

The influence of salt iodisation on the incidence of thyroid cancer

Wpływ jodowania soli na częstość występowania raka tarczycy

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Słowa kluczowe: rak tarczycy, jodowanie soli, wole tarczycy.

Abstract

The article analyses the relationship between iodine deficiency, the occurrence of thyroid cancer, and the effectiveness of salt iodisation. Iodine deficiency affects a large number of people around the world, including Poland, where both moderate iodine deficiency and an increase in the incidence of thyroid cancer are observed. The positive effect of salt iodisation on reducing thyroid goitre is noticeable. Additionally, the analysis shows a correlation between the BRAF mutation and an increase in the incidence of papillary cancer, especially in areas with excessive iodine intake. However, it is worth noting that proper iodine intake is associated with a decrease in follicular cancer. The increase in thyroid cancer cases is related to widespread ultrasonography, environmental pollution, diet, as well as recommendations to limit salt intake due to society's cardiological problems. A constant level of iodine in the body contributes to reducing the malignancy of thyroid cancer, confirming the importance of salt iodisation.

Streszczenie

W artykule analizowany jest związek między niedoborem jodu, występowaniem nowotworów tarczycy a skutecznością jodowania soli. Niedobór jodu dotyczy dużej liczby osób na świecie, w tym Polski, gdzie obserwuje się zarówno umiarkowany niedobór jodu, jak i wzrost częstości występowania nowotworów tarczycy. Pozytywny wpływ jodowania soli na zmniejszenie wola tarczycy jest zauważalny. Ponadto analiza wskazuje korelację między mutacją BRAF a wzrostem częstości występowania raka brodawkowatego, szczególnie w obszarach z nadmiernym spożyciem jodu. Warto jednak zauważyć, że prawidłowa podaż jodu wiąże się ze zmniejszeniem występowania nowotworu pęcherzykowego. Wzrost przypadków raka tarczycy jest związany z powszechną ultrasonografią, dietą, a także zaleceniami dotyczącymi ograniczenia spożycia soli ze względu na problemy kardiologiczne społeczeństwa. Stały poziom jodu w organizmie zmniejsza złośliwość nowotworów tarczycy, co potwierdza znaczenie jodowania soli.

Introduction

According to the World Health Organisation (WHO), 1.88 billion people around the world are at risk of iodine deficiency and up to one-third of the world's population lives in iodine-deficient areas [1]. Since 1990, international organisations, i.e. WHO, United Nations International Children's Emergency Fund (UNICEF), and International Council for the Control of Iodine Deficiency Disorders (ICCIDD), as well as committees for the control of iodine deficiency disorders, have been implementing iodine prevention programmes, whose goal is to ensure sufficient iodine supply at the population level mainly through the recommendation of salt iodisation [2].

In Europe, the iodisation period was between 1922 and 1997, depending on the country. Over the years,

a relationship between the incidence of thyroid cancer and the degree of salt iodisation has been observed. It has also been noted that gender, diet, and radiation exposure influence the incidence of this cancer. The incidence of follicular and papillary cancer was also examined in relation to the degree of iodisation and possible iodine deficiency [3].

Recommendations regarding iodine consumption in Poland

The proper development and functioning of the human body depends on an adequate supply of iodine, and the only way to obtain this substrate is through food, water, and air [4]. The largest amounts of iodine (about 50 µg/l) are present in the oceans and sea, while glacial and high mountain areas, far from

the coast, are characterised by very low concentrations of this element [2]. It is estimated that the highest iodine deficit in Poland occurs in mountainous regions [5]. The recommended daily dose of iodine in Poland differs from WHO recommendations only in the case of pregnant and breastfeeding women, who are recommended to take 250 µg of iodine per day. The remaining standards are presented in Table 1 [6].

The Beginnings of Salt Iodisation in Poland and in the World

Poland geographically covers areas with mild and moderate iodine deficiency. It is one of the few European countries that uses a mandatory model for the iodisation of table salt. Due to the supplementation, it belongs to the group of European countries with optimal iodine supplementation at the population level [7]. The first practices of iodising table salt began in 1935 but were discontinued between 1939 and 1945. They were resumed after the end of the war and continued until 1980. In the years from 1980 to 1989 in Poland, iodine prevention was practically non-existent, which coincides with the time when an increased number of cases in newborns was noticed [8]. There has also been an increase in the incidence of goitre in school-age children, adults, and pregnant women [9, 10]. At that time, a 3- to 5-fold increase in the incidence of differentiated thyroid cancer was documented in women over 40 years of age [11].

The tests, repeated in 1999–2005 using the “Thyromobil” ambulance, showed a significant reduction in endemic goitre in children aged 6 to 8 years, compared to data from 1994, when these tests were first carried out. After the introduction of effective prevention, iodine in the urine increased to 92%, while the incidence of goitre decreased to only 4.7%. The incidence of goitre in pregnant women decreased from 80% (data from 1993) to approximately 20% in 2000. Moreover, a reduction in the number of new cases of thyroid cancer in women was observed [12]. There were no side effects of iodine prophylaxis [13]. The rate of progression of thyroid cancer in women was considered slower, while the incidence was estimated to be 3–4 times higher in 2003 than in 1990 [11].

Throughout the world, the introduction period for iodised salt falls on different years. According to data collected by the WHO, this obligation was introduced in the 20th century. In the Balkan countries, the period of salt iodisation covers the years from 1935 to 1956, and for the Baltic countries, 1996. For eastern Europe, this period covers the years 1953–1997. In Western Europe, iodised salt was first introduced in Switzerland in 1922, and the latest obligation was introduced in Belgium in 1990. Data collected on iodisation in Southern Europe cover the years 1972–1997, and in Nordic countries it is the first half of the last century, with the exception of Denmark, which introduced this obligation only in 1998 [3]. Between

Table 1. Standards of the Institute of Food and Nutrition from 2017 for the daily intake of iodine [6]

Iodine supply dose [µg]	Target group
90	Children aged 0 to 5 years
120	Children aged 6 to 12 years of age
150	Children > 12 years of age and adults
220	Pregnant women
290	Breastfeeding women

2003 and 2011, the number of countries with iodine deficiency decreased from 54 to 32. At the same time, an increase was observed in the number of countries with an adequate intake of iodine reaching 105 countries. This represents increase of 38 countries [2].

Incidence of thyroid cancer

Thyroid cancer is the most common endocrine malignancy [14]. Scientists in Ukraine and Poland also noticed that thyroid cancer occurs 3 to 10 times more often in women than in men. A higher incidence of follicular thyroid cancer has been observed in iodine-deficient areas. In areas with increased radiation and insufficient iodine intake, the incidence of thyroid cancer is 6%, while in areas with increased radiation but adequate iodine supplementation it is 3.3%. In areas with normal levels of radioactivity and adequate iodine supplementation, it is only 2.1%. In the USA, the average incidence rate of this cancer is 6.8 new cases per 100,000 inhabitants, and in Europe it is 1.2–3 per 100,000 inhabitants. It ranges from 10% to 30% of all diagnosed thyroid cancers [15].

Reasons for the correlation of the incidence of thyroid cancer with iodine intake

Iodine deficiency may cause excessive TSH secretion, resulting in reduced thyroid hormone production, and therefore hypertrophy and hyperplasia of thyroid follicular cells, which can ultimately lead to the onset of cancer. After the Chernobyl disaster, a significant increase in cases of thyroid cancer was recorded because Romania was exposed to radioactive clouds. This exposure was unevenly distributed. This was due to the varying intensity of radiation depending on the geographical location. Compared to the years 1970 and 2001–2010, the incidence of thyroid cancer increased by 511%. A significant increase was observed 10 years after the explosion, while the detection of this cancer stabilised 25 years after the Chernobyl explosion. Most of the children diagnosed with thyroid cancer were born between 1996 and 2000. It was shown that children born between 10 and 15 years after the Chernobyl explosion were most affected by the effects of the explosion and accounted for approximately 65% of cases. However,

in the years 1984–1991, no major deviations were observed in the number of cases detected [16, 17].

In the Romanian population, signs of goitre are observed in approximately 35% of people, and approximately 20% of children have been diagnosed with iodine deficiency. Significant deficiencies in this element have also been observed in rural areas compared to urban areas. In 2002, it was found that non-iodised salt is still used in this country, and the largest percentage of it, as much as 37%, is used in rural areas, while in urban areas it is 31% [18].

In the years 2001–2004 and 2005–2008, studies were carried out to compare the incidence of thyroid cancer in Moldova. The number of recorded thyroid cancers was found to increase over time by up to 178%, while thyroidectomies decreased from 1734 (in 2001–2004) to 1449 (in 2005–2008). However, it was found that this may be influenced by the long latency period characteristic of this group of cancers. In Mures County, Romania, a positive effect of iodisation was observed on reducing the incidence of follicular cancer and increasing the incidence of papillary cancer [19].

Slovenia is considered an area with adequate iodine supply. Prevention consisted of salt iodisation in the amount of 10 mg kJ/kg in the years 1972–1998. Then, in the years 1999–2017, the amount of potassium iodide was increased to 25 mg kJ/kg. The effect of introducing a higher amount of iodisation was observed after 10 years. A decrease in the incidence of diffuse goitre was observed in adults and children. At the same time, the incidence of thyroid cancer has increased from 5.1/100,000 to 7.25/100,000; however, a reduction in the incidence of anaplastic thyroid cancer was observed [20, 21]. A similar situation regarding the incidence anaplastic cancer after higher salt iodisation has been reported in other endemic goitre regions in Argentina and the Tyrol region in Austria [22]. The risk of anaplastic thyroid cancer is influenced by insufficient iodine intake, a history of goitre, or previously coexisting differentiated thyroid cancer [23, 24]. The decrease in the incidence of anaplastic thyroid cancer in Slovenia is mainly attributed to the increased salt iodisation. Another factor contributing to the decline in anaplastic thyroid cancer in the Slovenian population was the reduction in the rate of goitre. Higher consumption of iodised salt is also believed to be a cause [25].

The Laboratory of Human Nutrition of the Faculty of Health Sciences and Technology of the Swiss Federal Institute of Technology in Switzerland and the University of Birmingham in the UK noted that differences in iodine intake between regions influence the incidence of different types of thyroid cancer. In the area of optimal iodine intake, there is a lower incidence of follicular thyroid cancer, but it is more aggressive and there are fewer papillary thyroid cancers. The ratio of papillary to follicular cancer in areas of optimal iodine intake is 3.4–6.5 : 1, and in areas deficient in iodine it is 0.19–1.7 : 1. Therefore,

it can be concluded that chronic iodine deficiency is a risk factor for the increased occurrence of follicular cancer, nodularity, and thyroid gland goitre [26].

In Germany, in the years 2003–2008, when the country had a proper iodine intake, an increase in the incidence of thyroid cancer was observed from 2.7 to 3.4 in men and from 6.5 to 8.9 per 100,000 cases of thyroid cancer per year, with the highest percentage being papillary thyroid cancer. The incidence of thyroid cancer was higher in the southern part of Germany, where salt iodisation was introduced later. Also in Austria, where salt iodisation took place in 1962, the incidence ratio of papillary to follicular thyroid cancer increased from 0.2 in the years 1952–1959 to 0.87 in the years 1970–1975. In Spain, the obligation to iodise salt dates back to 1985. Studies in the years 1978–2001 also noted an increase in the ratio of papillary cancer to follicular thyroid cancer from 2.3 to 11.5, as well as the incidence of thyroid cancer increased from 1.56 to 8.23 for women comparing the years 1978–1985 to 1994–2001 [27].

In China, the T1799A mutation of the BRAF gene was observed, which increased the risk of papillary cancer and its aggressiveness with excessive iodine consumption [28]. The excessive intake of iodine was due to the consumption of drinking water contaminated with iodine compounds. It should be noted that too much and too little iodine intake will predispose to the development of thyroid cancer, but correcting the amount of this element consumed may reduce the chances of developing this cancer or cause a change in the cancer subtype to a less malignant one [29].

Summary

Poland is an area with mild to moderate iodine deficiency. Currently, approximately 2 billion people around the world are at risk of iodine deficiency. This is a big problem on a global scale, because deficiency of this element predisposes to the development of goitre, which is a risk factor for thyroid cancer.

A positive effect of salt iodisation on reducing the occurrence of thyroid goitre was noticed. A correlation was observed between the BRAF mutation and a higher incidence of papillary cancer, and the mutation itself occurred more often in people living in areas with excessive iodine intake. It has been observed that thyroid cancer occurs more often in women (3–10 times) than in men, and the highest incidence occurs at the age of approximately 45–69 years. A decrease in the incidence of follicular cancer and an increase in papillary cancer is also observed with adequate iodine intake. Additionally, environmental pollution, diet, and consumption of highly processed foods were observed to have an impact on carcinogenesis, as well as recommendations to limit salt consumption due to society's cardiological problems. A constant level of iodine in the body also contributes to reducing the malignancy of thyroid cancer, which confirms the validity of salt iodisation.

Author contributions

Karolina P. Sas, Kamila Tokarczyk, and Damian Zieliński contributed equally to this work. All authors were involved in the study conception, data analysis, manuscript preparation, and approved the final version of the manuscript.

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Conflict of interest

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References

1. Universal Salt Iodization and Sodium Intake Reduction: Compatible, Cost-effective Strategies of Great Public Health Benefit. World Health Organization; 2022.
2. Pearce EN, Zimmermann MB. The prevention of iodine deficiency: a history. *Thyroid*. 2023; 33(2): 143-149.
3. <https://apps.who.int/iris/bitstream/handle/10665/108263/E68017.pdf?sequence=1>
4. Gérard AC, Poncin S, Caetano B. Iodine deficiency induces a thyroid stimulating hormone-independent early phase of microvascular reshaping in the thyroid. *Am J Pathol*. 2008; 172(3): 748-760.
5. Program for eliminating iodine deficiency in Poland for 2012-2016, Ministry of Health of the Republic of Poland, Warsaw 2012.
6. <https://ncez.pzh.gov.pl/abc-zywienia/jod-w-diece-jak-uniknac-niedoborat/>
7. Robertson A, Tirado C, Lobstein T, Jermini M, Knai C, Jensen JH, Ferro-Luzzi A, James WP. Food and health in Europe: a new basis for action. *WHO Reg Publ Eur Ser*. 2004; (96): i-xvi, 1-385.
8. Trofimiuk-Müldner M, Konopka J, Sokołowski G, Dubiel A, Kieć-Klimczak M, Kluczyński Ł, Motyka M, Rzepka E, Walczyk J, Sokołowska M, Buziak-Bereza M, Tisończyk J, Pach D, Hubalewska-Dydejczyk A. Current iodine nutrition status in Poland (2017): is the Polish model of obligatory iodine prophylaxis able to eliminate iodine deficiency in the population? *Public Health Nutrition*. 2020; 23 (14): 2467-2477.
9. Szybiński Z, Zarnecki A. Prevalence of goiter, iodine deficiency and iodine prophylaxis in Poland. The results of a nationwide study. *Endokrynol Pol*. 1993; 44(3): 373-388.
10. Szybiński Z; Polish Council for Control of Iodine Deficiency Disorders. Work of the Polish Council for Control of Iodine Deficiency Disorders, and the model of iodine prophylaxis in Poland. *Endokrynol Pol*. 2012; 63(2): 156-160.
11. Szybiński Z, Huszno B, Zemla B. Incidence of thyroid cancer in the selected areas of iodine deficiency in Poland. *J Endocrinol Invest*. 2003; 26(2 Suppl): 63-70.
12. Lewiński A, Szybiński Z, Bandurska-Stankiewicz E. Iodine-induced hyperthyroidism-an epidemiological survey several years after institution of iodine prophylaxis in Poland. *J Endocrinol Invest*. 2003; 26(2 Suppl): 57-62.
13. Szybiński Z. Iodine prophylaxis in Poland in light of the WHO recommendation on reduction of the daily salt intake. *Pediatr Endocrinol Diabetes Metab*. 2009; 15(2): 103-107.
14. Knobel M, Medeiros-Neto G. Relevance of iodine intake as a reputed predisposing factor for thyroid cancer. *Arq Bras Endocrinol Metabol*. 2007 Jul; 51(5): 701-712.
15. Schlumberger MJ. Papillary and follicular thyroid carcinoma. *N Engl J Med*. 1998 Jan 29; 338(5): 297-306.
16. Ward MH, Kilfoy BA, Weyer PJ. Nitrate intake and the risk of thyroid cancer and thyroid disease. *Epidemiology*. 2010 May; 21(3): 389-395.
17. Kermoison G, Draganescu C. Role of dietary and environmental factors on thyroid cancer in Romania: a brief review. *Diagnostics (Basel)*. 2022 Aug 13; 12(8): 1959.
18. Bartholomeusz C, Gonzalez-Angulo AM. Targeting the PI3K signaling pathway in cancer therapy. *Expert Opin Ther Targets*. 2012 Jan; 16(1): 121-130.
19. Kilfoy BA, Zhang Y, Park Y. Dietary nitrate and nitrite and the risk of thyroid cancer in the NIH-AARP Diet and Health Study. *Int J Cancer*. 2011 Jul; 129(1): 160-172.
20. Gabersček S, Zaletel K. Epidemiological trends of iodine-related thyroid disorders: an example from Slovenia. *Arh Hig Rada Toksikol*. 2016 Jun; 67(2): 93-98.
21. Zaletel K, Gaberscek S, Pirnat E. Ten-year follow-up of thyroid epidemiology in Slovenia after increase in salt iodization. *Croat Med J*. 2011 Oct; 52(5): 615-621.
22. Besic N, Gazic B. Dietary iodine intake, therapy with radioiodine, and anaplastic thyroid carcinoma. *Radiol Oncol*. 2020 May; 54(2): 187-193.
23. Harach HR, Galíndez M, Campero M. Undifferentiated (anaplastic) thyroid carcinoma and iodine intake in Salta, Argentina. *Endocr Pathol*. 2013 Sep; 24(3): 125-131.
24. Zivaljevic V, Slijepcevic N, Paunovic I. Risk factors for anaplastic thyroid cancer. *Int J Endocrinol*. 2014; 2014: 815070.
25. McIver B, Hay ID, Giuffrida DF. Anaplastic thyroid carcinoma: a 50-year experience at a single institution. *Surgery*. 2001 Dec; 130(6): 1028-1034.
26. Zimmermann MB. Iodine deficiency. *Endocr Rev*. 2009 Jun; 30(4): 376-408.
27. Feldt-Rasmussen U. Iodine and cancer. *Thyroid*. 2001 May; 11(5): 483-486.
28. Zimmermann MB, Galetti V. Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. *Thyroid Res*. 2015 Jun; 8: 8.
29. Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. *J Nutr*. 2012 Apr; 142(4): 744-750.

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