

Common herpes medication reduces HIV-1 levels, independent of herpes infection

March 13 2015



HIV-1 Virus. Credit: J Roberto Trujillo/Wikipedia

Case Western Reserve researchers are part of an international team that has discovered that a common herpes drug reduces HIV-1 levels—even when patients do not have herpes.

Published online in *Clinical Infectious Diseases*, the finding rebuts earlier scientific assumptions that Valacyclovir (brand name, Valtrex) required the presence of the other infection to benefit patients with HIV-1.

The result not only means that Valacyclovir can be used effectively with a broader range of HIV-1 patients, but also suggests promising new avenues for the development of HIV-fighting drugs. This insight is particularly significant given that some forms of HIV-1 have become resistant to existing medications.

"These results demonstrated that the mechanism by which Valacyclovir acts against HIV is not only through the presence of HSV-2," said senior author Benigno Rodriguez, MD, associate professor of medicine and infectious diseases, CWRU School of Medicine, co-Principal Investigator, Case Western Reserve University/University Hospitals Case Medical Center AIDS Clinical Trials Unit, and infectious disease specialist with UH Case Medical Center.

Even better, Rodriguez said, studies by these groups helped illuminate exactly how the medication decreases HIV-1 levels. Valacyclovir is activated in virus-infected cells, and then blocks the ability of HIV to reproduce.

The result? Reduced viral load.

HIV-1 can lead to the immune deficiency known as AIDS. The [herpes simplex virus 2](#) (HSV-2) causes periodic recurrence of genital herpes lesions, which increase the likelihood that a herpes sufferer may contract HIV through intimate contact. HSV-2 outbreaks are treated with either

Acyclovir or the newer generation Valacyclovir, which requires less frequent dosing.

Scientists previously thought that Valacyclovir helped reduce HIV levels and worked by decreasing the immune activation caused by HSV-2. With fewer immune cells to attack, the theory went, HIV-1 could not spread as widely. Yet Leonid Margolis, PhD, of the National Institutes of Health (NIH), believed another explanation might exist. After conducting laboratory studies with Acyclovir, an earlier sibling drug of Valacyclovir, Margolis saw that the medication clearly blocked HIV-1 reproduction, even when HSV-2 was absent. Those results helped spur [clinical trials](#) of Valacyclovir in people, and Margolis is senior author of the resulting journal article.

Beginning in June, 2009, patients from UH Case Medical Center and from IMPACTA, the Civic Association for Health and Education in Lima, Peru, started participating in the trials, which lasted until July, 2012. Under its protocols, half the patients took Valacyclovir twice daily for 12 weeks, while the other half took a placebo for the same period of time. After a two-week break from any medications, the two groups switched: those previously on placebo got 12 weeks of the Valacyclovir, and those who already had taken the medication now received placebos. When study participants took Valacyclovir, their HIV viral loads went down, and when they took the placebo, their HIV viral loads went up. Ultimately, a total of 18 patients participated.

"Our most recent clinical study demonstrates that acyclovir blocks HIV replication directly. The anti-HIV activity of [valacyclovir](#) does not depend on blocking the inflammation caused by herpes simplex virus 2," said Michael M. Lederman, MD, also a senior author. He is the Scott R. Inkley Professor of Medicine, Case Western Reserve University School of Medicine, and Principal Investigator of the Case Western Reserve University/University Hospitals Case Medical Center AIDS Clinical

Trials Unit and infectious disease specialist with UH Case Medical Center.

Lederman and Rodriguez, the two Cleveland-based members of the research team, believe that the data from this study can inform new drug development. Essentially, researchers would try to design agents based on the Valacyclovir's molecular structure - now proven to block HIV activity.

"The drug might be an agent that can be used safely in some people with HIV infection who have a form of HIV that is highly resistant to other antiretroviral drugs," Lederman said. "Valacyclovir might well augment the cocktail of medications they take for reducing HIV replication. Valacyclovir is a well-tolerated drug, and it doesn't have a lot of side effects."

Provided by Case Western Reserve University

Citation: Common herpes medication reduces HIV-1 levels, independent of herpes infection (2015, March 13) retrieved 3 May 2024 from <https://medicalxpress.com/news/2015-03-common-herpes-medication-hiv-independent.html>

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