr. Hsue added.

“We spend millions of dollars talking about which antiretroviral medications increase cardiovascular risk, but smoking cessation is much more important” for reducing the risk of MI in patients with HIV, she said.

Disclosures: Dr. Hsue reported having no conflicts of interest.