

Deficits of Gastric Acid Secretion Impair Absorption of Thyroxine

BY DOUG BRUNK
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Patients with multinodular goiter required a thyroxine dosage increase of 22%-34% if they had impaired secretion of stomach acids, results from a large controlled study demonstrated.

The finding suggests that "normal gastric acid secretion is important for the subsequent intestinal absorption of thyroxine," wrote the researchers, led by Dr. Marco Centanni of the department of experimental medicine and pathology at La Sapienza University, Rome.

"Although the clinical importance of these findings is fairly clear, the mechanism by which intestinal absorption of thyroxine is impaired in patients with hypochlorhydria is unknown. We may only speculate that oral thyroxine is administered as sodium salt that is less lipophilic than the native hormone, which enters target cells both through passive diffusion and in a carrier-mediated, inhibitable way. In this respect, achlorhydria due to atrophic gastritis, the production of ammonia, or both, which are characteristic of [*Helicobacter*] *pylori* infection, may alter the ionization status and the conformational characteristics of the thyroxine molecule and thus the efficiency of intestinal absorption of the hormone."

The group studied 248 patients with nontoxic multinodular goiter who were seen at a referral center for thyroid disease between 1999 and 2004. Of the 248 patients, 53 also had *H. pylori*-related gastritis and 60 had atrophic gastritis of the body of the stomach (31 with evidence of *H. pylori* infection and 29 without such evidence). The remaining 135 patients had no gastric disorders and served as the reference group (N. Engl. J. Med. 2006;354:1787-95).

All patients received an initial thyroxine dose of 50 µg per day and were followed for at least 30 months. The researchers evaluated the thyroid-pituitary axis every 4

months and, if needed, increased the thyroxine dose until a low serum thyrotropin level was achieved on at least two consecutive measurements. The thyrotropin level was considered low if it was between 0.05 and 0.20 mU per liter.

The researchers also studied the levels of serum thyrotropin in 11 women diagnosed with *H. pylori* infection 4-19 months after the study began, and in 10 women diagnosed with gastroesophageal reflux disease after the study began. These 10 women were given omeprazole along with thyroxine. Serum thyrotropin levels continued to be measured after treatment with omeprazole began.

Compared with patients in the reference group, all patients who had impaired secretion of gastric acid required statistically significant increases in their daily doses of thyroxine to achieve low levels of serum thyrotropin. The median thyroxine dose required of the 53 patients with *H. pylori*-related gastritis was 125 µg per day, which was a 22% median increase from that of the referent group.

The median thyroxine dose required of the 60 patients with atrophic gastritis of the body of the stomach also was 125 mg per day, which was a 27% median increase from that of the referent group. (Those with evidence of *H. pylori* infection required a median thyroxine dose of 150 µg per day, a median increase of 34% from that of the referent group, while those without such evidence required a median thyroxine dose of 125 µg per day, a median increase of 24% from that of the referent group.) Serum thyrotropin levels rose variably in the cohort of 11 women with newly diagnosed *H. pylori* infection.

"In some patients, a slightly higher dose of thyroxine was needed to restore thyrotropin suppression," the researchers wrote. "Likewise, the increase in the level of serum thyrotropin was variable in patients treated with omeprazole, although the suppressive effect of thyroxine on thyrotropin disappeared in all patients and was restored only at a substantially higher dose of thyroxine." ■

Smoking Not Tied To Hypothyroidism

WASHINGTON — Smoking was associated with an increased risk of subclinical hypothyroidism but no increase in clinical disease in unpublished data from the Danish Investigation of Iodine Intake and Thyroid Disease.

Dr. Peter Laurberg, a professor of endocrinology at Aarhus University Hospital in Denmark, reported on 140 subjects with spontaneous hypothyroidism; 42 were current smokers, 47 were previous smokers, and 51 were nonsmokers. Of 559 healthy control subjects, 193 were current smokers, 147 were previous smokers, and 219 were nonsmokers. "So there seems to be, in this study, no effect of smoking on development of overt hypothyroidism," he said.

The study followed a cohort of individuals prior to mandatory iodine supplementation in Denmark in 2000 and involves a prospective registry of hyper- and hypothyroid patients.

In an examination of smoking and subclinical disease, 1,619 smokers had a nonsignificant odds ratio of 1.15 for having subclinical hyperthyroidism compared with 2,800 nonsmokers. Alternatively, smokers had an odds ratio of 0.47 for subclinical hypothyroidism.

One proposed mechanism for this observation is that the liver detoxifies the cyanide in smoke to give thiocyanate, which reduces iodide transport into the cell in a manner similar to decreasing iodine intake. The thyroid cells compensate by trying to pump more iodide into the cell. However, the upregulation of these processes produces peroxide. "So if you are deficient over a long period without being severely deficient ... you get a thyroid with irregular growth and function and necrosis," said Dr. Laurberg.

Smokers also might be protected against autoimmunity, as they have lower levels of thyroid autoantibodies than nonsmokers, said Dr. Laurberg.

—Kerri Wachter

Biannual Dietary Counseling Improves Pediatric Outcomes

BY SHERRY BOSCHERT
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Giving families of infants and children individualized dietary counseling twice a year reduced the children's intake of fat and improved their insulin sensitivity by age 9 in a long-term randomized study.

The ongoing Special Turku Coronary Risk Factor Intervention Project for Children, a Finnish study, randomized healthy 7-month-old infants in 1990 to an intervention group (540 infants) or a control group (522 infants). The control group received the basic health education provided at well-baby clinics.

A physician and a dietitian provided individualized dietary counseling to the intervention group. Twice a year, families recorded what the child consumed for 4 consecutive days (including a weekend) within 3 weeks of the follow-up visit. The dietitian reviewed the list and suggested any changes needed to pursue a healthy diet low in saturated fat and cholesterol.

Clinicians recommend that children aged 3 and older get 55%-60% of energy from carbohydrates, 10%-15% from protein, and 30% from fat (with 10% or less

as saturated fat), reported Dr. Tuuli Kaitosaari of the University of Turku (Finland) and associates.

When the children reached age 7, the investigators took detailed laboratory measurements of a subset of 200 children seen consecutively for follow-up visits; of these, 167 also had blood samples taken at their 9-year follow-up visit. The 9-year-olds (78 in the intervention group and 89 in the control group) make up the current study population.

The children in the intervention group consumed significantly less total fat and less saturated fat than those in the control group. Scores on the homeostasis model assessment of insulin resistance (HOMA-IR) index at age 9 were lower in the intervention children, indicating better insulin sensitivity compared with controls (Diabetes Care 2006;29:781-5).

Multivariate analyses indicated that "our finding of decreased HOMA-IR in intervention children is to a large extent due to their lower saturated fat intake," Dr. Kaitosaari and associates said. Other factors that did not get measured in the study, such as exercise habits, also may partly explain the intervention's effect in lowering HOMA-IR scores, he added. ■

Consumption of Insoluble Fiber Boosts Insulin Sensitivity in Obese Patients

BY SHERRY BOSCHERT
San Francisco Bureau

Need another reason to help convince overweight and obese patients to have a healthy diet? A small, randomized, controlled study concluded that eating insoluble dietary fiber found in cereal, fruits, and vegetables improved insulin sensitivity, Dr. Martin O. Weickert reported.

Eating a diet high in insoluble fiber might be a safe, effective, and low-cost way to reduce insulin resistance in patients at risk of developing type 2 diabetes, said Dr. Weickert and his associates (Diabetes Care 2006;29:775-80).

Eating cereal fiber has been associated with a reduced risk of developing cardiovascular disease and type 2 diabetes in epidemiologic studies, but the underlying mechanism was not clear, said Dr. Weickert of the German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany.

Seventeen overweight or obese women with normal glucose metabolism and no serious health problems agreed to eat macronutrient-matched portions of bread at meal times, supplemented by standardized liquid meals, for 3 days. The

women were randomized to get oat fiber-enriched white bread or regular white bread, which served as the control. After a washout period of 7 days or more, the two groups crossed over to repeat the experiment using the other type of bread.

At the end of each 3-day period of bread eating, investigators measured whole-body insulin sensitivity and took blood samples. They conducted hydrogen breath tests to assess dietary adherence; previously they had shown that fiber consumption enhances colonic fermentation. The breath tests suggested that four women did not adhere to the study diet.

For the 17 women as a whole, 3 days of fiber-enriched bread significantly improved whole-body glucose disposal, equivalent to an 8% improvement in insulin sensitivity. Fasting insulin concentrations tended to be reduced after the days of fiber, an effect that might have been significant in a larger study, the investigators suggested.

A sub-analysis that excluded the four women who probably did not ingest the test meals found a highly significant improvement in whole-body glucose disposal after 3 days of fiber-fortified bread, equivalent to a 13% improvement in insulin sensitivity. ■