Better PrEP Adherence Linked to More Bone Loss

People who took daily Truvada 90% to 100% of the time were more likely to develop osteopenia or osteoporosis.

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A small proportion of people developed bone loss after they started using daily tenofovir disoproxil fumarate/emtricitabine (Truvada or generic equivalents) for pre-exposure prophylaxis (PrEP), and the more they took it, the greater the effect, according to a study presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2022).

It is well known that tenofovir disoproxil fumarate is associated with bone loss in HIV-positive people using it for treatment, but there is less evidence about its effects on HIV-negative people taking it for prevention. Some prior studies showed people on PrEP experience mild bone loss, which usually resolves after stopping Truvada. The newer tenofovir alafenamide/emtricitabine (Descovy) is easier on the bones and kidneys but more associated with weight gain and elevated lipids; with no generic equivalent, it is also a more expensive option.

Joseph Chang, MD, of Kaiser Permanente Medical Center in Los Angeles, and colleagues conducted a retrospective analysis to look at the link between Truvada PrEP and bone loss.

The study included 7,698 adults in Southern California who used Truvada for PrEP between 2012 and 2020. Data were extracted from the Kaiser Permanente HealthConnect System. Nearly all were men, and about a third each were in the 18 to 29 and 30 to 39 age groups. About a third were white, 40% were Latino, 10% were Asian and 7% were Black. About 40% had good adherence, as indicated by a "proportion of days covered" (PDC) by PrEP in the 90% to 100% range, while about 60% had suboptimal adherence below 90%.

The participants had no prior history of osteoporosis (substantial bone loss) or osteopenia (mild bone loss) as indicated by a T-score of -1 or less. However, they had all undergone a DEXA bone scan at some point during the study. Chang said DEXA scans were not part of routine PrEP monitoring and the researchers did not look at the reasons why people had the scans, leaving open the possibility that this group may have been at higher risks for bone problems than the overall population using PrEP.

Over an average follow-up period of 502 days, 217 participants (3%) developed osteopenia or

osteoporosis. The researchers noted that this is similar to the rate among HIV-positive people using treatment regimens that contain tenofovir disoproxil fumarate.

An initial analysis found that people with hepatitis B, cardiovascular disease, chronic kidney disease, impaired kidney function or hypertension were more likely to experience bone loss, but these factors were not statistically significant in an adjusted analysis that controlled for multiple variables.

However, people with better adherence to PrEP remained at greater risk for bone loss in the fully adjusted analysis. People in the 90% to 100% PDC category were significantly more likely to be diagnosed with osteopenia or osteoporosis compared to those with lower PDC adherence levels. In fact, more than 90% of those with osteopenia or osteoporosis were in the 90% to 100% PDC category compared with 9% in the below 90% adherence category. Obesity and younger age were associated with a lower risk of osteopenia or osteoporosis.

Reassuringly, no new cases of HIV were detected during the study period, even among participants with less than 90% adherence.

Based on these findings, the researchers suggested that counseling on the incidence of osteoporosis and osteopenia as well as routine screening should be considered for people starting daily Truvada for PrEP. “Annual to every other year DEXA may be advisable,” Chang said.

Because the amount of time spent on Truvada was the strongest risk factor for bone loss, they also suggested that future studies should explore whether on-demand PrEP, or “PrEP 2-1-1”—in which the pills are taken before and after sex rather than daily—might mitigate the risk of serious adverse effects.

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