High OGTT in Pregnancy Ups Later Diabetes Risk

BY MICHELE G. SULLIVAN
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Women who have an abnormal glucose tolerance test result during pregnancy but do not develop gestational diabetes still face an increased risk of developing type 2 diabetes later on, investigators reported.

The large retrospective study, published Jan. 25, concluded that even modestly elevated glucose levels double the risk of diabetes within the next 9 years. "The risk of subsequent diabetes ... likely occurs since these women have an intermediate form of glucose intolerance," with impaired β-cell functioning, wrote Dr. Darcy B. Carr of the University of Washington, Seattle, and her coauthors (Diabetes Care 2008 Jan. 25 [doi 10.2337/dcc07-1957]).

In this retrospective cohort study, the researchers analyzed diabetes risk over a mean 9-year follow-up period in 31,000 women without gestational diabetes who had an oral glucose tolerance test (OGTT) or oral glucose challenge test (OGCT) during their pregnancy. The mean age was 31 years; the median follow-up was 9 years.

The investigators found that the risk of later development of type 2 diabetes rose as the values of the normal OGTT value had double the risk of developing the disease, while women with levels greater than 7.3 mmol/L were three times more likely to do so. Women with no abnormal values on the OGTT were at no increased risk of developing type 2 diabetes, but those with one abnormal value were twice as likely to do so.

These associations remained significant even after the researchers controlled for age, primigravidity, and preterm delivery.

The finding is consistent with those from a previous, much smaller longitudinal study that reported higher frequencies of glucose intolerance in women with an abnormal OGTT value.

Dr. Carr and her colleagues noted that their study could not control for race, family history, or body mass index—important factors to consider when assessing diabetes risk. In addition, subsequent diabetes was not systematically assessed, which may introduce bias in those who were selected for testing, they wrote.

They also said their conclusions are not sufficient for them to make any screening or testing recommendations: "Whether women who fall within this intermediate range of glucose intolerance during pregnancy may benefit from increased diabetes surveillance as well as lifestyle recommendations proven to reduce the risk of developing diabetes is unknown."

IVF Twin Preganacies Raise Anxiety, but Not Depression

WASHINGTON — Anxiety—but not depression—was higher among women with twin pregnancies than in women with singleton pregnancies after in vitro fertilization, reported Dr. Farzad Jahangiri of Northwestern University, Chicago.

In this study, presented at the annual meeting of the American Society for Reproductive Medicine, Dr. Jahangiri and colleagues interviewed women at the confirmation of their pregnancies and again at 10-12 weeks’ gestation and 21-22 weeks’ gestation. The study included 48 singleton pregnancies and 13 sets of twins, and there were no significant demographic differences between the two groups.

The investigators found no differences in depression scores between the women with singleton vs. twin pregnancies at two of the three time points. By contrast, the women with twin pregnancies averaged higher (but not significant- ly higher) anxiety scores than the singleton group at 10-12 weeks and significantly higher anxiety scores at 22-23 weeks.

Psychological traits in singleton vs. twin IVF pregnancies have not been widely studied. But previous research has shown that women who are pregnant after IVF become less anxious as their pregnancies progress and their self-esteem increases.

The new findings of increased anxiety among women with IVF twin pregnancies during the second trimester can help clinicians discuss the risks associated with multiple gestations when they counsel women who are undergoing infertility treatments, and alerting them to the risks of the pregnancy. Depression was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). Anxiety was assessed using the Spielberger State and Trait Anxiety Inventory.

Monoclonal Antibodies for Ca, Asthma, and RA

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Excluding those classified as orphan drugs, there are 10 monoclonal antibodies currently on the market to treat non-Hodgkin’s lymphoma, asthma, or rheumatoid arthritis. Five are composed of various types of humanized immunoglobulin G (IgG) and two of murine IgG. The approved indications include metastatic carcinoma of the colon or rectum, squamous cell carcinoma of the head and neck, non-Hodgkin’s lymphoma, metastatic breast cancer, and moderate to severe chronic diseases such as asthma and rheumatoid arthritis.

The anti-neoplastic agents are alemtuzumab (Campath), bevacizumab (Avastin), cetuximab (Erbitux), gemtuzumab ozogamicin (Mylotarg), rituximab (Rituxan), panitumumab (Vectibix), tositumomab and iodine 131 (Bexar), and trastuzumab (Herceptin).

The ninth member of this group, rituximab (Rituxan), is also used as an antineuthamatic agent.

Exposure of the embryo and fetus should be expected when ever these antibodies are used in pregnancy. Although their molecular weights are very high, two are known to cross the placenta: Rituxan in humans and Herceptin in monkeys. The transplacental passage of the other anti-body has not been studied, but endogenous IgG levels are higher for Avastin, Mylotarg, and Vectibix.

Bexar, Campath, Erbitux, Mylotarg, Zevalin, and Rituxan may cause severe, infusion-related toxicity, including hypotension. Allergic reactions are high for Avastin, Mylotarg, and Vectibix.

Moreover, the long elimination half-lives ranging from about 2 to 19 days will place these antibodies at the maternal-fetal interface for prolonged periods. Animal reproduction studies have not been conducted with Bexar, Campath, Erbitux, or Zevalin. Studies in pregnant animals with Herceptin and Rituxan suggested high risk for humans, whereas the suggested low risk was greater for Avastin, Mylotarg, and Vectibix.

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Reports of exposure to Bexar and Mylotarg during pregnancy are unlikely. Bexar, indicated for non-Hodgkin’s lymphoma, contains radioactive iodine and is contraindicated in pregnancy. Mylotarg, a combination of gemtuzumab (IgG4k) conjugated with the cytotoxic antitumor antibiotic maytansine, is indicated for the treatment of patients with CD33-positive acute myeloid leukemia in first relapse who are 60 years of age or older. Mylotarg caused significant developmental toxicity at a small fraction of the human dose in the only experimental animal species tested. The therapeutic regimen for Zevalin, another agent for non-Hodgkin’s lymphoma, should preclude its use in pregnancy because it includes two radioactive components as well as Rituxan, and the risk to the embryo and fetus appears to be high.

Omalizumab (Xolair), a monoclonal antibody used for moderate to severe persistent asthma, selectively binds to human IgE and has a half-life of 26 days. It has not been studied in animals or humans, but probably crosses the placenta. Reproduction studies in monkeys suggest that the risk in human pregnancy is low, but the human pregnancy experience is limited. In clinical trials, 29 women became pregnant during treatment with Xolair, which was stopped when pregnancy was diag nosed.

Among these patients, there were 4 spontaneous abortions (SABs), 3 elective abortions, 11 normal deliveries, and 11 ongoing pregnancies. The number of SABs, all occurring in the first trimester, is within the expected incidence for recognized pregnancies.

A full assessment of the risk of monoclonal antibodies during pregnancy is not possible because of the very limited or absent human pregnancy data, including a lack of long-term evaluation of exposed offspring. Nevertheless, these agents are used for life-threatening diseases and, if indicated, should not be withheld from a pregnant woman—with the exception of Bexar, Mylotarg, and possibly Zevalin.

Exposure to monoclonal antibodies during human lactation has not been studied, but their excretion into human milk is likely. Xolair is excreted into the milk of monkeys and, after exposure during the gestation and 28 days of nursing, neonatal plasma concentrations ranged from 11% to 94% of maternal levels. Because the risk of infant toxicity from Xolair has not been determined, the safest course is to avoid breast-feeding if the mother is being treated. For the other antibodies, severe infant toxicity is a potential complication and consideration should be given to discontinuing nursing if the mother requires treatment.

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