Cisgender Women's Rectal Tissue May Be More Vulnerable to HIV Than Men's

What this means for women's HIV acquisition rates is unclear.

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Higher concentrations of some HIV pre-exposure prophylaxis drugs in rectal tissue may not be enough to protect cisgender women having anal sex from HIV acquisition, according to a small sub-study analysis in the journal AIDS.

It's been a scientific conundrum for as long as HIV pre-exposure prophylaxis (PrEP) has been around: Cisgender women having vaginal sex have a lower concentration of protective PrEP drugs at the exposure site than do men who have sex with men (MSM) having receptive anal sex. But the protective effects of PrEP drugs for receptive anal sex among women has been unclear. This is significant all on its own, but a computer model published in May also suggested that up to 41% of new HIV cases among cisgender women may be the result of anal sex.

In the AIDS study, Rogers Sekabira, BPharm, MHRS, a researcher at Baylor College of Medicine, and colleagues took samples of vaginal and rectal tissue from the 37 cisgender women and 54 MSM enrolled in HPTN 069/ACTG A5305. The study tested a PrEP combination of maraviroc (sold as Selzentry) plus emtricitabine (Emtriva), maraviroc plus tenofovir disoproxil fumarate (Viread) or tenofovir disoproxil fumarate plus emtricitabine (marketed as Truvada but now available as a generic). During the trial, researchers collected vaginal and rectal tissue samples and blood samples before they started taking the study drug, 24 weeks into the trial, 48 weeks into the trial and then one week after they stopped taking the drug.

Researchers then measured the concentration of each drug in the tissue and blood samples and tested the immune cells present in the tissue to determine the likelihood of HIV infections. Finally, they introduced a strain of HIV to the tissue samples to see how readily the virus could infect the cells.

Women were less adherent to the pills than their MSM counterparts: 79% of the women met the criteria for adherence versus 90% of the men. Up to 20% of both women and men had tissue and rectal fluid concentrations below the level of protection, however.

What's more, cervical drug tissue concentrations—that is, drug concentrations in the vagina—dropped below measurable levels in 43% to 91% of the samples. Indeed, detectable drug

levels in colorectal tissue for women didn't translate to vaginal protection; maraviroc vaginal concentrations were 12 times lower than rectal concentrations, emtricitabine levels were three times lower in vaginal tissue compared with rectal tissue and tenofovir levels were a full 276 times lower in vaginal tissue versus rectal tissue.

Whether that means drug levels won't protect women are unclear, said Craig Hendrix, MD PhD, of Johns Hopkins University, who also was involved in the study.

Plasma drug concentrations worked out a little more in women's favor. Maraviroc was twice as concentrated in women's blood samples compared with men's. In colorectal tissue, tenofovir was 12 times more concentrated in women's colorectal tissue samples versus men's, but emtracitabine was twice as concentrated in the rectal tissue of MSM than that of women.

Despite those levels, when researchers exposed the tissues to HIV and tested them for infection using a p24 HIV antigen test, they found that HIV was just as likely to be able to replicate and infect the rectal tissue of women when they were on treatment as before they started treatment—even if they were highly adherent to the medication. Plus, women's colorectal tissue was more susceptible to HIV acquisition at baseline in the study, at twice the rate of HIV acquisition among men.

In contrast, men's infectivity level started lower and then dropped as they took the drugs.

What this means for real-world HIV acquisition is unclear. Higher tissue infection rates in a lab don't mean that the women acquired HIV during the study. And the result is based on samples from just 11 women, as others didn't have all data available. Still, the finding perplexed the researchers, who wrote that the differences in drug tissue concentrations weren't big enough to explain the difference in HIV infectivity.

Hormonal differences between women and men could be to blame, but even that, Sekabira and colleagues wrote, is "only an explanation by exclusion"—meaning that, for lack of any other explanation, it's all they could figure.

"Some have argued the need for higher antiretroviral drug concentrations for oral TDF/FTC PrEP in cisgender women compared to MSM, to achieve the same level of protection as in MSM," he wrote. "Our findings suggest there may also be a physiologic, possibly hormonal differences in colorectal HIV infectivity that may be relevant to [transgender women] on gender-affirming hormone therapy."

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