HIV Therapy Decreases Bone Fracture Risk, Compared With Those Not on Treatment

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Compared with people living with HIV and not being treated for it, those using antiretroviral (ARV) therapy are less likely to experience a fracture related to frail bones, according to a research paper authored by Linda Mundy, MD, of GlaxoSmithKline and her colleagues, published in the June 1 issue of the journal AIDS.

The report's findings, notably that tenofovir (found in Viread, Truvada, Atripla and Complera) is associated with a reduced risk of bone fracture and that protease inhibitors have little effects on the risk one way or the other, are at odds with other recent papers. In addition to studies noting higher rates of osteopenia (mild/moderate bone mineral loss) and osteoporosis (significant bone mineral loss) among people living with HIV using these drugs, increased rates of wrist, back and hip fractures have also been observed.

In fact, a conflicting report waspublished in the April 24 issue of AIDS. This report, authored by Veterans Health Administration investigators, included final data from a study originally presented last July at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention in Rome. The investigators conclude that tenofovir and some protease inhibitors are associated with an increased fracture risk.

The analysis conducted by Mundy's group included 59,594 people living with HIV receiving care between January 1997 and March 2008; they were identified using a private administrative claims database.

Roughly half the patients included in the analysis had not received any ARVs. Among the 29,179 with no ARV experience, the average age was 39 and 58 percent were men. Among those who had been treated with ARVs, the average age was 42 and roughly 85 percent were men. Of note, those who never took ARVs were more likely to have experienced a past bone fracture (3.4 versus 0.7 percent) and less likely to have low body weight (4.3 percent versus 11.4 percent).

The final population selected for the comparison involved 2,477 individuals who experienced a fracture and 9,144 who did not during the 11-year study period.

The risk of bone fracture was higher, statistically speaking, among patients with traditional risk factors, including prior fractures, low physical activity, excess alcohol use, low body weight, hepatitis C coinfection and advanced HIV infection.

As for the risk associated with ARV therapy, Mundy's team found that those on treatment during the study period had a fracture risk that was about 36 percent lower than those who did not receive ARV therapy.

The decreased risk became more substantial with time, notably with the use of nucleoside and non-nucleoside drug classes. For example, compared with those not receiving ARV treatment, the risk of a bone fracture was reduced by 17 percent during the first five months of nucleoside reverse transcriptase (NRTI) treatment. Among those who had been on NRTIs for at least 20 months, the risk was reduced nearly 50 percent.

Protease inhibitor (PI) use had a null effect, at least during the first 18 months of treatment with this class of drugs. In other words, PIs neither lowered nor heightened the risk of bone fracture, compared with study subjects not using ARV therapy. Only after 18 months of treatment was a deviation noted—a 16 percent decrease in the risk of a fracture, compared with those not using ARV treatment.

In terms of specific drugs, the PIs Prezista (darunavir) and Invirase (saquinavir) and the non-nucleoside reverse transcriptase inhibitor (NNRTI) Rescriptor (delavirdine) were associated with an increased risk of bone fractures.

ARVs that had no or uncertain effects included the PIs Reyataz (atazanavir), Lexiva (fosamprenavir), Kaletra (lopinavir/ritonavir), Crixivan (indinavir), Viracept (nelfinavir), Norvir (ritonavir) and Aptivus (tipranavir); the NRTIs abacavir (found in Ziagen, Epzicom and Trizivir), Videx (didanosine) and Zerit (stavudine); and the entry inhibitor Fuzeon (enfuvirtide).

ARVs associated with a decreased risk of bone fracture included the NNRTIs efavirenz (found in Sustiva and Atripla) and Viramune (nevirapine) and the NRTIs Emtriva (emtricitabine), Epivir (lamivudine), zidovudine (found in Retrovir, Combivir and Trizivir) and tenofovir.

Looking specifically at tenofovir, which has been linked to lower bone mineral density and has also been associated with an increased risk of bone fractures in other studies, Mundy's team found a continual decrease in the risk. During the first four months of tenofovir treatment, the risk of a bone fracture was reduced by roughly 17 percent, whereas it was reduced by about 35 percent after 17 months of treatment.

"Together," Mundy's team concludes, "these drug-specific exposure-response relationships suggest an overall benefit of ARV treatment relative to the estimate of risk for fracture in subjects without ARV treatment."