Annals of Thyroid Research

Open Access

Austin Publishing Group

Special Article - Thyroid Gland

About Iodine and Salt Iodization in Brazil

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Received: April 14, 2020; **Accepted:** May 06, 2020; **Published:** May 13, 2020

Abstract

Iodine is an essential micronutrient present in very small quantities in the human body, with a fundamental action for the adequate synthesis of thyroid hormones, which are critical for cell differentiation, growth and metabolism. In the form of iodide, iodine is widely distributed in the environment, although in an irregular manner, occurring in abundant amounts in the oceans and in coastal areas and scarcely found on islands and mountains. The diet is the main source of iodine, whose intake varies according to the amount present in soil and water and according to eating habits. Governmental policies have been adopted to satisfy and guarantee the necessary daily supply of iodine, such as fortification of industrialized salt for domestic iodine consumption or addition to the bread commonly consumed in a given region, or the offer of iodized oil to the population, or even iodine supplementation through medications. One of the more significant metabolic problems due to dietary iodine deficiency is the presence of goiter (increased volume of the thyroid gland). In Brazil, since August 17, 1956, it is compulsory to iodize the salt used for domestic consumption. In 2013, ANVISA (a Brazilian governmental organ) changed the iodine concentration in industrialized salt from 20 to 60 mg/kg to 15 to 45 mg/kg salt in order to prevent thyroid diseases due to excessive iodine intake, since Brazilians ingest much salt in their diet. In 2007 we conducted a study for the assessment of iodine concentration in salt and urine samples of Ribeirão Preto schoolchildren and compared the values to the thyroid volume of these children. Iodine concentration was found to be above 100µg/L in urine in 100% of the urine samples and to be more than 300µg/L in 55.2% of the samples (values considered to be borderline by the WHO). No increase in thyroid volume was observed among these schoolchildren. In 2015, after the change of the regulation of salt iodination to 15 to 45 mg/kg salt, the study was repeated on schoolchildren of both sexes aged 8 to 10 years from the same schools studied in the previous investigation. We detected an improved standardization of iodine concentration in the salt samples delivered by the children, as well as a significant reduction of ioduria, with 10.9% of the urine samples showing less than 100µg/L and a 30.5% reduction of samples containing less than 300µg/L. An increase in thyroid volume of 7.9%, 5.19% and 0.85% was also observed in the 3 schools evaluated, respectively. This study suggests that is important to reavaluate the iodization situattion in Brazil.

Keywords: Iodine; Salt Iodization; Ioduria; Iodine deficiency; Goiter

Introduction

Iodine, from the Greek "iodes", which means "violet" [1], is an essential micronutrient present in very small quantities in the human body ($0.02285X10^{-3}$% adult body weight [2,3]. It is consumed in the water or in food as iodine (element with no charge) or iodide (ion with a negative charge), which is converted to iodine in the stomach.

Iodine is a fundamental nutrient for the appropriate synthesis of thyroid hormones, which are critical for cell differentiation, growth and metabolism. It represents 65% of the molecular weight of Thyroxine (T4) and 59% of Triiodothyronine (T3) [4,5]. In the iodide form, iodine is widely distributed in the environment, although in an irregular form, being found in abundant quantities in the oceans and coastal areas and in scarce amounts on islands and mountains [6].

The diet is the main source of iodine, whose plasma levels are also partially replaced by iodothyronine deiodination in the thyroid cells [6].

Iodine intake varies according to the quantity of iodine in the soil and water and to the eating habits of a given region [6].

The World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommend an iodine intake of 90 mg/day for children aged 0 to 5 years, of about 120 mg/day for children aged 6 to 12 years, of 150 mg/day for adults older than 12 years, and of 250 mg/day for pregnant and lactating women [7].

About 10% of ingested iodine is utilized by the thyroid in areas of iodine sufficiency and up to 80% is utilized in cases of iodine deficiency [8].

Most of the daily ingested iodine is eliminated through the urine as ioduria, which ranges from 100 to 300µg/L under normal intake conditions, and this excretion is a good indicator of dietary iodine intake [8].

Citation: Lúcia M. About Iodine and Salt Iodization in Brazil. Annals Thyroid Res. 2020; 6(1): 239-242.

The normal thyroid is the largest iodine reservoir in the organism, containing about 5 to 10 mg iodine, and functions as a reservoir of hormone and iodized thyrosines, being able to protect the organism from iodine deficiency for a certain period of time [9].

In the presence of iodine deficiency, the thyroid adapts by increasing its uptake with an initially diffuse increase in glandular mass which tends to become nodular in cases of chronic deficiency and by inducing preferential T3 secretion and increased TSH synthesis and release [10-13].

Excessive iodine intake on a chronic basis is also harmful, triggering goiter, chronic thyroiditis and subclinical hyperthyroidism in the exposed population [14,15].

The synthesis of thyroid hormones involves the following steps and utilizes the following proteins [16-20]:

1) Stimulation of follicular thyroid cells by TSH (Thyrotropin Hormone) at the TSH receptor protein site

2) Active iodine transport through the basement membrane into the follicular thyroid cells, with a concentration of intracellular iodine about 20 to 50 times higher than in plasma. This is an active process that uses the Sodium Iodide Symporter (NIS) which functions as a pump, co-transporting one iodine ion together with two Na^{+9} (sodium) ions and using the energy generated by Na^+/K^+ ATPase, which maintains a low concentration of intracellular Na^+. NIS also transports other ions such as pertectanate (TcO_4^-), Sulfocyanide (SCN^-), Perchlorate (CIO_4^-), and Nitrate (NO_3^-). Iodine transport by NIS is stimulated by TSH and by a mechanism of self-regulation, with NIS activity varying in an inverse manner in relation to intraglandular iodine concentration

3) Inside the follicular cells, iodine is transported to the colloid, an action performed by the protein pendrin, which acts as an iodine/chloride transporter

4) Iodine organification, whereby iodine is rapidly incorporated into the tyrosine residues of Thyroglobulin (Tg), a glycoprotein representing the principal content of colloid) by Hydrogen Peroxide (H_2O_2), a reaction catalyzed by the enzyme Thyoperoxidase (TPO)

5) Coupling of the iodotyrosine molecules in Tg forming the iodothyronines T3 and T4 through the action of Thyroperoxidase (TPO).

The processes of iodine oxidation and organification and the coupling reaction of iodotyrosines are catalyzed by TPO, which utilizes the H_2O_2 produced by the hydrogen peroxide generator proteins, NADPH-oxidase – the thyroid oxidase (ThOx 1 and ThOx 2) which are two dual oxidases (DUOX 1 and DUOX 2, the latter being more efficient for H_2O_2 production)

6) Colloid endocytosis, Tg proteolysis and release of free iodothyronines (T3 and T4)

7) IIntrathyroidal Deiodization of Monoiodoyrosine (MIT) and Diiodotyrosine (DIT) by the enzyme dehalogenase (DEHAL-1)

Before T4 secretion, part of it undergoes intrathyroidal deiodination and forms T3, increasing the quantity of released T3 and rendering the hormone synthesis more efficient.

The total plasma T4 content is about 45 times higher than the content of T3, with the main source of T3 production being the conversion of T4 to T3 by a deiodase enzyme in peripheral tissues.

Government policies are adopted in order to satisfy and guarantee the necessary daily supply of iodine, such as iodine fortification of industrialized salt for domestic consumption or the addition of iodine to bread in a given region, the offer of iodized oil to the population, or even iodine supplementation through medications.

One of the most significant metabolic problems due to dietary iodine deficiency is the presence of goiter (increased volume of the thyroid gland).

In 1918, when the United States of America were preparing to enter World War I, an examiner for the selection of soldiers in Hugoton County, Michigan, rejected about 30% of the potential recruits due to the presence of goiter and/or hypothyroidism. A study conducted at that same time on schoolchildren in the state of Michigan detected about 47.2% of the children examined with signs/symptoms of goiter and severe thyroid dysfunction [1].

At that time there was some debate about the severity of the situation around the belt of the American Great Lakes and about the iodine deficiency in that region. It was proposed to offer the children iodized syrup about 2 to 3 times a year, but that policy proved to be inadequate. In Rochester, New York, the proposal of adding iodine to the water consumed by the population of the city also failed [1].

In 1922, David Murray Cowie, a pediatrician at the University of Michigan, entered the fight against goiter by monitoring children with severe hypothyroidism and important intellectual damage leading to mental deficiency. One day, he had the opportunity to read a long monograph about the health authorities of Switzerland, another part of the world with iodine-deficient soil, which described a plan for the prevention of goiter by adding a specific amount of sodium or potassium iodide to the salt for domestic consumption commercially sold in the country. Cowie believed that, since everybody uses salt for the preparation of daily foods, he could convince the salt industries to change their product by adding iodine to it, a measure that could solve a serious public health problem. However, this proved not to be very easy and two years of intense work and education would be needed in order to obtain an effect [1].

Cowie was able to achieve the result that iodine would be added to virtually all salt processed in and around the state of Michigan and also that the chemist of Dow Chemical Company would demonstrate that the small quantity of iodine added to salt (about 0.1% of the total content) did not alter the flavor or function of salt [1].

Cowie, known since then as the "salt man", convinced the medical class that adding iodine to salt would not increase the risk of hyperthyroidism or heart damage. Working with a competent medical team, he was able to obtain a referendum from the Medical society of the state of Michigan regarding the use of iodized salt and, in addition, he traveled around the country offering public health lectures for the prevention of goiter and hypothyroidism with the use of iodized salt. Iodized salt started to be progressively commercialized throughout the country and the salt industry voluntarily switched to

the production of only iodized salt [1].

Attempts to solve the problem of chronic iodine deficiency in Brazil were based on federal laws and decrees indicating the mandatory addition of iodine to salt, although the objective was not fulfilled. Thus, in 1980, there were about 17 million Brazilians with endemic goiter due to iodine deficiency in the country [11].

Legislation concerning iodine addition to the salt consumed by the Brazilian population:

Law nº 1944 of August 14, 1953- makes it mandatory to iodize salt for human consumption in areas of endemic goiter [12].

Decree nº 39814 of August 17, 1956- delimits the areas of endemic goiter, extends iodination to the entire national territory and attributes to the Ministry of Health the responsibility for the importation of iodized supplements [13].

Law nº 6150 of December 3, 1974- revokes law nº 1944 of 1953, fixes at 100 mg/kg the iodine content of salt for human consumption, transfers the onus of iodination to the private initiative and determines that its enforcement be done by the states, territories and municipalities [14].

Decree nº 75697 of May 6, 1975- establishes quality and identification standards for salt destined to human consumption [15].

Decree nº 80563 of October 20, 1977- regulates the quality and presentation of salt for animal consumption [16].

Ministry order (MS) nº 1806 of October 24, 1994- increases the iodine content of the salt for human consumption to 40-60 mg/kg [17].

Law nº 9005 of March 14, 1995- determines that the Ministry of Health should establish the correct proportion of iodine in the salt consumed in Brazil and authorizes the supply of iodate to salt processing industries [18].

Resolution RDC 130 (ANVISA) of May 26, 2003- reduces the concentration of iodine in salt for human consumption to 20 to 60 mg/kg salt [19].

Resolution RDC nº 23 (ANVISA) of April 24, 2013 – provides for the iodine content of salt intended for human consumption and other measures. It reduces the iodine content of salt for human consumption from 20 to 60 mg to 15 to 45 mg/kg salt [20].

Case Series and Results

In 2007 a study was conducted in Ribeirão Preto, São Paulo state, on 300 schoolchildren of both sexes ranging in age from 8 to 10 years, from 3 schools of different socioeconomic levels (SCHOOL 1- lower level, SCHOOL 2- intermediate level, and SCHOOL 3- higher level). Iodine concentration was determined in samples of industrialized salt for domestic consumption provided by the children (The Ethics Committee of UNAERP – Project 063/06. Also, iodine concentration was determined in a casual urine sample obtained from the children and compared to their thyroid volume. In 2007, a marked discrepancy was observed among the iodine concentrations in the salt samples. Ioduria of more than 100µg/L was detected in all samples, and ioduria of more than 300µg/L (values considered to be borderline by the WHO) was detected in 55.2% of the samples. No increase in thyroid volume was detected in these schoolchildren [21-30]. In 2015, after a change in the regulation of salt iodination for domestic consumption from 20-40 mg I/kg salt to 15 to 45 mg I/kg salt due to the fact that ANVISA (the regulating governmental organ) considered that Brazilians ingested much salt and consequently much iodine with an increase in thyroid dysfunction [14,15-30], the study was repeated on 295 schoolchildren of both sexes aged 8 to 10 years from the same previously studied schools (The Ethics Committee of UNAERP- Project Plataforma Brazil – CAAE 37604700005498) . We observed an improved standardization of iodine concentration in the salt samples delivered by the children, as well as a significant reduction of ioduria, with 10.9% urine samples showing less 100 µg/L and a 30.5% reduction of samples containing more than 300 µg/L. Increased thyroid volume was also observed in 7.9%, 5.19% and 0.85% of children from SCHOOLS 1, 2 and 3, respectively [31-38].

Conclusion

Despite the limitations of the present study, it suggests the need to reevaluate the iodine situation in Brazil.

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