A short-term birth control pill for men? Mouse study hints its possible

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A guy pops a little pill just before he expects to get frisky with his

girlfriend.

But the pill isn't Viagra, as one might expect.

Instead, it's an on-demand contraceptive that will prevent pregnancy even if taken just before sex.

Researchers think they've discovered a way to create such a contraceptive pill for men, by inhibiting an enzyme that's key to a sperm's ability to swim.

Inhibiting this enzyme in lab mice using an experimental compound successfully prevented pregnancy, according to a new report published Feb. 14 in the journal *Nature Communications*.

"The effect started within 30 minutes after dosing and the mice were completely infertile for the subsequent two hours," said co-senior researcher Lonny Levin, a professor of pharmacology at Weill Cornell Medicine in New York City.

"By the following day, the mice were completely normal. The compound did not adversely affect the mice in any way, and their sexual behavior and ejaculate were completely normal," he added.

If proven to work in humans, such an approach "would be a tremendous advancement for the field," said Christopher Lindsey, program officer at the U.S. National Institute for Child Health and Human Development, which helped fund the study.

"The benefit of this is that unlike a hormonal approach where you'd have to take that drug for days, weeks, sometimes months, this would work similar to Viagra," Lindsey said. "You would only have to take it maybe a short time back before engaging in sexual activity."

Nearly half of all pregnancies are unintended, and the rate is even higher among teenagers in the United States, researchers said in background notes. This pill could revolutionize family planning.

The targeted enzyme is called soluble adenylyl cyclase (sAC). It contributes to fertility by helping sperm survive and swim upstream to the female egg.

"When sperm are deposited into the female reproductive tract, they actually have to be able to swim or move in order to be able to fertilize an egg," Lindsey said. "If you take away that motility, then the sperm don't move. They just sit there, and that is what this compound does, it prevents sperm from moving and maturing."

Some healthy men are naturally infertile due to a similar mutation that inhibits soluble adenylyl cyclase, Levin said.

To see whether a temporary inhibition of the enzyme would stop pregnancy, Levin and his colleagues tested the experimental drug on a group of lab mice. The compound was designed to specifically block soluble adenylyl cyclase.

The male and female mice got busy as expected, but no pregnancies were observed, researchers said. Sperm recovered from the female mice afterward remained incapacitated.

The compound wore off three hours later, and males recovered their fertility.

Men with naturally inhibited soluble adenylyl cyclase do have an increased risk of kidney stones, but that happens only when the enzyme is blocked for months or years, Levin said.

"A man would only have sAC inhibitors in their body temporarily so there would never be enough time with sAC inactive for stones to form," Levin said.

The drug used in the mice was a "tool compound"—a chemical used in the laboratory to investigate whether this approach would work, Levin said. Further work needs to be done to find the right enzyme blocker for humans.

"We don't consider it sufficiently advanced for taking into humans," Levin said of the compound. "Our current studies are focused on getting improved versions which are suitable for taking into clinical trials, which we hope can begin in the next two to three years."

But the researchers say this study proves the concept—an on-demand pill for male contraception is possible.

"Hopefully, someday men can be equal partners in family planning and people should not have to take a contraceptive every day of their lives in order to control their fertility," Levin said. "On-demand contraception allows a person to take birth control only when and as often as needed."

The approach is "promising," but there are still some potential hurdles to pass before such a pill is available for men, said Dr. Amin Herati, director of male infertility and men's health at Johns Hopkins Medicine in Baltimore.

"Many of these non-hormonal contraceptive therapies do not reach human use since human and murine [mouse] biology are not perfectly matched, and the success rates in human clinical trials may not be as robust as a vasectomy," Herati said. "Any contraceptive developed would need to match vasectomy as the current gold standard."

More information: Jochen Buck, On-demand male contraception via acute inhibition of soluble adenylyl cyclase, *Nature Communications* (2023). DOI: 10.1038/s41467-023-36119-6. www.nature.com/articles/s41467-023-36119-6