HIV and ARV Therapy Accelerate Bone Loss

June 30, 2009

Bone loss is common among people living with HIV before they begin antiretroviral (ARV) therapy, and it worsens upon starting treatment, especially if the regimen contains Combivir (zidovudine plus lamivudine), according to a new report published in the July 17 issue of AIDS. Though severe bone loss is associated with an increased risk of serious bone fractures, the Dutch study authors remind readers that this might be less of a concern among young people living with HIV.

Osteopenia and osteoporosis—mild-to-moderate and severe bone mineral loss, respectively—are increasingly being reported among people living with HIV. There have been reports suggesting that HIV itself may contribute to accelerated bone mineral loss, as well as studies indicating that protease inhibitors (PIs) can throw off the delicate cycle of bone metabolism. Less is known about the potential role of nucleoside reverse transcriptase inhibitors (NRTIs)—notably the thymidine analogue zidovudine, which has been implicated in other metabolic disorders—in the progression of bone loss in HIV-positive individuals.

A team headed by Marit van Vonderen, MD, of the VU University Medical Center in The Netherlands believes it is the first to publish a bone study comparing an NRTI-sparing regimen with a regimen containing both a PI and NRTI. The study conducted dual x-ray absorptiometry (DEXA) scans of the hip bone (femoral neck) and spine and looked for laboratory markers of bone metabolism at various time points over a two-year period among 50 men beginning HIV treatment for the first time. The study volunteers took either Kaletra (lopinavir/ritonavir) plus Combivir or Kaletra plus the non-nucleoside reverse transcriptase inhibitor (NNRTI) Viramune (nevirapine).

As has been documented in other studies, the prevalence of osteopenia was high even before HIV treatment was started. This is a significant finding in itself, given that the average age upon entering the study was 40—significantly younger than the approximate age of osteopenia diagnosis among those not living with HIV.
The researchers noted a rapid bone mineral density (BMD) decrease in both the femoral neck and lumbar spine after ARV therapy was started. While the BMD loss was documented in both groups of patients, it was significantly greater among those who received Kaletra plus Combivir compared with those using Kaletra plus Viramune.

In both groups, the researchers reported, lumbar spine bone loss appeared to stabilize in the second year of treatment, whereas progressive bone loss of the femoral neck was observed in the second year among those taking Kaletra plus Combivir.

Markers of bone formation (osteocalcin) and bone resorption (urine DPD/creatinine ratio) also increased significantly after ARV therapy in all study subjects. This, van Vonderen and his colleagues suggest, is indicative of increased bone turnover and a warning sign of increased bone loss, as has been seen in other studies involving hyperthyroidism and menopausal women.

While the finding of accelerated loss of bone mineral density, both before and during HIV treatment, is sobering, van Vonderen and his colleagues underscore that the risk of a serious bone fracture is dependent not only on decreasing BMD, but also on decreasing strength and agility that come with age. “As the absolute fracture risk is low in this age category,” the study authors write about their young, otherwise healthy HIV study population, “a clinically significant difference may only become apparent after longer follow-up with older age.”
