Most promising study to date on male contraceptive pill

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After decades of scientists trying to develop an effective male oral contraceptive, with previous attempts targeting testosterone having led to obesity, depression and high cholesterol, an “on demand” male contraceptive pill has now been developed that could be taken just before sex, and ultimately, be more effective than women’s birth control pills.

The team from Weill Cornell Medicine, New York, whose research on mice showed that all 52 attempts at impregnation during the study failed dismally, said the next step is repeating the study in a different pre-clinical model to lay the groundwork for clinical trials, and testing the effect on sperm motility in healthy human males.

Co-author Professor Jochen Buck said the therapy blocks a fertility protein for 24 hours, and the breakthrough is a potential “gamechanger” after their experiments showed the non-hormonal compound stopped mouse sperm cells in their tracks – preventing them from maturing.

The animals’ sexual functioning was normal: male lab rodents mated with females, but there were no pregnancies.

Lead author Dr Melanie Balbach said: “Our inhibitor works within 30 minutes to an hour. Every other experimental hormonal or non-hormonal male contraceptive takes weeks to bring sperm count down or render them unable to fertilise eggs.”

The drug temporarily disables an enzyme called sAC (soluble adenylyl cyclase), which triggers the cells to swim.

Balbach said: “Sperm recovered from female mice remained incapacitated. There were no side-effects. The compound wore off three hours later, and males recovered their fertility.”

A single dose rendered sperm immobile for up to two-and-a-half hours, with the effects persisting in the female reproductive tract after sex.

There were 52 attempts at impregnation and all failed. In contrast, peers treated with a placebo that acted as a control made a third of their partners pregnant.

After three hours, some sperm began regaining motility, with virtually all recovering a day later.

Co-author Professor Lonny Levin said: “The team is already working on making sAC inhibitors better suited for use in humans.”

They have already launched Sacyl Pharmaceuticals and are elated with their results, saying that when it comes to contraception, women's choices range from pills to patches to intrauterine devices. As a result, they traditionally bear most of the burden of preventing pregnancy.

It takes weeks to reverse the effects of other hormonal and non-hormonal male contraceptives in development, said Balbach, whereas this one wears off within hours. Men would take it only when, and as often, as needed.

The findings, published in the journal Nature Communications, are among the most promising to date, offering real hope of bringing it to fruition.

It would help reduce unintended pregnancies and abortions, as well as improving maternal health and decreasing infant mortality.

The female pill has enabled millions of women take control of their fertility and reproductive health since it became available in 1961.

Study details

On-demand male contraception via acute inhibition of soluble adenylyl cyclase

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Abstract

Nearly half of all pregnancies are unintended; thus, existing family planning options are inadequate. For men, the only choices are condoms and vasectomy, and most current efforts to develop new contraceptives for men impact sperm development, meaning that contraception requires months of continuous pretreatment. Here, we provide proof-of-concept for an innovative strategy for on-demand contraception, where a man would take a birth control pill shortly before sex, only as needed. Soluble adenylyl cyclase (sAC) is essential for sperm motility and maturation. We show a single dose of a safe, acutely-acting sAC inhibitor with long residence time renders male mice temporarily infertile. Mice exhibit normal mating behaviour, and full fertility returns the next day. These studies define sAC inhibitors as leads for on-demand contraceptives for men, and they provide in vivo proof-of-concept for previously untested paradigms in contraception; on-demand contraception after just a single dose and pharmacological contraception for men.

Nature Communication article – On-demand male contraception via acute inhibition of soluble adenylyl cyclase (Open access)

The Independent article – Male contraceptive pill stops sperm swimming: ‘Game changer’ (Open access)