FDA: Appropriate SSRI Use OK in Pregnancy

BY MICHELE G. SULLIVAN

Pregnant women taking selective serotonin reuptake inhibitors for depression may continue to do so, despite a 2006 warning that the drugs may predispose infants to persistent pulmonary hypertension, the Food and Drug Administration has announced.

That earlier warning was based on a single study indicating that infants exposed to the drug in utero after the 20th week of pregnancy were six times more likely to develop persistent pulmonary hypertension (PPHN) than nonexposed infants (N. Engl. J. Med. 2006;354:579-87).

"Since then, there have been conflicting findings from new studies evaluating this potential risk, making it unclear whether use of SSRIs during pregnancy can cause persistent pulmonary hypertension," the FDA said in a press statement.

The agency will update the drugs' warning labels to reflect data from new studies, which have produced conflicting results about the risk SSRIs may pose to an unborn child. Those studies include a large retrospective database study in 2009 that found no association between SSRI use and PPHN (Pharmacoepidemiol. Drug Saf. 2009;18:246-52), and a 2011 case-control study of 11,923 births that showed PPHN was associated with cesarean delivery but not with SSRI use in the second half of pregnancy (Am. J. Perinatol. 2011;28:19-24).

FDA officials concluded that the evidence is not sufficient to withhold SSRI treatment from pregnant women or take them off the antidepressants. "At present, FDA … recommends that health care providers treat depression during pregnancy as clinically appropriate," according to the agency's statement.

Dr. Gideon Koren, professor of pediatrics, pharmacology, pharmacy, medicine, and medical genetics at the University of Toronto, commented in an interview, "I support FDA's hesitation in confirming causation of SSRIs in causing PPHN. The available studies are split in their ability to show an association between SSRIs taken in late pregnancy.

"Critically, several studies have shown that depression itself is also associated with increased risk of PPHN. Hence it is quite possible that depression and not its treatment cause this rare risk ('confounding by indication')." Dr. Koren also heads the Research Leadership for Better Pharmacotherapy During Pregnancy and Lactation at the Hospital for Sick Children, Toronto, where he is director of the Motherisk Program.

Physicians and their patients should carefully weigh the risks and benefits of any antidepressant use in pregnancy, the FDA added, given that there are "substantial risks associated with undertreatment or no treatment of depression during pregnancy." Risks of untreated maternal depression can include low birth weight, preterm delivery, lower Apgar scores, poor prenatal care, failure to recognize or report impending labor, and increased risks of fetal abuse, neonaticide or maternal suicide, the FDA warned.

Both the American Psychiatric Association and the American College of Obstetricians and Gynecologists recommend monitoring pregnant women for depression and treating them appropriately.

Physicians should continue to report any possible adverse effects to the FDA's MedWatch program, www.fda.gov/MedWatch/report.htm.

Reporting forms can also be requested by calling 800-332-1088.

Dr. Koren said he had no relevant financial disclosures. ■

VIEW ON THE NEWS

Cautious Treatment Makes Sense

Even at the time of the first publication regarding the link between SSRIs and PPHN in 2006, the conclusion of the authors was that if the link is causal, the absolute risk for PPHN following late pregnancy exposure to SSRIs is very low. Thus, the recommendation that clinicians treat pregnant women appropriately for their symptoms was consistent with the initial findings, and continues to be so.

Since the initial publication, three others have appeared in full manuscript form and one in abstract form (now in press). The two published U.S. studies were either underpowered, or had limitations in classifying the outcomes, whereas the two Scandinavian studies confirmed the initial findings in large cohort or linked database studies. Importantly, the European studies that confirmed the association also came to the conclusion that SSRIs pose a small increased risk for a very rare outcome of pregnancy. Thus, the recommendation to treat only if needed, but not to avoid necessary treatment because of concern for PPHN continues to make sense.

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Overweight and Obese Women Deliver Fewer IVF Live Births

BY DAMIAN McNAMARA

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

VITALS

Major Finding: Compared with normal weight women undergoing IVF, a live birth was significantly less likely among overweight (adjusted OR, 0.96) and obese women in class I (0.63), class II (0.39), and class III (0.32).

Data Source: Retrospective cohort study of 4,609 women undergoing initial IVF at a single center in Boston.

Disclosures: Dr. Jones said she had no relevant disclosures.

ORLANDO – Obesity significantly lowers a woman's chance of delivering a live birth after in vitro fertilization, according to a retrospective study of more than 4,500 women.

Up to a 68% lower chance for a live birth was the major finding when researchers compared overweight and obese women to those with a normal body mass index (BMI). Women with a BMI greater than 25 kg/m^2 also had up to a 42% lower chance of embryo implantation and up to a 57% decline in clinical pregnancy rates compared with normal weight women.

The live birth rate declined as BMI increased, Dr. Stephanie Jones said. Compared with women with a normal BMI (18.50-24.99), the adjusted odds ratio (OR) for a live birth was 0.96 among overweight women (25-29.99); 0.63 for obesity class I (30-34.99); 0.39 for obesity class II (35-39.99); and 0.32 for those in obesity class III (BMI of 40 kg/m^2 or greater). They grouped women according to the World Health Organization BMI categories.

The clinical message is to counsel patients that even "a modest amount of weight loss might improve IVF success rates," Dr. Jones said at the meeting.

Dr. Jones and her associates examined outcomes after the first, fresh, autologous procedure for 4,609 women treated at Boston IVF in Brookline, Mass. from 2006 to 2010. Patients were aged 20-45 years.

A secondary outcome, the likelihood of implantation, was significantly different by BMI, compared with those with a normal BMI. Chances dropped for underweight women (BMI less than 18 kg/m^2) (adjusted OR, 0.92), as they did for overweight women (0.93) and those in obesity class I (0.69), class II (0.52), and class III (0.58).

The likelihood of clinical pregnancy dropped only slightly for underweight women (adjusted OR, 0.98). However, it decreased significantly for overweight women (0.90) and for women in obesity class I (0.70), class II (0.41), and class III (0.43).

Interestingly, the miscarriage rate did not differ significantly according to maternal BMI, said Dr. Jones, a third-year resident in the department of obstetrics and gynecology, Beth Israel Deaconess Medical Center, Boston.

The normal-weight reference group included 2,605 patients with a BMI of 18.5-24.99 kg/m^2. There were 92 underweight women (BMI less than 18 kg/m^2). The remaining patients included 1,027 overweight women, 477 class I obese; 275 class II obese, and 133 class III obese women. Baseline characteristics and rates of ectopic pregnancy, spontaneous abortion, and multiple birth did not differ significantly between groups.

In addition to its large sample size, the single-institution design of the study is an advantage, Dr. Jones said. Previous researchers reported an association between increasing obesity and lower IVF success, but most of these studies were small, unadjusted, and focused on pregnancy rates.

"The live birth rate is the outcome most significant to our patients," she said.

A systematic literature review found a decreased chance of IVF pregnancy (OR, 0.71) for overweight or obese women compared with normal weight women (Hum. Reprod. Update 2007;13:433-44). "But they only compared women in two groups – those with a BMI of 25 or less versus 25 plus," Dr. Jones said.

In another study reported at the 2009 ASRM meeting, researchers found a lower clinical pregnancy rate and lower birth weights as maternal BMI increased (Hum. Reprod. 2011;26:245-52). This report was multicenter "and they did not necessarily control for differences in provider factors," she said.

Dr. Jones and her associates also controlled for multiple potential confounders, including maternal age, paternal age, baseline follicle stimulating hormone levels, duration of stimulation, mean daily gonadotropin dose, peak estradiol, number of oocytes retrieved, use of intracytoplasmic sperm injection, embryo quality and number, transfer day, and number of embryos transferred. ■