Thyroid Disorder Guidelines Miss ACOG's Mark

BY PATRICE WENDLING
Chicago Bureau

VERONA, ITALY — Newly developed consensus guidelines recommend thyroid-function screening in high-risk pregnant women, but stop short of calling for universal screening.

An international task force, under the auspices of the Endocrine Society, examined 10 key topics related to pregnancy and thyroid. The end result was an 86-page, single-spaced document encompassing 35 recommendations, many of which were reached after a diplomatic search for compromise, Dr. Daniel Glinoer said at a joint meeting of the Italian Association of Clinical Endocrinologists and the American Association of Clinical Endocrinologists.

The difficulty stemmed from the paucity of prospective randomized trials in the field, the contrasting approaches of endocrinologists and ob.gyns. on some controversial issues, and the appearance of additional data even as the task force was writing the guidelines. "Altogether, this effort represented a tremendous challenge that was much more difficult than anticipated," said Dr. Glinoer, who represented the European Thyroid Association on the task force and is chief of the thyroid investigation clinic at the Centre Hôpitalier Universitaire Saint-Pierre, Brussels.

Despite compromises on many recommendations, the American College of Obstetricians and Gynecologists (ACOG) opted not to endorse the final guidelines. Dr. Sarah Kilpatrick, who represented ACOG on the task force, acknowledged that a great deal of time and work went into the guidelines.

"Unfortunately, the data available are not consistently good, and there are still many differences of opinion between endocrinologists and perinatologists about how to interpret the data and best manage pregnant women," Dr. Kilpatrick, professor and head of the department of ob.gyn. and vice dean of the college of medicine at the University of Illinois at Chicago, said in an interview. "ACOG did not endorse these guidelines because many of the recommendations made by the guidelines were based on poor evidence with a recommendation level of inconclusive."

For screening purposes, the task force identified high-risk women as those with a personal history of thyroid or autoimmune disorders; a family history of thyroid disorders; or a personal history of infertility or preterm delivery.

For maternal hypothyroidism, which affects 2.5%-3% of pregnant women, the task force recommends a targeted case-finding approach at the first prenatal visit or at diagnosis of pregnancy. The preconception thyroxine dosage should be adjusted to reach a serum thyroid-stimulating hormone (TSH) level no higher than 2.5 microIU/L. The thyroxine dosage usually needs to be incremented by 4-8 weeks of gestation, and these patients may require a 30%-50% increase in dosage, said Dr. Glinoer.

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If overt hypothyroidism is diagnosed during pregnancy, thyroid function tests should be normalized as rapidly as possible, in view of the potential obstetric complications and risks for the offspring associated with undisclosed prolonged hypothyroidism. Thyroxine dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5 microIU/L in the first trimester or less than 3 microIU/L in the second and third trimesters, or to trimester-specific normal TSH ranges, which Dr. Glinoer admitted haven't been universally established.

There was a consensus against advising termination of pregnancy, even if overt hypothyroidism is diagnosed late, he said.

If a subnormal serum TSH concentration is detected, hyperthyroidism must be distinguished from both normal physiology and hyperemesis gravidarum because of the adverse effects of overt hyperthyroidism on mother and fetus. Antithyroid drug (ATD) therapy should be either initiated for those with a new diagnosis of hyperthyroidism resulting from Graves' disease or adjusted for those with a prior history to maintain maternal free thyroxine levels in the trimester-specific normal pregnancy range, if available, or near the upper limit of the nonpregnant reference range, he said.

Because evidence suggests that methimazole may be associated with congenital anomalies, the task force recommends propylthiouracil (PTU) as first-line medication, especially during the first trimester. Methimazole may be prescribed if PTU is not available, or if a patient can't tolerate or has an adverse reaction to PTU.

The task force concluded that subtotal thyroidectomy may be indicated for maternal Graves' disease if there are severe adverse reactions to ATD therapy, if persistently high ATD doses are required, or if a patient is nonadherent to ATD therapy and has uncontrolled hyperthyroidism. The best time to perform surgery is the second trimester.

There is no evidence that treating subclinical hyperthyroidism improves pregnancy outcome, and it could potentially adversely affect the fetus, he said. ■

Mild Hyperthyroidism May Be Best Bet in Graves' Pregnancy

BY HEIDI SPLETE
Senior Writer

PHOENIX — Infants are rarely born with suppressed thyroid function if their mothers have Graves' disease but continue to take lower doses of thyroid medication during pregnancy, based on data from 249 pregnant Graves' disease patients.

Maternal free thyroxine (FT_4) levels just above normal (at least 1.9 ng/dL) were associated with normal FT_4 levels in the newborn, Dr. Naoko Momotani said at the annual meeting of the American Thyroid Association.

Although previous research has suggested that a mother's thyroid hormone level is linked to her newborn's health, this study is the first to show such a relationship, said Dr. Momotani of the Tokyo Health Service Association in Tokyo.

Graves' disease involves overactivity of the entire thyroid gland, which can cause underactivity of the thyroid in the developing fetus. When a pregnant woman with Graves' disease takes antithyroid medication, the TSH receptor antibodies are transferred to the fetus, which prevents fetal hypothyroidism.

"But the drug doses that are ideal for the mother might be too much for the fetus," Dr. Momotani said.

Keeping pregnant Graves' disease patients in a mild hyperthyroid state may be a noninvasive way to care for these women and prevent thyroid problems in the fetus, she said.

The women in the study took antithyroid drugs throughout pregnancy. The highest reported maternal FT_4 level was 4.1 ng/dL. Overall, 41 fetuses had elevated TSH, but none had a visible goiter at birth.

There were no cases of below-normal fetal FT_4 levels and only one case of elevated TSH in a fetus among women whose FT_4 levels were greater than 1.9 ng/dL (that is, higher than the upper normal range of 1.2-1.9 ng/dL).

By contrast, a total of 102 mothers had normal free T_4 levels (0.6-1.2 ng/dL) at the time of delivery, and 23 of their infants had low FT_4 and/or high TSH levels at birth. But only 1 of these 23 infants had an elevated TSH level when the infants were screened for congenital hypothyroidism. One infant had both suppressed TSH and normal free T_4 levels at birth, which suggested central hypothyroidism, and the mother's FT_4 in this case was 2.1 ng/dL.

It is important to remember that the range of FT_4 values in women with Graves' disease varies, and some infants may have initial suppressed thyroid function, but most of these infants do well with close follow-up, Dr. Momotani said. ■

Majority of Post–Heart Transplant Pregnancies End in Live Births

BY JEFF EVANS
Senior Writer

BOSTON — Live births occurred in 70% of heart transplant recipients who became pregnant after surgery, according to a review of 36 patients with 60 singleton pregnancies reported to the National Transplantation Pregnancy Registry.

Of 42 live-born children, 36 were healthy and developing well at the time of follow-up. Three children were receiving medical management for cardiomyopathy, the same diagnosis for which their mothers received transplants. Among the other three children, one underwent a hypospadias repair, one was treated for attention-deficit hyperactivity disorder, and one died from a traumatic injury, Lisa A. Coscia reported during a poster session at the 2006 World Transplant Congress.

These 42 children were born at a mean gestational age of 37 weeks (5 were premature) and with a mean birth weight of 2.67 kg. A cesarean section was performed in 14 deliveries. Neonatal complications developed in 11 cases.

In the 18 unsuccessful pregnancies, 11 fetuses were aborted spontaneously and 5 for therapeutic reasons. One woman had an ectopic pregnancy and another had a stillborn delivery, according to Ms. Coscia, a registered nurse in the department of surgery at Temple University, Philadelphia.

The 36 patients conceived their pregnancies a mean of 5 years after their transplants, although this ranged from as little as 0.2 years to as much as 15 years. They had an average age of 28 years at conception, ranging from 18 to 39 years.

During pregnancy, hypertension was the most common comorbidity (43%) among the women, followed by infections (14%), preeclampsia (11%), and gestational diabetes (3%).

Nine of the mothers (25%) died after pregnancy, although all of the deaths occurred more than 2 years post partum. These deaths were attributed to cardiac arrest (two), acute rejection (two), and in one patient each, vasculopathy, atherosclerosis, sepsis, lymphoma, and noncompliance. The other 27 mothers (75%) had adequate graft function at follow-up.

According to data collected by the U.S. Organ Procurement and Transplantation Network, the 5-year Kaplan-Meier patient survival rate for heart transplants performed in women between 1997 and 2004 (pregnancies not considered) is just over 69%.

The possibility of maternal death unrelated to pregnancy should be included during prepregnancy counseling, Ms. Coscia advised in her poster at the congress, which was sponsored by the American Society of Transplant Surgeons, the American Society of Transplantation, and the Transplantation Society. ■

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