Does Truvada Offer Protection Against COVID-19?

Studies of the link between tenofovir use and coronavirus infection or COVID-19 outcomes have yielded mixed results.

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Does taking tenofovir—widely used for HIV treatment and a component of the Truvada and Descovy pre-exposure prophylaxis (PrEP) pills—reduce the risk of acquiring the new coronavirus or developing severe COVID-19? This question remains open, as research has yielded conflicting findings. But most experts appear to agree that the effect, if it exists, is likely to be minimal.

Early in the pandemic, small studies and anecdotal reports suggested that people living with HIV were not more likely to acquire the new coronavirus or to develop severe COVID-19—and in fact, they might be at lower risk.

This led many to wonder whether antiretroviral drugs used for PrEP or HIV treatment might be protective against the new coronavirus, officially named SARS-CoV-2. Certain antiretrovirals have shown activity against SARS-CoV-2 in laboratory studies. One combination, Kaletra (lopinavir/ritonavir), appeared to help some COVID-19 patients but its promise was not borne out in randomized clinical trials.

HIV Treatment and COVID-19

After noticing that few HIV-positive people were developing severe COVID-19 at hospitals in Spain, Julia del Amo, MD, PhD, of the Ministry of Health in Madrid, and colleagues set out to study the link between specific nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and COVID-19 outcomes among people living with HIV.

The researchers analyzed outcomes among 77,590 people receiving antiretroviral therapy at HIV clinics in 60 Spanish hospitals between February and April 2020. Three quarters were men and 56% were age 50 or older. Most had good viral suppression and did not have advanced immune suppression.

As described in the Annals of Internal Medicine (online June 26; in print October 6), 236 people on antiretroviral treatment, or 30.0 per 10,000, were diagnosed with COVID-19—a bit lower than the rate for the general population in Spain. Of these, 21 were taking Truvada or a generic equivalent (tenofovir disoproxil fumarate/emtricitabine), 100 were taking Descovy (tenofovir

alafenamide/emtricitabine), 57 were taking Epzicom (abacavir/lamivudine) and 58 were taking other NRTIs.

A total of 151 people (64%) with HIV and COVID-19 were hospitalized, 15 (6%) were admitted to the intensive care unit (ICU) and 20 (8%) died. As expected, the risks of COVID-19 diagnosis, hospitalization, ICU admission and death were greater for men and for people older than 70.

Mortality, adjusted for age and sex, was higher among HIV-positive people compared with COVID-19 patients in the general Spanish population (3.7 versus 2.1 per 10,000 people). But the study authors noted that this is not a straightforward comparison because the "biological age" of people with long-standing HIV is estimated to be five to 10 years older than their chronological age.

The researchers found that people taking Truvada were about half as likely to be diagnosed or hospitalized with COVID-19 as those taking Descovy or other NRTIs. No one taking Truvada was admitted to the ICU or died.

Diagnosis rates per 10,000 people were 16.9 for those on Truvada, 39.1 for those on Descovy, 28.3 for those on Epzicom and 29.7 for those on other NRTIs. Hospitalization rates per 10,000 people were 10.5, 20.3, 23.4 and 20.0, respectively. People taking Truvada were 57% less likely to be diagnosed with COVID-19 and 48% less likely to be hospitalized than those taking Descovy. However, the authors did not report whether these differences were statistically significant, suggesting they might be due to chance.

"HIV-positive patients receiving [Truvada] have a lower risk for COVID-19 and related hospitalization than those receiving other therapies," the study authors concluded. "These findings warrant further investigation in HIV pre-exposure prophylaxis studies and randomized trials in persons without HIV."

To that end, the researchers have started a clinical trial to evaluate whether Truvada or hydroxychloroquine could help prevent SARS-CoV-2 infection or lessen COVID-19 severity among health care workers. (That study is still recruiting participants in Spain, according to the latest update from August 2020.)

The researchers suggested that tenofovir and other NRTIs might interfere with the activity of the SARS-CoV-2 polymerase enzyme (which the virus uses to copy its genetic material), as it does with HIV's reverse transcriptase enzyme; Truvada, which produces higher levels of tenofovir in the blood, may do so more than Descovy. Tenofovir also may have immunomodulatory effects that reduce excessive inflammation, which can lead to severe COVID-19 complications.

However, the study has limitations that could influence its results. First, the sample size was small, with only 21 people with HIV and COVID-19 taking Truvada. In addition, older people and those with underlying health conditions—known risk factors for COVID-19—may be more likely to be prescribed Descovy, which is easier on the kidneys and bones, rather than Truvada.

"[T]he people remaining on [Truvada] today are least likely to have many of the medical comorbidities associated with worse outcome in COVID-19—they're healthier at baseline," Paul Sax, MD, of Brigham and Women's Hospital in Boston, commented in a blog post. "Most older people with HIV, in particular those with renal or cardiovascular disease, now receive either [Descovy], or increasingly, a regimen that does not include either tenofovir or abacavir."

PrEP and COVID-19

Another Spanish study, published in Open Forum Infectious Diseases (online September 25), looked at the link between PrEP use and COVID-19 outcomes among HIV-negative people.

Oskar Ayerdi, of Hospital Clínico San Carlos in Madrid, and colleagues compared SARS-CoV-2 infection rates and clinical manifestations of COVID-19 among 409 people who used Truvada, 91 who used Descovy and 250 people who did not use PrEP. The study was done at a sexual health clinic in Madrid during May and June 2020.

Most study participants were gay and bisexual men; five were transgender women. The average age was approximately 37, and only about 9% were age 50 or older, so the group was at low risk for severe COVID-19 based on age. About three quarters reported community coronavirus exposure, about 17% reported occupational exposure and about 10% reported household exposure, with no significant differences between the PrEP and non-PrEP groups.

Nearly a quarter were reported to have comorbidities associated with COVID-19 risk, but the researchers counted tobacco use as a comorbidity, and this was by far the most common one. The next most common underlying health conditions were hypertension, severe asthma, liver disease, diabetes and undefined "severe" obesity, none of which exceeded 3%. Excluding smoking, Descovy users had lower rates of comorbidities than Truvada users.

The seroprevalence of SARS-CoV-2 antibodies (indicating prior infection) was 15.0% in the PrEP group compared with 9.2% in the non-PrEP group, a statistically significant difference. Among those taking PrEP, the rates were 14.7% for Truvada users and 16.5% for Descovy users, a nonsignificant difference.

Among those who tested positive for the coronavirus, 53.3% of Truvada users, 73.3% of Descovy users and 78.3% in the non-PrEP group had COVID-19 symptoms, differences that did not reach statistical significance. PrEP users had a shorter duration of symptoms (9.0 versus 11.5 days), but this difference also was not significant. Less than 3% received medications to treat COVID-19.

Four of the five people hospitalized with COVID-19 were taking PrEP, including one Descovy user who was admitted to the ICU.

The study authors suggested that the higher coronavirus infection rate among PrEP users could be related to this group having more sex. Although the coronavirus is not known to be directly sexually transmitted, it can spread through the air during sex and probably can be transmitted via kissing.

Taken together, the results of these two studies indicate that people living with or at risk for HIV should not rely on antiretrovirals to protect them against COVID-19 and therefore should take the same precautions recommended for the population at large, such as wearing masks, social distancing and limiting contact with people outside one's household.

For all POZ coverage of the new coronavirus, including how it affects people living with HIV, search the hashtag #COVID-19.

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