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Influence of selenium deficiency on the development of thyroid disorders - a literature review

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ABSTRACT:

Introduction and purpose: Selenium is essential for the proper course of many physiological and biochemical processes in the human body. It plays a large role in ensuring proper immunoendocrine function. The organ with the greatest amount of selenium per gram of tissue is the thyroid gland. This element builds enzymes involved in antioxidant processes - peroxidase, as well as deiodinases involved in the metabolism of thyroid hormones. There are scientific reports showing a beneficial effect of selenium supplementation in autoimmune diseases of the thyroid gland. The aim of this study is to summarize the current knowledge on the relationship between selenium deficiency and the development of thyroid dysfunction.

Description of the state of knowledge: There is a correlation between selenium deficiency and the functioning of the thyroid gland. It has been shown that selenium levels are often lowered in patients with autoimmune thyroiditis. Research shows that selenium supplementation may lower TPOAb and TgAb antibody levels in patients with Hashimoto's disease. In patients with Graves' orbitopathy, administration of selenium resulted in delayed progression of orbitopathy and less disease severity. There are reports that supplementation with this element may also increase the effectiveness of antithyroid drugs in patients with Graves-Basedow disease. There was also an association between selenium deficiency and the development of goiter and thyroid nodules.

Conclusions: Selenium plays an important role in the proper functioning of the thyroid gland. Although the specific role of selenium in the pathogenesis of thyroid disease is still under investigation, there are numerous reports saying that its deficiency may affect it. More research is needed on the relationship between selenium concentration and the regulation of thyroid function, because introducing it into the treatment regimen of thyroid disorders may give hope for better therapeutic effects.

Key words: selenium, thyroid, selenium deficiency, thyroid disorders

INTRODUCTION AND PURPOSE:

Selenium is a micronutrient that is crucial for the proper course of many physiological and biochemical processes in the human body. Scientific reports more and more often show how important this element is in ensuring proper immunoendocrine function. The organ with the greatest amount of selenium per gram of tissue is the thyroid gland [4, 11]. This element builds enzymes involved in antioxidant processes - peroxidase, responsible for the elimination of free radicals generated during the production of thyroid hormones, as well as deiodinases involved in the metabolism of thyroid hormones [4]. The relationship between the deficiency of this micronutrient and the development of thyroid disorders has been investigated for some time. There are scientific reports showing a beneficial effect of selenium supplementation in autoimmune diseases of the thyroid gland [6].

The main source of this element is food, its deficiencies mainly result from insufficient supply in the diet. Other factors, such as geographic area, also affect the selenium content in the body, due to the specificity of the soil. The recommended daily intake of selenium was estimated at 55 μg / d (range is 30–85 μg / d) [8]. Selenium deficiency in humans occurs when the dietary intake is less than 40 μg / day. At daily concentrations above 400 μg, selenium toxicity is observed [2, 19].

The aim of this study is to summarize the current knowledge on the relationship between selenium deficiency and the development of thyroid dysfunction.

DESCRIPTION OF THE STATE OF KNOWLEDGE:

There is a correlation between selenium concentration and the functioning of the thyroid gland. Selenium in the work of the thyroid gland is important for two reasons - by building peroxidase, it plays a role in antioxidant processes, by building deiodinase - a role in the action of thyroid hormones. The role of peroxidases in combating oxidative stress was demonstrated in one of the studies by the use of animal-derived thyroid cell culture [6]. Selenium deficiency caused improper iodination of certain proteins by peroxidases, which led directly to thyroid cell apoptosis or the exposure of atypical epitopes, which then became an easy target for the immune system. Incubation with low doses of selenium increased the activity of these enzymes and decreased the frequency of apoptosis [6].

Another study emphasized the role of selenium in the activity of deiodinases. A group of euthyroid people was analyzed; a correlation was shown between a decrease in serum selenium concentration and disturbed thyroid parameters - a reduced T3 / T4 ratio and higher TSH levels. It was associated with a decrease in the function of iodothyronine deiodinases responsible for the peripheral conversion of T4 to T3, which resulted in a reduced production of T3 and, consequently, an increased synthesis of TSH [6].

Therefore, more and more attention is paid to the potential role of selenium supplementation in the treatment of autoimmune thyroid disorders. It has been shown that in patients with thyroid diseases such as autoimmune thyroiditis or subclinical hypothyroidism, selenium levels are often reduced [2, 13]. One of the publications analyzes the effect of selenium administration during the treatment of Hashimoto's disease - chronic lymphocytic thyroiditis. It results in the production of antibodies to thyroid peroxidase - TPoAb and very often thyroglobulin - TgAb and the formation of lymphocytic infiltrates in the thyroid gland. The study found that in the group of patients who received selenium, TPOAb levels dropped by as much as 40%, and in 1/4 of patients the TPOAb concentration was completely normalized. Moreover, the echogenicity of the thyroid gland also improved in the subjects [4]. In another study, similar observations were made - the annual supplementation of physiological doses of selenium (80 μg / day) resulted in a decrease in TPoAb and TgAb levels. However, no significant effect on the concentration of T4 or TSH was shown [4, 12].

Many studies also focuses on the impact of selenium supplementation on the course of Graves-Basedow's disease. It is an autoimmune disease in which the production of TRAb antibodies against the TSH receptor stimulating this receptor occurs, resulting in an increased production of thyroid hormones and the development of symptoms of hyperthyroidism. The research data in this case is somewhat inconsistent. On the one hand, it has been shown that in patients whose disease returned, supplementation of this element may enhance the effect of antithyroid drugs and reduce the level of TRAb [2, 14]. On the other hand, a randomized clinical trial of patients with Graves-Basedow disease treated with methimazole did not show the effect of selenium in the short-term control of hyperthyroidism [15]. This inconsistency may result from the differences between the size of the patient groups, the duration of

treatment and follow-up, and the variable disease stage among patients [2]. Therefore, further research is needed to establish a more specific position on this matter.

A significant number of patients with Graves-Basedow disease, almost 50%, suffer from Graves orbitopathy [4]. A randomized, double-blind study assessed the effect of administering selenium or pentoxifylline in 152 patients with Graves' orbitopathy. This study showed that it was selenium treatment, rather than pentoxifylline, that resulted in reduced orbital involvement and delayed orbitopathy progression. These patients were also assessed after a six-month period without supplementation - the effect obtained during the first assessment was maintained [4].

Selenium supplementation in pregnant women with autoimmune thyroid disease is also becoming an issue of interest. There are hypotheses that since selenium has anti-inflammatory properties, it may be one of the elements in the therapy of pregnant women with autoimmune thyroid disease [16, 17, 7]. Three groups of pregnant women were examined in the period from the 10th week from the last menstruation to the year after childbirth. The first group of women with anti-TPO antibodies received selenomethionine 200 μg / day (S1), the second group with anti-TPO antibodies did not receive selenium (S0), while the third group was TPO-negative. During pregnancy, there was a significant decrease in anti-TPO antibodies in both the supplemented and non-supplemented groups, but the decrease was greater in the S1 group (62.4%) compared to the S0 group (43.9%). In the postpartum period, both groups had an increase in anti-TPO antibody titer, but the mean level and peak were lower in the S1 group compared to the S0 group. Also, the percentage of patients with postpartum thyroiditis and persistent hypothyroidism after pregnancy was significantly lower in the supplemented group compared to the non-supplemented group. This is the first such trial showing the positive effects of administering selenium to pregnant women with autoimmune thyroid disease [6]. On the other hand, in another study based on the analysis of the Polish population of pregnant women, Abroziak et al. observed selenium deficiency (<45 μg / l) in 0%, 3.4%, 28.6% and 4.5%, 18.2% and 35.5% of women with autoimmune thyroid disease (AITD) and in the control group, respectively in the first, second and third trimesters of pregnancy [20]. The decrease in TPOAb and TGAb was not related to the concentration of this element. TSH levels in newborns were also measured - no differences in the mean TSH levels in children of AITD mothers compared to healthy mothers (1.4 ± 1.4 mIU / l vs 1.8 ± 1.4 mIU / l). Moreover, no relationship was found between the TSH values in newborns and the concentrations of selenium or selenoprotein in the serum of their mothers [20]. The scientific data is therefore contradictory and there is no reliable evidence for selenium supplementation in pregnant women. The American Thyroid Association (ATA) in its 2017 guidelines does not recommend administering selenium during pregnancy due to the inconsistency of data from the literature [7]. This is a topic that still requires further analysis.

Part of the research focused on assessing the relationship between selenium deficiency and the volume of the thyroid gland and the tendency to form nodules within it. It has been shown that the low concentration of the element correlates with an increased risk of thyroid enlargement and the development of thyroid nodules [4, 18]. Therefore, there are more and

more hypotheses linking selenium deficiency with an increased risk of developing goiter and thyroid nodules [6].

CONCLUSIONS:

Selenium plays an important role in the proper functioning of the thyroid gland. It builds enzymes that are involved in the fight against free radicals and in the metabolism of thyroid hormones. More and more studies indicate a relationship between the deficiency of this element and the development of autoimmune diseases of the thyroid gland, goiter and thyroid nodules. Although the specific role of selenium in the pathogenesis of thyroid disease is still under investigation, there are numerous reports that its deficiency may affect it. More research is needed on the relationship between selenium concentration and the regulation of thyroid function, because introducing it into the treatment regimen of thyroid disorders may give hope for better therapeutic effects.

LIST OF REFERENCES:

1. Leonidas H. Duntas, Selenium and the Thyroid: A Close-Knit Connection, *The Journal of Clinical Endocrinology & Metabolism*, Volume 95, Issue 12, 1 December 2010, Pages 5180–5188, https://doi.org/10.1210/jc.2010-0191
2. Gorini, F.; Sabatino, L.; Pingitore, A.; Vassalle, C. *Selenium: An Element of Life Essential for Thyroid Function. Molecules* 2021, *26*, 7084. https://doi.org/10.3390/molecules26237084
3. Rayman M, DPhil [Oxon], *Selenium and human health,* The Lancet, Volume 379, Issue 9822, P1256-1268, March 31, 2012 DOIL https://doi.org/10.1016/S0140-6736(11)61452-9
4. Mara Ventura, Miguel Melo, Francisco Carrilho, *"Selenium and Thyroid Disease: From Pathophysiology to Treatment"*, *International Journal of Endocrinology*, vol. 2017, Article ID 1297658, 9 pages, 2017. https://doi.org/10.1155/2017/1297658
5. Mehdi Y, Hornick JL, Istasse L, Dufrasne I. *Selenium in the environment, metabolism and involvement in body functions.* Molecules. 2013 Mar 13;18(3):3292-311. doi: 10.3390/molecules18033292. PMID: 23486107; PMCID: PMC6270138.
6. Drutel, A., Archambeaud, F. and Caron, P. (2013), *Selenium and the thyroid gland: more good news for clinicians.* Clin Endocrinol, 78: 155-164. https://doi.org/10.1111/cen.12066
7. Hubalewska-Dydejczyk A, Duntas L, Gilis-Januszewska A. *Pregnancy, thyroid, and the potential use of selenium.* Hormones (Athens). 2020 Mar;19(1):47-53. doi: 10.1007/s42000-019-00144-2. Epub 2019 Nov 13. PMID: 31721136; PMCID: PMC7033058.

8. Rayman, M. (2008). *Food-chain selenium and human health: Emphasis on intake. British Journal of Nutrition, 100*(2), 254-268. doi:10.1017/S0007114508939830
9. Schomburg, L. *The other view: the trace element selenium as a micronutrient in thyroid disease, diabetes, and beyond*. *Hormones* 19, 15–24 (2020). https://doi.org/10.1007/s42000-019-00150-4
10. Yuan Z, Xu X, Ye H, Jin L, Zhang X, Zhu Y. *High levels of plasma selenium are associated with metabolic syndrome and elevated fasting plasma glucose in a Chinese population: A case-control study.* J Trace Elem Med Biol. 2015 Oct;32:189-94. doi: 10.1016/j.jtemb.2015.07.009. Epub 2015 Jul 26. PMID: 26302928.
11. R.C. Dickson, R.H. Tomlinson, *Selenium in blood and human tissues*, Clinica Chimica Acta, Volume 16, Issue 2, 1967, Pages 311-321, ISSN 0009-8981, https://doi.org/10.1016/0009-8981(67)90197-0
12. Nacamulli, D., Mian, C., Petricca, D., Lazzarotto, F., Barollo, S., Pozza, D., Masiero, S., Faggian, D., Plebani, M., Girelli, M.E., Mantero, F. and Betterle, C. (2010), *Influence of physiological dietary selenium supplementation on the natural course of autoimmune thyroiditis.* Clinical Endocrinology, 73: 535-539. https://doi.org/10.1111/j.1365-2265.2009.03758.x
13. Wu Q, Rayman MP, Lv H, Schomburg L, Cui B, Gao C, Chen P, Zhuang G, Zhang Z, Peng X, Li H, Zhao Y, He X, Zeng G, Qin F, Hou P, Shi B. *Low Population Selenium Status Is Associated With Increased Prevalence of Thyroid Disease*. J Clin Endocrinol Metab. 2015 Nov;100(11):4037-47. doi: 10.1210/jc.2015-2222. Epub 2015 Aug 25. PMID: 26305620.
14. Wang L, Wang B, Chen SR, Hou X, Wang XF, Zhao SH, Song JQ, Wang YG. *Effect of Selenium Supplementation on Recurrent Hyperthyroidism Caused by Graves' Disease: A Prospective Pilot Study*. Horm Metab Res. 2016 Sep;48(9):559-64. doi: 10.1055/s-0042-110491. Epub 2016 Jul 8. PMID: 27392116.
15. Leo M, Bartalena L, Rotondo Dottore G, Piantanida E, Premoli P, Ionni I, Di Cera M, Masiello E, Sassi L, Tanda ML, Latrofa F, Vitti P, Marcocci C, Marinò M. *Effects of selenium on short-term control of hyperthyroidism due to Graves' disease treated with methimazole: results of a randomized clinical trial.* J Endocrinol Invest. 2017 Mar;40(3):281-287. doi: 10.1007/s40618-016-0559-9. Epub 2016 Oct 12. PMID: 27734319.
16. Ventura M, Melo M, Carrilho F. *Selenium and Thyroid Disease: From Pathophysiology to Treatment.* Int J Endocrinol. 2017;2017:1297658. doi: 10.1155/2017/1297658. Epub 2017 Jan 31. PMID: 28255299; PMCID: PMC5307254.
17. Negro R, Greco G, Mangieri T, Pezzarossa A, Dazzi D, Hassan H. *The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies*. J Clin Endocrinol Metab. 2007 Apr;92(4):1263-8. doi: 10.1210/jc.2006-1821. Epub 2007 Feb 6. PMID: 17284630.
18. Rasmussen, Lone Banke, Lutz Schomburg, Josef Köhrle, Inge Bülow Pedersen, Birgit Hollenbach, Antonia Hög, Lars Ovesen, Hans Perrild, and Peter Laurberg. "Selenium status, thyroid volume, and multiple nodule formation in an area with mild iodine

deficiency", *European Journal of Endocrinology* 164, 4 (2011): 585-590, accessed Aug 23, 2022, https://doi.org/10.1530/EJE-10-1026

19. Lenny H. E. Winkel, C. Annette Johnson, Markus Lenz, Tim Grundl, Olivier X. Leupin, Manouchehr Amini, and Laurent Charlet, *Environmental Science & Technology* 2012 *46* (2), 571-579DOI: 10.1021/es203434d

20. Ambroziak U, Hybsier S, Shahnazaryan U, Krasnodębska-Kiljańska M, Rijntjes E, Bartoszewicz Z, Bednarczuk T, Schomburg L. *Severe selenium deficits in pregnant women irrespective of autoimmune thyroid disease in an area with marginal selenium intake*. J Trace Elem Med Biol. 2017 Dec;44:186-191. doi: 10.1016/j.jtemb.2017.08.005. Epub 2017 Aug 4. PMID: 28965575.