A Review About Selenium, An Essential Micronutrient

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Abstract: Selenium (Se), which is integrated into selenoproteins, is present in high concentrations in the thyroid gland. Se is regarded by the scientific community as a subject of rising interest. Schwarz was curious about the liver necrosis that occurs in lab rats that consume a torula yeast-containing diet. The issue was solved by switching from torula yeast to Saccharomyces yeast. Schwarz was able to use this experience to demonstrate the selenium deficiency of torula and to discover the first disease that was selenium responsive. Different investigational sequences are needed for common thyroid disorder such hypothyroidism, hyperthyroidism, and thyroid nodules in order to help with creating a diagnosis and treatment strategy. Women of childbearing age frequently experience thyroid issues, which call for a specialised treatment plan. Understanding uncommon thyroid diseases enables individualised workups in these situations. In the 1970s, plasma Se levels ranged from 0.63 to 0.76 mmol/L, which was among the lowest values ever recorded worldwide due to the poor dietary intake of selenium (25 mcg/day). The plasma selenium concentrations have grown by 70% as a result of the addition of selenium to fertilisers. A significant symptom of autoimmune hyperthyroidism, which frequently affects people with Graves' illness, is Graves' orbitopathy (GO). The thyroid gland expresses the majority of the known selenoproteins. Selenium shortage results in a decrease in these enzymes' expression and activity, which raises T4 levels while lowering T3 levels. The most prevalent types of autoimmune thyroid illness are Graves' disease and Hashimoto thyroid. More than 1% to 2% of the world's population is affected by AITD, which is often diagnosed in women between the ages of 30 and 50.

Introduction

A micronutrient called Selenium(Se) was originally identified in 1817[1]. The amount of selenium in the body depends on the demographics, nutrition, and geographic location of the population (mostly on the soil composition)[1, 2]. The importance of this micronutrient in preserving metabolism, cellular homeostasis, and immune-endocrine function has been documented in scientific studies during the past few years. Selenium, which is integrated into selenoproteins, is present in high concentrations in the thyroid gland. The removal of oxygen free radicals produced during the synthesis of thyroid hormones by some of these selenoproteins strengthens the antioxidant defence in the thyroid. Because it is a component of iodothyronine deiodinases, selenium is crucial for the metabolism of thyroid hormones. Numerous substances that are essential for the synthesis and metabolism of thyroid hormones are required for normal thyroid function[3]. Unsurprisingly, thyroid dysfunction may be exacerbated by selenium insufficiency. Selenium is regarded by the scientific community as a subject of rising interest. The way selenium is thought about has changed thanks to Schwarz and Foltz. Schwarz was curious about the liver necrosis that occurs in lab rats that consume a torula yeast-containing diet. The issue was solved by switching from torula yeast to Saccharomyces yeast. Schwarz was able to use this experience to demonstrate the selenium deficiency of torula and to discover the first disease that was selenium responsive[4]. Selenium can be found in both inorganic and organic forms, such as selenomethionine and selenocysteine (selenite and selenate)[1]. The organic form appears to be the best formulation for supplementation or treatment since it has better absorption[5]. Vegetable sources, particularly cereals, selenium yeast, and other selenium supplements all include selenomethionine[1]. Because methionine is replaced by selenium in body proteins, selenomethionine-containing supplements tend to have more bioavailable selenium. In contrast, animal foods are the principal source of selenocysteine, a selenium counterpart of the amino acid cysteine. Dietary supplements typically contain the inorganic forms (selenate and selenite). Due to a syndrome known as myxedematous endemic cretinism, which was characterised by an iodine and selenium deficiency, hypothyroidism, myxoedema, developmental issues, and intellectual incapacity, the crucial role of selenium in thyroid function came under scrutiny[6]. Even while selenium consumption in Europe does not consistently approach the acceptable amounts, selenium overdoses with harmful effects can sporadically take place. Selenosis is a condition that often develops when daily intake of this micronutrient exceeds 400g[7]. This uncommon condition, which can be caused by acute poisoning or protracted exposure to high amounts of selenium, was primarily described by epidemiological investigations in populations living in locations with high soil selenium

content[8]. Severe nausea, vomiting, abdominal discomfort, diarrhoea, hair loss, brittle nails, peripheral neuropathy, and the distinctive garlic smell in perspiration and breath are all signs of selenium toxicity[9]. The amount of selenium in the plasma directly relates to the amount of selenium consumed and is positively correlated with the nutrient's organic availability. In a study conducted in Belgium, meat items were shown to be the greatest source of selenium (31%) and were followed by fish (19%), pasta or rice (12%), and bread or cereals (11%)[4]. The small intestine absorbs the majority of the selenium. Reduced selenium levels are reported in smokers and the elderly for reasons that are yet unclear; selenium depletion has also been linked to the consumption of eggs, white rice, alcohol, and coffee.

Thyroid disease

Different investigational sequences are needed for common thyroid disorder such hypothyroidism, hyperthyroidism, and thyroid nodules in order to help with creating a diagnosis and treatment strategy. Women of childbearing age frequently experience thyroid issues, which call for a specialised treatment plan. Understanding uncommon thyroid diseases enables individualised workups in these situations. When determining if someone has an excess or shortage of thyroid hormone based on symptoms or risk factors, Thyroid Stimulating Hormone (TSH) should be tested.

- When thyroid nodules or a goitre are found.
- When monitoring simple thyroxine replacement treatment, at least 4-6
- Weeks should pass after a dose modification to allow for the establishment of a steady state, and once the medication is stable, every year.
- Before and early in the first trimester of pregnancy in persons who are taking levothyroxine or who have thyroid dysfunction risk factors.

A screening test for possible thyroid dysfunction is the measurement of TSH. Thyroxine (T4) and triiodothyronine(T3), two circulating thyroid hormones, exert strong negative feedback control over TSH release from the anterior pituitary (T3). TSH is an extremely sensitive indicator of thyroid dysfunction since a tiny increase in thyroid hormone synthesis causes a logarithmic suppression of TSH, and the opposite is also true[10]. TSH assays are reliable, and interference is infrequent. A normal TSH level effectively rules out thyroid hormone excess or insufficiency for the reasons listed above and because central thyroid malfunction (pituitary or hypothalamic diseases) is uncommon[11]. Hypothyroidism symptoms are vague and poorly correlated with thyroid hormone insufficiency. TSH is so frequently employed as a screening test for a variety of clinical presentations with a low pre-test probability for thyroid disease, such as fatigue, metabolic syndrome, and mental health issues. In most cases, a TSH result within the normal range (typically 0.5–4.0 mIU/L, and reported for each assay) in a situation with a low pre-test likelihood precludes thyroid dysfunction and typically does not need to be repeated for a number of years[12,13]. A concordant measure of a normal FT4 with a normal TSH result confidently excludes incident thyroid dysfunction if pre-test probability is high. Contrarily, hyperthyroidism frequently manifests as symptoms and has a stronger clinical and biochemical link. The daily intake of selenium is variable according to the geographical area, as mentioned previously. Indeed, in Europe, dietary selenium intake is about 40µg per day, and in the USA, it was reported to be 93µg per day in women and 134µg per day in men[2]. Table 2 shows the recommended daily allowances of selenium for adults[14,15]. In general, no difference exists in the recommended dietary

Selenium and Selenoproteins

Dietary Se can be found in a wide range of foods, including grains, vegetables, seafood, meat, dairy products, and nuts[15]. Se is required in trace levels. According to a study from Belgium, meat items account for 31% of dietary selenium intake, followed by fish (19%), rice or pasta (12%), and bread or cereals (11%)[16]. In the small intestine, selenium is absorbed most commonly (50–80%). Only 5% of selenium is eliminated in perspiration or saliva, with the kidneys excreting 60% of it and the colon excreting the remaining 35%[17]. Se shortage affects 15% of the world's population, according to estimates, and selenium intake varies greatly between countries. Dietary selenium consumption in Europe is about 40mcg per day. The dietary selenium consumption in the USA varies from 93mcg per day for women to 134mcg per day for men[18]. In the UK, men should get 75 micrograms of selenium per day, while women should get 60 micrograms [17]. Selenium type, soil pH, organic matter content, and ions are some of the variables that affect how readily available selenium is to the food chain and contribute to the variation in consumption around the globe[19]. The Ministry of Agriculture and Forestry introduced a multi-nutrient fertiliser containing sodium selenate in 1984 to improve the Se intake. Regular monitoring has been done of the plasma Se level in healthy Finnish people. In the 1970s, plasma Se levels ranged from 0.63 to 0.76 mmol/L, which was among the lowest values ever recorded worldwide due to the poor dietary intake of selenium (25 mcg/day). The plasma selenium concentrations have grown by 70% as a result

of the addition of selenium to fertilisers; this level is higher than the average plasma selenium value in Europe but lower than that reported in Canada or the USA[20]. Selenocysteine(Sec) is a substitute for selenium. Se largely affects biological processes by becoming incorporated into selenoproteins. The complicated selenoprotein manufacturing pathway used by all cell types incorporates dietary Se. There are 25 known human genes that produce selenoproteins[21]. Selenoprotein expression is necessary for life, as shown by the embryonic lethality of mice lacking the Sec tRNA[Ser]Sec gene, which is needed for selenoprotein translation[22]. Selenoprotein expression alterations are caused by variations in tRNA[Ser]Sec expression. Distinct subclasses of selenoproteins, notably the housekeeping and the stress-related selenoproteins, express two different Sec tRNAs that differ only by a single methylation base occurring on the 2′-O-hydroxyribosyl moiety at position 34. The research of selenoproteins proteins has recently been expanded thanks to Carlson et al recent demonstration of novel techniques for the isolation and sequencing of selenocysteines tRNA[23]. Serine (Ser) gets charged onto a tRNA (tRNA Sec) to create a Ser-tRNA Sec, which starts the selenoprotein manufacturing process. The Ser-tRNA Sec's seryl-tRNA residue is subsequently phosphorylated and changed into selenocysteyl-tRNA (Sec-tRNA Sec). Through the action of cis elements found in selenoprotein mRNA and protein factors including SECIS binding protein 2 (SBO2) and Sec specific translational elongation factor, the Sec tRNA is employed as Sec transfer into selenoproteins (EF Sec). The thioredoxin reductases, which play a role in the control of redox status and defence against oxidative damage, are among other well-studied selenoproteins[24].

Potential Role of selenium supplement

Selenium is found in high concentrations in the thyroid gland, and selenium and selenoproteins are recognised to be crucial for thyroid function. Low selenium levels have been discovered in the African region of Zaire, where myxoedema is endemic, supporting this theory and pointing to an oligoelement function. There has been investigation on selenium's effects on thyroid physiopathology. The thyroid gland expresses the majority of the known selenoproteins. Selenium shortage results in a decrease in these enzymes' expression and activity, which raises T4 levels while lowering T3 levels. The most prevalent types of autoimmune thyroid illness are Graves' disease and Hashimoto thyroid. More than 1% to 2% of the world's population is affected by AITD, which is often diagnosed in women between the ages of 30 and 50[25]. Although the pathophysiology of AITD is not fully understood, new genome-wide association studies[27] have suggested the existence of both common and distinct susceptibility genes[26]. Selenoprotein activity and quantity have recently been linked to single nucleotide polymorphisms (SNPs) in the selenoprotein genes, which may affect illness risk. Our team's earlier research, which was published, revealed a connection between the genetic variation of the SELENOS (SEPS1) promoter and the chance of developing Hashimoto's thyroiditis (HT). Patients with autoimmune thyroid diseases have been shown to have lower serum selenium concentrations (below 70 g/L)[28]. In order to determine if supplementation might have an effect on the development of thyroid immune mediated illness, several investigations were conducted in individuals with AITD, particularly in regions with low to borderline selenium levels. The majority of research indicate that selenium supplementation may reduce thyroid autoantibodies in the blood, although the trials up to this point have been inconsistent in terms of patient count, selenium supplement type, duration, thyroid ultrasonography assessment, and serum selenium measurement. Patients with AITD who use selenium supplements appear to have altered immunological and inflammatory responses. Enhancing plasma Glutathione Peroxidasw(GPX) and Thioredoxin reductase(TR) activity and lowering hazardous levels of hydrogen peroxide (H2O2) and lipid hydroperoxides(LHP) are the main strategies that have been put forth [29,30]. The most prevalent and well-known cause of thyroid dysfunction in the postpartum period is postpartum thyroiditis (PPT). PPT preventative and treatment strategies have been proposed, including selenium supplementation. In the study by Negro and collaborators[32], selenium supplementation was linked to a significant reduction in the anti-TPO antibody titre and a significant improvement of the ultrasound thyroiditis pattern in pregnant women with autoimmune thyroiditis. In Al-Kunani and collaborators' study[31], women who experienced spontaneous abortion had lower selenium capillary levels than the group who had achieved term gestation. Along with it, the prevalence of postpartum thyroid dysfunction and long-term hypothyroidism significantly decreased. These imply that a higher risk of thyroid illness is linked to poor Se status. Both groups in this study demonstrated Se deficient status (80 g/L), however there was no statistically significant difference between them. This could be attributed to the limited sample size and similar dietary patterns in the Nanjing area. The association between the mean Se level in Nanjing and the incidence of HT requires further research. In humans, selenoproteins with antioxidant and immunoregulatory capabilities carry out Se's biological tasks. In this study, serum GPx3 and SePP1 levels were also measured to assess Se status. Consistent with the results of baseline Se, SePP1 levels were slightly lower in patients with HT than in healthy subjects, but this trend was not statistically significant. In contrast, GPx3 levels showed statistical difference between groups, suggesting that patients with HT have lower antioxidation capacity. Supplementing with se may also guard against autoimmune thyroiditis, however the evidence is conflicting. Se supplementation is a promising adjuvant therapy for HT, according to the first meta-analysis of individuals with HT receiving L-T4 therapy.

Effect on Selenium on Graves' disease

A significant symptom of autoimmune hyperthyroidism, which frequently affects people with Graves' illness, is Graves' orbitopathy (GO). In 152 individuals with mild Graves' orbitopathy, Marcocci and associates conducted a randomised, double-blind, placebo-controlled trial to compare the effects of selenium and pentoxifylline[33]. At six months, they discovered that selenium medication, but not pentoxifylline, was linked to better quality of life, fewer ocular involvements, and a halt in the course of Graves' orbitopathy. The patients were then re-evaluated at 12 months (after 6 months without selenium, pentoxifylline, or placebo supplementation). Several studies have focused on the significance of selenium in thyroid function and autoimmune processes in order to determine whether supplementing with this micronutrient may have an effect on the development of thyroid disease. The development of Hashimoto's thyroiditis, a disorder marked by the presence of anti-thyroperoxidase and anti-thyroglobulin antibodies, is actually influenced by selenium intake. Clinical trials have recently been developed to address some of these unresolved issues. A current randomised controlled trial with 472 autoimmune thyroiditis patients receiving levothyroxine has been called the CATALYST trial (also known as the "chronic autoimmune thyroiditis quality of life selenium trial") (LT4). Their main goal is to compare the impact of a 200 g selenium-enriched yeast supplement over a 12-month period to a placebo on thyroid-related quality of life. LT4 dosage, serum T3/T4 ratio, serum Thyroid Peroxidase Antibody (TPOAb) concentration, plasma selenium concentration, and immunological and oxidative stress indicators are secondary objectives that will be assessed in comparison to placebo. In this trial, unlike several others on the subject, plasma selenium concentrations will be monitored on a regular basis to gauge selenium intake. Additionally, this study will be the first to examine the mechanisms by which selenium functions in autoimmune thyroiditis and the impact of selenium supplementation on LT4 dose. This trial is expected to end in 2018 under the research protocol[34].

Conclusion

Though the evidence is not as yet clear-cut, the organic form (selenomethionine), due to its pharmacokinetics, is likely to be more advantageous in long-term prevention, and supplementation efforts, while the inorganic form (sodium selenite) has proven effective in an acute, e.g., sepsis, clinical setting. Recent data indicate that functional selenoprotein single-nucleotide polymorphisms (SNPs) may interfere with Se utilization and effectiveness.

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