Hypothyroidism during pregnancy

ABSTRACT

QUESTION I have a 27-year-old patient diagnosed with hypothyroidism in the 8th week of pregnancy. She received conflicting opinions regarding risk for her baby and wants to get more information. I also found conflicting information in the literature. How should I advise her?

ANSWER Pregnant patients with untreated hypothyroidism are at increased risk of obstetric complications. Adequate treatment with thyroid hormones greatly reduces the frequency of these complications. Observational studies suggest that children whose mothers had hypothyroxinemia in early pregnancy have lower IQs than matched controls. Another study has shown that even if levothyroxine therapy is started after the first trimester, there is an excellent chance children will have normal neuropsychologic development.

RÉSUMÉ

QUESTION Une de mes patientes de 27 ans qui en est à sa huitième semaine de grossesse vient de recevoir un diagnostic d’hypothyroïdie. Les avis qu’on lui a donnés concernant le risque pour son enfant sont contradictoires et elle veut avoir plus d’information. J’ai moi aussi trouvé des renseignements conflictuels dans les ouvrages scientifiques. Quels conseils devrais-je lui donner?

RÉPONSE Les patientes enceintes dont l’hypothyroïdie n’est pas traitée présentent un risque accru de complications obstétriques. Un traitement adéquat au moyen d’hormones thyroïdiennes réduit considérablement la fréquence de telles complications. Des études par observation laissent entendre que les enfants dont la mère a souffert d’hypothyroïdie au début de sa grossesse ont un quotient intellectuel plus bas en comparaison des sujets de contrôle. Une autre étude a fait valoir que même si une thérapie à la lévothyroxine est commencée après le premier trimestre de la grossesse, il y a d’excellentes chances que ces enfants aient un développement neuropsychologique normal.

Hypothyroidism occurs during pregnancy relatively frequently. A nation-wide US survey showed that 4.6% of the population 12 years old and older had hypothyroidism and that 4.3% of all women suffered from thyroid disease or goitre, or were taking thyroid medication. Routine prenatal screening showed that 2.2% of pregnant women in their second trimester had thyroid-stimulating hormone (TSH) levels at or above 6 mU/L. Pregnant patients with hypothyroidism are at increased risk of obstetric complications, such as fetal death, gestational hypertension, placental abruption, and poor perinatal outcome. Adequate treatment with thyroid hormones greatly reduces the frequency of these maternal complications.

Until 12 weeks’ gestation, before the fetal thyroid begins to produce thyroid hormones, the developing brain is critically dependent on circulating levels of maternal thyroxine ($T_4$). A recent trial demonstrated that thyroid insufficiency in pregnant rats disrupted migration of neurons in the fetal cortex and hippocampus, leading to aberrant location of neurons in the adult offspring’s brain. Children born to women with high serum TSH concentrations at 17 weeks’ gestation who were not treated for hypothyroidism had 7-point lower IQs.
Motherisk Update

than matched controls. A prospective cohort study has shown that low levels of free thyroxine (fT₄) at 12 weeks’ gestation are associated with impaired psychomotor development at 10 months old.

Treatment

Two thyroid hormones, levothyroxine (L-T₄) and liothyronine (L-T₃), are available in Canada. Liothyronine can be used occasionally when quick onset of action is required, but is less desirable for chronic replacement therapy because it requires frequent dosing and because it produces a transient elevation in triiodothyronine concentrations.

A desiccated hormone preparation, derived from animal thyroids, is also available in Canada. It contains both thyroxine and triiodothyronine, but because it has highly variable biologic activity, it is not recommended as the primary alternative for thyroid hormone therapy. Levothyroxine is considered a safe and effective replacement treatment for hypothyroid pregnant patients and is not teratogenic. A large population-based case-control study found that only 12 babies were born with major malformations to mothers with a history of hypothyroidism who were being treated with thyroid hormones during pregnancy. These cases had no homogenous pattern of defects.

It is generally accepted that severe maternal hypothyroidism during the second trimester can result in irreversible neurologic deficits. Maternal hypothyroxinemia (fT₄ below the lowest 10th percentile and TSH within the reference range of 0.15 to 2.0 mU/L) at later stages can lead to less severe, and partially reversible, fetal brain damage. Even partial treatment of maternal hypothyroidism during pregnancy appears to be beneficial for offspring. A recent cohort study found that infant neurodevelopment was not adversely affected by hypothyroxinemia during the first trimester if fT₄ concentrations were subsequently corrected.

Should we then treat all pregnant women with high TSH levels but no clinical hypothyroidism? We believe this decision must await results of randomized controlled trials of treatment.

Dose adjustment of L-T₄ during pregnancy

Several studies have now confirmed that L-T₄ requirements in most women with existing hypothyroidism increase substantially during pregnancy. Absorption of T₄ occurs in the small intestine; it can absorb from 50% to 80% of the dose. An empty stomach improves absorption. Sucralfate, cholestyramine resin, and aluminum hydroxide can interfere with L-T₄ absorption. Concomitant administration of drugs that induce hepatic cytochrome P450 (CYP) enzymes, mainly CYP3A4, such as phenytoin, carbamazepine, and rifampin, enhance biliary excretion of L-T₄. Hormonal and physiologic changes could indicate a need to adjust dosages during pregnancy.

Special attention should be paid to prenatal vitamins because they contain iron and calcium, both of which potently inhibit absorption of L-T₄. A recent study found L-T₄ dosage adjustments were not required if prenatal vitamins were taken 4 hours after ingesting L-T₄.

Therapeutic drug monitoring of L-T₄

Because adverse effects for both mother and baby are not due to high serum TSH per se but to low free T₄ concentrations, decisions regarding treatment should be based on serum free T₄ concentrations rather than on serum TSH concentrations. If the L-T₄ dose was increased during pregnancy, it should be reduced gradually after delivery and thyroid function evaluated repeatedly.

Levothyroxine and breastfeeding

The quantity of thyroid hormone transferred into human milk is too low to affect plasma thyroid hormone levels in neonates. The American Academy of Pediatrics considers L-T₄ compatible with breastfeeding and has reported that no observable change is seen in nursing infants whose mothers are taking L-T₄.

References


