DOES IODINE CAUSE THYROID CANCER?

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One of the major public health accomplishments of the twentieth century has been the global iodization of salt with substantial reduction in iodine deficiency disorders (IDD), including thyroid nodules & goiters; hypo- and hyperthyroidism; and physical and mental retardation. Iodine supplementation, initially introduced in a few countries in the early part of the last century, was followed by more extensive projects since the 1960s; currently, it is estimated that more than 100 countries have salt iodization programs. Despite this apparent success, I-deficiency still persists in parts of Europe, much of Africa and in many areas of Asia.

WHO (World Health Organization) defines severe iodine deficiency as I intake < 20 mcg/day and adequate with I 100 mcg or more per day. Recommended daily iodine intake is around 90 mcg for children; 150 mcg for adults; and 250 mcg during pregnancy and lactation. Iodine intake is easily assessed by measurement of iodine concentration in a random urine sample (1).

During these decades of increasing iodine intake worldwide, population studies have demonstrated a significant rise in the incidence of thyroid cancer which led many experts to wonder if iodine is causally related to this increase. Davies & Welch were among the first to show that the incidence of thyroid cancer in the U.S. increased substantially during the past several decades (2). Other reports have also confirmed that worldwide the incidence of thyroid cancer significantly increased from 1.5 to 11.6 per 100,000 population in the last five decades (3). Most believe this major change is attributed largely to the widespread availability and application of sensitive imaging, mainly ultrasound, and partly due to introduction of better health screening programs. To be sure, some of this increase may be real, possibly caused by pollution, radiation, or other causes. These measures have resulted in the detection of small, incidental thyroid masses. Despite the huge increase in incidence, mortality from thyroid cancer has remained either mostly stable or marginally changed (4).

The discovery of small thyroid tumors, followed by surgical treatment, has led many to believe that we now both overdiagnose and overtreat small thyroid cancers (2, 3). Data show that 90% of these cancers are papillary thyroid carcinomas (PTC), frequently smaller than 2 cm, and associated with low morbidity (2).

The issue of iodine and thyroid cancer is further complicated by the fact that the rise in cancer incidence does not necessarily parallel iodine intake. For example, the increase in PTC incidence in the U.S. has occurred despite a decline in iodine intake largely due to less iodine in diet and increasing use of non-iodized cooking salts. And in Denmark, increased cancer incidence occurred while daily iodine intake remained stable, decades before iodized salt was introduced in 2000 (5). Moreover, in Iceland, a country with excess iodine intake, thyroid cancer is reported to also have increased (6). Animal studies have shown variable results, but seem to suggest that I-deficiency is a weak initiator but a strong stimulator of follicular cell-derived thyroid cancer. In a comprehensive review of the subject, Zimmerman & Galetti (1) concluded that "iodine deficiency acts as a promoter rather than as an initiator of thyroid carcinogenesis [...and] iodine excess appears not to be an initiator, but may be a weak promoter."

How could iodine deficiency cause thyroid cancer? One mechanism could be that chronic TSH stimulation in I-deficiency results in progressive thyroid follicular cell proliferation, leading to carcinogenesis. Alternatively, chronic thyroid cell stimulation may promote mutagenesis, resulting in mutations known that cause cancer. It is established that thyroid follicular cells are TSH-dependent, hence the rationale for using thyroxine therapy to suppress TSH in patients with differentiated thyroid cancer. Iodine deficiency is also known to be associated with an increased risk of follicular thyroid cancer and anaplastic cancer. Other molecular mechanisms may also be identified (7).

Facts are that, during the preceding several

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decades, iodine intake has increased worldwide and, at the same time, the incidence of small PTCs has increased. Is there a causal relationship here? The answer seems to be no. In some countries, the rise in cancer is associated with stable or decreased iodine intake. Ample evidence points to the fact that the rising incidence of thyroid cancer can be attributed mostly to small tumors detected by improved technology and population screening. And, animal studies show that low dietary iodine may act as a promoter but not initiator of thyroid cancer. Finally, increasing iodine intake seems to result in less aggressive thyroid cancers, PTC, and iodine deficiency is associated with more aggressive forms, such as follicular and anaplastic cancers in the general population.

In conclusion, I-deficiency may be a risk factor for follicular thyroid cancer. While iodine supplementation has been temporally associated with an increase in thyroid cancer incidence, a clear cause & effect relationship is not established. Therefore, we should continue global iodination programs and educate the public, as well as advocacy groups, that these efforts are not causing thyroid cancer.

Conflict of interest

The author declares that he has no conflict of interest.

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