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Iodine Supplementation in Euthyroid Pregnant Women Does Not Alter Maternal Free T₄ Levels

Elizabeth N. Pearce

Brucker-Davis F, Panaia-Ferrari P, Gal J, Fénichel P, Hiéronimus S. Iodine supplementation throughout pregnancy does not prevent the drop in FT₄ in the second and thirds trimesters in women with normal initial thyroid function. Eur Thyroid J 2013;2:187-194.

SUMMARY

Background

Observational studies have demonstrated that maternal hypothyroxinemia is associated with adverse neurodevelopmental outcomes in offspring (1,2). Hypothyroxinemia may result from iodine deficiency, but there are also physiologic alterations in free T₄ levels throughout pregnancy, and normal trimester-specific ranges for free T₄ are not well defined. The aim of this study was to determine how much of the decrease in maternal free T₄ after the first trimester of pregnancy is mediated by iodine deficiency. Mildly iodine-deficient, euthyroid pregnant women were randomly assigned to receive iodine supplementation and compared with a control group receiving no supplementation. Thyroid function was assessed throughout gestation.

Methods

This was a prospective, randomized trial in pregnant women. Women with a singleton pregnancy, with normal baseline thyroid-function tests (TSH <2.5 mIU/L and FT₄ above the 10th percentile) and negative TPO antibodies were enrolled between July 2007 and July 2008. All women were enrolled before 12 weeks of gestation. Women with baseline urine iodine concentrations ≥400 µg/L and women taking iodine supplements before the start of the study were excluded. A total of 111 women were randomly assigned to receive prenatal multivitamins with or without 150 µg/day of potassium iodide. All women received dietary instructions about optimizing iodine intake. Treatment was started at enrollment (median, 10 weeks of gestation) and continued through 3 months post partum. Pill counts were obtained at each visit. Thyroid-function tests, urinary iodine measurements, TPO antibodies, thyroglobulin anti-

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bodies, thyroxine-binding globulin (TBG), and serum thyroglobulin were obtained at enrollment, week 22, week 33, and 3 months postpartum. Thyroid ultrasound was performed at baseline, at week 33, and at the postpartum visit. Comparisons between groups were performed using χ^2 and Fisher's exact tests for categorical data and Mann-Whitney testing for continuous data.

Results

A total of 86 of the 111 women were followed until delivery, and 36 were followed to 3 months postpartum. Ten women taking iodine-containing supplements and only one woman in the control group dropped out because of nausea and vomiting. Median urinary iodine excretion was similar in the treatment and control groups at baseline (111 $\mu\text{g/L}$ vs. 103 $\mu\text{g/L}$), and 84% of

women in both groups reported using iodized salt. In the treatment group, urinary iodine increased to 161 $\mu\text{g/L}$ by the third trimester, whereas in the controls the urinary iodine concentration decreased to 76 $\mu\text{g/L}$ ($P < 0.001$). Free T₄ decreased by 15% in treated women and 21.6% in the controls between the first and second trimesters ($P = 0.27$), and then remained stable in the third trimester. Total T₄, free T₄, free T₃, TSH, TBG, and thyroid volume did not differ between groups at any time point. Serum thyroglobulin was lower in the treated group than in controls at the second-trimester and postpartum visits ($P < 0.01$).

Conclusions

Iodine supplementation in mildly iodine-deficient, antithyroid antibody-negative, euthyroid pregnant women did not alter maternal free T₄ levels.

ANALYSIS AND COMMENTARY ● ● ● ● ●

Serum free T₄ and free T₃ concentrations typically decrease after the first trimester of pregnancy. This is due, at least in part, to the fall in serum level of human chorionic gonadotropin (hCG), a stimulator of the thyroidal TSH receptor, after weeks 8 to 10 of gestation. In this study, an decrease of approximately 20% in free peripheral thyroid hormone levels was observed in both groups between the first and second trimesters, with no concomitant increase in TSH. The ratio of total T₄ to TBG followed the same pattern as free T₄, arguing against free T₄ assay artifact as a reason for the observed decline in free T₄. These data suggest that the free T₄ decline after the first trimester is physiologic, not pathologic, and is not the result of mild iodine deficiency. There is a need for trimester-specific, assay-specific reference ranges for free T₄ to guide clinical decision-making.

Strengths of the study include its randomized, prospective design and the fact that iodine supplementation was started relatively early in gestation. The supplementation dose of 150 μg of iodine daily is in agreement with ATA and Endocrine Society guide-

lines (3,4). However, results may not be generalizable to antithyroid antibody-positive women or to those with baseline hypothyroxinemia or TSH elevations, who might be more susceptible to the development or worsening of thyroid hypofunction in the setting of iodine deficiency. There was more gastrointestinal intolerance of iodine-containing prenatal multivitamins, leading to differential dropout, in the treatment group. It is important to note that effects of iodine supplementation on fetal and neonatal thyroid function and developmental outcomes were not assessed.

These data should not be interpreted as a reason to avoid iodine supplementation for iodine-deficient pregnant women. Even mild maternal iodine deficiency in pregnancy has been associated with deleterious effects on child cognition (5,6). In the present study, iodine supplementation prevented a rise in serum thyroglobulin levels, a marker for iodine deficiency, and normalized urinary iodine concentrations. Supplementation with 150 μg of iodine daily in mildly deficient regions has been demonstrated to be safe; supplementation should optimally be started before a woman conceives.

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