Defining the Risk Factors for Kidney Damage in Patients Using Tenofovir

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HIV-positive patients with high blood pressure and on medications known to increase the risk of kidney damage are at the highest risk for kidney damage if tenofovir—the active drug in Viread and a component of Truvada and Atripla—is used as a component of antiretroviral (ARV) therapy, according to a study reported at the XVII International AIDS Conference (IAC) in Mexico City. The study also suggests a higher risk of kidney problems among those using tenofovir in combination with a protease inhibitor (PI), but a lower risk among those using it in combination with a non-nucleoside reverse transcriptase inhibitor (NNRTI) as first-line ARV treatment.

Regimens containing tenofovir are favorable treatment options. However, there are concerns that it may cause significant kidney damage (nephrotoxicity) in some patients. One way to reduce the risk is by checking kidney function—using creatinine clearance testing—before starting the drug. Patients with normal pre-treatment creatinine clearance are still at risk of nephrotoxicity, but it hasn't been clear which HIV-positive patients are at the greatest risk for kidney problems while using the drug.

Chelsea Castellano, MD, of Duke University Medical Center in Durham, North Carolina, and her colleagues studied the risk factors for nephrotoxicity among patients using tenofovir; they reported the results at IAC. Her group analyzed 1,574 patients, 744 of whom had been on tenofovir for at least three months.

According to Dr. Castellano's presentation, the rate of kidney toxicity was similar between those treated with tenofovir and those not treated with the drug. Thirty-five tenofovir-treated patients, or 4.7 percent, experienced signs of kidney problems, compared with 4.2 percent of those receiving ARV regimens that didn't contain tenofovir.

The researchers noted that kidney function improved in 16 of 20 tenofovir-treated patients with documented nephrotoxicity, once the drug was discontinued.

The researchers then looked at possible risk factors for kidney damage, including patients' ARV treatment histories, pre-existing kidney disease, CD4 counts (including the lowest and highest counts recorded), viral load, high blood pressure, diabetes, chronic pain (which often signals the use of non-steroidal pain medications known to cause nephrotoxicity), hepatitis B and C, obesity, smoking, cancer and heart failure.

The greatest predictors of kidney toxicity were concurrent use of a protease inhibitor, chronic pain,

high blood pressure, the presence of other health problems and the use of other nephrotoxic medications. The risk was 3.79 times higher among those using tenofovir with a protease inhibitor, 4.58 times higher among those with chronic pain, 4.79 times higher among those with high blood pressure, 5.43 times higher among those with other health problems, and 6.36 times higher among those using other nephrotoxic medications.

According to Castellano's report, 100 percent—a total of 25 patients—of those using tenofovir while they had uncontrolled high blood pressure and were also using other nephrotoxic drugs experienced kidney problems while taking tenofovir. When both factors were absent, however, only 3 percent experienced kidney problems.

"Tenofovir use should be avoided in patients with hypertension requiring other nephrotoxic drugs, especially if given with a PI," Castellano and her fellow authors recommended. "Use as part of initial NNRTI-based therapy is low risk for nephrotoxicity."
