Adding Metformin Doesn't Help With Ovulation

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Adding metformin to a clomifene citrate regimen did not significantly increase the probability of ovulating or becoming pregnant in women who had polycystic ovary disease and were treated with clomifene citrate alone.

This conclusion was based on results of a trial conducted at 20 Dutch hospitals where 228 women were randomized to receive either clomifene citrate (Clomid) in combination with metformin (Glucophage) or clomifene citrate with a placebo (BMJ 2006;doi:10.1136/bmj.38867.631551.55). The researchers, led by Etelka Moll, registrar for obstetrics and gynecology at the center for reproductive medicine at Academic Medical Center, Amsterdam, found comparable ovulation rates in the two groups, the primary outcome measure, and no statistically significant differences in pregnancy, spontaneous abortion, and clomifene resistance rates, the secondary outcome measures.

"The effects of metformin on ovulation may not be sufficiently strong to improve on the already high ovulation rates with clomifene citrate in these women," the authors wrote.

Of the 111 women in the clomifene citrate plus metformin group, 64% ovulated. Of the 114 in the clomifene citrate plus placebo group, 72% ovulated. In the metformin group, 40% had an ongoing pregnancy, compared with 46% in the clomifene and placebo group. Spontaneous abortions occurred in 12% of the metformin group and 11% of the control group. None of these differences was statistically significant.

The authors note that their trial population was less obese than women evaluated in previous studies of the combined therapy, reflecting a normal range of women with polycystic ovary syndrome (PCOS)—around 35%-60% of such women are obese. Lean women are less likely to benefit from insulin sensitizers such as metformin because they are less insulin resistant.

Patients in the metformin group were significantly more likely to drop out of the study due to side effects, the authors said.

Clomifene citrate stimulates ovulation by increasing follicle-stimulating hormone and luteinizing hormone levels. Of women with PCOS treated with clomifene citrate, 75% will ovulate. Metformin, which potentiates insulin action, stimulates ovulation by reducing insulin and androgen levels. ■

Bariatric Surgery May Resolve PCOS for Some

BOSTON — Bariatric surgery may resolve symptoms of polycystic ovary syndrome in obese women with the condition, Dr. Héctor Escobar-Morreale reported at the annual meeting of the Androgen Excess Society.

"In some women, the syndrome is so driven by insulin resistance that it may resolve completely with weight loss," said the endocrinologist, of the Hospital Ramón y Cajal in Madrid.

Among women seeking weight-loss advice at his endocrinology practice, Dr. Escobar-Morreale found a PCOS prevalence of 28%, more than five times the prevalence among lean women in Madrid. This discovery prompted him to examine the prevalence of the disorder among 36 obese women referred for bariatric surgery, and to also track the effect of surgically induced weight loss on their symptoms.

In this group of women, 17 (47%) were diagnosed with PCOS according to the 1990 National Institutes of Health criteria. Follow-up data at 1 year were available on 12 of them.

By 12 months, the women had lost an average of 41 kg and their hirsutism had resolved. Significant decreases were noted in their sex steroid levels: Total testosterone dropped from a mean of 69 ng/dL to 19 ng/dL. Insulin sensitivity returned to normal and regular menstruation was restored. Among 10 women who were tested, all had hormonal evidence of ovulation.

Of course, Dr. Escobar-Morreale said, bariatric surgery is a serious proposal and is indicated only for morbidly obese patients who have repeatedly failed to lose weight. "Lifestyle modification should be attempted first," he said.

—Michele G. Sullivan

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