INCREASED DIETARY INTAKE OF NITRATE MAY CAUSE THYROID CANCER IN MEN

Kilfoy BA, Zhang Y, Park Y, Holford TR, Schatzkin A, Hollenbeck A, Ward MH. **Dietary nitrate** and nitrite and the risk of thyroid cancer in the NIH-AARP Diet and Health Study. Int J Cancer 2011;129:160-72. doi: 10.1002/ijc.25650. Epub November 18, 2010.

BACKGROUND

The incidence of thyroid cancer has been increasing during the past few decades. Ionizing radiation is the only well-established causative factor. The present study considered the possibility that nitrate and nitrite intake could play a role, based on the fact that nitrate competitively inhibits iodide transport into the thyroid gland. Also, nitrate is reduced to nitrite by oral bacteria, and nitrite reacts with amines and amides in vivo to form nitrosamines and nitrosamides that are potent carcinogens for animals.

METHODS

The authors used a database of the NIH-AARP Diet and Health Study that was initiated in 1995–1996 when an extensive baseline questionnaire was mailed to 3.5 million AARP members 50 to 71 years of age. A total of 567,169 questionnaires were determined to have been satisfactorily completed. The nitrate and nitrite content of over 3000 foods was determined by review of the literature. Based on a food-frequency questionnaire, the nitrate and nitrite intake of each person was calculated. The major contributors to nitrate intake were lettuce, spinach, and broccoli, and the major contributors to nitrite intake were cold cuts, pasta, and bread. A total of 370 cases of thyroid cancer were identified in this population during a 7-year span, 200 in women and 170 in men; 70% were papillary cancers.

Clinical

THYROIDOLOGY

RESULTS

The incidence of thyroid cancer was 17 in 100,000 patient-years. The mean dietary nitrate intake was 88 mg/day and the mean nitrite intake was 1.2 mg/day. Among men in the highest quintile of nitrate intake, there was a 2.3-fold increased risk of thyroid cancer (95% confidence interval [CI], 1.3 to 4.0). There was a 3-fold increased risk of follicular thyroid cancer in men in the highest quartile of nitrate intake, but this was not found in women. Nitrite intake was associated with an increased trend for follicular thyroid cancer in men but not in women. A borderline significant interaction was found for smoking status and nitrite intake in women with a nonsignificant trend for thyroid cancer in the highest quintile of nitrate and nitrite intake.

CONCLUSIONS

Among men, increasing nitrate intake was positively associated with thyroid cancer, with a relative risk of 2.3 for the highest quintile versus the lowest (95% CI, 1.3 to 4.0), but there was no significant trend with intake among women. Nitrite intake was not associated with risk of thyroid cancer for either men or women.

COMMENTARY • • • • • • • • • • • • • • • • •

Studies to explain the increasing incidence of thyroid cancer are worthwhile. The hypothesis tested by this study is based on the finding that nitrate competitively inhibits iodide uptake by the thyroid. Furthermore, reduced iodide uptake causes increased thyrotropin stimulation, and this could promote thyroid carcinogenesis. Studies with cultured cells that contained the sodium-iodide symporter showed that nitrate has about one eighth the affinity of iodide for the symporter (1). Although thiocyanate generated from smoking was thought to be the main anionic inhibitor of iodide uptake (1), nitrate could also play a significant role. Because the main source of dietary nitrate is leafy vegetables, it is possible that pesticides used in agriculture may be responsible for promoting thyroid cancer.

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The finding that higher nitrate intake increases the risk for thyroid cancer in men but not in women requires explanation. The same group found a significant association of nitrate intake with thyroid cancer in older women in Iowa (2) and could not offer an explanation for not corroborating this finding in the present larger study. I agree with the conclusion that the role of nitrate in thyroid carcinogenesis is worthy of further study.

– Jerome M. Hershman, MD

References

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