

## Certain HIV meds have patients packing on pounds

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the life-saving antiretroviral drug cocktails used to treat HIV may trigger weight gain, new research warns.

The concern stems from tracking patients taking antiretroviral therapy (ART). Since the mid-1990s, the therapy has relied on various drug combinations to essentially outwit HIV, controlling viral loads and turning a once-deadly infection into a manageable condition.

But the new research is raising questions about one drug featured in many ART recipes: tenofovir alafenamide, also known as TAF.

There's no question that TAF works. The researchers noted that it is both effective and welltolerated. And TAF has gained popularity in recent years because it poses less risk to kidney and bone health than another medication, called tenofovir disoproxil fumarate (TDF).

But the new study found that over 18 months, patients on an antiretroviral regimen containing TAF gained nearly 4 pounds on average, compared to about 1.5 pounds among patients on drug cocktails containing TDF.

That resulted in nearly 14% of normal weight TAF users becoming overweight or obese, compared with just over 8% of their TDF counterparts, the findings showed.

"TDF and TAF are common parts of these combo drugs and most ART regimens," said Dr. Michael Horberg, director of Kaiser Permanente's division of HIV/AIDS and STDs. "That's why this study is so important."

Horberg, who was not involved with the study but reviewed the findings, pointed out that both drugs are also part of most so-called PrEP regimens. PrEP (pre-exposure prophylaxis) is designed to (HealthDay)—A commonly prescribed component of prevent HIV infections from taking hold in the first place, "so an even greater number of people [are] maybe using it for that," he said.

> Horberg said the newer TAF medication has been regarded as "the answer" to the main problem with the older TDF drug, which raised creatinine levels in some patients, an indicator of worsening kidney function.

"And, in the most part, that's true," Horberg said.

He said the new study is critical, however, because weight gain and worsening lipid levels are "not small issues either." Lipids are fatty substances that can build up and clog arteries.

Most people don't want to gain weight because of medication, "and rising lipids can be associated with cardiovascular disease (heart attacks, strokes), which we want to prevent in people with HIV also," Horberg said.

1/3



For the study, a team led by Dr. Bernard Surial of Bern University Hospital in Switzerland, reviewed weight gain data collected from more than 3,400 Swiss HIV patients between 2016 and 2019.

All had been taking an antiretroviral cocktail containing the older TDF drug for at least six months, before switching to an ART regimen containing the newer TAF drug.

Weight gain among patients who made the switch was then stacked up against nearly 900 patients who stuck with TDF during 18 months of tracking.

In that time, the researchers found that not only were weight gains much more significant among TAF users, but so were rises in their cholesterol and triglyceride levels, which can signal increased risk of heart trouble.

Horberg said the findings come as little surprise.

"Our patients were noticing this weight gain before we were," he said. "And we used to say 'oh, it's not the meds. You're just eating more because you're doing better.' Well, we now know that's not true. And if they weren't having any kidney problems, we For patients with borderline kidney disease or may have been trying to fix a problem that didn't exist" in switching therapies.

So what does this mean for treatment options going forward?

"Frankly, this has to be done on a case-by-case basis," Horberg said.

One consideration is money, he noted, as TDF is now a generic medication and much cheaper than TAF.

"We want everyone to have these medications available, including for PrEP," Horberg said. "But weight gain is a serious issue, and many patients do not like how it makes them feel or look," PrEP takers included.

If weight gain is due to the medication, they'll stop taking it, Horberg said, so a balance must be struck. If there are kidney concerns, it's important to switch. If not, doctors should discuss the pluses

and minuses of any change with their patients, he suggested.

Dr. Rajesh Gandhi, a fellow at the Infectious Diseases Society of America, and chairman of the HIV Medicine Association, also reviewed the study findings.

"This weight gain difference is something we pay attention to because we're trying to keep people healthy for decades, not for years," Gandhi said.

The medicines that revolutionized HIV treatment in the mid-1990s effectively got the virus under control, but they don't eliminate it. That means once a patient starts taking ART meds, they continue for the rest of their lives, making side effects a concern, he explained.

"Today, there are far fewer side effects than when ART came on the scene," Gandhi said. "And the weight gain found among those taking the newer formulation of tenofovir was relatively small. And not everyone was affected. But there was a difference."

osteoporosis, the new formula has a lot of advantages, Gandhi said, adding that more research into weight gain concerns is needed.

In the meantime, decisions about which formulation to use should be based on a discussion with each patient's health care provider "and decided case by case," he said.

The study was published online March 16 in the Annals of Internal Medicine.

More information: Learn more about antiretroviral therapy at the U.S. National Institutes of Health.

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