REVIEW ARTICLE

Journal of Pre-Clinical and Clinical Research 2024, Vol 18, No 4, 345-352
www.jpccr.eu

Correlation between selenium levels and thyroid cancer – a literature review

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Durmała K, Pyc G, Bęben D, Kowalewski J, Mączka J, Dąbrowska A, Dudzik M, Majewski K, Sielicka U, Pakos K. Correlation between selenium levels and thyroid cancer – a literature review. J Pre Clin-Clin Res. 2024; 18(4): 345–352. doi: 10.26444/jpccr/195942

Abstract
Introduction and Objective. Selenium is one of the micronutrients in the human body that has antioxidant, immunomodulatory, anticancer properties and affects thyroid hormone conversion. Selenium accumulates to the greatest extent in thyroid tissue. There is evidence that selenium supplementation may have an effect on reducing the risk of thyroid cancer. The aim of this review is to evaluate the existence of an association between selenium concentrations and thyroid cancer, based on the current literature.
Review Methods. Information was sought using PubMed, Google Scholar, Cochrane databases, academic textbooks, and data from various organizations, e.g. FDA, EFSA, ESMO. A total of 5 publications were included in the review.
Brief description of the state of knowledge. Selenium deficiency interferes with the conversion of thyroid hormones to their active form, which can result in hormone deficiency and excessive TSH secretion. In turn, high levels of TSH are considered a risk factor in the development of thyroid cancer. One study found an association between low serum selenium levels and the occurrence of thyroid cancer. Another study only confirmed an association between low selenium concentrations and the progression of already existing cancer. In contrast, a third study did not confirm the presence of any correlation.
Summary. The results of the study varied, which may be due to complex mechanisms and the influence of many factors on the relationship studied. It is also possible that beneficial effects on the thyroid correlate with a certain range of selenium concentrations. However, further research is needed to prove this.

Key words
risk factors, thyroid hormones, selenium, micronutrients, thyroid neoplasms

INTRODUCTION AND OBJECTIVE

Currently, cancer is the second cause of premature death worldwide. With the incidence of cancer steadily increasing, long-term projections predict that cancer may dominate cardiovascular disease (CVD) as the leading cause of death in most countries during this century [1]. Consequently, in recent years researchers have become interested in exploring the impact of nutrition and micronutrients in the diet on the human body and on the occurrence of diseases. This is with a view to seeking new methods of prevention, diagnosis as well as treatment.

Selenium is an element that is one of the micronutrients in the human body. Although it is not needed in large quantities for the body to function properly, it has extremely important functions, and is found in many organs, most abundantly accumulated in the thyroid gland [2]. It is also interesting to note that even in a selenium-deficient state, the thyroid gland still has the highest amount of this element in the body [3]. Additionally, it has been shown to have antioxidant, immunomodulatory and anticancer properties [4, 5, 6].

Selenium is commonly found in the environment, with its distribution in soil varying according to latitude; for example, in parts of the United States, Colombia and Venezuela, the content in soil is extremely high, while in Asia, in some provinces of China, especially in a belt stretching from the north-east to the south-central part of the country, and in parts of the Congo, soils are clearly deficient [7]. The selenium content of the soil translates to a certain extent into the content of the element in plants. However, this is not a simple relationship, as it depends on the selenium uptake capacity of plants, which is influenced, for example, by soil pH, soil ion content, occurrence of microbial organisms, or climate [8]. In animals, their internal regulatory mechanisms maintain constant selenium levels in tissues, despite consuming plants with varying amounts of selenium [9].

In the human body, the selenium content depends mainly on the diet, which is particularly influenced by the intake of

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Received: 06.08.2024; accepted: 14.11.2024; first publised: 22.11.2024

plant foods. The food with the highest selenium content is Brazil nuts, as 6 nuts provide as much as 544 ug [10], while the average daily requirement in Europe is 70 ug [11]. This is followed by fish and meat, and cereal products, such as pasta and oatmeal. In view of this, it is important to note when conducting surveys that the results of blood selenium concentrations in subjects may vary depending on where they live.

Table 1. Selenium content of selected foods [10]

Food	Selenium, Se per 100 g (μg)
Brazil nuts, dried, unblanched	1920
Tuna, yellowfin, cooked	108
Tuna, white, canned in oil	60.1
Salmon, Atlantic, farmed, cooked	41.4
Cod, Atlantic, cooked	37.6
Pork, ground, cooked	35.4
Beef, flank, steak, cooked, broiled	28.9
Lamb, ground, cooked, broiled	27.7
Chicken, meat only, cooked, roasted	24.6
Bread, whole-wheat	38.6
Bread, white wheat	16.1
Pasta, whole-wheat, cooked	36.3
Pasta, unenriched, cooked	26.4
Rice, white, long-grain, unenriched, cooked	7.5
Rice, brown, long-grain, cooked	5.8
Cereals, oats, regular and quick, unenriched, cooked with water	5.4
Egg, whole, cooked, fried	33.1
Milk, fluid, 1% fat	3.3
Yogurt, plain, whole milk	2.2

The US Institute of Medicine has estimated the recommended daily allowance (RDA) for selenium at 55 ug/day for men and women aged 19–50 years [12]. The US Food and Drug Administration (FDA) has also proposed a daily value for selenium of 55 micrograms for adults [13], while the European Food Safety Authority (EFSA) in the European Union (EU) has set a value of 70 ug/day for selenium as an adequate intake (AI) [11]. Of course, the daily requirement for selenium is determined for a given population depending on the bioavailability of the element, gender, age, pregnancy or lactation [12].

Many studies have positively verified the role of selenium as a preventive factor in cancer [14]. In 2008, the FDA reported that selenium supplementation may reduce the risk of certain cancers, but noted that the evidence is limited and inconclusive. One such cancer is cancer of the thyroid [15] where a steady increase in the incidence has been observed worldwide over the past three decades [16]. Therefore, it remains the most common malignancy of the endocrine system [17]. Given the growing interest in selenium and the intensive research on its effects on the body, it was decided to perform a literature review to summarise the current knowledge on the correlation between selenium levels in the body and thyroid cancer.

Table 2. Selenium. Recommended Dietary Allowance (RDA) and Tolerable Upper Intake Level (UL) [12]

Age	Recommended Dietary Allowance (RDA) [mcg]	Tolerable Upper Intake Levels (UL) [mcg]
Birth to 6 months	15	45
Infants 7-12 months	20	60
Children 1-3 years	20	90
Children 4-8 years	30	150
Children 9-13 years	40	280
Teens 14-18 years	55	400
Adults 19-50 years	55	400
Adults 51-70 years	55	400
Adults 71 years and older	55	400
Pregnant teens and women	60	400
Breastfeeding teens and women	70	400

Table 3. Incidence of the ten most prevalent cancers worldwide in 2022, both sexes, all ages [18]

Rank	Cancer	No. of cases	Percent
1st	Lung	2 480 675	12,4
2nd	Breast	2 296 840	11,5
3rd	Colorectum	1 926 425	9,6
4th	Prostate	1 467 854	7,3
5th	Stomach	968 784	4,9
6th	Liver	866 136	4,3
7th	Thyroid	821 214	4,1
8th	Cervix uteri	662 301	3,3
9th	Bladder	614 298	3,1
10th	NHL	553 389	2,8
-	Others	7 318 583	36,7
-	All cancers	19 976 499	-

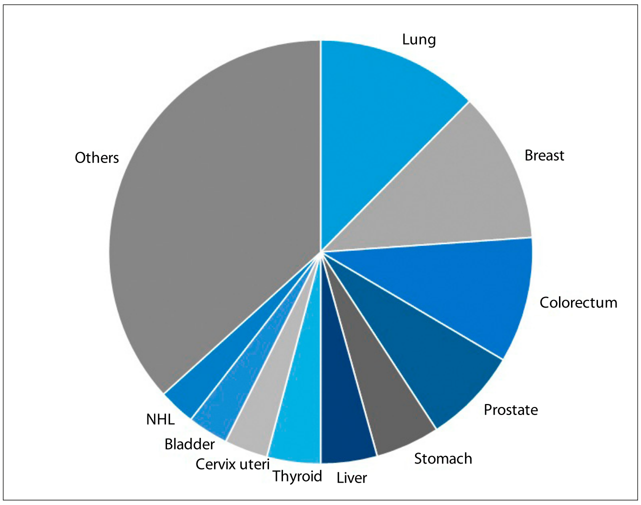

Figure 1. Incidence of the ten most prevalent cancers worldwide in 2022, both sexes, all ages [18]

REVIEW METHODS

To compile this review, the electronic databases PubMed, Google Scholar and the Cochrane Library were searched for publications dated up to 7 July 2024. Kowledge from academic textbooks was used, as well as data from organisations such as the Institute of Medicine in the United States, the Food and Drug Administration (FDA), the European Food Safety Authority (EFSA), and the European Society of Clinical Oncology (ESMO).

Using the key words: 'selenium', 'selenoproteins', 'micronutrients', 'micorelements, 'trace elements', in combination with the terms 'thyroid', 'thyroid hormones', 'thyroid disease', 'thyroid cancer' and 'cancer risk' among more than 200 scientific articles covering all types were matched. In order to present reliable information in the review, articles published before 2010 were not considered due to older reaserch methods that could influenece the results. The results were then ranked in terms of clinical trials, cross-sectional studies and meta-analyses. In addition, relevant articles citing others according to the references provided, were manually searched.

The primary inclusion criteria were the determination of body selenium levels and the confirmation of thyroid cancer by histology. This method is the 'gold standard' and definitively confirms a cancer diagnosis.

Exclusion criteria primarily concerned inappropriate studies, such as reviews, case reports or editorials. Papers were rejected if they were interfered in a way that could, in the opinion of the authors of this review, influence the results, e.g. selenium supplementation was deliberately used in a correlation study or selenium concentrations were assessed during therapy, e.g. radioiodine treatment.

The aim of the review was to present the topic in a reliable, objective and generalised way; therefore, papers were selected independently of gender, age, ethnicity and region of residence of the population. Nevertheless, it was realized that such a broad spectrum of factors could have an ambiguous effect on determining the results. Finally, five publications were included in our review on which were based the analysis of the association between human selenium concentrations and thyroid cancer.

DESCRIPTION OF THE STATE OF KNOWLEDGE

The role of selenium. Selenium occurs in the environment in 2 forms. In the inorganic form as selenates and in the organic form by forming amino acids, the most important of which are selenomethionine and selenocysteine. Amino acids, on the other hand, build enzymes, among which glutathione peroxidases, thioredoxin reductases, iodothyronine deionidases and selenoproteins are distinguished [19].

Many selenoproteins have antioxidant functions involving the inactivation of reactive oxygen species (ROS). Glutathione peroxidases and thioredoxin reductases have similar properties. Reactive oxygen species (ROS) are unstable oxygen-containing molecules that readily enter into chemical reactions. They are formed in the body during various processes, both physiological and pathological, e.g. inflammation. The body successively inactivates them thanks to specialised enzymes. ROS do not pose a threat unless there is an imbalance, either as a result of their excessive formation or an impairment of their neutralisation mechanisms. This can lead to an unfavourable phenomenon called oxidative stress, which is associated with ageing and can lead to many diseases, including diabetes, atherosclerosis, cardiovascular, neurodegenerative or cancer [4].

Another important group are the iodothyronine deionidases (DIOs), which are involved in the conversion of thyroid hormones. They exist in several forms that can act in 2 ways: some of them convert inactive thyroxine (T4) into active triiodothyronine (T3) by removing the iodine molecule, while others act in reverse and deactivate the hormones. Deionidases are found not only in the thyroid gland, but also in other organs, e.g. brain, skin, heart, kidneys [20].

In selenium deficiency, there is a decrease in enzyme activity. Neutralisation of reactive oxygen species does not occur efficiently and the resulting oxidative stress causes apoptosis and cell death. Thyroid hormone conversion is also impaired, which impairs thyroid function [2].

Studies confirm that selenium has complex immunomodulatory properties [5]. It affects not only the cellular response, but also the humoral response. Excess selenium enhances the proliferation and differentiation of helper lymphocytes (Th) into Th1 cells, through interactions with interleukin 2 (IL-2) and interferon gamma (INFs), which play an important role in the body's immune responses. Also, NK cells respond to higher concentrations of selenium by increasing their cytotoxicity. Furthermore, by influencing macrophage function, selenium favours a change in the activation of pro-inflammatory macrophages (M1) into anti-inflammatory macrophages (M2). This has been associated with a state of significant selenium deficiency, which may influence inflammatory reactions, including autoimmunity [21, 22] or favour infections [23].

Anti-cancer properties are also among selenium's remarkable qualities. Due to the observed beneficial effects of selenium on the immune system, researchers have investigated the effects of selenium on cancer cells. However, the results have been mixed, showing an effect that is dependent on the selenium supplementation dose [6]. At low doses of selenium, the effect was beneficial and focused on an antioxidant role protecting cells, while high doses promoted the occurrence of oxidative stress [24]. Given the relationship presented and the increasing incidence of cancer, new concepts are emerging for the use of selenium in supporting cancer treatment as a chemoprotective agent. However, this is a very complex topic that requires a lot of new research on an ongoing basis [25, 26].

One of the factors implicated in the formation of thyroid cancer includes high levels of thyrotropic hormone (TSH), a relationship which has been confirmed by numerous scientific studies [27, 28]. Thyrotropic hormone (TSH) is produced and secreted by the anterior lobe of the pituitary gland. Via its receptors (TSHR), it acts on the thyroid gland, stimulating cells to produce and secrete the thyroid hormones triiodothyronine (T3) and thyroxine (T4).

Xu et al [29] in their meta-analysis also confirm the correlation of increased serum TSH levels in patients with an increased risk of papillary thyroid cancer (PTC). At the same time, they point out that TSH affects already existing tumour cells, stimulating them to divide further [30]. This is corroborated by the control group which showed that healthy individuals have no significant risk of thyroid cancer. In view of this, the association of increased TSH and thyroid cancer would particularly apply to individuals with thyroid nodules containing abnormal cells [31]. Selenium may also potentially contribute to the relationship presented. As indicated previously by the authors of the current review, selenium-containing enzymes iodothyronine deionidases affect thyroid hormone conversion by activating or deactivating them. The researchers postulate a theory in which the formation of triiodothyronine and thyroxine may be impaired in the case of selenium deficiency. A decrease in these hormones stimulates the pituitary via negative feedback to over-secrete TSH. In contrast, increased TSH levels can affect cell proliferation and tumour growth [32].

Method of selenium measurement. Attention should also be paid to the way selenium levels are determined, which can vary from one study to another. The most commonly used indicator is the plasma and serum concentration of the element, which reflects recent selenium intake. In addition, the universality of this method makes it possible to compare results with other tests. However, it should be borne in mind that the plasma selenium concentrations may be reduced due to inflammatory response and high CRP [33]. To assess the long-term selenium content of the body, determination in hair and toenails is used. This is one of the forms in which selenium is excreted from the body, which shows whether the element was present within the range of normal values. A prerequisite for this determination is that the dietary availability of selenium for the study group was constant. Similarly, the determination of selenium in whole blood (including erythrocytes) indicates the long-term status of the element concentration [34].

Overview of medical research. Taking everything into account, scientists have begun to consider whether there is a link between selenium concentrations and the occurrence of thyroid diseases, including cancer. The studies to date answering this question vary in their results – some show the presence of a relationship [35, 36, 37], while others do not [38]. In view of these contradictions, this is a complex topic which has not been fully investigated and requires further research.

A study by Baltaci et al [39] conducted in 2016, was based on the examination of trace element levels, including selenium in serum and thyroid gland tissue in patients diagnosed with thyroid cancer before and after surgery. The results showed that pre- and post-operative serum selenium levels in the study group were significantly lower than in the control group, while selenium levels in thyroid tissue were higher. Serum selenium was also measured on day 15 post-operation, at which time selenium levels in the study group were found to be similar to those in the control group.

Similar results were obtained in a recently published study by Ge et al [32], conducted on a group of 284 patients diagnosed with papillary thyroid cancer (PTC) who underwent total thyroidectomy. The researchers focused in not only on the relationship between serum selenium levels and the incidence of thyroid cancer, but also decided to go one step further and looked at the relationship between serum selenium levels and pathological features of papillary thyroid cancer in the patients. These features were tumour grade, lymph node metastasis grade, tumour size and number of metastatic lymph nodes. In addition to finding that serum selenium levels in women with PTC were lower than in men, the study also found a negative correlation of selenium levels with the number of lymph node metastases. However, regarding the stage and pathological subtype of PTC, no significant correlation was found. The researchers also observed that serum selenium concentrations in patients with bilateral tumours were significantly lower than in patients with unilateral tumours. There was a similar correlation for multifocal and unifocal tumours. Therefore, the conclusion was drawn that high serum selenium levels may be a protective factor in patients with papillary thyroid cancer.

A similar study was conducted by Jonklaas et al [40]. The authors selected a group of 65 patients undergoing thyroidectomy for thyroid cancer, suspected thyroid cancer, or nodular disease, in whom serum selenium levels were examined, among others. Analysis of the results did not confirm the existence of an association between serum selenium levels and the occurrence of differentiated thyroid cancer (DTC). However, it did show that there was a correlation of low selenium concentrations with the progression of already existing thyroid cancer. In contrast, the researchers stressed that the mechanism of this correlation is unknown. It is also not known whether it is the low selenium levels that influence greater tumour advancement, or whether it is the other way around and it is the advanced disease that causes low concentrations of the element.

The differences in the results of the Ge et al. and Jonklaas et al. studies may be due to the selection of the study group. In the case of the Ge et al. study, only cases with papillary thyroid cancer (PTC) were included, whereas the Jonklaas et al. study reviewed patients with differentiated thyroid cancer (DTC).

In the study by O'Grady et al [41], the researchers investigated the association of micronutrients, including selenium, with the incidence of thyroid cancer. The study initially included a large prospective cohort of 566,398 men and women in the United States, which, after applying exclusions, included 482, 807 participants. A questionnaire was used to assess dietary intake over the previous 12 months. The results, howevrer, did not reveal an association between a quintile of selenium intake and the incidence of thyroid cancer. On the other hand, the authors themselves emphasise that the use of the questionnaire was not objective and may have contributed to an erroneous assessment of dietary selenium content. On the one hand, this may be due to the fact that the study group lived in a large area where the selenium content of the soil varies considerably, which translates into differences in dietary content. On the other hand, the questionnaire did not provide direct (numerical) values for the study to refer to. For an objective assessment, determination of selenium concentrations in serum or nail sections would have been a better choice, although with such a large cohort this would create significant difficulties in conducting the study.

A similar use of a questionnaire was used in a study by Xu et al. [38] who determined the association between selenium intake and thyroid cancer in postmenopausal women aged 50–79 years. A total of 161, 808 women were recruited, but after applying the selection criteria, 147, 348 women were included with a mean age of 63.15 y at baseline. Both dietary selenium and selenium supplementation were assessed. The results of the study did not confirm the presence of a correlation. However, this study, like the previous one by O'Grady et al., was based on a questionnaire; therefore

Table 4. Characteristics of the studies

Authors	Study type	Study aim	Studied group	Se estimated method	Main results	Country
Baltaci et al.	Cross-sectional study	Comparison of serum selenium levels and thyroid tissue selenium levels in patients before, after, and 15 days after thyroidectomy, compared to control groups	Case group: 15 women and 15 men with the thyroid cancer Control group: 10 women and 10 men not diagnosed with thyroid cancer	Selenium estimated in serum and thyroid tissue samples	1. Pre- and post-operative serum selenium levels significantly lower than levels in the control groups 2. Post-operative selenium levels in thyroid tissue significantly elevated than the levels in the control groups 3. 15 days after the operation, serum selenium levels had returned to control group values	Turkey
Ge et al.	Cross-sectional study	Examining of association between serum selenium levels and pathological features of papillary thyroid cancer (PTC)	Group of 284 patients both genders with the papillary thyroid cancer	Selenium estimated in serum samples	1. Serum selenium levels of PTC lower in female patients than in malre patients 2. Serum selenium levels of PTC patients negatively correlated with the number of lymph node metastasis 3. No significant correlation found between serum selenium levels and the stage and pathological subtype of PTC.	China
Jonklaas et al.	Cross-sectional study	Investigation of the relationship between serum selenium levels and disease stage	Group of 65 patients both genders qualified for thyroidectomy due to differentiated thyroid cancer (48 patients) and for benign thyroid disease (17 patients)	Selenium estimated in serum samples taken 2 - 4 weeks prior to thyroidectomy	1. No significant association between low serum selenium levels and diagnosis of differentiated thyroid cancer 2. Association between lower serum selenium levels and higher thyroid cancer stage	United States, Washington, DC
O'Grady et al.	Prospective study	Assessment of correlation of dietary selenium intake with thyroid cancer risk	Cohort included 482,807 participants both sexes	Selenium estimated by questionnaire included usual dietary intake and use of supplements	1. No evidence of an association between quintile of selenium intake and incidence of total thyroid cancer	United States
Xu et al.	Prospective study	Examination of the association between dietary selenium intake and risk of thyroid cancer in post-menopausal women	Group of 147 348 women, mean age 63.15 y at baseline (age 50 to 79 y)	Total selenium intake including dietary and supplemental selenium measured by food frequency questionnaire (FFQ)	1. No significant association between total selenium intake and thyroid cancer risk were found 2. No significant association between total selenium intake and the risk for papillary thyroid cancer were found	United States

the selenium concentrationweare not objective and only informative. It was also limited by the study group, which only included postmenopausal women within a certain age range, therefore the results could not be applied to the whole population.

Factors influencing discrepancies in test results. A source of reliable and credible research is the standardisation of the method of measurement. This consists of a number of factors, the most important of which appears to be the possibility to compare the results obtained in different studies. If studies provide similar conclusions, this increases the credibility of the hypothesis. This also makes it possible to verify the methodology, as well as to identify and reduce errors.

Laboratory availability, equipment and capacity are important. Among other things, the prevalence of a measurement method, its cost, sensitivity or duration influences the evaluation of a sample in a laboratory. In addition, depending on the method, reference values may vary which affects interpretation of the results. Properly conducted, standardised testing promotes the sharing of results between scientists, which promotes development and supports innovation.

Another factor is the variability of selenium levels in soil in different regions, which translates into the content of this element in the human body. This is one aspect that creates difficulties in correctly determining the initial selenium concentration at the very beginning of the study. When comparing the results of two populations, each inhabited area with a different content of the element in the soil, the final results may differ, leading to ambivalent conclusions. For this reason, in order to maintain objectivity, it is necessary to standardise the results in terms of geographical differences.

The human ageing process affects biological changes which, in turn, affect the results of medical tests. There is a slowing down of metabolism in the body, a decline in the functioning of the immune system, a weakening of the regenerative capacity, and the development of chronic diseases. Lifestyle changes are observed through reduced physical activity and restrictions to resources, such as economic resources, which can translate into access to healthcare and therapeutic options. In addition, seniors are often on permanent medication, which can have an impaired view on objective tests.

Gender also has a significant impact on test results for a number of reasons in which hormone levels differ in their impact and role on the body. An example is the crucial importance of selenium for proper spermiogenesis and male fertility. During testosterone production, excessive production of reactive oxygen species (ROS) occurs, which have a damaging effect on delicate reproductive cells. Selenium-containing molecules have antioxidant properties and therefore have a protective effect on the processes of sperm formation and normal sperm growth [42].

Many diseases may manifest themselves differently and some genetic diseases are inherited in a gender-specific manner. Other differences may include health behaviours, such as physical activity, healthy diet, use of healthcare or predisposition to addictions. Ethnic origin also determines the approach to a study. The main aspect is genetic differences between individuals. It is well known that given groups have an individual metabolism and thus a greater predisposition to certain diseases, or a different response to medication.

The examples citedabove are only some of the factors that influence medical research and understanding these differences is crucial for developing effective public health recommendations. In the case of selenium deficiency, supplementation guidelines are intended to be based on the geographical and demographic factors outlined above. Adapting them should take into account new data and the health needs of the population to ensure adequate well-being.

Statistical significance is alsoa key factor which may influence the discrepancy in determining the role of selenium in thyroid cancer. Many studies have relied on flawed methodology; for example, they had low statistical power, meaning that the study group was too small or there was insufficient data to determine a correlation. On the other hand, by considering too large a group, real differences can be overlooked. The study design is not served by the lack of a placebo control and the failure to use a double-blinded trial. Also, the use of an inappropriate statistical test may be associated with a discrepant summary. When evaluating a study, attention should be paid to the comprehensiveness of the subject and the presence of many variables; thus, the greater their number, the more often it is impossible to take all of them into account. Therefore, an ideal study does not exist and in each case there may be concerns about the statistical significance of the results and errors in the analysis.

To minimise these concerns, a detailed study design is suggested, a meticulous study of the methodology, an assessment of the included population, or a careful consideration of factors that may influence the confounding of results.

Can test results have an impact on other thyroid diseases? Although this review has focused on thyroid cancer, it is also worth mentioning the possible impact on other thyroid diseases, such as chronic autoimmune thyroiditis (Hashimoto's disease) or Graves-Basedow disease, both of which are among the most common autoimmune disorders. Their pathogenesis is influenced by factors in the form of genetic susceptibility, epigenetic and environmental factors and, above all, immunological disorders [43].

One environmental aspect is nutritional status, which includes selenium deficiency [44]. In a study carried out on a Chinese population, a correlation was found between higher serum selenium concentrations and a lower probability of developing, among other things, autoimmune thyroiditis (Hashimoto's disease) [45]. Another study observed a significant effect of selenium supplementation on improving the condition of patients with mild orbitopathy in the course of Graves-Basedow disease [46]. Therefore, any study evaluating selenium levels can serve in the analyses not only related to thyroid cancer, but also to other thyroid diseases. In addition, some work has linked Hashimoto's or Graves-Basedow's disease to an increased risk. Although these conclusions are occasionally questioned, there exists a proportion of people worldwide in whom Hashimoto's disease or Graves-Basedow's disease co-occurs with thyroid cancer. It can therefore be concluded that research on the role of selenium can provide valuable information about thyroid and body health.

Effects of selenium deficiency or excess. In view of the increasing importance of selenium and the demonstration of its effects on the body, supplementation with this element may be beneficial. However, it should be borne in mind that a significant selenium deficiency or excess leads to serious diseases that can be health-threatening or even life-threatening. Selenium deficiency rarely overtly contributes to disease. However, in areas where content in the soil is very poor, it can cause serious diseases [49]. This is particularly the case in China, Tibet, Siberia and North Korea. One example is Keshan disease, a congestive cardiomyopathy that mainly affects children and young women of childbearing age. Another example is Kashin-Beck disease affecting the musculoskeletal system. It is a type of osteoarthritis, causing destruction and deformation of the bones, resulting in reduced mobility in the joints. Fortunately, both diseases are successfully treated with selenium supplementation.

In contrast, a significant excess of selenium in the diet can cause severe intoxication, i.e. selenosis [50], the most common symptoms of which are nausea, vomiting, diarrhoea, brittleness and loss of nails, hair loss, fatigue and behavioural changes in the form of irritability.

In addition, numerous studies confirm an increased risk of developing type 2 diabetes mellitus (DM2) when selenium intake exceeds recommended values. One of the consequences of long-term selenium exposure is the excessive activity of glutathione peroxidase 1 (GPx1) which disrupts the intracellular balance of reactive oxygen species (ROS), resulting in increased β-cell mass, dysregulation of insulin secretion and, consequently, impaired insulin sensitivity [51].

Thus, it can be concluded that there is a U-shaped relationship between selenium concentrations and disease occurrence. It is therefore recommended to follow the recommendations for daily selenium intake as well as periodic monitoring of blood concentrations of the element.

SUMMARY

Despite the relatively limited knowledge avasilable about selenium and its inconspicuous effects on the body, it is known that it has important functions in the proper functioning of the thyroid gland and the production of thyroid hormones. As is well known, thyroid hormones play a key role in maintaining homeostasis in the body by acting on virtually all body tissues.

To date, numerous studies have demonstrated the effects of selenium on thyroid diseases, including Graves-Basedow disease, Hashimoto's disease, congenital iodine deficiency syndrome and thyroid cancer. In addition, selenium has been shown to have antioxidant, immunomodulatory and anticancer effects, which are used in the development of new strategies in medicine, such as treatment.

During the authors review of the current knowledge and research, studies with differing results were found. Some confirmed the existence of a correlation between low selenium concentrations and the occurrence of thyroid cancer, while others rejected this correlation; still others only showed an association between low selenium concentrations and the progression of an already existing cancer. Each of the papers has advantages and disadvantages that affect a clear assessment of the correlation that occurs. Difficulties arise from the number of variables, including the selection of the study group, the area in which the group resides, the selenium content of the diet, or how the selenium levels were determined. It could be asked whether high selenium levels are therefore preferable, as they may protect against the onset or progression of cancer. But it should be noted that high levels of selenium do not necessarily confirm a lower risk of cancer, as high levels may be associated with proper, conscious healthy eating, which in itself is an important modifiable risk factor in cancer incidence.

Finally, a rational approach regarding supplementation must be maintained. In some conditions, such as insufficient dietary selenium supply, supplementation is beneficial. On the other hand, an excess of the element can cause dangerous health consequences. The best option, therefore, is supply under periodic monitoring of selenium concentration in the blood.

It is certain that the relationship studied is not a simple one, but rather a complex mechanism dependent on many factors. It is also possible that the beneficial effect of selenium on thyroid function depends on a specific range of concentrations of the element in the body. However, this needs to be further assess by research.

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