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Childhood Obesity and Increased Childhood Weight Gain Are Associated with an Increased Risk for Hypothyroidism and TPO Antibody Positivity in Adulthood

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Ong KK, Kuh D, Pierce M, Franklyn JA; on behalf of the Medical Research Council National Survey of Health Development Scientific Data Collection Teams. Childhood weight gain and thyroid autoimmunity at age 60-64 years: the 1946 British Birth Cohort Study. J Clin Endocrinol Metab. February 22, 2013 [Epub ahead of print].

SUMMARY

Background

In previous observational studies, complex associations between thyroid status and body weight have been described. Hypothyroidism causes modest increases in body weight, but obesity is also associated with increased levels of both TSH and serum T_3, which decrease with subsequent weight loss (1, 2). A recent study demonstrated a higher risk for TPO-antibody positivity in obese as compared with normal-weight adults (3).

Methods

This was a prospective observational cohort study using data from the UK Medical Research National Council Survey of Health and Development. A total of 2547 women and 2815 men were initially included in this cohort, representing a socially stratified sample of all births across the United Kingdom within a single week in 1946. Birth weights were recorded, and height and weight were measured at multiple time points between ages 2 and 64. At ages 60 to 64, a total of 3163 subjects were sent survey that included questions regarding diagnoses of thyroid disease and use of thyroid medications. Self-reported diagnoses of thyroid disease were validated by questionnaires sent to participants' primary care providers. In addition, thyroid-function tests (serum TSH, free T_4, and TPO antibodies) were obtained in 2143 participants at ages 60 to 64. In individuals with abnormal TSH and/or free T_4 values, free T_3 concentrations were also measured. Body-mass index (BMI), weight, and height were converted into standardized scores. Overweight/obesity at age 14 was defined as a BMI in the top decile. Weight gain between 0 and 14 years was adjusted for birth weight and by height gain from ages 2 to 14. Analyses were stratified by sex. Logistic regression was used to determine odds ratios for taking levothyroxine (L-T_4) and for having a thyroid disorder in those with and those without overweight/obesity at age 14 and by childhood weight gain. Cross-sectional associations between BMI and thyroid function at ages 60 to 64 among euthyroid participants were also assessed.

Results

At ages 60 to 64, 10.9% of women and 2.3% of men reported use of L-T_4. TPO antibodies were positive in 11.5% of women and 3.3% of men. Women who reported L-T_4 use had higher BMI and body weight at ages 60 to 64 than women not taking L-T_4 (BMI, 28.9 vs. 27.8; P = 0.04; weight, 75.9 kg vs. 72.8 kg; P = 0.03); this difference was not observed in men. The women taking L-T_4 also had higher body weights at all other time points assessed, starting at age 6. Body weight, but not BMI, was higher in TPO-positive than in TPO-negative women at ages 60 to 64 (75.3 kg vs. 72.4 kg; P = 0.04) as well as at earlier time points; this

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difference was not observed in men. In women, but not in men, greater weight gain between birth and age 14 was associated with an increased likelihood for L-T_4 use and for TPO antibody positivity at ages 60 to 64. The women who had been overweight or obese at age 14 were more likely to have positive TPO antibodies at ages 60 to 64, but were not significantly more likely to use L-T_4. In men, overweight or obesity at age 14 was associated with higher likelihood for L-T_4 use, but not for TPO antibody positivity, at ages 60 to 64. After adjustment for weight at age 14, there were no cross-sectional associations between adult weight or BMI at ages 60 to 64 and either L-T_4 use or TPO antibody positivity. Among the 1712 euthyroid, TPO antibody-negative individuals in the cohort, free T_4 was inversely associated with BMI, but there were no associations between BMI at ages 60 to 64 and serum TSH values.

Conclusions

This study demonstrates that in women, childhood overweight/obesity and more rapid childhood weight gain are associated with an increased risk for hypothyroidism and TPO antibody positivity later in life.

ANALYSIS AND COMMENTARY

An association between higher birth weight and adult hypothyroidism had previously been described in a single small study (4). Conversely, in a birth cohort study of 293 women in Finland, lower birth weight and lower weight in childhood were associated with higher risk for hypothyroidism as an adult (5). It is unclear why the results of the larger study by Ong and colleagues are discordant with the Finnish data. There is no clear mechanism to explain why childhood adiposity should predict thyroid dysfunction or autoimmunity. In addition, it is unclear whether effects of childhood obesity and weight gain on adult thyroid function and thyroid autoimmunity are truly sex-specific or whether there were simply too few cases of thyroid dysfunction in the men in this cohort to see associations.

Strengths of this study include its prospective design, representative study sample, and long length of follow-up. Limitations include the loss to follow-up of 28% of the initial cohort, incomplete questionnaire response rates, lack of interval thyroid antibody or thyroid-function measurements prior to ages 60 to 64, and the use of self-report (although validated in most cases by physician questionnaires) to ascertain L-T_4 use. Information about potential confounders, such as family history of obesity and of thyroid dysfunction, was not ascertained.

Rates of childhood obesity have more than doubled in children and tripled in adolescents in the past 30 years, with more than one third of U.S. children and adolescents considered overweight or obese in 2010 (6). These facts, together with the data of Ong and colleagues, suggest that there may be substantial increases in the incidence of hypothyroidism and thyroid autoimmunity in the United States over the next several decades.

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