Tenofovir Vaginal Gel Blocked HIV Transmission

BY MITCHEL L. ZOLER

FROM THE 18TH INTERNATIONAL AIDS CONFERENCE

VIENNA — The unqualified success of tenofovir vaginal gel in cutting the spread of HIV infection in a randomized, 3-year study of more than 800 women produced heady excitement among conference attendees, as well as sober recognition that the gel needs more testing and is likely at least 3 years away from a marketed product.

After 30 months, the 422 women who completed the study in the tenofovir gel group had a 39% relative cut in their rate of new HIV infections, compared with the 421 completers in the placebo arm. The infection rate curves began to diverge within the first 6 months of the study and then continued to separate. Among the 38% of women who used the gel during more than 80% of their events, the active gel cut the HIV infection rate by a relative 54%. Concurrently with the meeting report, the results appeared in an article online (Science 2010;doi:10.1126/science.1193748).

"The CAPRISA [Center for the AIDS Program of Research in South Africa] 004 study is the first step. Additional studies are urgently needed to confirm and extend the findings," said Dr. Salim S. Abdool Karim, director of CAPRISA in Congella, South Africa, and a professor of clinical epidemiology at Columbia University, New York, who presented the results.

Sheena McCormack, a clinical epidemiologist with the Medical Research Council in London, said the report was "proof of concept of microbicides" as a viable way to interrupt HIV transmission, and proof of concept of an antiretroviral drug for prophylaxis. "But it is not ready to roll out globally. Five other prophylaxis effectiveness trials are in process. This is a step in the right direction, but just one step in the path."

VITALS

Major Finding: Women who applied a 1% tenofovir vaginal gel before and after sex had a significant 39% relative cut in HIV infection rate during 30 months of treatment, compared with placebo.

Data Source: CAPRISA 004, a randomized, placebo-controlled study of 843 women.

Disclosures: Gilead, which supplied the tenofovir gel, licensed its use in Africa to CONRAD, a nongovernmental organization in Arlington, Va. Dr. Salim S. Abdool Karim said that he had no conflicts.

It was actually a highly successful first step along two different paths. Not only did the results show a significant cut in the HIV incidence rate from nine cases per 100 women-years with placebo to six cases per 100 women-years with use of tenofovir gel before and after sex, but the regimen also cut the transmission rate of herpes simplex virus type-2 (HSV2) in half.

The apparently completely independent ability of tenofovir gel to block HSV2 transmission "is a major bonus," commented Tim Farley, Ph.D., a statistician in the department of reproductive health and research for the World Health Organization in Geneva. "It will be relatively easy to confirm in a non-HIV infected population. I wouldn't be surprised if getting the HSV2 indication goes faster because it's easier to do; HSV2 is not life threatening."

CAPRISA 004, a proof-of-concept trial, ran at two South African clinic locations: a rural site in the KwaZulu-Natal Midlands, and an urban site in Durban. The researchers randomized 889 eligible women, all HIV negative and sexually active. Participants applied either a 1% tenofovir vaginal gel or placebo gel once up to 12 hours before sex, and then a second time within 12 hours following sex. People in the region where the study took place have a low rate (less than 1%) of anal sex.

The prespecified HSV2 analysis focused on women in the study who were HSV2 negative at baseline, 202 who completed the tenofovir arm and 224 who completed the placebo arm. Other marketed drugs similar in class to tenofovir, such as cidofovir and adefovir, have activity against HSV, so it was worth checking if tenofovir gel did too, said Dr. Karim. The active gel cut new HSV2 infections by a relative 51% over 30 months, compared with placebo. The analysis showed that the tenofovir gel blocked the HIV and HSV2 infections "by two independent mechanisms. We see protection against HSV2 in women who were HIV negative and in HIV positives," he said.

The study also showed no sign of tenofovir resistance in women who became infected despite use of the drug, a benign adverse effect profile, no safety issues in pregnancy, and no increase in HIV risk behavior. During the study, all women received regular counseling that reinforced the need for condom use whenever possible. The purpose of the gel was to give women protection when a condom wasn't used.

A pharmacology study showed very low concentrations of tenofovir appearing in the women's blood, while high levels of tenofovir in cervicovaginal fluid linked with better HIV protection.

"I was struck by the lack of any degree of [HIV] resistance from the topical application of this drug," said Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, Md. He speculated that tenofovir penetrates the mucosal surface of the vagina and enters submucosal dendritic and T cells where it blocks HIV replication and thus prevents infection from starting. ■

STDs More Prevalent in Men on Erectile Dysfunction Drugs

BY SHARON WORCESTER

FROM THE ANNALS OF INTERNAL MEDICINE

Men who use pharmacologic treatment for erectile dysfunction have higher rates of sexually transmitted diseases than do nonusers both before and after they receive a prescription for ED drugs, according to the findings of a retrospective cohort study of 1,410,806 men over age 40.

The rate of sexually transmitted diseases in the year before receiving a prescription was 214 per 100,000 ED drug users, compared with 106 per 100,000 nonusers. In the year after receiving a prescription, the rate was 105/100,000 ED drug users, compared with 65/100,000. The adjusted odds ratios were 2.80 and 2.65 for an STD in ED users in the year before and after a prescription, respectively, Dr. Anupam B. Jena of Massachusetts General Hospital, Boston, and colleagues reported.

The finding of increased risk both before and after receiving a prescription suggests that the association seen in this study has more to do with the types of patients who use ED drugs, than with the actual use of ED drugs, the investigators said (Ann. Intern. Med. 2010;153:1-7).

"Risk assessment for STDs and counseling about safe sexual practices" should accompany the prescription of ED drugs, they wrote, citing their findings as well as those from prior studies showing that condom use declines with age. The investigators also noted research linking ED drug with high-risk behavior in men who have sex with men.

For their study, the investigators used a database of insurance claims from 1997 to 2006, including data on 33,968 men with at least 1 filled prescription for an ED drug, and 1,376,838 men with no ED drug prescription. They adjusted for age and comorbid conditions, and found that the differences in STD rates between ED drug users and nonusers were due largely to HIV infection.

The adjusted odds ratios for HIV infection in the year before and after an ED drug prescription were 3.32 and 3.19, respectively.

They noted, however, that overall rates of STDs remain low, so routine testing for STDs in men requesting ED treatment would probably not be cost effective. ■

VITALS

Major Finding: The rate of STDs in the year before receiving a prescription was 214 per 100,000 ED drug users, compared with 106 per 100,000 nonusers, and the rate in the year after receiving a prescription was 105 per 100,000 ED drug users, compared with 65 per 100,000 (adjusted odds ratios of 2.80 and 2.65 for an STD in ED users in the year before and after a prescription, respectively).

Data Source: A retrospective cohort study of 1,410,806 men.

Disclosures: The Bing Study Center for Health Economics and the RAND Roybal Center for Health Policy Simulation sponsored the research for this study. Dr. Jena received support from the National Institutes of Health and the Agency for Healthcare Research and Quality.

MY TAKE

Counsel About Safe Sex After Age 40

Sex after age 40 years remains safer than during adolescence, but the age-related differences in risk have been eroding in recent decades as the rate of STDs in older adults increased, Dr. Thomas Fekete wrote in an editorial.

The increase has occurred in tandem with dramatic increases in the use of the drugs for erectile dysfunction, at least in the last decade, and the findings of Dr. Jena and associates regarding an increased rate of STDs in men over age 40 who use ED drugs (as compared with nonusers) serve as a reminder that STD counseling should not stop at age 40 years (Ann. Intern. Med. 2010;153:49-50).

Indeed, the higher baseline risk for STDs among men who use ED drugs, as demonstrated in this study, must be addressed when prescribing the drugs to these patients and thus enhancing the opportunity for transmission of STDs, he said, noting that although counseling about safer sex practices should not wait until a patient requests ED treatment, "the presence of higher rates of serious STDs, such as HIV infection, in men who use ED drugs compared with those who do not make it critical that all ED drug prescriptions be accompanied by assessment of STD risk and counseling about safe sex."

DR. FEKETE *is professor of medicine and chief of infectious diseases at Temple University, Philadelphia.*