Study explains potential failure of oral contraceptives with obese women

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Researchers have identified a potential biological mechanism that could explain why oral contraceptives may be less effective at preventing pregnancy in obese women, as some epidemiological studies have indicated.

Although conventional oral contraceptives appear to eventually reach the effective blood concentrations needed in the body to prevent conception in obese women, it appears to take twice as long, leaving a "window of opportunity" every month where the contraceptive may not be at a high enough level to prevent a pregnancy.

The findings are of particular importance, researchers noted in their study, because about 30 percent of all adults in the U.S. are obese and the birth control pill is one of the most popular forms of contraception in the nation.

"We don't have enough data yet to recommend that physicians change their clinical practice for use of oral contraceptives with patients who are very overweight," said Ganesh Cherala, an assistant professor in the College of Pharmacy at Oregon State University. "However, until more studies are done, women may wish to consult with their physicians about this issue and consider a backup method of contraception at some times of the month."

The study was just published in the journal *Contraception*, by scientists from OSU, Oregon Health and Science University, University of

Colorado at Denver, Oregon National Primate Research Center, and the University of Southern California. The research was supported by the National Institutes of Health.

The underlying problem, Cherala said, is that oral contraceptives, like most drugs, are initially tested in "healthy" people, which rarely includes people who are more than 130 percent of their ideal body weight.

"When we first test drugs for safety and efficacy, we generally do not include people with a high body mass index," Cherala said. "But body weight and amounts of fat can seriously change the pharmacokinetics, or way drugs act and are processed in the body. There's a growing awareness that we need to more carefully consider obesity and other factors that affect drug absorption, distribution, metabolism and other factors."

Conventional oral contraceptives, Cherala said, are thought to be relatively "lipophilic," or tend to concentrate in fat tissue. However, the researchers in this study said they were somewhat surprised to find that the affinity of these drugs for fat tissue was not significantly different between obese and normal body weight subjects.

Rather, the researchers found that contraceptive drug levels in both obese women and those of normal weight eventually were about the same, but it took longer to achieve that level in very overweight women.

The study showed it took an average of about five days for the drugs to achieve their maximum concentration in women of normal weight, an average of 10 days for obese women, and even longer than that for some individuals. One woman in the study took more than 20 days to reach a "steady state" drug concentration. Women of normal weight who follow their oral contraceptive directions should have appropriate protection against pregnancy. But the delay in reaching a steady state drug

concentration raises questions about how well oral contraceptives may work for obese women.

Increasing the drug dosage might help address this issue, Cherala said, but also adds other health concerns.

In fact, the researchers noted in their report that many clinicians actually prescribe lower-dose oral contraceptives to obese patients in an effort to decrease their risk of venous thrombosis. These are blood clots in the legs or elsewhere that can increase the risk of stroke and heart attacks.

The study was done with 20 women of ages 18 to 35, all of them healthy and seeking contraception, 10 of whom were of normal weight and 10 with a "body mass index" of more than 30 - a common measure of obesity.

According to Dr. Alison Edelman, lead author of the study and assistant director of the Family Planning Fellowship at Oregon Health and Science University, the participants in this study were purposely selected for obesity in order to explore this issue. But several demographic studies have shown that even women just considered "overweight," with a body mass index of 25-30, may also be at increased risk of contraceptive failure.

"Although our research has found this interaction between obese women and oral contraceptives, we don't have enough information yet to recommend changes in clinical practice, other than choosing a contraceptive option that works better for both normal weight and obese women, like an intrauterine device," Edelman said.

For future work, she said, studies of contraception would be more useful if they included participants that reflect the general population, including women with different body mass indexes. The biological underpinnings

of how oral contraceptives work, their effects on the hypothalamic-pituitary-ovarian axis, has only been studied in women of normal weight, the researchers noted in their study.

At present, Cherala said, there is no readily available test that would tell a woman how long it would take for her to reach an effective concentration level of a particular contraceptive, and this does vary with the individual. However, scientists are continuing research on that issue, and they may ultimately develop tests or methods that would improve drug efficacy for women who wish to use oral contraceptives.

Source: Oregon State University (news : web)