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DISBALANCE OF MICROELEMENTS AS ONE OF THE INSUFFICIENTLY EXPLORED CAUSES OF THYROID DISFUNCTION

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Abstract:

The causes of thyroid dysfunction are varied. These can lead directly to the pathology of the thyroid gland itself, as well as diseases of the pituitary and hypothalamus. In other cases, a violation of the synthesis of thyroid hormones causes a deficiency of microelements, which in the composition of thyroid hormones or affect their transformation, for example, iodine or selenium. But there are other trace elements that are involved in the metabolism of thyroid hormones, which participation is less studied. The review is dedicated to this microelements.

Keywords

Thyroxine, triiodothyronine, microelements, subclinical hypothyroidism

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INTRODUCTION:

There are about 215 million people in the world suffering from diseases of the thyroid gland (TG) according to WHO [1, 2]. The clinical and social significance of thyroid pathology is inferior only to diabetes [3, 4]. One of the most common thyroid dysfunction is subclinical hypothyroidism (SH). This term refers to clinical and laboratory syndrome due to persistent deficiency of thyroid stimulating hormone (TSH) in the human body or a decrease the biological effect of thyroid hormones (TH) on target cells [5]. According to statistics, the prevalence of hypothyroidism in Russia is 3.7 - 21%, with the most common in women older than 50 years old [6]. For every 1,000 women older than 50 years old, there are 19 suffering from hypothyroidism, which may be due to hormonal alteration of the body during menopause. In 95% of the total number of patients, the primary form of hypothyroidism is diagnosed [7–9].Secondary hypothyroidism is a pathological condition that arises due to insufficient production of TSH by the pituitary gland [10,11]. HS, which cannot be attributed to any of described forms, occurs in 5% of cases. It occurs due to the acquired resistance of the tissues to thyroid hormones or may be associated with impaired transformation of thyroxin (T4) into triiodothyronine (T3) at the level of peripheral tissues. The causes of hypothyroidism can be varied [12]. It can be genetically determined resistance to T3 [13,14] or a violation of T4 deiodination process [14]. Interest to studying the role of the effect of imbalance of microelements on the functioning of vital body system, the volume of research, scientific works and publications devoted to this problem increase every year.

Today it has been established that microelements have a direct impact on the functioning of organs and systems, and also take part in the synthesis and metabolism of enzymes and hormones, including thyroid [8]. Excessive and insufficient intake of trace elements leads to disruption of this process [15].

Some factors that explain the insufficient effect of thyroid hormones are discussed in this review.

The metabolism of hormones and their constituent components, such as iodine, is influenced by such trace elements as selenium, zinc, chromium, iron and some others. One of the common causes of hypothyroidism is iodine deficiency in the environment, as it is a part of TG - T4 and T3. Conversion of T4 to more active T3 is the most significant link in the metabolism of thyroid hormones. This process is carried out in the course of monodeiodination of thyroxin in the tissues with the participation of selenium-dependent deiodinases [16-18]. The role of selenium in the metabolism of thyroid hormones is studied. Selenium was discovered by the Swedish chemist J. Y. Berzelius in 1817. For the first time the need for it was proven in 1957. But at that time, the biochemical mechanisms of action of selenium were not fully understood and clear. The association of selenium deficiency with the development of Keshan and Kashin-Bek disease was described thirteen years later [19]. Rayman M.P. described the relationship between moderate selenium deficiency and increased risk of developing cancer, infectious diseases, male infertility, neurological diseases, including Alzheimer's and Parkinson's in a review article [20]. Disruption of TG metabolism, manifested in the development of GHT, was noted by the endocrine system [21].

To date, determined the daily need for selenium for humans. It is 50-500 mg / day. If you use selenium more than 700 mcg / day, there is a risk of poisoning [18, 22]. All biological effects of selenium on the human body are carried out through the expression of selenoproteins. They are about 30. They contain selencysteine in their active center, which is encoded by 25 corresponding genes [23]. Most of them have their own well-defined function: 1) they are involved in maintaining the oxidative balance of the cell — glutathione peroxidase, thioredoxinreductase; 2) inhibit apoptosis and regulation of cell growth (decrease in the level of thioredoxin); 3) participate in the conversion of T4 into reversible or active T3 - 1st and 2nd class deiodinases [22]. There are several selencysteine-containing proteins are expressed in the thyroid gland, mainly in thyrocytes. These proteins include 3 forms of glutathione peroxidases (cGPx, pGPx, PHGPx), 1-type 5-deiodinase and selenoprotein P [24]. Thyrocytes form a large amount of peroxides (H_2O_2), which are the substrate for the synthesis of thyroid peroxidase (TPO) on the cell surface. This process takes place for the implementation of the electron acceptance reaction. The formation of hydrogen peroxide is a limiting stage in the metabolism of thyroid hormones and this stage is controlled through a system of secondary messengers. The production of peroxides leads to the iodination of tyrosine residues that are present in thyroglobulin synthesized by the follicular cells of the gland. After this, the protein changes its structure in such a way that the tyrosine residues approach each other, facilitating the condensation reaction between them. The process of iodization of tyrosyl residues and the condensation reaction occur on the outer surface of the thyrocyte apical membrane. Hydrogen peroxide, which can easily penetrate the outer surface of the apical membrane

and activate thyroid peroxidase, accumulates at the site of thyroid peroxidase [21]. The thyroglobulin iodization process is triggered in this way. This mechanism is strictly controlled by glutathione peroxidase (GPx), under the action of which peroxide is reduced to water. An excess of peroxides can diffuse into thyrocyte, where it will immediately restore to water under the action of GPx, thioredoxinreductase (TRx), and peroxisome catalase. Thus, in the case of selenium deficiency, GPx activity decreases. Therefore, there is an accumulation of excess amounts of hydrogen peroxide and an increase in the activity of thyroid peroxidase. Consequently, it can be judged that the GPx system is central to the iodization process, and the extra thyroid selenium content determines the activity of this system [18].

In addition, the effect of selenium deficiency on TG metabolism depends on whether it is accompanied by iodine deficiency [25]. In the case when deficiency of selenium is determined, for example, in patients with phenylketonuria who are on a low protein diet, the thyroid function is maintained within the normal range. Then much attention is paid to the decrease in the activity of glutathione peroxidase, which causes an intensification of oxidative stress [26]. As shown by the results of a study conducted in 1993, Beckett G.J., Nicol F., Rae P.W. et. al., selenium deficiency potentiates a decrease the thyroid function arising on the background of iodine deficiency [27]. Selenium is an element of iodotyroninedeiodinase [28]; therefore, it should not be ruled out that its deficiency may lead to insufficient synthesis of this enzyme. Impaired transformation of thyroxin into triiodothyronine in the liver and kidneys, as well as iodine metabolism and TG formation is a consequence of this deficiency [18, 29, 30].

The selenium-containing oxidoreductases are represented by 3 types of iodothyronine deiodinases (D1, D2, D3), which catalyze the activation (D1 and D2) and inactivation (D3) of thyroxine (T4) with the formation of active triiodothyronine (T3) and reverse T3 (rT3) in deiodination reactions].

Deiodinases have tissue and organ specificity, which is determined by their different localization and functions in human tissues and organs [32]. Thus, D1 is mainly expressed in the liver, kidney, thyroid and pituitary; D2 - in the thyroid, heart, central nervous system (CNS), pituitary, skeletal muscles, brown adipose tissue and placenta; D3 - in the pregnant uterus, placenta, liver, brain and skin of the embryo. Different types of deiodinases catalyze the reactions of central (in the thyroid gland) and local (in other organs and tissues) deiodination. T3 production in the thyroid gland and control of its level in the blood are mainly provided by D1, while D2 and D3 regulate the deiodination in other organs and tissues [30]. Zinc also occupies one of the leading positions in the metabolism of the thyroid hormones [33]. It is an important essential trace element, an integral component of the composition of metalloenzymes and determines the catalytic activity by participating in the metabolism of hormones. The trace element is indispensable for the functioning of DNA and RNA polymerases, which are responsible for the transfer of genetic information, the biosynthesis of cellular components and repair. The recommended daily intake of zinc in the diet is 11 mg for men and 8 mg for women [33, 34]. The most important aspect is the effect of zinc on the synthesis of thyroid hormones through the realization of their effects. Zinc is contained in 20 transcription factors needed to modulate the expression of the thyroxin gene [35, 36]. Data on the effect of zinc concentration on thyroid hormone levels are not straightforward. Research results G. Napolitano et al. on the example of patients with trisomy 21 chromosome pairs and hypothyroidism and A.K. Baltaci et al. study in rats showed that a diet rich in zinc leads to a decrease in thyroid stimulating hormone levels and an increase in T3 concentration [37]. A correlation is observed between zinc deficiency and thyroid gland volume, which is manifested in an increase in AT titer to thyroid stimulating hormone receptors (TSH) and their stimulating effect on thyroid growth, as well as phagocytosis disorder, increased release of cytokines by macrophages (growth factors): a transforming alpha growth factor , transforming growth factor beta [33, 38, 39]. Zinc inhibits the toxicity of lead and copper and affects to the secretion of thyroid-stimulating hormone, the glycoprotein of the anterior pituitary gland, which stimulates the synthesis and release of thyroid hormones: thyroxine and triiodothyronine [40].

Also studied the role of chromium. One of the manifestations of its biological activity is the interaction with the thyroid gland. The need for chromium varies, according to available data, in the range of 50–200 mcg per day. The standard diet contains 33-125 micrograms of chromium, and for the elderly 5-115 micrograms. The difference between the recommended and actual consumption of chromium is 2 times less due to the consumption of highly purified products that are poor in chromium [18], which in turn leads to a deficiency of this trace element. There is a direct relationship between the concentration of chromium and the function of the thyroid gland, which was revealed during the examination of the mineralograms of human hair.

As a result of research, it was revealed that, under certain conditions, chromium is able to replace iodine in thyroid hormones. Giving physiological doses of chromium to rats, experiencing iodine deficiency, judging by the histological picture of the thyroid gland, increases its functional activity [AT Goncharov. 1968], while elevated doses of chromium inhibit thyroid function at animals receiving a normal amount of iodine [18]. Chromium accumulates in large quantities in the thyroid gland, in iodine-deficient biogeochemical regions, at humans and animals. This occurs due to a decrease in its concentration in organs and tissues [A. Sorkina. 1963]. There is evidence that after thyroidectomy, the chromium content in animals decreases, and when animals receive thyroid hormones, it rises again [Lifshits M.L., 1980] [18,36]. Thus, we can conclude that there are signs of SG in case of chromium deficiency.

Before proceeding to consider the effect of iron on the thyroid gland, it is necessary to note a number of functions that it provides. So iron-containing biomolecules perform 5 main functions: electron transport (cytochromes, iron seroproteins), transport and oxygen storage (hemoglobin, myoglobin), participate in the formation of active centers of redox enzymes (sulphoperoxide dismutase, oxidase), as well as selenium. And also provide transport and deposit of iron, the conversion of phenylalanine to tyrosine. Let us dwell on the last two functions [13, 14, 36]. An excess of iron deposition leads to the emergence of a special form of complications - hemochromatosis. It is accumulation of hemosiderin, due to changes in the metabolism of ferritin. For example, iron deposition occurs in various organs, including the thyroid gland, which leads to disruption of its structure and function [18]. Iron is directly involved in the conversion of phenylalanine - an essential amino acid used in the body to synthesize tyrosine, being a catalyst for the process and, as a result, further contributing to the conversion of tyrosine to thyroid hormones [14]. Cobalt has a negative effect on the metabolism of hormones. In excess, it inhibits thyroid peroxidase, which iodizes the tyrosine residues of thyroglobulin. [18, 36]. An interesting fact is that a negative effect on the function of the thyroid gland has not only an excess, but also a deficiency of this trace element. It was established that at physiological concentrations cobalt is necessary for the synthesis of TG at rats. The giving of this trace element to animals that are deficient in chromium leads to a decrease in the number of thyroid follicles and an increase in the height of the epithelium lining them. Farm animals and people from biogeochemical provinces with a reduced level of cobalt in the environment or an unfavorable ratio with iodine have endemic thyroid dysfunction [Kovalsky VV, 1974].

Lithium is a conditionally essential trace element that participates in the metabolism of thyroid hormones. It specifically accumulates in thyrocytes and causes an increase in the thyroid at humans, and formation of colloidal goiter was noted at rats [Sheard M.N., 1980 Wenzel R., 1984]. In experimental studies L.V. Gerbilsky (1987) was established that colloid retention occurs in rat gland follicles, and a significant decrease in the number of resorption vacuoles, thyrocyte heights and a decrease in the diameter of their nuclei under the action of lithium. In addition, the inclusion of radioactive iodine in the thyroid gland is dramatically reduced, the level of T4 and T3 in the serum decreases, which indicates a delay in the removal of hormones from the thyroid gland, which is characteristic of colloid goiter [36].

CONCLUSIONS:

The data presented indicate that the causes of hypothyroidism are diverse and not well understood. The function of the thyroid gland can affect both the excess and the lack of certain trace elements, therefore this problem is of particular relevance not only for understanding the causes and mechanisms of thyroid dysfunction, but also for choosing the tactics of treating patients with thyroid pathology. Therefore, the importance of the influence of a number of trace elements on the metabolism of thyroid hormones requires further study.

REFERENSES:

1. Budnevsky AV, Kaverzina MY [et al.] Quality of life and treatment of subclinical hypothyroidism in patients with coronary heart disease // Applied Informational Aspects of Medicine. 2011; 14(1): 52-57.
2. Shiryaev OYu, Yankovskaya VL, Budnevsky AV [et al.] Psychosomatic Aspects of Chronic Heart Failure // International Journal of Biomedicine. 2017; 7(3): 248-250.
3. Goncharov NP, Peterkova VA, Kolesnikova GS Secondary hypothyroidism: features of diagnosis and treatment // Endocrinology Problems. 2002; 48(6): 26-30.
4. Kravchenko AYa, Chernykh AA, Budnevsky AV [et al.] Relationship between within-visit blood pressure variability and kidney function in patients with arterial hypertension. International Journal of Biomedicine. 2017; 7(2): 91-95.
5. Verbovoy AF Hypothyroidism. Farmateka. 2015; 10(303): 8-11.
6. Podzolkov AV, Fadeev VV [et al.] Hypothyroidism, subclinical hypothyroidism,

highly normal level of TSH // Clinical and experimental thyroidology. 2009; 5(2): 4-16.
7. Starkova NT [et al.] Guidelines for clinical endocrinology // SPb .: Peter Press. 2002: 13-17.
8. Budnevsky AV, Kravchenko AYa, A.A. Feskova [et al.] Possible causes of the failure of monotherapy in subclinical hypothyroidism L-thyroxine // Clinical medicine. 2015; 93(10): 14-18.
9. Sawin CT, Castelli WP, Hershman JM [et al.] The aging thyroid. Thyroid deficiency in the Framingham Study // Arch Intern Med. 1985; 145: 1386-1388.
10. Yamada M., Mori M. [et al.] Mechanisms of central hypothyroidism / // Nat ClinPractEndocrinolMetab. 2008; 4(12): 683-694.
11. Gavrilova TA, Morgunova TB, Fadeev VV.[et al.] Secondary hypothyroidism: modern approaches to diagnosis and treatment // Medical advice. 2017; 3: 64-67.
12. Hypothyroidism / V.V. Fadeev, G.A. Melnichenko [et al.] // A guide for doctors. CJSC "RCT North press". - 2002. - P. 45-48.
13. Dedov II, Melnichenko GA, Fadeev VV [et al.] Endocrinology. Textbook for universities. 2007: 185-190.
14. Skvortsov VV, Tumarenko AV [et al.] Endocrinology/ Textbook for universities. 2015: 88-100
15. Verbovoy AF [et al.] Hypothyroidism and cardiovascular diseases // Farmateka. 2015; 17(310): 36-41.
16. Petunina NA, Trukhina LV [et al.] Diseases of the thyroid gland // GEOTAR-media. 2011: 75-80
17. Petunina NA, Trukhina LV [et al.] Hypothyroidism // Breast cancer. 2013; 21(12): 664-666.
18. Avtsyn AP, Zhavoronkov AA, Rish MA [et al.] Human trace elements // 1991.
19. Levander OA, Beck MA [et al.] Interacting nutritional and infectious diseases of Keshan disease: insights from Coxackie virus // E. Biol. Trace Elem. Res. 1997; 56: 5–21.
20. Rayman MP [et al.] The importance of selenium to human health // Lancet. 2000; 356: 233–241.
21. Arner ES, Holmgren A [et al.] Physiological functions of thioredoxin and thioredoxinreductase // Eur. J. Biochem. 2000; 267: 6102–6109.
22. Pirola I., Gandossi E., Agosti B. [et al.] Selenium supplementation could restore patients with autoimmune thyroiditis // Endokrynol Pol. 2016; 67(6): 567-571.
23. Kryukov GV, Castellano S, Novoselov SV [et al.] Characterization of mammalian selenoproteomes // Science. 2003; 300: 1439–1443.
24. Kohrle J. [et al.] The deiodinase family: selenlenoenzymes regulating thy roid hormone availability and action // Cell. Mol. Life Sci. 2000; 57: 1853–1863.
25. Yu L., Zhou L., Xu E. [et al.] Levothyroxine monotherapy versus levothyroxine and selenium combination therapy in chronic lymphocytic thyroiditis // Endocrinol Invest. 2017. 40(11): 1243-1250.
26. Vanderpas J., Peter F., Wiersinga W. [et al.] Selenium and iodine deficiency as risk factors for goiter and hypothyroidism // The Thyroid and Environment. 2000; 17(1): 33-39
27. Beckett GJ, Nicol F, Rae PW [et al.] Effects of combined iodine and selenium deficiency on thyroid hormone metabolism in rats // Am. J. Clin. Nutr. 1993; 57: 240–243.
28. Rasic-Milutinovic Z, Jovanovic D, Bogdanovic G [et al.] Potential Influence of Selenium, Copper, Hypothyroidism and Hypothyroidism // ExpClinEndocrinol Diabetes. 2017; 125(2): 79-85.
29. Imai. H, Nakagava Y Biological significance of phospholipid hydroperoxide glutathione peroxidase (PHGPx, GPx4) in mammalian cells // Free Rad. Biol. Med. 2003; 34: 145–169.
30. Shabalina EA, Morgunova TB, Orlova SV [et al.]Selenium and the thyroid gland // Clinical and experimental thyroidology. 2011; 7(2): 7-18.
31. Bianco AC, Kim BW [et al.] Deiodinases: Impacting thyroid hormone action / // J. Clin. Invest. 2006; 116:2571–2579.
32. Germain St. DL, Hernandez A, Schneider MJ [et al.] Insights into the role of deiodinases from studies of genetically modified animals // International Journal of Thyroid. 2005; 15: 905–916.
33. Vinichenko DS, Kvitkova LV, Zinchuk S [et al.] On the relationship between the development of diffuse-toxic goiter of severe and moderate severity with the security body's zinc // Vrach-aspirant. 2016; 76(3):71–80.
34. Baltaci AK, Mogulkoc R [et al.] Leptin, NPY, Melatonin and Zinc Levels in Experimental Hypothyroidism and Hyperthyroidism: The Relation to Zinc // Biochem Genet. 2017; 55(3): 223-233.
35. Notova SV, Barysheva ES, S.V. Lebedev [et al.] The effect of trace elements on the morphofunctional indicators of the thyroid gland // Bulletin of the Orenburg State University. 2006; 2S(52): 64-67.
36. Avtsyn AP, Zhavoronkov AA, Rish MA [et al.] Principles of classification of diseases of biogeochemical nature // Archive of pathology. 1983; 45(9): 3-11.

37. Napolitano G, Palka G, Lio S [et al.] Is zinc deficiency a cause of subclinical hypothyroidism in Down syndrome // Ann Genet. 1990; 33(1): 9-15.
38. Haase H, Rink L [et al.] Multiple impacts of zinc on immune function // Metallomics. 2014; 6(7): 1175-1180.
39. Kvitkova LV, Vinichenko DS, Borodkina DA [et al.] The role of zinc deficiency in the development of cardiovascular complications in patients with diffuse toxic goiter // Clinical and experimental thyroidology. 2017; 13(4): 30-39.
40. Maxwell C, Volpe SL [et al.] Effect of zinc supplementation on thyroid hormone function. A case study of two college females //Ann NutrMetab. 2007; 51(2): 188-194.