Vaginal Ring Upsets Metabolism Less Than the Pill

Evidence suggests that oral contraceptives augment insulin resistance and related long-term risks.

BY FRAN LOWRY
Orlando Bureau

WASHINGTON — The contraceptive vaginal ring has fewer metabolic adverse effects than do oral contraceptives and may be a better alternative for insulin-resistant women, those with diabetes, and women with metabolic syndrome at increased risk for cardiovascular disease, Dr. Karen Elkind-Hirsch and colleagues wrote in a poster presented at the annual meeting of the American College of Obstetricians and Gynecologists.

Combined oral contraceptives remain the first line of treatment for women who desired birth control or cycle control with contraceptive steroids. Although much effort has been directed toward minimizing their potential thromboembolic and cardiovascular disease risks, much less attention has been given to their metabolic effects, wrote Dr. Elkind-Hirsch, scientific director of the Woman's Health Research Institute in Baton Rouge, La.

There is some evidence that oral contraceptives may aggravate insulin resistance and exert other untoward metabolic effects that might increase a woman's long-term risk for diabetes and heart disease. Delivering low-dose oral contraceptives via a nonoral route such as the vaginal ring might provide efficacy and good cycle control with less risk, they wrote.

To test this, the investigators randomized 30 women aged 18-40 years to either the vaginal ring or to a low-dose monophasic oral contraceptive for five continuous menstrual cycles. They tested the effects of both methods of birth control on carbohydrate metabolism, using insulin sensitivity indices derived from fasting and oral glucose tolerance tests.

All patients were similar with regard to age, weight, and metabolic parameters at baseline. However, by the end of the treatment period, the researchers noted that insulin sensitivity measured with a glucose tolerance test was significantly decreased in women taking the oral contraceptive pill, compared with women using the vaginal ring. The pill also significantly increased insulin resistance from baseline to after the treatment period when fasting levels alone were measured.

The study results confirm that low-dose oral contraceptives can adversely impact metabolic function, Dr. Elkind-Hirsch and her colleagues concluded. "So many women of reproductive age have insulin resistance or type 2 diabetes now," she said in an interview. "What birth control can we put them on that will not make this worse?

"The other issue is obesity. When you give the contraceptive drug vaginally, you're right at the source, so you can give less. We don't have to go orally, thus bypass the liver, and the ring delivers the drug at a more steady state than the pill,"she added.

She added that the "women loved the ring. Everyone who had been randomized to the ring really loved it. There was no breakthrough bleeding, no matter how high their [body mass indexes] were. Not to get the breakthrough bleeding on such a low dose was very nice, and I think that was due to the steady-state vaginal delivery." ■

Insulin Levels Higher Among Obese Teens Taking Medroxyprogesterone

BY DIANA MAHONEY
New England Bureau

BOSTON — The use of medroxyprogesterone may impair insulin and glucose metabolism in obese adolescents, thus increasing the long-term health risks of young women in an already vulnerable population, Dr. Nancy E. Fritz said at the annual meeting of the Society for Adolescent Medicine.

In a small retrospective study, Dr. Fritz and colleagues in the Cook County Bureau of Health Services' division of adolescent medicine in Chicago collected information on height, weight, laboratory values, contraceptive use, and obstetric history from the charts of 56 adolescent girls (mean age 17 years) from three urban school-based health centers who were participating in an obesity management program. With the exception of two Hispanic girls, participants were African American.

All participants had a body mass index of at least 95% for their age and all had at least one additional risk factor for type 2 diabetes mellitus. As part of the obesity management program, all of the young women had undergone screening for fasting glucose, lipids, and insulin levels.

The study participants were sorted into one of three groups based on contraceptive use: 22 medroxyprogesterone (Depo Provera) users, 13 oral contraception users, and 21 women who did not use hormonal contraception, Dr. Fritz reported in a poster presentation.

The three groups did not differ significantly by age, body mass index, glucose, cholesterol, triglyceride, HDL cholesterol, or LDL cholesterol levels.

The medroxyprogesterone group was more likely to have gained weight before the time of blood work than were the other two groups, "which is consistent with data from previous studies showing an association between medroxyprogesterone use and weight gain," Dr. Fritz noted.

The results also showed significantly higher mean insulin levels in the medroxyprogesterone group compared with both the oral contraceptive and nonhormone groups. Insulin levels tended to be higher among the never-pregnant vs. previously pregnant medroxyprogesterone users, but the finding was not statistically significant.

The insulin increases do not appear to be a function of weight gain in this population, as the insulin levels among oral contraception users and nonusers who were gaining weight were not significantly different from those who were losing weight, Dr. Fritz said. However, the association between insulin increases and weight gain and loss could not be reliably calculated for the medroxyprogesterone users because, she noted, "only three of this group did not gain weight."

The association between medroxyprogesterone use and both increasing weight and increased insulin levels independent of body mass index in obese at-risk adolescents raises the possibility that the contraceptive also may increase risks for metabolic syndrome and/or diabetes in this subgroup, Dr. Fritz said.

Although enlightening, the data from this study are "too preliminary, too retrospective, and too small" to make a definitive statement about how to address this issue clinically, she said. "We need a larger prospective study looking at this in teenagers of various weights, ethnicities, and other risks. For now we need to keep an open mind."

Studies already have shown that medroxyprogesterone makes heavy teens heavier, "and that alone probably increases their risks for all of the bad things, so we can tell our patients that," Dr. Fritz said. "If it also messes with insulin levels and glucose metabolism above and beyond the weight issue, which our work suggests, things get more complicated, as they do when you consider the fact that African American kids, who are already at higher risk for diabetes, are probably the ones most likely to use [medroxyprogesterone] these days, and therefore the ones most likely to get pregnant if we steer them away from it."

The challenge, she added, "is figuring out how to factor all of those ethical decisions into a discussion with a concrete teenager. Which is worse, teenage pregnancy or increased diabetes mellitus risks? I would say the latter, but not everyone would agree with me." ■

FDA Approves 'Follow-On' Human Growth Hormone

BY ALICIA AULT
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The Food and Drug Administration has approved the first "follow-on" version of a human growth hormone, Omnitrope, a recombinant somatotropin made by Sandoz International GmbH.

The approval is notable in that it raises questions about the FDA's process for approving generic biologics. The agency says it still does not have the authority to license such generics. In the case of Omnitrope, the agency determined that it is not therapeutically equivalent to the human growth hormones currently on the market. Thus, Omnitrope is not considered a generic, but is instead deemed to be a follow-on product because it is "sufficiently similar" to Pfizer Inc.'s Genotropin, said the FDA.

After Omnitrope manufacturer Sandoz sued the FDA last year, a federal court ordered the agency to make a decision on the hormone's application.

Pfizer had filed a petition to block Omnitrope's approval, objecting to Sandoz's use of Pfizer data in its application, which was submitted in mid-2003. Sandoz, meanwhile, sued the FDA last September to force some action on its long-languishing application. In early April, a federal court ordered the agency to move one way or another.

The FDA said its Omnitrope approval did not set an automatic precedent for the approval of other follow-on or generic biologics, as human growth hormone has certain characteristics that make it uniquely suited to a relatively simple approval. Recombinant human growth hormone has only one known active ingredient, and its mechanism of action, toxicity, and efficacy is well understood, said the FDA.

Sandoz used both published data from Pfizer and conducted its own trial in pediatric patients to prove Omnitrope's safety and efficacy. In the 89-patient study, 44 children received Omnitrope and 45 another Genotropin for 9 months in a daily subcutaneous injection of 0.03 mg/kg. At 9 months, height velocity was similar for both, with a mean of 10.7 cm per year.

Omnitrope was approved for growth failure in pediatric patients and growth hormone deficiency in adults. The warnings and precautions for Omnitrope are similar to those for other growth hormone formulations. Patients with diabetes or glucose intolerance should be watched carefully as the drug can induce insulin resistance, according to the FDA-approved label.

In a press release announcing the approval, Sandoz did not comment on whether Omnitrope would cost less than competitors. ■