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VITAMIN D AND AUTOIMMUNE THYROIDITIS - STUDYING THE RELATIONSHIP

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ABSTRACT: This article discusses the role of vitamin D in patients with autoimmune thyroiditis (AIT). The authors found that vitamin D levels were low in patients with AIT. In the article, the authors showed an inverse correlation between thyroid-stimulating hormone, antibodies to thyroperoxidase and thyroglobulin and vitamin D content, which indicates that vitamin D deficiency is also one of the pathogenetic links in the course of AIT.

Keywords: Vitamin D, autoimmune thyroiditis, hypothyroidism.

ВИТАМИН D И АУТОИММУННЫЙ ТИРЕОИДИТ – ИЗУЧЕНИЕ ВЗАИМОСВЯЗИ

АННОТАЦИЯ: В данной статье обсуждается роль витамина D у больных с аутоиммунным тиреоидитом (АИТ). Авторы обнаружили, что у пациентов с АИТ уровень витамина D был низким. В статье авторы показали обратную корреляцию между тиреотропным гормоном, антителами к тиреопероксидазе и тиреоглобулину и содержанием витамина D, что указывает на то, что дефицит витамина D также является одним из патогенетических звеньев течения АИТ.

Ключевые слова: Витамин D, аутоиммунный тиреоидит, гипотиреоз.

D VITAMINI VA AUTOIMMUN TIROIDIT – O`ZARO ALOQALARNI O'RGANISH

ANNOTATSIYA: Ushbu maqolada autoimmun tireoidit (AIT) bilan og'rigan bemorlarda D vitaminining roli muhokama qilinadi. Mualliflar AIT bilan og'rigan bemorlarda D vitamini darajasi past ekanligini aniqladilar. Maqolada mualliflar tireotrop gormoni, tireoperoksidaza va tireoglobulinga qarshi antitelolar va D vitamini o'rtasidagi teskari bog'liqlikni ko'rsatdilar, bu D vitamini etishmovchiligi AIT kechish jarayonida patogenetik bog'lanishlardan biri ekanligini ko'rsatadi.

Kalit so'zlar: D vitamini, autoimmun tireoidit, gipotireoz.

Introduction

Autoimmune thyroiditis (another name is Hashimoto's thyroiditis) is a chronic autoimmune inflammatory disease of the thyroid gland with a hereditary predisposition, accompanied by its lymphocytic infiltration followed by replacement with fibrous tissue, which is a common cause of primary hypothyroidism [2,11,14,16].

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The prevalence of Hashimoto's thyroiditis is 800 cases per 100,000 people when assessed by a review of published articles and 4,600 cases per 100,000 when assessed by biochemical signs of hypothyroidism and autoantibodies to the thyroid gland [1,2,15]. Etiological factors are stress and environmental conditions, leading to surges of adrenaline and cortisol, adrenal insufficiency, followed by a decrease in the adaptation syndrome, resulting in an increase in autoimmune diseases, including AIT; Endogenous factors – genetic predisposition, additional external factors (viruses, various infections, and others) are necessary to realize a predisposition to the development of autoimmune disease; Individuals with histocompatibility antigens HLA DR3 (atrophic form), DR5 (hypertrophic form) are predisposed to AIT [2,4,7]. The disease is caused by a partial defect in immunological control – a deficiency of T-lymphocyte suppressors, and therefore the survival of a prohibited forbidden clone of T-lymphocytes occurs. The interaction of the forbidden clone of T – lymphocytes with antigens triggers the immune process according to the type of delayed hypersensitivity , inflammatory mediators are released – lymphokines, tumor necrosis factor and other cytotoxic substances.Helper T lymphocytes act on B lymphocytes, which turn into plasma cells and form antibodies to thyroglobulin and microsomal fraction (TPO). Antibodies on the surface of follicular epithelial cells, combining with killer T–lymphocytes, have a cytotoxic effect, cause their destruction, reducing the secretion of T3, T4 and increase TSH, which leads to an increase in thyroid goiter (hypertrophic form of AIT) [8,10,17]. Vitamin D is not only the main regulator of calcium-phosphorus metabolism, but also participates in the control of various processes and functions in the body. The final active substrate, calcitriol, formed as a result of step–by–step synthesis from inactive precursors, is a true hormone D in terms of its mechanism of action and its characteristics. Vitamin D is involved in calcium metabolism and bone mineralization [9,18,21]. In addition, vitamin D receptors are located on the surface of immune and cancer cells [11,15,17]. First of all, the role of vitamin D is due to its effect on the immune system. In this regard, special attention is now being paid to the problem of vitamin D provision in patients with autoimmune diseases [10]. Vitamin D receptors were found on almost all immunocompetent cells: CD4+ and CD8+, lymphocytes, antigen-presenting cells, including macrophages and dentdrite cells [5,6,7,17,20]. The level of vitamin D receptors changes as the cells of the immune system mature. Naive T lymphocytes contain a small number of receptors, and mature forms are characterized by a high level of expression of the vitamin D receptor. During the differentiation of monocytes into macrophages and dendritic cells, the number of vitamin D receptors decreases [8,20]. This pattern reflects the sensitivity of immunocompetent cells to vitamin D, which may play a role in the fine regulation of the immune response. Macrophages, being carriers of vitamin D receptors, show greater sensitivity to vitamin D. Macrophages and dentrite cells synthesize the active form of vitamin D themselves, due to the expression of the enzyme a 1- gyroxylase in them, the activity of which, unlike renal localization, is regulated not by parathyroid hormone, but by cytokines [11,12,17,19]. The aim of the study was to study the relationship between vitamin D deficiency and immunological markers of the thyroid gland in patients with autoimmune thyroiditis.

Research methods. The study was conducted in the department of 2-therapy and endocrinology of the multidisciplinary TMA clinic. The study included 100 patients aged 18 to 45 years with autoimmune thyroiditis. Among them, 85 (85%) women and 15 (15%) men, with an average age of 31.5±13.5 years. Laboratory tests were carried out: the concentration of vitamin D - 25(OH)D in blood serum, levels of thyroid-stimulating hormone (TSH), free

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thyroxine (sv.T4), antibodies to thyropyroxidase (AT-TPO), antibodies to thyroglobulin (AT-TG), total calcium, as well as ultrasound data of the thyroid gland.

A clinical examination and ultrasound of the thyroid gland were performed using the SonoScape SSI-6000 device (China) with a 7.5 MHz sensor at the initial treatment, then annually. The obtained values of the thyroid volume were estimated according to the standards calculated relative to the surface area of the body. Goiter was diagnosed if the upper limit of normal values was exceeded. Serum levels of TSH, T4, as well as titers of AT-TPO and AT-TG were determined by ELISA using a set of reagents from Alkor Bio. The normal values were TSH 0.3-4.0 mUl/l, sv. T4 – 8.9-17.2 ng/ml, AT-TPO – 0-30ME/ml, AT-TG – 0-100 IU/ml. The assessment of the degree of vitamin D provision was carried out at the level of 25 (OH)D in blood serum (enzyme immunoassay, Rayto analyzer, China) in 100 women using the criteria of the International Society of Endocrinologists (2011) [13] and recommendations of the Russian Association of Endocrinologists, the Russian Association for Osteoporosis [3.13]. The value of 25 (OH) was taken as the normal vitamin D supplySerum D is above 75 nmol/l (30 ng/ml), for deficiency – 50 to 75 nmol/l (20-30 ng/ml), and for deficiency – a level below 50 nmol/l (20 ng/ml).

The combination of elevated test levels with normal T4 levels was regarded as subclinical hypothyroidism, and at lower levels as manifest hypothyroidism.

Statistical processing of the obtained results was carried out using the "STATISTICA for Windows" system in accordance with the type of data and the number of study groups. The criterion of statistical reliability of the obtained conclusions was considered to be the generally accepted value of $p < 0.05$ in medicine.

The results of our own research

The analysis of thyroid hormone indicators revealed: euthyroidism in 46 (46.0%) patients with an average TSH level of 2.9±0.9 mMU/ml; hypothyroidism in 56 (56.0%) patients. Among them, patients with subclinical hypothyroidism (SG) prevailed - 37 (66.0%) compared with manifest hypothyroidism (MG) – 19 (34.0%). According to hormonal studies with SG and MG, the TSH content in the blood was 7.5±1.5 mMU/ml and 17.3±2.3 mMU/ml ($p<0.001$), sv.T4 - 10.6±1.1pg/ml and 7.5±0.9 pg/ml, respectively. The control group consisted of 20 people who did not suffer from autoimmune thyroiditis and other thyroid pathologies, whose average age was 32.3±7.9 years. In patients with autoimmune thyroiditis, the average vitamin D content was 17.7±3.4 ng/ml ($p<0.05$) versus control - 26.7±7.9 ng/ml.

Among these patients, 54 (54.0%) had insufficiency, 26 (26.0%) vitamin D deficiency, determined by the level of 25 (OH)D in blood serum (<20 ng/ml deficiency, 20-30 ng/ml insufficiency). 20 (20.0%) patients had a normal vitamin D content. In the control group, it was revealed: vitamin D deficiency in 12, the normal content of this vitamin in 8 subjects.

At the same time, vitamin D deficiency was not detected in the control group. The level of calcium in the blood of patients ranged from 1.9 to 2.5 mmol/l, on average 2.2±0.5 mmol/l, and there were no significant differences in the study groups, however, in patients with multiple sclerosis, this indicator was lower and amounted to 1.89±0.05 mmol/l compared with groups with hypertension and euthyroidism.

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Table.1

Indicators of thyroid status and immunological markers of the thyroid gland in the examined patients

Parameter	Euthyroidism (n-46)	Subclinical hypothyroidism (n-37)	Manifest hypothyroidism (n-19)	The control group (n-20)
Sv. T4 (ng/ml)	11,5±3,0	10,6±1,1	7,5±0,9*	14,3±2,9
TTG (mUl/l)	2,9±0,9	7,5±1,5*	17,3±2,3<	2,3±1,1
AT-TPO (IU/ml)	215,8±30,6*	259,8±37,1*	590±18,1<	17,1±4,5
AT-TG (IU/ml)	98,4±7,8	104,2±9,9*	111,9±7,3*	57,7±8,5

Note: the presence of reliability in relation to the control, the level of statistical significance *- p<0.05-< p<0.001

The T4 level in the group with SG was within the normal range, but differed from the control group and was 16% lower. In patients with MG, this hormone was reduced by 25% (p<0.05). There was a significant increase in AT-TPO in patients with MG compared with SG and euthyroidism (590±18.1 IU/ml versus 259.8±37.1 IU/ml and 215.8±30.6 IU/ml, p<0.001). AT-TG were similarly increased, so in the SG group, this indicator was 104.2±9.9IU/ml (p<0.05), with MG 111.9±7.3IU/ml (p<0.05) and in the group with euthyroidism 98.4±7.8 (p<0.05), (in the control group this indicator It was 57.7±8.5IU/ml.

Table.2

The content of vitamin D in the blood of the examined patients

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Parameter	Euthyroidism (n-46)	Subclinical hypothyroidism (n-37)	Manifest hypothyroidism (n-19)	The control group (n-20)
Vitamin D (ng/ml)	23,5±4,2 (9-31)	19,6±3,2* (11-27)	11,5±2,2* (7-26)	26,7±5, (18-39)

Note: the presence of reliability in relation to the control, the level of statistical significance *- p<0.05

The blood vitamin D level in individuals with HYPERTENSION was lowered and amounted to 19±3.2 ng/ml. Whereas, in individuals with MG, vitamin D levels (11.5±2.2 ng/ml) were lower in comparison with the group of patients with euthyroidism by 40% (p<0.05) and by 24% (p<0.05) with subclinical hypothyroidism. An analysis of the literature data showed that hypothyroidism is associated with immunosuppression, and vitamin D deficiency, in turn, has a significant effect on both thyroid function and immunity [19,22].

During ultrasound examination of the thyroid gland, the volume of the latter averaged 24.7=3.4 cm/3 (p<0.05) compared with the control group - 13.5=2.5 cm/3. Comparing the average values of thyroid volume in the control group with the studied groups, it was revealed: the average volume of the thyroid gland was 13± 2.5 cm /3 (control), in the group with MG - 11±3.0 cm/3, SG - 24.9±7.2 cm/3 (P<0.05) and euthyroidism - 23.3±5.9 cm/3 (P<0.05). Thus, in the groups with SG and euthyroidism, the volume of the thyroid gland was 48% larger and 35% larger, respectively, compared with the MG group. At the same time, hypertrophic form was detected in 45 (45%), atrophic in 9 (9%) and diffuse nodular forms of thyroid in 31 (31%) patients. The remaining patients have 15 (15%) the volume of the thyroid gland was within normal values. To compare whether there is a relationship between the studied parameters, we conducted a correlation analysis. The study of correlation analysis showed that there are certain connections between vitamin D deficiency in the blood and thyroid hormone levels – TSH and immunological markers, for example, vitamin D levels in the blood negatively correlated with TSH (-60), AT-TPO- (-0.89) (P<0.001), AT-TG (-0.76) (P<0.001) blood. The same relationship was found between deficiency and normal vitamin D levels in the blood with TSH and immunological markers. A negative relationship was found between vitamin D and TSH (-0.43) (P<0.05), with AT-TPO (-0.56) (P<0.05) and AT-TG (-0.44) (P<0.05). A negative relationship was also found in the group with normal vitamin D content with AT-TPO (-0.34) (P<0.05) and AT-TG (-0.31) (P<0.05). This means that vitamin D content affects the course of autoimmune thyroiditis, exacerbating immunological disorders. According to foreign authors, screening for vitamin D deficiency is recommended for all patients with AIT, especially if there are functional disorders [11]. A positive relationship was also found between the total calcium content and vitamin D content in the D-deficient and deficient groups.

Table.3

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Correlation analysis between level 25(OH)D in the blood and hormonal, immunological parameters in the examined women.

	The value of Spearman's rank correlation coefficient (R)		
Parameter	**The normal content is 25(OH)D, 30-100 ng/ml n-54**	**Deficit of 25 (OH) D, 20 ng/ml n-26**	**The disadvantage is 25 (HE)D, 20-30 ng/ml n-20**
Sv. T4 (ng/ml)	0,20	-0,49*	-0,41*
TTG (mUl/l)	0,22	-0,60*	-0,43*
AT-TPO (IU/ml)	-0,34*	-0,89**	-0,56*
AT-TG (IU/ml)	-0,31*	-0,76**	-0,44*
Total calcium, mmol/l	0,23	0,45*	0,49*

Note: the level of statistical significance *- $p<0.05$; **-$p<0.001$

In conclusion, it should be noted that there is no unambiguous answer to the question whether vitamin D deficiency is the cause of the development of AIT, but it has a certain significance during the course of the disease. This is indicated by the presence of a relationship between the content of vitamin D in the blood and hormonal and immunological markers of the thyroid gland. It is necessary to examine the level of vitamin D in the blood and, if there is a shortage, safely prescribe therapeutic doses of this vitamin in order to maximize the effectiveness of therapy for autoimmune thyroiditis.

CONCLUSIONS:

1. In patients with autoimmune thyroiditis, the vitamin D content is probably lower (17.7±3.4 ng/ml) than in practically healthy individuals (26.7±7.9 ng/ml; $p<0.05$). Vitamin D deficiency prevailed among patients, which was 54.0%, deficiency 26.0% and normal content was 20.0% of patients.

2. A probable positive correlation has been established between vitamin D content and total calcium, as well as a negative probable correlation with TSH, AT-TPO and AT-TG levels. Thus, the data of the correlation analysis showed that there are certain connections between

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vitamin D deficiency in the blood and thyroid hormone levels - TSH and immunological markers, while the level of vitamin D in the blood was negatively correlated with TSH (-60), AT-TPO (-0.89) (P<0.001), AT-TG (-0.76) (P<0.001) of blood. A positive relationship was also found between the total calcium and vitamin B content in groups with and without vitamin D deficiency.

3. It is necessary to study the level of vitamin D in the blood and, if it is deficient, safely prescribe therapeutic doses of this vitamin in order to maximize the effectiveness of therapy for autoimmune thyroiditis.

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