Monitor for and Treat Mild Hypothyroidism in Pregnancy

BY MARY ELLEN SCHNEIDER
New York Bureau

PHILADELPHIA — Physicians should test pregnant women for subclinical hypothyroidism and treat the condition to prevent possible fetal and developmental abnormalities, according to Dr. Stephanie L. Lee, director of the Endocrine Clinics at Boston Medical Center.

For the first 15 weeks of development, the fetus is dependent on the mother’s thyroid hormone. “So if Mom is hypothyroid, then baby is hypothyroid during that critical development period,” Dr. Lee said at Endocrinology in the News sponsored by Boston University.

The risks of fetal loss and impaired development have been borne out in recent studies, she said. For example, a study that looked at the consequences of mild hypothyroidism among pregnant women found that the fetal death rate was four times greater in women with elevated levels of thyroid-stimulating hormone (TSH).

The researchers measured TSH in serum samples taken from women during their second trimester as part of their routine prenatal care. Of 9,403 women with singleton pregnancies, 2.2% (209 women) had TSH levels of 6 mU/L or greater. The rate of fetal death was 1.98% among the women with elevated TSH, compared with 0.5% in women with TSH levels less than 6 mU/L (J. Med. Screen. 2006;7:127-30).

In another study by the same group of researchers, the results of IQ testing in children born to women who had untreated hypothyroidism during pregnancy were compared with those of children of women who had normal serum thyrotropin levels during pregnancy. Among the children of 48 women with untreated thyroid deficiency, the IQ scores were on average 7 points lower than those of the children of 124 women with normal thyroid levels. In addition, among children of mothers with untreated thyroid deficiency, 19% had IQ scores of 85 or less, compared with 5% of the other children (N. Engl. J. Med. 1999;341:549-55).

These are two bits of information that suggest that maternal hypothyroidism is a very serious condition and needs to be treated and monitored, said Dr. Lee, who had no commercial support to disclose.

Dr. Lee recommends testing as soon as pregnancy is confirmed in women with a strong family history of hypothyroidism, who have a goiter on exam, or who were taking thyroid hormone prior to conception. She advises continuing to monitor these patients every 4-5 weeks through the first 20 weeks of gestation. After 20 weeks, she increased the demand from the fetus to slow or stop, Dr. Lee said.

“Because these pregnant women do not see their [obstetricians] until week 12 or 13, it really is up to the internist to make sure that they know that they have to get the thyroid levels checked,” Dr. Lee said.

The Endocrine Society made similar recommendations in clinical practice guidelines released in 2007. The society advises physicians to measure TSH in women at high risk for thyroid disease.

Maternal Hyperglycemia Tied to High Fetal Insulin, Birth Weight

BY MARY ANN MOON
Contributing Writer

Maternal glucose levels that were high but below the diagnostic threshold for gestational diabetes were strongly associated with high fetal insulin levels and birth weights in a large international study.

There were also weaker—but still significant—associations between maternal hyperglycemia that fell short of overt gestational diabetes, as well as a host of neonatal problems that included hypoglycemia in the neonate, the need for cesarean delivery, premature delivery, shoulder dystocia, or birth trauma, the need for intensive neonatal care, hyperbilirubinemia, and preeclampsia.

These findings “indicate the need to reconsider current criteria for diagnosing and treating hyperglycemia during pregnancy,” said Dr. Boyd E. Metzger of the University of Florida.

The study subjects underwent standard oral glucose tolerance testing at 24-32 weeks’ gestation at 15 medical centers in nine countries. Cord blood specimens were obtained at delivery to assess serum C-peptide levels, and rates of fetal β-cell function.

High levels of fasting, 1-hour, and 2-hour plasma glucose were strongly correlated with birth weight above the 90th percentile in both infants and children of the 90th percentile, and the rates of these problems were found to increase as the plasma glucose levels increased, the investigators reported (N. Engl. J. Med. 2008;358:1991-2002).

There were weaker but significant correlations between maternal hyperglycemia and two other primary outcomes: one for cesarean delivery and clinical neonatal hyperglycemia, as well as five secondary outcomes. A recent meta-analysis that was presented at the annual meeting of the American Academy of Pediatrics in July showed that maternal glucose intolerance early in pregnancy and the development of gestational diabetes were associated with increased insulin resistance and fetal macrosomia.

Considering the strong evidence of safety and efficacy, it is time for the FDA to remove the antiemetic doses of droperidol from the black box warning.

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Drugs in Pregnancy and Lactation

Droperidol and the Black Box Warning

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In December 2001, the Food and Drug Administration placed a black box warning on droperidol (Inaprosine) because of concerns about QT prolongation and torsades de pointes. This action took the medical and pharmaceutical communities by surprise and created tremendous controversy. Although the labeling information always contained warnings of serious and even life-threatening arrhythmias, droperidol had a 30-year history of safe and effective use in a range of patients.

Since its release in 1970, droperidol had been one of the preferred antiemetics for the prevention and treatment of postoperative nausea and vomiting (PONV) and the treatment of hyperemesis gravidarum (HG). But the agency’s action resulted in a marked decrease in its use for both indications.

In the early 1990s, manufacturing problems curtailed the availability of parenteral prochlorperazine, the other preferred antiemetic for these indications. With no other viable alternatives, there was an increase in the use of ondansetron (Zofran), which was expensive, but is now available as a generic.

What remains unresolved is the use of droperidol in clinical situations, in which it is the preferred agent for PONV, including after cesarean section, and for HG.

Several small studies that compared droperidol and ondansetron for PONV found no differences between the two in terms of efficacy and toxicity. However, a large study with more than 2,000 subjects concluded that droperidol (1.25 mg IV) was superior to ondansetron (4 mg IV) for both vomiting and nausea (Anesth. Analg. 1998;86:731-8).


A 2005 study of droperidol (0.625-1.25 mg) for antiemetic prophylaxis during general anesthesia in outpatient surgery observed no significant increase in the corrected QT (QTc) interval, compared with saline (Anesthesiology 2005;102:1101-9). A 2007 Mayo Clinic study reported no documentations of QTc prolongation or ventricular arrhythmias (Chest 23:133-9).

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