Daily dose of HIV drug reduces risk of HIV infection

November 23 2010

A daily dose of an oral antiretroviral drug, currently approved to treat HIV infection, reduced the risk of acquiring HIV infection by 43.8 percent among men who have sex with men. The findings, a major advance in HIV prevention research, come from a large international clinical trial published online Nov. 23 by the *New England Journal of Medicine*. The study, titled "Chemoprophylaxis for HIV Prevention in Men," found even higher rates of effectiveness, up to 72.8 percent, among those participants who adhered most closely to the daily drug regimen.

"We now have strong evidence that pre-exposure prophylaxis with an antiretroviral drug, a strategy widely referred to as PrEP, can reduce the risk of HIV acquisition among men who have sex with men, a segment of the population disproportionately affected by HIV/AIDS," says Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. "Additional research is needed, but certainly this is an important finding that provides the basis for further investigating, developing and employing this prevention strategy, which has the potential to make a significant impact in the fight against HIV/AIDS."

"No single HIV prevention strategy is going to be effective for everyone," adds Dr. Fauci, "and it is important to note that the new findings pertain only to the effectiveness of PrEP among men who have sex with men and cannot at this point be extrapolated to other populations. Therefore, we must continue to conduct PrEP research

among other study populations, such as women and heterosexual men, to provide a comprehensive picture of its potential utility as an HIV prevention tool."

NIAID sponsored the study, also known as iPrEx, through a grant to the J. David Gladstone Institutes, a non-profit independent research organization affiliated with the University of California at San Francisco. Additional study funding was provided by the Bill & Melinda Gates Foundation. Gilead Sciences, based in Foster City, Calif., donated the study drug.

Led by study chair Robert M. Grant, M.D., of the Gladstone Institute of Virology and Immunology, and study co-chair Javier R. Lama, M.D., of Investigaciones Medicas en Salud, a Peruvian-based research organization, the iPrEx study enrolled a total of 2,499 men who have sex with men and transgendered women who have sex with men. All participants were at least 18 years old and HIV-negative at time of enrollment. The study, which began in June 2007, was conducted at 11 sites in Brazil, Ecuador, Peru, South Africa, Thailand and the United States.

The study participants were randomly assigned to receive either a daily antiretroviral tablet containing combination emtricitabine (FTC 200 milligrams) and tenofovir (TDF 300 milligrams), known by the brand name Truvada, or a placebo pill. Before enrollment, all participants received detailed information about the possible risks and benefits of participating in the trial. Once enrolled, they were evaluated for HIV infection monthly for the duration of their participation in the study. The average enrollment was 1.2 years. In addition, all participants were routinely counseled about safe sex practices and provided condoms and treatment for other sexually transmitted infections.

In the final analysis, 100 cases of HIV infection occurred among

participants in the iPrEx study. Of those, 36 HIV infections occurred among the 1,251 participants who received the antiretroviral therapy compared with 64 HIV infections among the 1,248 participants who received the placebo. This level of effectiveness in reducing the risk of HIV infection, 43.8 percent, is statistically significant. Furthermore, the drug's ability to reduce the risk of HIV acquisition was greater among those volunteers who were more adherent to the daily drug regimen. Participants who took the drug on 50 percent or more days as measured by pill count, bottle count and self reporting experienced 50.2 percent fewer HIV infections. Those who took the drug on 90 percent or more days had 72.8 percent fewer HIV infections.

The researchers concluded that consistent with earlier, smaller studies leading up to this trial, Truvada appeared to be safe and well-tolerated for its use in the iPrEx study. Side effects were mild and infrequent and included a small number of participants with transient nausea and mild elevations in creatinine, a naturally occurring molecule filtered by the kidneys. These elevations resolved spontaneously or with discontinuation of the drug. Additionally, very little drug resistance occurred with no instances of tenofovir resistance and three cases of emtricitabine resistance (one participant in the placebo group; two participants in the active drug group). The two cases of emtricitabine in the active drug group occurred among individuals who were in the stages of acute HIV infection at the time of enrollment, but who tested negative for HIV. Both groups of study participants reported a decrease in the number of sexual partners and increased condom use.

"The iPrEx study provides important evidence that PrEP works to reduce HIV infection risk among gay and bisexual men," says Dr. Grant. "The need for new HIV prevention methods is critical. PrEP, in combination with other prevention methods, such as HIV testing, counseling and consistent condom use, could represent a major step forward for efforts to control the global epidemic."

Correct and consistent condom use and a reduced number of sexual partners remain the most effective ways for gay and bisexual men to protect against HIV infection.

"A variety of expert and community advisory groups at the federal, state and local levels are looking closely at the study data and will move forward in a deliberative and measured way over the coming months to determine whether and how these findings should be incorporated into ongoing HIV prevention programs," says Howard K. Koh, M.D., assistant secretary for health at the U.S. Department of Health and Human Services.

Participants in the iPrEx study are being informed of the results and counseled on the need to continue safe sex practices. Individuals who acquired HIV infection during the study were referred to appropriate medical care. Investigators will conduct a follow-on study in which all HIV-negative iPrEx participants will be offered the combination drug for 18 months. That study, which will begin in 2011, is designed to provide additional information about the drug's long-term effectiveness and safety as well as participant risk behavior and pill-taking practices.

More information: Manuscript: www.nejm.org/doi/full/10.1056/NEJMoa1011205

The NIAID-sponsored VOICE www.niaid.nih.gov/news/newsrel … 009/Pages/VOICE.aspx study, which launched in Sept. 2009, is examining three different, once-daily HIV prevention strategies in women: a combination pill, a pill containing only tenofovir, and a tenofovir-based vaginal gel. The study is expected to enroll as many as 5,000 women in three African countries, and results are expected in 2013.

For additional information about the iPrEx study, see the Questions and

Answers www.niaid.nih.gov/news/QA/Pages/iPrExQA.aspx and and visit the iPrEx News Web site www.iprexnews.com. Visit the NIAID HIV/AIDS portal for more information about NIAID's HIV/AIDS research. www.niaid.nih.gov/topics/hivai … s/Pages/Default.aspx

Provided by National Institutes of Health