MOTHERISK *UPDATE*

Managing hypothyroidism during pregnancy

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abstract

QUESTION One of my pregnant patients is taking levothyroxine for hypothyroidism. I prescribed her iron because she was anemic, but she continues to be weak and to have high levels of thyroid-stimulating hormone (TSH). Increasing her dose of levothyroxine did not seem to affect her TSH levels.

ANSWER Many women need higher doses of levothyroxine during pregnancy. You should continue to monitor her TSH levels carefully and be aware that iron given during pregnancy might form an insoluble complex with thyroxine in the gestational tract.

résumé

QUESTION Une de mes patientes qui est enceinte prend de la lévothyroxine pour une hypothyroïdie. Je lui ai prescrit du fer parce qu'elle est anémique, mais sa faiblesse persiste et elle présente des taux élevés de thyréotropine (TSH) qui ne semblent pas influencés par une augmentation de la dose de lévothyroxine.

RÉPONSE De nombreuses femmes ont besoin de plus fortes doses de lévothyroxine durant la grossesse. Vous devriez continuer à surveiller de près ses taux de TSH et aussi savoir que le fer pris durant la grossesse pourrait former un complexe insoluble avec la thyroxine dans les voies gestationnelles.

Maternal hypothyroidism affects between 0.19% and 2.5% of pregnancies, depending on race and geographic area.[1-4] Many hypothyroid women (>70%) have anovulatory cycles and, when they conceive, have high rates of fetal loss in the first trimester (more than twice as many spontaneous abortions as normal women).[3] Studies have shown that the fetuses of hypothyroid women have 10% to 20% more congenital anomalies, 20% more perinatal mortality (stillbirth and neonatal death), and 50% to 60% higher rates of impaired mental and somatic development than those of non-affected women.[1,3] Maternal complications include overt anemia, preeclampsia, abruptio placentae, cardiac dysfunction, and hypertension.[4]

Effects of hypothyroidism

Two recent studies[5,6] have shown that low maternal thyroid hormone concentrations during early gestation might be associated with substantially lower IQ scores in children when tested at school age. Also, the children of hypothyroid women with high concentrations of TSH due to inadequate doses of levothyroxine have impaired psychological development compared with carefully matched control children.[6] It is important to note that the IQs of children of women who had high TSH concentrations but did not exhibit clinical hypothyroidism were also affected. Eventually many of these women developed clinical disease.[7] **Table 1** shows the range of results of thyroid function tests in nonpregnant, pregnant, and hypothyroid pregnant women.[1-4]

All hypothyroid women require daily, lifelong treatment. Levothyroxine is the treatment of choice. Administration of levothyroxine alone is preferable because the hormone content of the synthetic drug is more reliably standardized; this medication has replaced desiccated thyroid tablets as the mainstay of therapy.

Thyroxine (T_4, levothyroxine) is de-iodinated to T_3 in the extrathyroidal tissues, so it most closely duplicates the normal physiologic process.[1] During pregnancy, many women need more thyroxine than they did before they were pregnant, so it is important to monitor TSH and thyroid hormone levels periodically for correct dosage and biologic effectiveness. The bioavailability of levothyroxine might differ somewhat among marketed brands of the drug.[8] Clinical experience has not shown increased risk of fetal abnormalities when

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Table 1. Results of thyroid function tests

THYROID HORMONES	NORMAL FUNCTION	NORMAL PREGNANT FUNCTION	HYPOTHYROID FUNCTION
Thyroid-stimulating hormone	5 μU/mL	Unchanged	Increased
Total T_4	4-12 μg/dL	Increased	Decreased
Free T_4	0.8-2.7 ng/mL	Unchanged	Decreased
T_3	75-195 ng/mL	Increased	Decreased
Thyroxine-binding globulin	Age and sex dependent	Increased	Unchanged

T_4—thyroxine, T_3—triiodothyronine.

Table 2. Drugs that might affect levothyroxine dose requirements

MEDICATION	MECHANISM OF INTERACTION
Iodine	Interferes with thyroid hormone synthesis and release
Lithium	Interferes with thyroid hormone synthesis and release
Carbamazepine	Increases thyroxine clearance
Phenytoin	Increases thyroxine clearance
Phenobarbital	Increases thyroxine clearance
Rifampin	Increases thyroxine clearance
Amiodarone	Decreases conversion from T_4 to T_3 and possibly inhibits T_3
Aluminium hydroxide	Interferes with intestinal absorption
Cholestyramine	Interferes with intestinal absorption
Sucralfate	Interferes with intestinal absorption
Salicylates	Decrease thyroxine-binding globulin
Androgens	Decrease thyroxine-binding globulin, inhibit metabolism
Estrogens	Decrease thyroxine-binding globulin, inhibit metabolism
Corticosteroids	Decrease thyroxine-binding globulin, decrease thyroid-stimulating hormone, block conversion of T_4 to T_3
Prenatal vitamins	Interfere with intestinal absorption

T_4—thyroxine, T_3—triiodothyronine.

hormones are administered during pregnancy.[9]

When to take levothyroxine

The best time to take levothyroxine is early in the morning on an empty stomach. Some women, particularly during the first trimester, might not be able to tolerate medications at that time of day due to morning sickness, and it is probably better to allow them to take levothyroxine later when they are not experiencing nausea and vomiting. Insisting on administration of the medication early in the morning (regardless of patients' symptoms) might lead to skipping this important medication too often.

Many pregnant women take ferrous sulfate during pregnancy. This medication could form insoluble ferric-thyroxin complexes in the gastrointestinal tract and result in reduced absorption of levothyroxine. Ingestion of these two drugs should be separated by at least 2 hours.[1] Other medications that might affect levothyroxine absorption are shown in **Table 2**.[1,2,10]

Conclusion

Maintenance of thyroid hormone levels within the normal range is vital for pregnant woman to ensure optimal maternal and fetal health. Improved outcomes of pregnancy in hypothyroid women have been achieved through efforts to identify and treat these women. Euthyroidism must be reached and maintained in a timely fashion. Levothyroxine is the treatment of choice. Levels of both TSH and thyroid hormone need to be monitored periodically, and concurrent administration of other medications should be carefully followed.

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