

Comparative Screening for Thyroid disorders: in an iodine deficient community: A Retro prospective Study

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Received date: April 01,2017 ; Accepted date : September 09,2017 ; Published date: January 01,2018

Citation for this Article : M.Nasrollahzadeh, Comparative Screening for Thyroid disorders: in an iodine-deficient community: A Retro prospective Study. J. Endocrinology and Disorders Doi: [10.31579/2640-1045/015](https://doi.org/10.31579/2640-1045/015)

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Abstract

Thyroid disorders are conditions that affect the thyroid gland, a butterfly-shaped gland in the front of the neck. The thyroid has important roles to regulate numerous metabolic processes throughout the body. Different types of thyroid disorders affect either its structure or function.

The thyroid gland is located below the Adam's apple wrapped around the trachea (windpipe). A thin area of tissue in the gland's middle, known as the isthmus, joins the two thyroid lobes on each side. The thyroid uses iodine to produce vital hormones. Thyroxine, also known as T₄, is the primary hormone produced by the gland. After delivery via the bloodstream to the body's tissues, a small portion of the T₄ released from the gland is converted to triiodothyronine (T₃), which is the most active hormone. The function of the thyroid gland is regulated by a feedback mechanism involving the brain.

2 billion individuals worldwide have insufficient iodine intake, with those in south Asia and sub-Saharan Africa particularly affected. Iodine deficiency has many adverse effects on growth and development. These effects are due to inadequate production of thyroid hormone and are termed iodine-deficiency disorders. Iodine deficiency is the most common cause of preventable mental impairment worldwide. Assessment methods include urinary iodine concentration, goitre, newborn thyroid-stimulating hormone, and blood thyroglobulin. In nearly all countries, the best strategy to control iodine deficiency is iodisation of salt, which is one of the most cost-effective ways to contribute to economic and social development. When iodisation of salt is not possible, iodine supplements can be given to susceptible groups. Introduction of iodised salt to regions of chronic iodine-deficiency disorders might transiently increase the proportion of thyroid disorders, but overall the small risks of iodine excess are far outweighed by the substantial risks of iodine deficiency. International efforts to control iodine-deficiency disorders are slowing, and reaching the third of the worldwide population that remains deficient poses major challenges.

Introduction

Thyroid Disease

The thyroid is a butterfly-shaped gland located in the front of the neck just above the trachea. It weighs approximately 15 to 20 grams in the adult human. The thyroid produces and releases into the circulation at least two potent hormones, thyroxine (T₄) and triiodothyronine (T₃), which influence basal metabolic processes and/or enhance oxygen consumption in nearly all body tissues. Thyroid hormones also influence linear growth, brain function including intelligence and memory, neural development, dentition, and bone development (Larsen, 2003).

The thyroid gland produces T₄ and T₃ utilizing iodide obtained either from dietary sources or from the metabolism of thyroid hormones and other iodinated compounds. About 100 µg of iodide is required on a daily basis to generate sufficient quantities of thyroid hormone. Dietary ingestion of iodide in the United States ranges between 200 and 500 µg/day and varies geographically; ingestion is higher in the western part of the United States than in the eastern states. The specialized thyroid epithelial cells of the thyroid gland are equipped with a Na/I symporter that helps concentrate iodide 30 to 40 times the level in plasma to ensure adequate amounts for the synthesis of thyroid hormone. The iodide trapped by the thyroid gland is subsequently oxidized to iodine by the enzyme thyroid peroxidase. The iodine then undergoes a series of organic reactions within the thyroid gland to produce tetraiodothyronine or thyroxine (T₄) and triiodothyronine (T₃).

T₃ is also produced in other tissues such as the pituitary, liver, and kidney by the removal of an iodine molecule from T₄. T₄ is considered to be more of a pro-hormone, while T₃ is the most potent thyroid hormone produced. T₄ and T₃ are both stored in the thyroglobulin protein of the thyroid gland and released into the circulation through the action of pituitary derived thyrotropin (thyroid stimulating hormone or TSH). A normal individual produces from the thyroid gland approximately 90 to 100 µg of T₄ and 30 to 35 µg of T₃ on a daily basis. An estimated 80 percent of the T₃ produced daily in humans is derived from peripheral metabolism (5'-monodeiodination) of T₄, with only about 20 percent secreted directly from the thyroid gland itself. On a weight basis, T₃ is about 3 to 5 times more potent as a thyroid hormone than T₄ and is believed to be the biologically active form of the hormone.

Hyperthyroidism and hypothyroidism are common conditions that have life-long effects on health. About 5 percent of U.S. adults report having thyroid disease or taking thyroid medication. In a cross-sectional study of 2,799 well-functioning adults ages 70 to 79, 9.7 percent of black women, 6 percent of white women, 3.2 percent of black men, and 2.2 percent of white men reported a history of hyperthyroidism. In the same study, 6.2 percent of black women, 16.5 percent of white women, 1.7 percent of black men, and 5.6 percent of white men reported a history of hypothyroidism.

Hyperthyroidism has several causes. Graves' disease, the most common intrinsic cause, is an autoimmune disorder associated with the development of long-acting thyroid stimulating antibodies (LATS).

Single or multiple thyroid nodules that produce thyroid hormones can also cause hyperthyroidism. The use of excessive doses of the thyroid hormone supplement levothyroxine is also a common cause.

Definition of Screening and Casefinding

Screening can be defined as “the application of a test to detect a potential disease or condition in a person who has no known signs or symptoms of that condition at the time the test is done.” By this definition, screening with thyroid function tests may identify asymptomatic individuals as well as patients who have mild, nonspecific symptoms such as cold intolerance or feeling “a little tired.”

Thyroid Function Test

At the present time, serum-based tests available by immunoassay for measuring the concentration of thyroid hormones in the circulation include total (TT₄ and TT₃) and free (FT₄ and FT₃) hormone. In addition, direct measurements of thyroid hormone binding plasma proteins, thyroxine binding globulin (TBG), transthyretin (TTR)/prealbumin (TBPA), and albumin are also available. However, the thyroid test measurement that has the greatest utility for evaluating patients suspected of thyroid disease is the third-generation thyroid stimulating hormone (TSH, thyrotropin) assay. Most third-generation TSH assays today that can reliably detect differences of 0.02 µU/ml or better (interassay imprecision <20 percent) can easily distinguish both hyper- and hypothyroidism from euthyroidism (normal thyroid function) and may differentiate the patient suffering from the “euthyroid sick syndrome” from true hyperthyroidism. Other methods in thyroid testing include the measurement of thyroid gland autoantibodies, including antithyroid peroxidase (TPOab), antithyroglobulin (Tgab), and antibodies against the TSH receptor (Trab). All of these thyroid test methods are routinely available on automated immunoassay instruments located in most hospital and reference laboratories with tight (<10 percent) method between run coefficients of variation.

Thyroid Function Testing in the Elderly

The prevalence of both low and high serum TSH levels (with normal serum free T₄ results) is increased in elderly subjects compared with younger people. With respect to high serum TSH values, the increase is thought to represent an increased prevalence of autoimmune thyroiditis, especially in women, as will be discussed. The higher prevalence of low serum TSH values may be due to thyroid nodular disease or unrecognized non-thyroid illness.

Design

The first screening study where elderly subjects with varying amounts of iodine supply but from the same geographical and ethnographical region (Carpathian basin) were compared, and all hormone measurements and ultrasonography were performed by the same laboratory or person.

Patients

Nursing home residents were screened for thyroid disorders from: (A) an iodine- deficient area, Northern Hungary ($n=119$; median age 81 years; median iodine excretion (MIE) 0.065 µmol/mmol creatinine (equivalent to 72 µg/g creatinine); (B) an area of obligatory iodinated salt prophylaxis since the 1950s, Slovakia ($n=135$; median age 81 years, MIE 0.090 µmol/mmol creatinine (equivalent to 100 µg/g creatinine)) and (C) an abundant iodine intake area, Eastern Hungary ($n=92$; median age 78 years; MIE 0.462 µmol/mmol creatinine (equivalent to 513 µg/g creatinine)).

Measurements

TSH, T₄, free T₄, T₃, thyroglobulin (Tg), antibodies to Tg (AbTg) and to thyroid peroxidase (AbTPO), iodine excretion, ultrasonography of the thyroid gland.

Results

In regions A, B and C, the prevalence of unsuspected clinical hypothyroidism was 0.8%, 1.5% and 7.6% ($P = 0.006$), with all cases except one being antibody positive (Ab+). The occurrence of subclinical hypothyroidism was 4.2% in region A, 10.4% in region B and 23.9% in region C ($P<0.001$), but only 3 of 22 cases with subclinical hypothyroidism from region C were Ab-. The overall prevalence of Ab positivity (either antiTg+ or antiTPO+) was similar in the three regions (A, 19.3%; B, 24.4%; C, 22.8%). The occurrence of hyperthyroidism (clinical plus subclinical) was 3.4% in region A, 3.0% in region B and 0% in region C (not significant). The rate of elevated Tg levels was similar in the three regions. The prevalence of goitre was 39.4%, 16.4% and 12.2% ($P<0.001$), respectively in regions A, B and C. In euthyroid subjects the mean ultrasonographically determined thyroid volume was 21.9 ml in region A, 13.6 ml in region B and 15.1 ml in region C (ANOVA $F=5.76$; $P=0.0038$). There was no significant difference in the occurrence of cases with hypoechogenic echotexture of the thyroid gland.

Accuracy of Screening Tests

Screening for thyroid dysfunction can be done using a history and physical examination, antithyroid antibodies, or thyroid function tests, including various assays for TSH and T₄. Today the TSH test is usually proposed as the initial test in screening because of its ability to detect abnormalities before serum thyroxine and triiodothyronine levels are abnormal. When used to confirm suspected thyroid disease in patients referred to an endocrine specialty clinic, the sensitive TSH has a sensitivity above 98 percent and a specificity greater than 92 percent for the clinical and functional diagnosis.

The accuracy of a TSH when used to screen primary care patients has been difficult to evaluate. The greatest difficulty is in classifying a patient who has an abnormal TSH, normal T₄ and T₃ levels, and no evidence supporting thyroid disease on physical examination. Those who consider the TSH to be the “gold standard” determination of disease would define such a patient as a “true positive.” Others argue that patients who have an abnormal TSH but who never develop complications and never progress should be considered “false positives.” They argue that these patients happen to have TSH levels outside the 95-percent reference limits for the general population but never truly had a thyroid disorder.

Conclusions

The screening for hypothyroidism in nursing home residents living in iodine- rich regions is justified by the high prevalence of unsuspected clinical hypothyroidism. The high prevalence of antibody positivity in old age is independent of the iodine supply, but iodine supply has a determining role in the development of autoimmune hypothyroidism in the aged. Most cases of subclinical hypothyroidism in iodine- rich regions are not of autoimmune origin. In old age, hypoechogenic texture of the thyroid gland is not predictive of thyroid dysfunction.

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