SELENIUM MAY PREVENT GOITER AND THYROID NODULES

Rasmussen LB, Schaumburg L, Kohrle J, Pedersen IB, Hollenbach B, Hög A, Ovesen L, Perrild H, Laurberg P. **Selenium status, thyroid volume, and multiple nodule formation in an area with mild iodine deficiency.** Eur J Endocrinol 2011;164:585-90. Epub January 17, 2011.

SUMMARY

BACKGROUND

Selenium plays an important role in the function of the thyroid gland. It is found in high concentration in the thyroid gland, is incorporated as selenocysteine into a number of antioxidant selenoproteins, and contributes to the antioxidant defense by protecting the thyrocytes from any excess hydrogen peroxide that is produced during thyroid hormone biosynthesis. The association between serum selenium concentration and thyroid volume and goiter development is controversial, with positive, negative, and no association reported.

METHODS

The objective was to study the associations between serum selenium concentration and thyroid volume, both before (C1) and after (C2) iodine fortification was introduced in Denmark. Additional objectives were: (a) to examine the association between serum selenium concentration and prevalence of thyroid nodules and (b) to investigate associations between serum selenium concentration and risk for enlarged thyroid gland.

Subjects were participants in the Danish Investigation of Iodine Intake and Thyroid Diseases (DanThyr) study. Two cross-sectional studies were carried out, the first (C1) in 1997–1998 and the second (C2) in 2004–2005. Two groups, one of women and one of men, were randomly selected: women 18 to 22, 40 to 45, and 60 to 65 years of age and men 60 to 65 years of age. Analyses were performed on 805 participants (405 from C1 and 400 from C2), from whom all the variables of interest were available

Thyroid ultrasounds before and after iodine fortification were interpreted by the same two sonographers. Thyroid enlargement was defined as a thyroid volume >18 ml for women and >25 ml for men, which corresponds to the mean +3 SD values in iodine-sufficient populations. The structure of the gland was classified as normal, diffuse (no registered nodules), solitary nodule >10 mm in diameter (one thyroid nodule), or multinodular (more than one thyroid nodule). In the event of more than three nodules in a lobe, only the three largest nodules were registered.

All participants were asked to give a urine sample that was analyzed for iodine.

Blood samples were obtained for measurement of serum selenium concentration. The limit of detection was 15 µg/L. Human serum concentrations typically range between 50 and 200 µg/L. Interassay variation was 7%, and intraassay variation was 5% during the determinations.

RESULTS

Thyroid volume decreased significantly from the first to the second cross-sectional study. Before fortification, thyroid volume was 12.5 ml, versus 11.9 after fortification ($P<0.05$). Urinary iodine excretion increased at the same time, 97 µg/day before fortification to 148 µg/day after fortification ($P<0.001$).

Median serum selenium concentration decreased slightly, but significantly, by 5% during this period. It was 99.2 µg/L before fortification and 95.0 µg/L after fortification ($P<0.05$). Iodine excretion and serum selenium concentration were weakly but significantly positively correlated ($r = 0.2$, $P<0.001$).

In the combined cohort, the serum selenium concentration was significantly negatively associated with thyroid volume. The significant negative association between serum selenium concentration and thyroid volume was found in the entire group of women, but did not reach significance in the subgroup of women 60 to 65 years of age. In men (all 60 to 65 years),

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there was no association between thyroid volume and serum selenium concentration).

The serum selenium concentration was significantly negatively associated with risk for enlarged thyroid gland; the association was significant before iodine fortification, but not after iodine fortification. Furthermore, the risk for an enlarged thyroid gland increased with lower serum selenium concentrations in women but not in men. Low serum selenium concentrations tended to increase the risk for multiple thyroid nodules of more than 10 mm in diameter. In contrast, serum selenium did not influence the risk for solitary nodules.

CONCLUSIONS

The serum selenium concentration has an effect on thyroid volume and probably multiple nodule formation in areas with mild iodine deficiency; however, the association is weak and appears to be confined to women. The results of the present study as well as some previous studies suggest that sufficient selenium intake is one of the environmental factors that may add to the prevention of goiter and thyroid nodules. Prospective intervention studies are needed to evaluate the potential role of selenium in patients suffering from goiter and thyroid nodularity.

COMMENTARY

The majority of the literature on the effect of selenium on thyroid hormone metabolism and of selenium supplementation therapy originates in Europe. As discussed by the authors, the role of selenium supplementation in preventing goiter or reducing thyroid volume is controversial, perhaps sex- and age-dependent, and related to iodine in the diet. Two recent studies demonstrated the beneficial effect of selenium supplementation in reducing thyroid peroxidase (TPO) antibody titer in women with Hashimoto's thyroiditis. In one study from Greece, l-selenomethionine 200 µg a day given for 12 months caused a significant decrease in serum anti-TPO levels in the first 6 months of treatment, with an additional 8% decrease when the treatment was extended for another 6 months, while withdrawal of the drug caused a 4.8% increase in anti-TPO concentrations (1). In a study from Italy, selenium, 200 µg daily, was given to women during pregnancy and the postpartum period, who were then compared to control pregnant TPO-positive women who were being given placebo therapy. Postpartum thyroiditis and permanent hypothyroidism were significantly lower in the group receiving therapy as compared with the control group (28.6 vs. 48.6%, $P<0.01$; and 11.7 vs. 20.3%, $P<0.01$, respectively) (2). Let me add a note of caution on the potential adverse effects of selenium supplementation. During a mean (±SD) follow-up of 7.7±2.7 years in a group of persons without diabetes who were receiving selenium supplementation or placebo, type 2 diabetes developed in 58 selenium recipients and in 39 placebo recipients (hazard ratio, 1.55; 95% confidence interval, 1.03 to 2.33). The conclusion by the authors was that selenium supplementation does not seem to prevent type 2 diabetes, and it may increase the risk for the disease (3).

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