

Antiretroviral drugs may protect against sexual transmission of HIV

A new study in macaques suggests that antiretroviral drugs used to treat HIV could also protect people from getting the AIDS virus, especially if two drugs are taken in combination before exposure to the virus occurs.

Published in the open access journal *PLoS Medicine*, the study found that macaques which were repeatedly exposed to SHIV (a virus closely related to HIV) but received antiretroviral drugs were less likely to become infected than exposed macaques that received no anti-HIV medication. The best protection was seen in macaques that had received a combination of two drugs. The study, led by José Gerardo García-Lerma and Walid Heneine from the US Centers for Disease Control and Prevention, is the culmination of a series of experiments designed to show how similar studies in humans -- some of which are planned and in progress -- can be optimally designed.

Although HIV treatment has rapidly advanced since the introduction of antiretroviral drugs in the 1990s, the absence of an effective vaccine means the virus continues to spread, infecting 2.5 million people each year. Pre-exposure prophylaxis (PrEP) -- the prevention of infection by treating people with drugs before they are exposed to the germ in question -- is often used to prevent malaria, but has not yet been shown to be effective against sexual transmission of HIV.

To simulate a common route of HIV transmission in humans, the researchers exposed the macaques to low weekly doses of SHIV that were given rectally. Five groups of macaques were all exposed to the virus in the same way, but they were given different dosages and combinations of antiretroviral drugs.

Three groups received drugs daily: the first was only injected with one anti-HIV drug, emtricitabine (FTC); the second group received a daily dose of this drug by mouth in combination with an oral form of another anti-HIV drug called tenofovir; the third was injected with FTC and a high dose of tenofovir every day. A fourth group was also injected with FTC and a high dose of tenofovir, but macaques in this group were only treated shortly before and after the weekly exposures to HIV. For comparison a fifth group of macaques received no anti-HIV drugs.

The results showed that macaques from any of the four groups that received drugs were less likely to become infected than those in the fifth (control) group. All of the macaques receiving the combination of both FTC and the high dosage of tenofovir were protected from infection -- whether they were from the group that received these drugs daily, or only around the time of exposure to infection. The results suggest that higher doses and combinations of drugs worked better than single or low doses, and also that PrEP may not need to be taken every day to be effective.

The researchers also observed some risks that emphasize the need for careful design of human PrEP studies. They found some viral resistance to one of the drugs, FTC, in macaques that became infected. In addition, doses of tenofovir that resulted in maximum protection for macaques are higher than would be safe in humans.

In a related perspective article, Myron Cohen and Angela Kashuba from the University of North Carolina (Chapel Hill, NC, USA), uninvolved with the study, note that the results “highlight an exciting and potentially important use” of antiretroviral drugs to prevent sexual transmission of HIV.

Citation: García-Lerma JG, Otten RA, Qari SH, Jackson E, Cong M, et al. (2008) Prevention of rectal SHIV transmission in macaques by daily or intermittent prophylaxis with emtricitabine and tenofovir. *PLoS*

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