Hrana u zdravlju i bolesti, znanstveno-stručni časopis za nutricionizam i dijetetiku (2022) 11 (1) 29-36
Food in Health and Disease, scientific-professional journal of nutrition and dietetics (2022) 11 (1) 29-36

THE EFFECT OF IODINE INTAKE FREQUENCY FROM SALT AND SALT-CONTAINING PRODUCTS ON THYROID DYSFUNCTION

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professional paper

Summary

The human body needs small quantities of iodine per day. In 1990, the World Health Organization (WHO) Assembly adopted the universal salt iodization as the method of choice for eliminating iodine deficiency. In order to examine the influence of the frequency of iodine intake from salt and salt-containing products on thyroid dysfunction, a questionnaire was created and its answers were analyzed. The results of the study showed that there are significant statistical differences between subjects with thyroid dysfunction who consume less salt in food and have a reduced frequency of consumption of salt-containing products compared to subjects in the control group.

Keywords: iodine, salt, thyroid dysfunction

Introduction

A major factor in iodine deficiency is low concentration of iodine in the consumed food (Benoist et al., 2004). The recommended daily intake of iodine for infants is 50 µg/day, children (1-6 years) 90 µg/day, children (7-12 years) 120 µg/day, adults and children (over 12 years) 150 µg/day, and for pregnant and lactating women 200 µg/day (WHO, 1996). In order to ensure the intake of 150 µg of iodine per day through iodized salt, the World Health Organization and the United Nations International Children's Fund (UNICEF) in 1996. recommended that the iodine content in salt is 20-40 mgI/kg (ZZJZ, 2006). In 1990, the World Health Organization Assembly adopted the universal method of iodization of salt as the method of choice for the elimination of iodine deficiency disorders (IDD). This strategy is based on the fact that: (a) salt is one of the few goods consumed by the entire population; (b) salt consumption is fairly stable throughout the year; (c) salt production is usually in the hands of several producers; (d) salt iodization technology is easily feasible and available at a reasonable cost (Benoist et al., 2004).
This recommendation was based on data indicating iodine loss from the place of production to its delivery the household, and that 20% of iodine is lost by cooking before use. Also, iodized salt does not cause side effects nor does iodine from iodized salt carry risks for people who already have enough iodine in their bodies (Ranganathan and Reddy, 1995).
Sources of salt intake in the human body through diet can be roughly classified into two groups. As a spice, kitchen salt is added in small amounts to enhance the flavor of dishes (Yee et al., 2011). Another source of salt intake is in the form of preservatives. Significant sources of hidden salt are found in semi-ready and ready foods such as: cured meats, pâtés, hard cheeses, cheese spreads, snacks (chips, chopsticks, peanuts and pistachios), ready-made sauces, mustard, mayonnaise, hamburgers, bagged soups, corn and cereal flakes. Baked goods, especially bread, are a major source of kitchen salt and account for 25-30% of the daily salt intake (Ugarčić-Hardi et al., 2010) (Table 1). Iodized salt from processed foods is an important source of iodine, especially for adults. The use of iodized salt by the food industry should be enforced along with population monitoring to ensure sustainability of optimal iodine intake (Chotivichien et al., 2021). It is concerning that the use of kitchen salt in the preparation of food as a spice but also as a preservative in various products greatly exceeds the daily needs of the human body, which are small, only 5 g/day of salt is needed (WHO, 2006).
According to a study conducted in Croatia, the intake of kitchen salt in both sexes is over twice the recommended amount (as recommended by the WHO). The highest daily intake was 29.9 g for men and 19.4 g for women. A statistically significant correlation was observed between body mass index and kitchen salt intake in the whole group of respondents (Đurić et al., 2011). Reducing dietary salt intake from the current values of 9-12 g/day to the recommended level of less than 5-6 g/day will have major positive effects on cardiovascular health. The World Health Organization and the Food and Agriculture Organization (FAO) recommend consuming less than 5 g of salt per day (Sung Kyu Ha, 2014). During a study that was conducted on the Italian population, researchers have come to the conclusion that whit a daily consumption of 5 g of salt iodized at 30 mg/kg, the estimated daily iodine intake

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resulted within the range of optimal iodine intake in all age groups. In children the recommended iodine intake is achieved with a daily consumption of 3 g of iodized salt (Pastorelli et al., 2015).

Table 1. Iodine content in various dietary products (Pennington and Spungen, 2010)

Product	Quantity of product	Amount of iodine (μg)
Cod	85 g	99
Corn grits	1 cup	68
Milk, 2% fat	240 ml (1 cup)	56
Milk, fat free	240 ml (1 cup)	51
White bread	50 g (2 pieces)	46
Beef liver, cooked	85 g	36
Beans, cooked	90 g (1/2 cup)	35
Potatoes, baked	110 g	34
Whole wheat bread	50 g	32
Egg, boiled	50 g	24
Oatmeal, cooked	1 cup	16

Potassium iodide (KI) and potassium iodate (KIO_3) are substances mainly used for salt iodization. In a mixture with salts KI is less stable compared to KIO_3. KI can be used for iodization of highly purified salt, but that salt has be stored in dry conditions and should be consumed a few months after production. Otherwise, iodine stabilizers need to be added, such as Sodium Thiosulfate or Calcium Hydroxide, 1 g of stabilizer per 1 kg of salt iodinated with KI. KIO_3, recommended by the World Health Organization for salt iodization, is generally stable and resistant to evaporation. KIO_3 should be used for iodization of salt that is less purified and if it's assumed that the salt will be exposed to heat or humidity, and will be stored or transported for a long time (Tahirović, 2004).

To date, the available results are conflicting, depending on the country (Table 2.), salt iodization policy, as well as time frame of data collection. However, ensuring an optimal iodine supply by salt fortification, without exceeding the current recommendation by the World Health Organization for salt intake, seems to be an achievable goal (Nista et al., 2022). Iodine fortification of kitchen salt has recently been increased in Switzerland from 20-25 mg/kg to ensure iodine sufficiency in the population, whereas in Germany fortification still remains at a mean level of 20 mg/kg implying a growing risk of increasing iodine deficiency rates if general salt intake drops (Esche et al., 2020).

The human body contains 15-20 mg of iodine, 70-80 % of which is concentrated in the thyroid. Of the total amount of iodine ingested, 15% goes to the thyroid within 24 hours. Excess iodine is excreted through urine (Ristić-Medić et al., 2009). The thyroid is an endocrine gland located in the front lower part of the neck, and its hormones help the body use energy, enable the proper function of the heart, brain, muscles and other organs (ATA, 2014).

The thyroid secretes Triiodothyronine (T_3), Thyroxin (T_4) and Calcitonin. The biosynthesis of thyroid hormones depends on the intake of exogenous iodine through food and water. Iodine is absorbed through the small intestine and transferred through plasma to the thyroid where it is concentrated, oxidized, and then incorporated into Thyroglobulin (Tg) to form Monoiodotyrosine (MIT) and Diiodotyrosine (DIT), later on T_4 and T_3. Thyroglobulin undergoes proteolysis, and the released hormones are secreted into the circulation, where specific binding proteins transfer them to target tissues (Rousset et al., 2015).

Control of thyroid hormone secretion is achieved by a '*negative feedback mechanism*'. The Hypothalamus secretes the Thyrotropin-releasing hormone (TRH), which affects the adenohypophysis by stimulating the secretion of thyroid-stimulating hormone (TSH), which has a role in all of the stages of thyroid hormone synthesis (Corvilain et al., 1988).
Disorders of the thyroid gland occur due to certain irregularities in its performance or as a result of enlargement of the gland (Khan et al., 2002). Women are more likely to get sick than men, and the symptoms of the disease sometimes go unrecognized (Ashwell et al., 1999). People at increased risk for thyroid dysfunction are those with a family history of such disorders, gland dysfunction after childbirth or surgery, women aged 55 and older, and people from regions with endemic iodine deficiency (Stockigt, 2003). The most common thyroid dysfunction are Hypothyroidism and Hyperthyroidism. Hypothyroidism refers to decreased production of thyroid hormones leading to clinical manifestations of thyroid insufficiency. Hyperthyroidism is excessive production and / or secretion of thyroid hormones (Persani, 2012). A study conducted in China did not show a significant association between salt consumption and the current high prevalence of goiter in that country during 2011-2013 (Liang et al., 2017).

Table 2. Average iodine intake in daily salt intake in some countries of the region

Country	Iodine limit in kg of salt (mgI/kg)	Mean value of iodine in kg of salt (mgI/kg)	Recommended average daily salt intake (g)	Average daily iodine intake (μg)	Average amount of daily iodine intake in 6 g salt/day (μg)
Serbia	12-18	15	6	72-108	90
Slovenia	20-30	25	6	120-180	150
B&H	20-30	25	6	120-180	150

Source: Rulebook on quality and other requirements for salt intended for human consumption and food production, Official Gazette of Serbia and Montenegro, 31/2005; Rulebook on the quality of salt, Official Gazette of the Republic of Slovenia, No. 70/03, 31/04, 45/08 - ZKme-1 and 46/18; Rulebook on salt for human consumption, Official Gazette of B&H number: 39/09

Materials and methods

This study consisted of a questionnaire on eating habits and lifestyle to determine whether the frequency of iodine intake from salt has an impact on thyroid dysfunction. The questionnaire was standardized and developed by using general recommendations and guides on proper nutrition as well as recommendations of associations of patients with thyroid disorder (WHO, 2006; ATA, 2017). The questions in the questionnaire were formulated using the Likert scale for offered questions (Wuensch, 2009). This scale enabled better processing and quantification of the offered answers, as well as the calculation of statistical significance and correlation factors.
The subjects were people aged 28-73 years with thyroid dysfunction and a group of healthy people. A pilot group of 20 respondents aged 30 to 60 years was used to validate the questionnaire. The validation of the questionnaire examined metric characteristics, and whether the questions used in the questionnaire were appropriate and showed the correlation we were looking for. Verbal expressions offered in response were used as quantifiers of the frequency of consumption of individual foods.
The questionnaire on the eating habits of the respondents and their lifestyle looked like this:

Name and surname ____________________________ Age _______ years

Weight: ______ Height: ______ BMI: ________

Disease (round): Hypothyroidism Hyperthyroidism

Circle the answers to the following questions.

1. Food I eat: a) I don't add extra salt b) I try and then add salt c) I add salt first and then I eat

2. In your opinion, you consume:

a) Foods with a very low salt intake b) moderately salty foods c) very salty foods

3. Do I consume cured meat products in my diet?

a) Daily b) 3-5 times a week c) 2-3 times a week e) once a week e) never

4. How much bread do you eat per day?

a) More than half a loaf of bread b) half a loaf of bread c) more than 5 slices

d) 3-5 slices e) two slices

5. Do you consume pies and other pastry dishes in your diet?

a) Daily b) 3-5 times a week c) 2-3 times a week e) once a week e) never

Subjects were divided into two groups of 100: test (I1) and control (K1). Subjects from group (I1) were persons with Hypothyroidism, and subjects from group K1 were persons with good thyroid function.
Statistical analysis was performed using SPSS software version 23.0 (SPSS, Inc., Chicago, Illinois). Continuous variables with normal distribution were expressed as mean ± standard deviation, and continuous variables whose distribution is not normal were expressed as median and interquartile range (IQR). Normal data distribution was evaluated by Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical variables were expressed as a number (percentage). The T-test was used to compare the two independent groups of continuous variables following the normal distribution, and the Mann-Whitney U test was used for the continuous independent variables following the normal distribution. The Wilcoxon signed rank test was used to compare two dependent continuous variables that do not follow the normal distribution. A chi-square test or Fisher's exact test was used to compare categorical variables if the number of variables in any cell of the contingency table was less than 5. A P-value <0.05 was considered statistically significant.

Results and discussion

One hundred respondents were included in the examined and control group at the beginning of the research and the same number of them completed the questionnaire on eating habits. The initial characteristics of the respondents are shown in Table 3. The mean age of the respondents in the examined group was 57 years (IQR, 46-65), and the majority of the respondents were women (90/100, 90%). The mean age of the subjects in the control group was 51 years (IQR, 41–58), and the majority of the subjects were women (66/100, 66%). The average body mass index (BMI) was 28.11 for the subjects of the examined group and 27.17 for the subjects of the control group. Decreased thyroid activity is thought to lead to obesity and thus to an increase in BMI, probably as a result of decreased metabolism (Åsvold et al., 2009). According to the results in this study there are no significant differences in BMI between the two groups which can be explained by the fact that in the control group consisted of a higher number of men whose BMI is higher than women, which brought the mean value closer to the BMI of the respondents in the examined group. Significant differences in height were detected between the subjects of the examined and control group, which was to be expected since the control group consisted of more men who are usually slightly taller than women. This data did not affect the course of the research.

Table 3. Initial characteristics of the respondents in the study

Data on respondents	Examined group (n= 100)	Control group (n = 100)	p value
Age (median,Q1 - Q3)	57 (46-65)	51 (41-58)	<0.001
Sex	10 Male/90 Female	34 Male/66 Female	<0.001
Weight (kg) (mean value ± standard deviation)	76±13	79±15	0.133
Height (m) (mean value ± standard deviation	1.64±0.08	1.69±0.1	0.007
BMI (median,Q1 - Q3)	28.11 (25.14-30.83)	27.17 (24.83-29.73)	0.327

Statistically significant at the level of $p<0.05$

To determine the impact of the frequency of intake of iodine from salt and salt-containing products, the answers to the questions from the questionnaire were compared between control and examined group of respondents. Their statistical processing showed that there are significant differences in the frequency of consumption of salt and salt-containing products between the subjects of the examined and controlled groups (Table 4).

Table 4. Estimation of frequency of salt and salt-containing foods intake for examined and control groups

Questions	Examined group (n = 100)	Control group (n = 100)	p value
The food I consume: (median, Q1 - Q3)	1 (1-2)	2 (2-3)	<0.001
In your opinion you are consuming: (median, Q1 - Q3)	1 (1-2)	2 (2-2)	<0.001
I consume cured meat products in my diet: (median, Q1 - Q3)	2 (1-2)	3 (3-4)	<0.001
How much bread do you eat per day (median, Q1 - Q3)	3 (2-3.25)	4 (3-5)	<0.001
Do you eat pies and other doughy dishes? (median, Q1 - Q3)	2 (2-3)	3 (3-4)	<0.001

Statistically significant at the level of $p <0.05$

It was estimated that in the pediatric population, approximately 65–73 % of the total iodine intake was derived from food and 27–35 % from iodized salt and that iodized salt actually only contributed to 20% of the total salt intake (Iacone et al., 2021). Iodine in iodized salt does not carry risks for people who already have enough iodine. Salt iodization at the current level of enrichment (15–30 ppm iodine) does maintain intake in a safe daily range for all populations, regardless of their iodine status (Ranganathan and Reddy, 1995). In a cross-sectional study conducted by Yu et al (2021), researchers did not provide information on side effects using iodized salt nor did they specifically consider adverse effects, and we can be sure that adverse effects are small or almost non-existent. In order to examine the side effects of iodized salt it would require a large study of at least two years, not focusing on the rate of goiter and urinary iodine excretion, and paying special attention to the mental and physical development of children and mortality (Clar et al., 2002). In a study conducted between the years 1990 and 1999. involving 26.010 respondents, Huang et al. (2001) concluded that iodized salt intake and the incidence of hyperthyroidism had a significant correlation. However, the typical model of the change of disease patterns incidence needs further study. The high incidence of thyroid diseases caused by high iodine intake has been contentious. Zhao et al. (2014) investigated the relationship between iodine intake and thyroid diseases through the comparison of urine iodine concentration (UIC) of patients with thyroid diseases and healthy volunteers and through assessment of iodine intake among the residents. The susceptibility of thyroid diseases among subjects was significantly associated with the female sex (odds ratio (OR) = 3.3), older age (OR = 2.1), and high iodine intake (OR = 1.3). In conclusion, high iodine intake was likely to lead to the occurrence of thyroid diseases, such as Hashimoto thyroiditis, nodular goiter, and hyperthyroidism, through a long-term mechanism.

Subjects in the focus group usually do not add additional salt to the food they consume. There is a statistically significant difference between the examined and control groups regarding the frequency of salt intake ($p<0.001$) but we also need to take into account the addition of salt to food during cooking, this fact is unknown to us and we cannot say with certainty that the subjects in the focus group consume less iodine without adding salt to their food. The method of food preparation could also affect the iodine content in the final product. The loss of iodine depends on the cooking method and the frequency of adding salt during cooking. Minimum losses were found during shallow frying where cooking time of salt was 1 minutes and 15 s and maximum during pressure cooking where cooking time of salt was 26 minutes (Rana and Raghuvanshi, 2013).

Furthermore, according to the respondents, they tend to use food with a low salt intake, while most of the respondents in the control group stated that they consume moderately salty food ($p<0.001$).

At the top of the list of foods as sources of iodine in the diet are cured meat products as well as whole grain bread and other pastry dishes (Pennington and Spungen, 2009). Baked goods are a major source of salt and account for 25-30% of the daily salt intake (Ugarčić-Hardi et al., 2010). Bread is widely considered to be the food that provides the most dietary salt. As such, it is one of the key public health targets for a salt reduction policy (Quilez and Salas-Salvado, 2012). Research has shown that commercially prepared foods (including bread and pizza) are decreasing the amount of iodized salt (Ugarčić-Hardi et al., 2010). Purchasing data suggests that bread and cereal products are responsible for approximately 18% of normal daily unrestricted sodium intake; this percentage may be substantially higher in subjects attempting to follow a reduced sodium diet by avoiding added salt and salty sauces and meats (Daugirdas, 2013).

There is a statistically significant difference between the examined and control groups in the frequency of intake of cured meat products ($p <0.001$) as well as the daily consumption of bread ($p<0.001$). We do not know the quantities of the consumed portion so some of the subjects may have a higher intake of salt from cured meats in one consumption, than the other who has consumed three or more portions. Therefore, the obtained results of the questionnaire must be observed with caution.

Alternative substances and processing technologies for reducing or replacing sodium in meat products are being actively researched with the goal of the industrial development and manufacture of low-salt meat products. Studies have shown that sodium chloride cannot be replaced or reduced by over 50% using a single process (Kim et al., 2021).

Respondents of the examined group consume more than 5 slices of bread per day, while in the control group there very varying answers (some consume more than 5 slices per day, others consume ½ loaf of bread and more than half a loaf of bread per day). If one considers the cuisine of the region, it is to be expected that pies and doughy dishes are consumed several times during the week. There are certain statistical differences in the responses to this question. While the examined group consumed pie and doughy dishes mostly once a week, and a couple of responses said 2-3 times a week, most of the responses of the control group stated that baked goods were consumed 2-3 times a week. In a study conducted in Croatia, salt content varied widely between bakeries, with an average content of 2.30±0.22 g per 100 g of bread, which is almost twice the threshold content (1.4%) defined by the Croatian National Regulation on Cereals and Cereal Products (Delaš Aždajić et al., 2019). According to the obtained results we can conclude that the respondents of the examined group consume more salt by consuming larger amounts of bread and pies than the respondents of the study group.

Conclusion

Based on the research, obtained results and discussion, it can be concluded that there is a statistically significant difference in the answers given by the subjects of the examined and control group, regarding the frequency of salt intake and other foods labeled as sources of salt in the diet. Subjects of the control group consume larger amounts of salt and salt-containing food in their diet, thus ensuring the daily needs for iodine. Subjects in the examined group, despite suffering from thyroid dysfunction (hypothyroidism) which additionally signals iodine intake, have lower salt intake and salty foods resulting in reduced iodine intake and prolonged disease.

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