Fast-dissolving insert found safe, shows promise as method for preventing HIV through anal sex

February 22 2023

Credit: Pixabay/CC0 Public Domain

A fast-dissolving insert being developed as an "on-demand" HIV prevention method was found to be safe and well-tolerated in the first

study of its use rectally. The results, which were presented today at the Conference on Retroviruses and Opportunistic Infections (CROI 2023) in Seattle, also found the insert delivered high levels of the anti-retroviral drugs tenofovir alafenamide (TAF) and elvitegravir (EVG) to rectal tissue and fluid, with very little drug circulating elsewhere in the body, and results of laboratory tests suggesting the insert could potentially provide protection for up to three days after use.

The TAF/EVG fast-dissolving insert, which resembles an oral tablet, was originally conceived as a product to prevent HIV acquired through vaginal sex. The Phase I study, known as MTN-039, was designed to evaluate the safety and feasibility of the insert as an on-demand method—to be used at or around the time of sex—for people who engage in receptive anal intercourse. By some estimates, the risk of acquiring HIV through anal sex is up to 20 times greater than through vaginal sex.

"Not everyone wants to take a tablet every day or go to a clinic for long-acting injectable PrEP," said Sharon Riddler, M.D, a professor of infectious diseases at the University of Pittsburgh School of Medicine, referring to currently approved methods, such as daily oral pre-exposure prophylaxis (PrEP) and injections of cabotegravir given every two months.

"Finding the insert was safe and delivered high concentrations of drug within the rectum—at the site of potential infection—with low systemic exposure, supports its continued evaluation as an alternative method of HIV prevention," added Dr. Riddler, who led the study for the Microbicide Trials Network (MTN).

MTN-039 enrolled 23 HIV-negative participants at the University of Pittsburgh and the University of Alabama at Birmingham, six of whom were assigned female at birth. Participants received a single dose of the

insert in the clinic, and researchers collected samples of blood, rectal fluid and rectal tissue to assess drug levels at different time points that day and in the three days that followed. After a period of up to seven weeks, participants returned to the clinic and were administered two of the inserts at the same time, and as before, tests were conducted over the next three days to determine how much drug gets into and remains in the blood, rectal fluid and rectal tissue.

Only one adverse event, a mild case of redness around the anus (anal erythema), was deemed possibly related to use of the insert. Both doses—the single insert and two inserts—achieved high levels of drug in rectal tissue and fluid, and through a laboratory test of rectal tissue that mimics how HIV infects cells of the rectum, researchers found both doses able to suppress HIV for up to 72 hours, with two inserts (double the dose of one) providing greater suppression of HIV in the tissue.

Each insert contains 20 mg of TAF and 16 mg of EVG. TAF is a nucleotide reverse transcriptase inhibitor that blocks the HIV virus from replicating and making copies of itself, while EVG is an integrase inhibitor that prevents HIV from integrating into the DNA of host cells. While TAF also acts against herpes simplex virus (HSV), tests of rectal tissue conducted as part of MTN-039 were not designed to investigate its potential for suppressing HSV infection.

"The MTN-039 study has provided important information about the safety of the TAF/EVG insert used rectally as well as its potential efficacy, augmenting the data collected in our Phase I study of the insert as a vaginal product. Both clinical studies, which involved single administration (rectal or vaginal), have shown high and long-lasting drug levels compatible with protection against HIV. We are very encouraged by these results as we plan the next set of studies of this promising and unique product, which we believe would fill a gap in existing HIV prevention methods," commented Gustavo Doncel, M.D., Ph.D.,

professor of obstetrics and gynecology at Eastern Virginia Medical School and scientific and executive director of CONRAD, which is developing the TAF/EVG fast-dissolving insert.

Together with recently published animal studies demonstrating high efficacy when applied before or after viral exposure, these first-in-human clinical trials support CONRAD's plans to test the on-demand insert for proof-of-concept effectiveness as a dual-compartment, vaginal and rectal, microbicide, Dr. Doncel added.

As part of the U.S. Agency for International Development (USAID)-funded MATRIX project, CONRAD is also planning to conduct a second study of the insert used vaginally, which like MTN-039, will evaluate its safety and where and how the drugs are taken up in the body, but after multiple repeated doses. In addition, laboratory tests of tissue samples will be conducted to assess its potential activity against both HIV and HSV. The study, which will enroll 60 women at three sites in the U.S., Kenya and South Africa, will be the first to evaluate the insert in African women.

Provided by Microbicide Trials Network