Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

WOMEN OF CHILDBEARING AGE MAY BENEFIT FROM IODINE SUPPLEMENTATION SEVERAL MONTHS BEFORE CONCEPTION

Moleti M, Di Bella B, Giorgianni G, Mancuso A, De Vivo A, Alibrandi A, Trimarchi F, Vermiglio F. **Maternal thyroid function in different conditions of iodine nutrition in pregnant women exposed to mild-moderate iodine deficiency: an observational study.** Clin Endocrinol (Oxf) 2011;74:762-8.

SUMMARY

BACKGROUND

In a previous study by the same research group (in a mildly iodine-deficient area in Italy), thyroid function in pregnant women who had regularly used iodized salt for at least 2 years before becoming pregnant was compared with that of women who began using iodized salt upon becoming pregnant. That study showed that prolonged use of iodized salt was associated with a very low prevalence of maternal thyroid insufficiency during pregnancy. Therefore, it could be speculated that a high percentage of women of child-bearing age is likely to have iodine levels that are inadequate for the increased needs during pregnancy unless they are supplemented. The aim of the study was to examine the effect of different conditions of nutritional iodine intake on maternal thyroid function throughout gestation in a cohort of healthy, antithyroid peroxidase antibody (anti-TPOAb)–negative women from a mild-to-moderately iodine-deficient area.

METHODS

The study comprised 433 anti-TPOAb–negative women; excluded were those who were taking thyroid medications, those who had started iodine supplementation later than the first trimester, those who had used prenatal preparations whose iodine content was not at least 150 µg, or those who reported intermittent use of iodine supplements. The information on iodine intake was obtained from a patient questionnaire. Three study groups were obtained: The 150-µg-iodine (150-I) group comprised 168 women. They introduced iodized salt into their diets upon becoming pregnant or some time prior to pregnancy and received a daily iodine supplement of 150 µg per day from early pregnancy (range, 6 to 12 weeks; median, 9) to term.

The iodized-salt (I-salt) group included 105 women who had regularly used iodized salt for at least 2 years prior to becoming pregnant.

The no-iodine (no-I) group comprised 160 women who disregarded recommendations about iodine supplementation. Therefore, none of these women were taking prenatal preparations containing iodine or regularly using iodized salt.

In assessing maternal thyroid function, the authors considered both serum free thyroxine (T_4) and thyrotropin (TSH) internal trimester-specific reference intervals, previously calculated in a cohort of consecutive healthy and anti-TPOAb–negative pregnant women. TSH, free triiodothyronine, and free T_4 were measured at each sampling, whereas TPOAb were tested at the first sampling only. Urinary iodine excretion (UIE) was obtained from sporadic samples.

RESULTS

There was no difference in age and parity between the three groups. Conversely, median UIE was higher in the 150-I group than in either the I-salt ($P<0.001$) or no-I ($P<0.0001$) groups, and consistent with a more adequate, although still insufficient, dietary iodine intake for pregnancy (estimated iodine intake, 200 µg per day). UIE significantly increased from the early first (67.2 µg/L) to the late third (133.7 µg/L) trimester in the 150-I group only ($P<0.001$).

Serum free T_4 concentrations declined over the course of the observation period in all groups. Overall, the extent of this decline was roughly the same (approximately 20%) in all three groups, irrespective of iodine supplementation. Free T_4 concentrations were consistently higher in the I-salt group than those in both the 150-I and the no-I groups. No difference in

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free T_4 concentrations could be observed between the 150-I group and the no-I group at any time.

During the first half of gestation, changes in TSH concentrations were similar in the three groups. After a prompt, although not significant, decline between the early and late first trimesters, serum TSH levels increased in all three groups, peaking between weeks 14 and 19. However, this increase was statistically significance only in the 150-I group ($P<0.05$). Thereafter, TSH concentrations plateaued until the end of pregnancy in all three groups. The lowest TSH concentrations were consistently observed in the I-salt group.

Prevalence of raised TSH and decreased free T_4: Overall, in 44 of 168 (26.2%) of the 150-I group, 16 of 105 (15.2%) of the I-salt group, and 47 of 160 (29.4%) of the no-I group, TSH values were found to exceed the trimester-specific upper limit. A comparison of the three groups showed the prevalence of raised TSH throughout pregnancy to be slightly higher in the 150-I group than in the I-salt group ($P = 0.048$; odds ratio, 1.97; 95% confidence interval, 1.05 to 3.72), but not different from that found in the no-I group ($P = 0.51$). The prevalence of decreased free T_4 over the course of pregnancy was 8.3%, 9.5%, and 20% in the 150-I, I-salt, and no-I groups, respectively.

CONCLUSIONS

The regular use of iodine-containing supplements proved effective in reducing the risk of inappropriately low free T_4 levels during pregnancy. The observed TSH increase in the 150-I group may be due to a transient stunning effect on the thyroid gland, occurring as a result of the abrupt increase in daily iodine intake. While the importance of gestational iodine supplementation is undisputed, the authors believed that in mild-to-moderately iodine-deficient areas, women considering conception should be advised to take iodine supplementation for several months prior to becoming pregnant. Given the large number of unplanned pregnancies, such a strategy would reasonably guarantee the adequate replenishment of maternal intrathyroidal iodine stores and prevent any possible adverse effect on the mother and fetus.

COMMENTARY

In euthyroid adults, the average daily iodine requirement is estimated to be about 95 µg per day, and the corresponding recommended nutrient intake for men and nonpregnant or lactating women is 150 µg per day (1). During pregnancy, the demand for iodine increases because of increased maternal TSH production, which occurs very early in gestation; the transfer of T_4 and iodide from the mother to the fetus; and a presumed increased loss of iodide through the kidney (2). Overall, these factors cause an estimated rise in the daily iodine requirement of at least 50% to 70%, with the recommended daily iodine intake for pregnant women of 250 µg per day. In a recent issue of *Clinical Thyroidology*, Elizabeth Pierce (3) commented on the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey studies on iodine status in the U.S. population and stated "the fact that pregnant women in the samples from these two surveys were mildly iodine-deficient is quite worrisome." Dr. Pierce concluded that until new studies identify particular U.S. women at risk for iodine deficiency, "all pregnant women are best advised to take a prenatal multivitamin containing 150 µg of iodine daily."

The study by Moleti et al. indicates that iodine supplementation should be started months, perhaps even 2 years before conception, to ensure a euthyroid state throughout pregnancy, avoiding potential relative mild hypothyroidism in women who start iodine supplementation after conception. The

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incidence of hypothyroidism in pregnancy is estimated to be around 4%, with most of the women having subclinical disease; the women who were detected were newly diagnosed or those with iodine deficiency (the incidence is very low in the United States), or about 40% of women who were on levothyroxine therapy at the time of the first obstetrical visit (4). It was shown that women on levothyroxine ($L\text{-}T_4$) therapy with a preconception serum TSH <1.3 mIU/L (5), attained a normal serum TSH (<2.5 mIU/L) at the first obstetrical visit. Therefore, it appears reasonable, until further studies confirm the work of Moleti et al., to advise all women in the United States who are of reproductive age to add an extra 150 µg of iodine daily to their regular diet, and in addition to advise those on $L\text{-}T_4$ therapy to maintain their serum TSH levels at not more than 1.3 mIU/L. The exception is women who have undergone thyroidectomy for thyroid cancer, who usually require a lower serum TSH level. As we all know very well, unplanned pregnancy is not a rare event in our daily practice.

— Jorge H. Mestman, MD

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