Review article

Overview of Iodine Intake

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Abstract

Iodine is an essential element for human health. Food is the primary source of iodine, but the iodine content of local foods depends on the iodine content of the soil. Therefore, a low iodine concentration in soil and water results in plants and animals with low iodine content. Numerous effects of iodine deficiency on growth and development are known as iodine deficiency disorders. Iodine deficiency has been identified as the most common cause of brain damage in the world and is linked to its effects on infant and child growth and development. Supplementation of table salt with iodine was introduced in the 20th century. Croatia was one of the first countries to introduce the supplementation of table salt with potassium iodide at a concentration of 10 mg/kg in 1953 and 25 mg/kg in 1993. In 2003, the Croatian population reached iodine sufficiency, but given the excessive salt intake (11.6 g/day) and additional sources of iodine in the diet, the question arises, are we consuming too much iodine? This article gives a short overview of iodine intake.

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Discovery of iodine and history of iodine supplementation

Purple vapour was first discovered in 1811 by the chemist Courtois during the production of saltpeter. The production of saltpeter required soda, which was obtained from the ashes of seaweed. The chemical reaction required to make saltpeter resulted in the formation of insoluble material at the bottom of metal vats. The material was cleaned out using acid and heat, which led to purple vapour crystallising on the bottom of the vats. However, iodine was only discovered two years later by Sir Humphry Davy and Gay-Lussac (1). The use of iodine in medicine started in 1819 with Coindet, a physician from Geneva who administered a tincture of iodine to goitre patients, which resulted in the swelling going down within a week. The link between iodine and the environment was not confirmed, although the French chemist Chatin proved that the iodine content in water and food was insufficient in the areas commonly affected by goitre. The first paper on the link between iodine deficiency and goitre was published in 1851 (2). Chatin's discoveries on the link between environment and iodine deficiency were neglected until the end of the 19th century. In 1896, the presence of iodine in the thyroid gland was discovered by Baumann and Roos (3). Switzerland was the first country to introduce iodine as prophylaxis against goitre and cretinism. Since 1922, Switzerland has had a continuous program of supplementation of salt with iodine, with the level of iodine eventually being raised from 15 mg/kg in 1980 to 20 mg/kg in 1998 (3, 4).

Role of iodine, iodine deficiency disorders and optimal iodine intake

The thyroid gland of a healthy adult stores 70-80% of the total iodine content in the body, which ranges from 15 to 20 mg. It also uses about 80 µg of iodine per day for the synthesis of thyroid hormones. Iodine is essential for the synthesis and production of thyroid hormones (triiodothyronine – T3 and thyroxine – T4) and for normal thyroid function. The thyroid hormones control the metabolic processes in our body. Their production is controlled and influenced by the pituitary gland and its hormone thyrotropin (thyroid-stimulating hormone – TSH). TSH increases the uptake of iodine from the blood into the thyroid gland and stimulates the production of thyroid hormones, which is regulated through feedback. When the level of thyroid hormones in the blood is low or decreases, increased TSH is released from the pituitary gland. TSH stimulates the function of the thyroid gland, causes cell growth and proliferation of thyroid tissue, and, in case of chronic iodine deficiency, can lead to an enlargement of the thyroid gland known as a goitre. Goitre is one of the most common diet-related diseases (5). In addition, when iodine intake is very low, thyroid hormone production decreases despite elevated TSH levels, leading to hypothyroidism (6, 7). Numerous effects of iodine deficiency on growth and development are known as iodine deficiency disorders. Iodine deficiency has been identified as the most common cause of brain damage in the world and it is related to its impact on the growth and development of infants and children (8,9).

Table 1. Recommended daily intake of iodine (12)

	Children 0-5 years	Children 6-12 years	Adults	Pregnant and lactating women
Intake (µg)	90	120	150	250

The spectrum of iodine deficiency disorders includes mental retardation, hypothyroidism, goitre and varying degrees of other growth and developmental disorders (10). Chronic iodine deficiency is also associated with an increased risk of developing follicular thyroid cancer (11).

According to Zimmerman and Andersson, the recommended daily dietary intake for iodine is as shown in Table 1.

Iodised salt regulations

One of the greatest public health challenges worldwide is the lack of essential vitamins and minerals in the daily diet. This issue is widespread among women and young children in low- and middle-income countries (13). This can lead to serious health issues and economic consequences, which only adds to the global burden of disease (14,15). This also applies to iodine and the issue of high prevalence of disorders caused by insufficient iodine intake (16). To overcome this issue, many national nutrition strategies started promoting programs to eliminate iodine deficiency disorders in the 1990s, after the World Summit for Children and the Joint United Nations Children's Fund (UNICEF)/WHO Committee on Health recognised the benefits of iodisation of table salt (17-19). Iodisation of salt has been recognised as the best preventive measure to eliminate iodine deficiency disorders at the population level (20). Not only is the iodisation of salt technically feasible, but salt is also consumed in standard quantities by all segments of the population worldwide (21).

Between 1942 and 2021, 123 countries worldwide established a legal framework for mandatory iodisation of table salt and 21 countries introduced legislation for voluntary iodisation of table salt (22). According to estimates made by UNICEF, an average of 88.7% of households worldwide consumed table salt with some form of iodine in 2021. Most households using iodised table salt are in the East Asia and Pacific region (92%) and in South Asia (89.9%) (23). On the other hand, there are also countries with excessive iodine intake, such as South Korea (449 µg/L), Djibouti (335 µg/L), Cameroon (>300 µg/L), Honduras (356 µg/L) and Colombia (407 µg/L). The reasons for the increased iodine concentration are related to diet, groundwater and drinking water, which are naturally rich in iodine, as well as to high amounts of iodine added to salt considering the per capita intake of salt (22).

Although the legal regulations on compulsory or voluntary iodine intake via table salt have greatly reduced the issue of iodine deficiency disorders, there are still regions where almost one billion people do not have access to iodised table salt(22). One way to ensure the necessary supply of iodised table salt for such persons is to promote the Universal Salt Iodization (USI) Initiative, which is one of the most economical, convenient and effective strategies to increase the intake of iodised table salt (24). The initiative could be improved through cooperation between relevant stakeholders at local, regional and national levels, in the food industry and in the scientific community. Nowadays, EU member states introduce various strategies and legal frameworks to combat iodine deficiency, but there are still countries such as Norway (75 µg/L), Finland (96 µg/L) and Germany (89 µg/L) that are deficient in iodine from table salt (22). To combat iodine deficiency, it is necessary to identify potential barriers and adopt a uniform approach to the development of a single regulatory framework at the EU level based on the guidelines of WHO, without exception. Furthermore, such a uniform approach should allow national governments to implement measures in line with their culture and to remove barriers to marketing for the purpose of raising awareness of iodine deficiency disorders among the general public (25).

1. *Dietary sources of iodine and fortification of salt with iodine*

Unlike most essential nutrients, the status of iodine in our body is not related to socioeconomic factors, but rather to the climate in which we live(16). The iodine content of local foods depends on the iodine content in the soil. Therefore, a low concentration of iodine in the soil and water will result in plants and animals with low iodine content. Most of the iodine on our planet is found in the oceans. Also, the iodine content in the soil varies depending on the region. If the soil is older and more exposed to external factors, it is more likely that iodine will be washed out by soil erosion. People who depend on local foods produced in iodine-deficient areas must also rely on foods fortified with iodine(26, 27). Humans receive iodine through food, food supplements and water, mainly in the form of iodide (27, 28). Iodine concentrations vary both between food groups and within the groups themselves. Foods containing iodine include seafood, eggs, milk and dairy as well as iodised salt. The iodine content of milk and eggs depends on how animals are fed (iodine-enriched feed) and on the hygiene on the farm (28). The natural iodine content in most foods and beverages is low, and the most commonly consumed foods provide 3 to 80 µg per meal (5). In Croatia, all table salt used for food is iodised by adding 25 mg of iodine per kilogram of salt in order to prevent diseases related to insufficient iodine intake and Croatia is recognised as an iodine sufficient country (29, 30). The urinary iodine test is a well-known, inexpensive and easily accessible method of determining iodine status (31). A nationwide project named Epidemiology of Hypertension and Salt Intake (EH-UH 2) is currently active in Croatia. One of its main objectives is to determine iodine intake from a 24-hour urine sample and to assess whether there is a risk of exposure to low iodine concentrations if the recommended daily salt intake limit of 5 grams is observed (Strategic Plan for Reduction of Salt Intake) (32, 33).

Iodine toxicity

Excessive iodine intake usually occurs when people take iodine supplements to improve thyroid function. Several types of seafood, including shrimp, cod, tuna and seaweed, are rich in iodine. In cultures where a lot of seaweed is eaten, people sometimes consume thousands of milligrams of iodine per day. It is estimated that people in Japan consume between 1,000 and 3,000 mg of iodine daily, mainly from seaweed. This leads to iodine-induced hyperthyroidism and goitre in Japan. However, the same research also points out that the higher iodine intake may play a role in the low cancer rates and high life expectancy in Japan (8). Exceeding the maximum permissible amount of iodine can lead to poisoning and iodine toxicity may eventually lead to iodine goitre, hypothyroidism, or myxoedema (35). Also, excessive iodine intake can have a negative impact on patients with breast cancer due to the stimulation of the transcriptional activity of oestrogen receptor α (ER-α), resulting in an elevated risk of developing thyroid cancer (36). Chronic toxicity develops only if iodine intake exceeds 2 mg/day. In some sensitive individuals, ingestion of iodine-containing substances may lead to thyroid dysfunction due to high iodine exposure. Under certain circumstances, excessive iodine intake can have harmful effects on the thyroid gland after just one exposure to an iodine-containing substance (35). Patients with iodine deficiency and patients with a pre-existing thyroid condition may be sensitive to iodine levels considered safe for the general population. Neonates, older people and pregnant women may also be more susceptible to iodine excess (37). It is very difficult to get iodine poisoning from food alone, so iodine poisoning is usually a result of taking too many iodine supplements (38). Acute iodine poisoning is rare and the symptoms of iodine poisoning range from relatively mild to severe, depending on the amount of iodine. Mild symptoms of iodine poisoning include diarrhoea, burning in the mouth, nausea and vomiting. Very large amounts of iodine can cause a metallic taste in the mouth, increased salivation, irritation of the digestive system and acne-like skin changes. Severe symptoms of iodine poisoning include swelling of the airways, blue skin discoloration (cyanosis) and low heart rate. Iodine poisoning can also lead to kidney failure (39).

Certain medications can also increase the amount of iodine in the body. Amiodarone, a drug used to regulate heart rate and rhythm, contains 75 mg of iodine in each 200 mg tablet, which is one hundred times more than the standard recommended daily intake (40). Various drugs, such as propranolol (in high doses), the anti-thyroid drug propylthiouracil, dexamethasone, the cholecystographic agents (ipodate and iopanoic acid) and the previously mentioned amiodarone can inhibit the conversion of T4 into T3 (41). Potassium iodide supplements and the contrast medium used for CT scans also contain iodine (9). Elemental iodine is an oxidising irritant and can cause lesions in case of direct contact with the skin, while exposure to iodine vapours causes irritation of the lungs, eyes and skin.

Diagnosis and assessment of iodine toxicity is an important part of the health care team's approach to providing treatment, enhancing care coordination and establishing communication necessary to improve patient outcomes. Iodine toxicity is a rare condition that requires a comprehensive initial diagnosis and a heightened level of suspicion. Patients may present with vague signs and symptoms. Although medical history may reveal toxicity, the cause is difficult to determine without further investigation. The consequences of iodine toxicity depend on the cause and severity. However, to improve outcomes, it is recommended that an interprofessional group of experts be consulted to monitor the patient's vital signs and educate the patient and their family (42).

Discussion

Iodine is an essential mineral for healthy functioning of the human body, but only in moderate amounts. Iodine boosts thyroid function and consequently increases metabolism, supports a healthy pregnancy and prevents cretinism, and promotes heart health by stimulating the production of hormones that regulate heart rate and blood pressure. Over one billion people around the world still do not have access to iodised salt and therefore suffer from iodine deficiency (10, 11). After the Second World War, the prevalence of goitre and cretinism in the endemic areas of the Republic of Croatia was high (43, 44). The highest prevalence was found in the village of Rude and in the Samobor and Žumberak mountains, where almost 85% of school children suffered from goitre and 2.3% of children suffered from cretinism. The first intervention involving iodised salt was made in 1953 and set at 10 mg per kilogram of salt. This intervention led to a threefold reduction in goitre in children and complete elimination of cretinism (44, 45). Fifteen kilometres from the Adriatic coast, in the region of Grobnik, Croatia, goitre was endemic before iodised salt prophylaxis. In 1963, the prevalence of goitre was 63% in school children and 34% in adults. A second survey was conducted in 1981 and the prevalence of goitre was 18% in school children and 11% in adults. In 2001, another survey on the prevalence of goitre was conducted in the Grobnik region. The results showed that the prevalence of goitre was 6.6% among school children and 6.4% among adults. A significant decrease in prevalence was achieved among school children, but not among adults due to the hereditary thyroid disease in the indigenous population (11.7%) (46). The high prevalence of goitre led to an increase in the potassium iodide content in salt from 10 mg/kg to 25 mg/kg (47). In the period from 2002 to 2009, urine samples of school children were analysed to determine the iodine concentration using a median urinary iodine concentration [UIC] of 68 μg/L. The results showed that the iodine concentration in 2009 was significantly higher than in 2002, indicating that there were hidden sources of iodine in the diet besides salt (29).

The first legal document regulating the general iodisation of salt in the Republic of Croatia was introduced in 1953, prescribing 10 mg of potassium iodide (KI) per kilogram of salt (48). In the 1990s, at the initiative of the then chairman of the National Committee for Eradication of Goitre and Control of Iodine Prophylaxis, Professor Zvonko Kusić, two new legal documents were introduced: Instructions on Iodisation of Table Salt (Official Gazette 84/96) and the Salt Iodisation Regulation (Official Gazette 15/97), which led to a further increase in the prescribed amount of iodine in table salt (48). The initiative for universal iodisation of salt in Croatia allows for iodisation of table salt to be applied at three levels: in households, food industry and animal feed production. The Croatian model of table salt iodisation complies with all guidelines of the WHO, International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and UNICEF and it has been internationally recognised as one of the models for addressing this emerging public health issue (48, 49).

Conclusion

This article provides an overview of iodine discovery and its physiological role in our bodies, at the same time explaining the optimal iodine intake in relation to different dietary sources and environments. Iodine toxicity and iodine deficiency disorders are also addressed, which raises the question of whether we really know how much iodine we consume per day. Another question is, if we ingest too much salt, are we placing ourselves at the risk of excessive iodine intake? The answer to those questions could be found in different initiatives and projects, such as the EH-UH 2, for which a comprehensive and detailed strategic approach should be defined to assess the amount of iodine intake across the population.

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