

Tenofovir, leading HIV medication, linked with risk of kidney damage

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(Medical Xpress) -- Tenofovir, one of the most effective and commonly prescribed antiretroviral medications for HIV/AIDS, is associated with a significant risk of kidney damage and chronic kidney disease that increases over time, according to a study of more than 10,000 patients led by researchers at the San Francisco VA Medical Center and the University of California, San Francisco (UCSF).

The researchers call for increased screening for kidney damage in patients taking the drug, especially those with other risk factors for [kidney disease](#).

In their analysis of comprehensive VA [electronic health records](#), the study authors found that for each year of exposure to tenofovir, risk of protein in urine – a marker of kidney damage – rose 34 percent, risk of rapid decline in kidney function rose 11 percent and risk of developing [chronic kidney disease](#) (CKD) rose 33 percent. The risks remained after the researchers controlled for other kidney disease risk factors such as age, race, diabetes, hypertension, smoking and HIV-related factors.

For individual patients, the differences in risk between users and non-users of tenofovir for each year of use were 13 percent vs. 8 percent for protein in urine, 9 percent vs. 5 percent for rapidly declining kidney function and 2 percent vs. 1 percent for CKD. “However, these numbers are based on the average risks in our study population, and patients with more risk factors for kidney disease would be put at proportionately higher risk,” said principal investigator Michael G. Shlipak, MD, MPH,

chief of general internal medicine at SFVAMC and professor of medicine and epidemiology and biostatistics at UCSF.

Patients were tracked for an average of 1.2 years after they stopped taking tenofovir. They remained at elevated risk for at least six months to one year compared with those who never took the drug, suggesting that the damage is not quickly reversible, said Shlipak. “We do not know the long-term prognosis for these patients who stop tenofovir after developing kidney disease,” he cautioned.

The implications for patients already on or starting antiretroviral therapy are “mixed,” said Shlipak. “The best strategy right now is to work with your health care provider to continually monitor for kidney damage. Early detection is the best way to determine when the risks of tenofovir begin to outweigh the benefits.”

Shlipak noted that HIV, itself, increases the risk of kidney damage, while modern antiretroviral treatments clearly reduce that overall risk. “Patients need to be aware of their kidney disease risks before they start therapy, and this should influence the medications that they choose in consultation with their doctor,” he said. “For an otherwise healthy patient, the benefits of tenofovir are likely to exceed the risks, but for a patient with a combination of risk factors for kidney disease, tenofovir may not be the right medication.”

Tenofovir is used to decrease viral load and increase immune cell count in people infected with the virus. It is currently considered the preferred first line treatment for HIV because of its potency, overall low toxicity, and convenience of dosing. It is sold under a variety of names, by itself and in combination with other medications.

The study examined the [medical](#) records of 10,841 HIV-positive veterans in the national VA health care system who were new users of

antiretroviral therapy from 1997 to 2007. It was published electronically in the journal AIDS on January 9.

Lead author Rebecca Scherzer, PhD, a researcher and statistician at SFVAMC and UCSF, said that the observational study was the largest and most conclusive indication so far of tenofovir's association with kidney damage. "There have been a number of previous, smaller studies suggesting that this drug might be associated with kidney disease, but the results were mixed," she said. "Those studies may have missed this association because they were too small, lacked appropriate lab data or excluded subjects with pre-existing renal impairment or risk factors for kidney disease."

To be sure that tenofovir was the culprit, Scherzer and her colleagues looked for associations between 18 other antiretroviral medications and the same three measures of kidney disease: protein in urine, rapid decline in function and progression to CKD. None were associated with higher risk.

Shlipak noted that the study results are particularly strong because two of the risk factors – decline in function and CKD – indicate kidney function, while protein in urine indicates physical damage to the kidney. "These are independent markers," he said. "To see the same drug cause both types of kidney disease gives you a very objective signal that something real is happening here."

Shlipak emphasized that, despite tenofovir's association with progressive kidney disease, it is an important component of effective antiretroviral therapy that may be required in many patients to control viral load.

The VA is the largest provider of HIV care in the United States, said Shlipak. "We could not have done this work without access to the VA's system of electronic medical records," he said. "In particular, the data

kept by the VA Clinical Care Registry, located at the VA Palo Alto Health Care System, were essential to this study.”

Co-authors of the study are Michelle Estrella, MD, of Johns Hopkins School of Medicine; the late Andy I. Choi, MD, MAS, of SFVAMC and UCSF; Steven G. Deeks, MD, of San Francisco General Hospital; and Carl Grunfeld, MD, PhD, of SFVAMC and UCSF.

The study was supported by funds from the National Institutes of Health, the National Center for Research Resources, the American Heart Association and the Department of Veterans Affairs, some of which were administered by the Northern California Institute for Research and Education.

Tenofovir: Q&A for Patients and Providers

What is the new finding about HIV/AIDS drugs and associated kidney problems?

Tenofovir, an anti-retroviral drug used to treat HIV, was associated with an increased risk of kidney disease in an observational study of 10,841 HIV-infected veterans who were new users of antiretroviral therapy between 1997 and 2007. The study found that tenofovir is associated with an elevated risk of kidney disease, even in persons without pre-existing risk factors for kidney disease, and that this toxicity to the kidney may not be reversible.

The study showed that for each year that a person uses tenofovir, there is a 34 percent higher risk of developing protein in the urine, which is an important sign of kidney damage; an 11% higher risk of rapidly declining kidney function, and a 33% higher risk of developing chronic kidney disease. These risks are all independent of the other factors that

cause kidney disease, such as age, diabetes, hypertension, smoking, hepatitis C infection and HIV-related factors.

How much extra risk is this?

Overall in the study, the differences in risk between users and non-users of tenofovir each year were: 13% vs. 8% for protein in urine, which is an important marker of [kidney damage](#) 9% vs. 5% for rapidly declining kidney function; and 2% vs. 1% for developing chronic kidney disease. However, these numbers are based on the average risks in the study population, and patients with more [risk factors](#) for kidney disease would be put at proportionately higher risk when they use tenofovir.

Which drugs are we talking about?

In the study, the risk appeared to be unique to tenofovir. Other antiretroviral drugs showed weaker or inconsistent associations with kidney disease events, and none was associated with higher risk for even two of these three adverse kidney disease outcomes.

Should I stop taking these drugs if I am already taking them now?

This decision should be made on an individual basis, in consultation with your physician. The decision should involve weighing the risks/benefits and discussion of alternative treatment options. Tenofovir is an important component of effective antiretroviral therapy that you may need to control your viral load. If you remain on tenofovir, you may need more frequent monitoring of your kidney function and your level of urine protein. You are likely at increased risk of kidney disease if you have diabetes, high blood pressure, cardiovascular disease or hepatitis C. African Americans, Hispanics, Pacific Islanders, Native Americans and

older adults are also at increased risk.

What are the symptoms of kidney problems? Should I be taking tests to monitor my kidney function?

Most people do not have any symptoms until their kidney disease is advanced. So, kidney disease is typically detected by screening tests of blood and urine.

Moving forward, what questions should I ask my doctors?

You should ask your doctor about whether you need routine monitoring of blood and urine samples to measure the following: serum creatinine, proteinuria, and microalbuminuria. You should also ask your doctor to calculate your estimated glomerular filtration rate (eGFR). You may want to have a discussion about alternative treatment options.

What about the prophylactic use of these drugs to prevent HIV progression and transmission?

A study of HIV pre-exposure prophylaxis (PrEP) using once-daily oral [tenofovir](#) was presented at the XVIII International Conference on AIDS (AIDS 2010), which included 323 men. This study found no indication of significant safety issues, including kidney problems or bone loss. However, this study may not have been large enough to detect increases in risk for kidney disease.

Where can I get more information?

You may get more information from [HIV/AIDS](#) websites such as

[Project Inform](#) or [HIV InSite](#). You can also contact your doctor if you have additional questions about your anti-retroviral medications or risk for kidney disease.

Provided by University of California, San Francisco

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