Obesity-related fertility issues may be improved by correcting blood sugar levels

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Reproductive hormone levels in females with obesity may be partially restored by lowering blood glucose levels, leading to improved fertility, according to a study published in the *Journal of Endocrinology*.

The study indicates that altered levels of reproductive hormones in a well-established mouse model of obesity may be partially restored by a common type 2 diabetes medication that reduces blood glucose levels. Many women with obesity that experience fertility issues also have altered levels of reproductive hormones. Currently there is no effective therapy to address this. Development of a therapy that not only improves women's' metabolic health but also treats obesity-related infertility would be a significant advancement, with the potential to improve many people's quality of life.

Although fertility problems are well established in women with obesity, there remains a lack of effective and targeted treatments to address them. Obesity is a growing health epidemic, which means more women are being affected by reproductive difficulties. Obesity-related fertility issues are complex but evidence suggests that, in part, they may be linked to changes in energy metabolism, which lead to altered levels of reproductive hormones that can then disrupt the menstrual cycle and ovulation. People with obesity are at a greater risk of developing type 2 diabetes and often have high blood glucose levels, as well as other metabolic changes.

The MC4R gene knock-out (KO) mouse is a well-characterized model of obesity, which also exhibits irregular reproductive cycles with altered hormone levels that lead to declining fertility. The mouse reproductive cycle is similar to that of humans, in that the profile of hormone level changes is analogous, although it is much shorter in duration, so the MC4R KO mouse is a good, representative model for initial investigations of metabolic and reproductive function in obesity.

Dapagliflozin is a drug commonly used to treat type 2 diabetes, where it reduces blood glucose levels and improves other markers of metabolic health but its effects on reproductive health and fertility have yet to be investigated.

In this study, Professor Chen and colleagues at the University of Queensland in Australia, investigated the effects of dapagliflozin treatment on metabolic health and reproductive hormone levels in the MC4R mouse model of obesity. After just eight weeks of treatment blood glucose levels were normal, body weight was reduced, the reproductive cycle was normalized and levels of reproductive hormones and ovulation were partially restored, compared with non-treated mice.

"We often see low fertility in women with obesity in clinical practice", comments primary author, Dr. Cui, a visiting fellow from Chengdu Women and Children Hospital in China, "so this research provides hope for a future, effective treatment."

Professor Chen comments that "these data suggest that normalizing blood glucose metabolism with dapagliflozin in obesity may be a promising route for at least partially restoring reproductive function. This could improve fertility in women where no other successful therapy is currently available."

However, Professor Chen cautions that "although encouraging, these studies were conducted in mice and much more work needs to be done to confirm that these findings could be replicated effectively in women. However, people with obesity are at much greater risk of developing type 2 diabetes, so the known health benefits of correcting blood glucose levels may be extended to also improving fertility in those affected."

The team now intend to further investigate the therapeutic benefits of using dapagliflozin to improve reproductive function by examining the molecular pathways involved, which could identify better targets for future fertility treatment in women.

More information: Ling Cui et al, Dapagliflozin partially restores reproductive function in MC4R KO obese female mice, *Journal of*

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