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Clinical Care of Women with Hypothyroidism during their Reproductive Years Requires Awareness of the Consequences by Patients and Clinicians

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Vadiveloo, T, Mires GT, Donnan PT, Leese GP. Thyroid testing in pregnant women with thyroid dysfunction in Tayside, Scotland: the thyroid epidemiology, audit and research study (TEARS). Clin Endocrinol (Oxf) 2013;78:466-71.

SUMMARY

Background

Early in normal pregnancy, thyroxine demands increase by 30% to 50%, and these demands are easily achieved in women not affected by thyroid pathology. The objective of these authors was to study a representative group of women of the U.K. population on thyroxine-replacement therapy to assess the pattern of serum TSH determination before and during pregnancy and the proportion of women who have their dose of thyroxine adjusted according to the recommendation of recently published guidelines.

Methods

Population

Health care data on pregnant women in Tayside, Scotland. Five principle databases were used to identify pregnant women on thyroxine therapy in the study population. These databases covered primary, secondary, and private health care. All pregnant women who were 18 years or older and who delivered between January 1, 1993, and March 31, 2011 in Tayside were identified. Patients were included in the study if they had at least three thyroxine prescriptions prior to pregnancy, at least one of which was within 6 months prior to pregnancy. The main outcome study was the number of TSH assays performed during pregnancy and the changes in dosage of thyroxine pre-

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scribed during pregnancy; the main analysis was performed using TSH trimester-specific ranges (0.4 to 2.5 mU/L in the first trimester and 0.4 to 3.0 mU/L in the second and third trimesters). Gestation was confirmed with either first- or early-second-trimester ultrasound scan.

The mean (±SD) age of these women was 32.1±5.2 years. The percentage of pregnant women who were prescribed thyroxine increased from 0.4% (95% CI, 0.3 to 0.7) in 1994 to 2.3% (95% CI, 2 to 3) in 2010

Results

The authors identified 950 pregnant women who had thyroxine prescribed prior to pregnancy. Overall, 96.9% of these women had at least one TSH assay performed during or just prior to pregnancy, 81.2% of them in the first trimester. In the first trimester, of 423 (55%) women who had elevated TSH, only 18 (4.3%) had at least one low FT_4 or T_4 level. Low or suppressed serum TSH was detected in about 15% of women in the last 2 months before conception or in the first trimester. In women with an elevated serum TSH in the first trimester, thyroxine dosage was increased in only 39.2%. There was a significant decrease in the median serum TSH during pregnancy—2.5 mU/L at 6 weeks, 2.6 mU/L at 12 weeks and 1.4 mU/L at 24 weeks, representative of active adjustment of the levothyroxine dose.

Conclusions

Many patients on long-term thyroxine therapy had a TSH above the reference range during pregnancy and especially, 55% of them, during the first trimester of pregnancy. Serum TSH concentration declined during pregnancy, reflecting active management. However, the decline in TSH occurs too late in pregnancy. It should be adjusted earlier.

ANALYSIS AND COMMENTARY

It is well established that in the first trimester of human pregnancy there is an increased demand for thyroid hormones, by about 30% to 50%. This increased demand is due to several factors, among them the half-life prolongation and increase in serum TBG level, an increase in renal iodine excretion, and the thyroid-stimulating effect of human chorionic gonadotropin. As a result of these changes, there is a slight FT_4 increase, albeit within the normal reference range, and a lowering of serum TSH, with a significant number of normal pregnancies with serum TSH values below 0.3 mIU/L and even with suppressed values. This increase in thyroid production provides transplacental passage of maternal thyroid hormones to the fetus, since the fetal hypothalamic–pituitary–thyroid axis is fully functioning only by 14 to 18 weeks of gestation. In women with normal thyroid-gland function, this increase in thyroid demand is easily compensated; however, women on thyroid-replacement therapy because of hypothyroidism (previous ablation or intrinsic thyroid disease) or those euthyroid women with chronic autoimmune thyroiditis, are at risk for hypothyroidism early in pregnancy, since the diseased or absent thyroid gland is unable to compensate for this increase in thyroxine demand. Even mild hypothyroidism in early pregnancy has been reported to affect maternal, obstetrical, and neonatal outcome, and motor and intellectual performance in their children, although not all the studies have consistent outcomes (1, 2). The most common maternal complications in women with hypothyroidism and even in euthyroid women with chronic thyroiditis are spontaneous miscarriages and preterm labor. Therefore, it is imperative to educate women of childbearing age who have thyroid disease and those on thyroid-replacement therapy about the importance if achieving an appropriate serum TSH level before contemplating pregnancy and to have the results of thyroid-function tests assessed shortly after conception. One study addressed the issue of thyroxine adjustment early after conception, with

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the recommendation to increase the thyroxine dose by about 25% of the prepregnancy dose (taking two extra doses of L-T_4) at the time of pregnancy diagnosis until thyroid-test results are available (3). In another study, the authors suggested keeping serum TSH around 1 mIU/L at the time of pregnancy planning, which will secure a serum TSH of <2.5 mIU/L in early pregnancy in almost 82.8% of the studied women (4). This concept could be applied to women on thyroxine-replacement therapy who are contemplating pregnancy, but not to those with euthyroid chronic thyroiditis. It is assumed that detecting and correcting hypothyroidism early in pregnancy would prevent pregnancy complications (5). As this and other studies have shown (6), over 40% of women on thyroxine-replacement therapy have a serum TSH above the trimester-specific reference range at the first obstetrical visit. Since the first obstetrical visit in the majority of women is after 8 weeks of gestation, prevention of hypothyroidism early in pregnancy should be a medical priority. Medical identification of these women is a public health necessity, similar to the identification of women in the prediabetic stage before conception. A proper medical and family history, along with detection of thyroid autoimmunity on physical examination (presence of goiter, vitiligo) and a determination of serum TSH and TPOAb will diagnose women with euthyroid thyroiditis who are at risk for hypothyroidism after conception. Since more than 50% of pregnancies in this country are unplanned, it will require a strong effort from our medical and obstetrical societies to provide patients and health care professionals proper medical education in order to avoid hypothyroidism early in pregnancy in women at risk.

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