Early trial suggests rectal microbicide is safe, could significantly reduce HIV transmission

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(Medical Xpress) -- A topically applied microbicide gel containing a potent anti-HIV drug has been found to significantly reduce infection when applied to rectal tissue that was subsequently exposed to HIV in the laboratory, according to a new study by the UCLA AIDS Institute. The gel was also found to be safe and acceptable to users.

The first-ever phase 1 clinical trial of the rectal HIV-prevention drug known as UC781, a non-nucleoside reverse transcriptase inhibitor, is described in the current edition of the online journal PLoS ONE.

The trial represents the first use of this novel approach to obtain early insights into the drug's potential to prevent real-life infections during sexual exposure. In addition, it represents an important contribution to efforts aimed at strategically preventing HIV transmission during receptive anal intercourse.

While anal-receptive intercourse is known to be the main route for new HIV infections in men who have sex with men, far more women than men worldwide practice anal intercourse. The risk of HIV infection, per sex act, is anywhere from 20 to 2,000 times greater with receptive anal sex than receptive vaginal sex — particularly if there are other infections present, such as herpes, gonorrhea or chlamydia, according to the study's lead author, Dr. Peter Anton, a professor of medicine in the division of digestive diseases at the David Geffen School of Medicine at UCLA.

The significant reduction in the ability of HIV to infect tissues treated

with the drug was surprising, Anton said, as this was a new index in clinical trials. Typically, phase 1 clinical trials focus primarily on safety.

"While the main goal of this trial was also to evaluate safety, these new tests enabled us to evaluate, indirectly, whether this drug and route of delivery might potentially reduce new HIV infections," said Anton, who is also a member of the UCLA AIDS Institute. "Of course, it is very gratifying that the results were so impressive. This approach reflects the kind of intensive analyses these dedicated participants in these early trials are willing to tolerate to help us evaluate a drug's potential earlier in the pipeline of drug development."

Anton also noted that although this is the first time this infectibility analysis has been used in a human clinical trial, the results were quite significant.

Until now, microbicide clinical trials have focused on vaginal transmission. These trials, fortunately, have had successful results in the past year, after nearly a decade of disappointment. But the development of a microbicide prevention gel for rectal application has only been under way for the past five to six years.

In the current trial, researchers tested a formulation of the gel that was created for vaginal use in human trials and that contained two concentrations of UC781. They enrolled 36 male and female subjects at UCLA who were not infected with HIV, and they collected blood and rectal tissue samples at baseline, before participants were randomized to either a placebo group or to receive one of two concentrations of UC781. All participants were given the placebo or active drug as a single exposure by the team's clinicians, with research samples collected 30 minutes later for analysis.

After two to three weeks, the participants resumed the second part of the

trial by applying the gel or placebo once daily over seven days on their own at home. Afterwards, they returned to the clinic for another collection of samples. All participants completed the study once they were enrolled. In-depth interviews with each participant assessed their acceptability of the current form of the product.

Though the microbicide used for this study was formulated for vaginal use, the same team of researchers has also developed a rectal-specific microbicide gel, which they plan to start testing in a clinical trial in January 2012.

Dr. Ian McGowan of the University of Pittsburgh was the co-lead investigator. Other researchers were Terry Saunders, Julie Elliott, Elena Khanukhova, Robert Dennis, Amy Adler, Galen Cortina, Karen Tanner, John Boscardin, William G. Cumberland and Ying Zhou, all of UCLA; Lorna Rabe of the University of Pittsburgh; Ana Ventuneac and Alex Carballo-Diéguez of Columbia University; and Timothy McCormick, Henry Gabelnick and Christine Mauck of CONRAD.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023243

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