Maternal Hyperglycemia Tied to High Fetal Insulin

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 an international study of 716 pregnant women. There were also weaker—but still significant—associations between maternal hyperglycemia and two other primary outcomes of this study (cesarean delivery and clinical neonatal hyperglycemia), as well as five secondary outcomes. A similar dose-response relationship was seen between maternal fasting glucose levels and birth outcomes for these problems, Dr. Metzger and his associates reported in the New England Journal of Medicine.

The researchers assessed the 23,316 gravid women “to clarify the risk of adverse neonatal outcomes associated with gestational maternal hyperglycemia.” They compared fasting plasma glucose levels of 70 to 100 mg/dL (3.9 to 5.5 mmol/L) with increased plasma glucose levels.” 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, an indicator 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 and C-peptide levels above the 90th percentile, and the rates of these problems increased as plasma glucose levels increased. There were weaker but significant correlations between maternal hyperglycemia and two other primary outcomes of this study (cesarean delivery and clinical neonatal hyperglycemia), as well as five secondary outcomes. A similar dose-response relationship was seen between maternal fasting glucose levels and birth outcomes for these problems, Dr. Metzger and his associates reported in the New England Journal of Medicine.

In a separate study of gestational diabetes published in the same issue, Dr. Janet A. Rowan of Auckland City (New Zealand) Hospital and her associates in the Metformin in Gestational Diabetes trial found that metformin was “noninferior” to insulin in safety and efficacy, and was preferred by patients with overt disease. In that open-label study, Dr. Rowan and her associates compared oral metformin with insulin therapy in 731 women who had overt gestational diabetes and were followed at 10 New Zealand and Australian obstetric hospitals.

The composite outcome of numerous neonatal complications, including hyperglycemia in the infant, was no different between the metformin group and the insulin group, at 32% in both. There were no differences between the two groups in neonatal anthropometric measures or in umbilical cord serum insulin concentrations. The women preferred metformin to insulin. However, 46% of those who took metformin eventually required supplemental insulin as well, Dr. Rowan and her associates reported at the New England Journal of Medicine.

Follow-up further data on the offspring are needed to determine the long-term safety of metformin use in pregnancy, they noted.

Expert: Itching in Pregnancy May Be Intrahepatic Cholestasis

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO—Check serum bile acids to determine if severe itching during pregnancy is the result of intrahepatic cholestasis of pregnancy, advises a dermatologic pathologist.

“Intrahepatic cholestasis of pregnancy is about the only dermatosis of pregnancy that has poor outcomes for the unborn,” Dr. Senait W. Dyson said at a meeting sponsored by Skin Disease Education and Treatment Foundation.

An uncommon problem in the United States, intrahepatic cholestasis of pregnancy (also called prurigo gravidarum or obstetric cholestasis) is a reversible form of cholestasis that presents in late pregnancy and persists until delivery.

The disease increases the risk of intrauterine fetal distress and leads to a three- to fourfold increase in the risk of stillbirth.

It typically presents during the third trimester and resolves within days after delivery. Clinically, the problem is characterized by generalized, severe pruritus without primary skin lesions, said Dr. Dyson, director of dermatopathology at the University of California, Irvine. Upon enrollment of the palms and soles is common. You’ll seldom see jaundice with intrahepatic cholestasis of pregnancy.

The main diagnostic finding is increased serum bile acids in all cases, resulting from impaired bile flow. Elevated serum bile acid levels greater than 4.07 mg/mL (10 micromol/L) in these pregnant women are diagnostic, Dr. Dyson said.

Some patients will have abnormal liver function tests. Histology is nonspecific, with minimal biliary obstruction tests will be negative.

Prolonged disease causes vitamin K deficiency and increases the risk for bleeding in the mother. It is not clear whether the bleeding risk increases in the infant. Check prothrombin times in women with intrahepatic cholestasis of pregnancy (especially in Chile and other Latin American countries), she said.

Antihistamines will help control the pruritus. Ursodeoxycholic acid (UDCA), the only approved medication to treat primary biliary cirrhosis, also helps improve pruritus in patients with intrahepatic cholestasis of pregnancy, Dr. Dyson said.

Dr. Dyson reported that when they arrive in the operating room, or to interventional radiology, not to stop the bleeding, “Dr. Mahadevan said.

The patients were still moderately coagulopathic when they arrived in the ICU, with an initial transfusion in a 1:1 ratio. Nevertheless, Dr. Mahadevan noted, because of the way the massive-transfusion guidelines have been set up, none of the patients received FFP until after they received 6 U of packed red cells.

Upon arrival in the ICU following initial resuscitation in the ED, the patients’ INRs were still high (1.6, plus or minus 0.1). Finally, they would start receiving packed red cells and FFP in a 1:1 ratio, Dr. Mahadevan said.

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Consider Using FFP Earlier in Cases of Massive Transfusion

BY CAROLYN SACHS
Contributing Writer

A published study of 97 severely injured patients at the University of Texas, Houston, indicated there is a need for earlier administration of fresh-frozen plasma.

In that open-label study, Dr. Mahadevan and his associates compared oral metformin with insulin therapy in 731 women who had overt gestational diabetes and were followed at 10 New Zealand and Australian obstetric hospitals.

The composite outcome of numerous neonatal complications, including hyperglycemia in the infant, was no different between the metformin group and the insulin group, at 32% in both. There were no differences between the two groups in neonatal anthropometric measures or in umbilical cord serum insulin concentrations. The women preferred metformin to insulin. However, 46% of those who took metformin eventually required supplemental insulin as well, Dr. Rowan and her associates reported at the New England Journal of Medicine.

Follow-up further data on the offspring are needed to determine the long-term safety of metformin use in pregnancy, they noted.

In his presentation, Dr. Mahadevan stressed that “we should be assuming the severity of coagulopathy on ICU admission correlated with an increase in mortality. Dr. Mahadevan observed. If your INR was greater than 2, you had a 50% mortality, which, obviously, is significant,” he commented.

Learning from this study, Dr. Mahadevan stressed that “we should be assuming that these patients are coagulopathic, and we should be using FFP right out of the gates,” with an initial transfusion in a 1:1 ratio with packed red blood cells.

Based on the study’s findings, the University of Texas investigators recommended that in 97 severely injured patients who required a massive transfusion of at least 10 U of packed red blood cells during their first 24 hours in the university hospital. “These patients were sick enough that they eventually had to go to the operating room, or to interventional radiology, to stop the bleeding,” Dr. Mahadevan said.