Study Suggests Cause of Tenofovir's Bone and Kidney Problems

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Compared with the nucleoside analog abacavir, tenofovir is more likely to increase levels of a hormone responsible for regulating calcium in the blood, potentially explaining the increased risk of bone mineral density loss and kidney problems in people living with HIV using the drug. These results, published in the July issue of *AIDS Research and Human Retroviruses*, indicate that parathyroid hormone (PTH) levels are raised substantially soon after the drug is started and that these elevations are most likely to be seen in people with low vitamin D levels.

Tenofovir has been linked to bone and kidney problems in a minority of people who take the drug. Though neither problem is common, tenofovir has been linked to more serious kidney disease and bone fractures in previous studies. Thus far, however, the actual cause of the complications has not been well characterized.

Several studies have hinted that elevated PTH levels could be one cause. PTH is a hormone that boosts calcium levels in the blood by speeding up the removal of minerals from bones and slowing down the excretion of calcium by the kidneys. When PTH remains high—a problem called hyperparathyroidism—bone strength and kidney function can become impaired.

To explore the possible link between elevated PTH and tenofovir, Mar Masiá, MD, from the Universitario de Elche, in Alacante, Spain, and her colleagues, compared PTH levels between two groups—31 people starting a new antiretroviral (ARV) regimen with tenofovir (found in Viread, Truvada and Atripla) and 26 starting a regimen including abacavir (found in Ziagen and Epzicom). The study duration was 48 weeks, and the participants in both groups were similar in most regards.

Masiá's team found that people taking tenofovir had higher PTH levels than those taking abacavir for at least 36 weeks after starting treatment, with significant elevations in PTH documented after just four weeks of starting the tenofovir-inclusive regimen.

After controlling for multiple factors, including vitamin D and calcium levels, the team found that tenofovir was independently associated with elevated PTH levels. What's more, they found that having low vitamin D levels significantly increased the likelihood that a person would have high PTH levels.

Masiá and her coauthors acknowledge that the study was small and didn't randomize those who were assigned to take tenofovir versus abacavir. This means that a larger randomized study might give a different result.

The study was also unable to determine whether tenofovir directly affects PTH or indirectly does so through an effect on vitamin D levels. But because vitamin D deficiency was a key variable in the risk, Masiá's team reiterated the conclusions of other studies that have underscored vitamin D problems in people living with HIV. "Patients with baseline suboptimal [vitamin D] levels are at higher risk for developing the highest PTH levels, and therefore vitamin D supplementation might be considered in these patients, even in the absence of overt [vitamin D] deficiency, when their doctors are willing to start tenofovir-based [treatment]," the authors conclude.

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