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IMPACT OF SELENIUM IN RESTORATION OF THYROID FUNCTION AND OUTCOMES OF ANTI-TUBERCULOSIS CHEMOTHERAPY IN THYROIDAL DYSFUNCTION

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The effect of selenium on thyroid status and outcomes of chemotherapy was studied at examination of 180 tuberculosis patients with the pathological structural changes of thyroid. A subclinical hypothyroidism was diagnosed at this category of patients. Subclinical hypothyroidism progressed under antituberculosis chemotherapy. Prescribing of selenium nitric restored thyroid function with the increasing of blood level of free thyroxine and decreasing of thyroid stimulating hormone and also optimized the results of chemotherapy with increasing the percentage of tuberculosis patients stopped bacilli excretion and healing of the cavities in lungs. Thus sodium selenite was recommended like accompanying medicine if antituberculosis chemotherapy.

Key words: tuberculosis; thyroid; selenium; chemotherapy outcomes.

Thyroid hormones play a vital role in Mycobacterium tuberculosis infection the hypothyroidism and TB cohorts were matched with the control group in a 1:4 ratios. The risk of developing TB in patients with hypothyroidism was 2.91 times higher than that in those without hypothyroidism (95 % confidence interval [CI], 1.50–3.65) [1, 2]. Selenium is required for the antioxidant function and for the metabolism of thyroid hormones. The content of selenium (Se) in 1 g of thyroid tissue (thyroid gland) is greater than in other organs [3]. For normal functioning of the thyroid gland and maintenance of thyroid homeostasis, not only iodine, but also Se is needed. In regions with severe iodine deficiency, selenium deficiency increases hypothyroidism and leads to myxedema and cretinism [4]. With autoimmune thyroiditis in conditions of selenium deficiency, an inverse relationship was observed between the level of selenium in the blood and the volume of the thyroid gland, as well as the severity of thyroid hypoechogenicity [5]. Most authors pay attention to the positive effect of selenium supplements on the immune system and the regulation of production of reactive oxygen radicals and their metabolism. Selenium reduces the level of antithyroid antibodies in patients with

Hashimoto's disease and in pregnant women [3-5]. Thus, selenium status can play a role in the development of thyroid pathology.

Objective – to study the role of selenium for restoration of thyroid function and outcomes of antituberculosis chemotherapy in tuberculosis patients with thyroid pathology.

Patients and methods

180 patients with pulmonary tuberculosis and changes in the volume and /or structure of the thyroid gland were monitoring. Changes in the volume and/or structure of the thyroid gland were attributed to pathological changes in the thyroid gland, which was established by ultrasound examination on the diagnostic apparatus SSF-240A manufactured by Toshiba Medical Systems. The diffuse pathology of the thyroid gland with heterogeneity of its structure and heterogeneity of acoustic density with gland hyperplasia, hypoplasia or without a change in its volume prevailed. Patients were divided into 6 groups: observation group 1a – patients with tuberculosis (TB) and subclinical hypothyroiditis (SH), received selenium (Se) on the background of standardized antituberculosis chemotherapy [6] (TB + SH + Se) and comparison group 1b – patients with tuberculosis with TB and SH, received standardized antituberculosis chemotherapy only; observation group 2a – patients with co-infection TB/HIV with SH who received selenium on the background of standardized highly active antiretroviral therapy (HAART) – (TB/HIV + SH + Se) and comparison group 2a – patients with co-infection TB/HIV with SH (TB/HIV + SH), received antituberculosis chemotherapy and HAART only; observation group 3a – patients with multidrug-resistant tuberculosis with resistance to at least both rifampin and isoniazid, received selenium on the background of individual antituberculosis chemotherapy (MDR TB+SH + Se) and the comparison group 3b – patients with multidrug-resistant tuberculosis with SH, who received selenium (MDR TB + SH). The average age of the patients was 34.43 years. In gender terms, men predominated – 87 %. All patients were examined before the start of treatment and after 2 months of

chemotherapy according to the standards of examination of patients with tuberculosis. Patients in the intensive phase of treatment were standardized or individualized, and patients with MRI had individualized anti-tuberculosis chemotherapy according to accepted treatment standards.

Patients with co-infection also received highly active antiretroviral therapy (HAART) regardless of the T-lymphocyte content in the blood. Selenite sodium was added to the complex treatment of patients of observation groups at 200 micrograms per day for 2 months. The comparison groups did not receive the selenium preparation and served as a control. In the serum of venous blood, the levels of selenium (Se) in the laboratory Synevo on Perkin Elmer 4110 analyzer, as well as the levels of free thyroxine (free T₄), thyroid-stimulating hormone of the pituitary (TSH), antibodies to thyroglobulin (a/TTG) and thyroperoxidase (a/TPO) by the immune-enzymatic method with the help of the ALCOR BIO kit on the Tecan Sunrise spectrophotometer (Austria). Biochemical indices before and after 2 months of therapy were compared between the respective groups of monitoring and control. In addition, the efficacy of treatment (% of cessation of bacterial release and healing of destruction) was compared during the intensive care phase.

Statistical processing of the obtained data was carried out by the method of variation statistics with the help of the standardized package of calculations of Microsoft Excel XP. The probability of divergence of the mean values was determined by the t test of Student. The critical level of significance (P) for testing statistical hypotheses was assumed to be 0.05.

Patients with co-infection also received highly active antiretroviral therapy (HAART) regardless of the T-lymphocyte content in the blood. Selenite sodium was added to the complex treatment of patients with observation groups at 200 micrograms per day for 2 months. The comparison groups did not receive the selenium preparation and served as a control. In the serum of venous blood, the levels of selenium (Se) in the Synevo laboratory (Germany) on the Perkin Elmer Zeeman AAS 4110 analyzer, as well as the levels of free thyroxine (freeT₄), thyroid-stimulating hormone of the pituitary (TTG), antibodies to thyroglobulin (a/TTG) and thyroperoxidase (a/TPO) by the immune-enzymatic method with the help of the ALCOR BIO kit on the Tecan Sunrise spectrophotometer (Austria). Biochemical indices before and after 2 months of the therapy were compared between the respective groups of observation and control. In addition, the efficacy of treatment (% of stopping of bacterial excretion and healing of cavities) was compared during the intensive phase of chemotherapy.

Results and discussion

Patients with tuberculosis and pathological changes of the thyroid gland (group 1a) have a lower average serum

level of serum (66 µg/l) at a norm of 74-130 µg/l. A low-normal mean free thyroxine (11.12 pmol/L) and an increase in the level of TSH (4.30 µIU/ml) in this group (Table 1) indicate the development of subclinical hypothyroidism. An increase in the level of antithyroid antibodies to thyroperoxidase and thyroglobulin in this group of patients is a marker of an autoimmune process in the thyroid gland. At the end of the intensive care phase after a 2-month appointment of sodium selenite, the average selenium content significantly increases to 95.39 µg/l in patients in this group. The level of free thyroxine in these patients is significantly increased to 13.32 pmol/l, and the mean level of TSH is reliably reduced to 2.12 µIU/ml in comparison with the control group (group 1b), in which chemotherapy is observed an average level of free thyroxine and an increase in the average level of TSH in comparison with the baseline levels of these hormones. The level of antibodies to TPO significantly decreases both in comparison with baseline (from 42.64 to 4.30 IU/ml) and when compared with the comparison group (42.64 and 4.32 IU/ml).

The results indicate the restoration of thyroid function under the influence of selenium in patients with tuberculosis, as well as the protective effect of this microelement in the chemotherapy process with respect to the thyroid

Structural changes in the thyroid gland in co-infection TB/HIV are accompanied by selenium deficiency (63.27 µg/L) (group 2a). The appointment of sodium selenite restores the level of selenium to normal (94.69 µg/l). In this group of patients, a decrease in its hormonal activity is also noted, as evidenced by the mean low-normal value of the free thyroxine level (9.89 pmol/L) and a fairly high level of TSH (3.43 IU/ml). In the comparison group (group 2b), chemotherapy in the intensive phase leads to an increase in the mean level of TSH (from 3.43 to 4.12 IU/ml), which indicates the weakening of the thyroid status of the patient with co-infection with tuberculosis/HIV under the influence of antituberculosis drugs. The appointment of sodium selenite in the observation group of patients with co-infection leads to a significant increase in the mean free thyroxine level within the normal values (12.97 pmol/L) and a decrease in the TSH level to the norm (1.87 µIU/ml), i.e. optimizes the functional state of the thyroid gland without prescribing thyroid hormones. In the co-infected group receiving sodium selenite, there was also a significant decrease in the average level of antibodies to thyroperoxidase both in comparison with baseline (from 31.12 to 2.12 IU/ml) and in comparison with the comparison group (2, 12 and 6.77 IU/ml).

In the group of patients with multi-drug resistant tuberculosis and pathological changes in the thyroid gland before treatment, the lowest average selenium level was observed when compared with other groups (56.66 µg/l)

(group 3a). In the same group, there is a low-normal average level of free thyroxine (10.22 pmol/l) with normal TSH values (1.08 IU/ml). In the comparison group (group 3b), against the background of intensive chemotherapy, a decrease in the average level of free thyroxine to a low-abnormal value was recorded (from 10.71 to 8.33 pmol/l). The administration of sodium selenite in observation group 3a, restoring the normal selenium content in the blood to 107.0 µg/l, not only prevents a further decrease in free thyroxine, as in comparison group 3b, but also causes its significant increase within normal physiological values (14.34 pmol/l).

The results of the study demonstrate the damaging effect of tuberculosis infection on the thyroid gland and the presence of subclinical hypothyroidism in tuberculosis patients with structural disorders of the thyroid gland. The data obtained confirm the ability of anti-tuberculosis drugs to reduce thyroid function, as noted by numerous studies [7]. Sodium selenite, compensating for selenium deficiency in the body of tuberculosis patients with impaired thyroid gland structure, restores thyroid function in observation groups (groups 1a, 2a and 3a), while in comparison groups (groups 1b, 2b and 3b) during the phase intensive chemotherapy, a further weakening of thyroid function is noted. The results of the study also confirm the ability of selenium to reduce the titer of antibodies to thyroid peroxidase, which is reflected in a number of publications [3].

Thus, sodium selenite has a protective and stimulating effect on the thyroid gland of tuberculosis patients with

thyroid pathology and subclinical hypothyroidism and can be recommended as a therapy to accompany chemotherapy in these individuals.

When assessing the effect of selenium on the outcomes of chemotherapy in tuberculosis patients by the end of the intensive therapy phase, it was found that in observation group 1a, bacterial excretion stopped in 24 % of patients, which is 6.66 % more than in the comparison group. In the same group, the rate of cavity healing was 10 % higher when compared with the control group (group 1b) (Table 1).

In the group of patients with tuberculosis/HIV co-infection who received selenium (group 2a), abacillation by the end of the intensive therapy phase occurred in 20 cases (66.66 %), in the comparison group – in 14 cases (46.66 %) (group 2b). Healing of cavities in this group occurred in 13 (43.33 %) – 10 % more when compared with the comparison group – 10 cases (33.33 %). In patients with multidrug-resistant tuberculosis with thyroid pathology who received sodium selenite, abacillation by the end of the intensive therapy phase occurred in 15 cases (50.0 %), and healing of cavities occurred in 10 cases (33.33 %). The corresponding figures in the comparison group were 17 cases (56.66 %) and 7 cases (23.33 %). The results obtained reflect the positive effect of selenium on the results of chemotherapy, increasing the stopping of bacterial excretion by 6.66 % – 20 % and the healing of cavities by 10 % when compared with the control.

Table 1

Outcomes of chemotherapy in tuberculosis patients with thyroid pathology depending on selenium levels

Parameters	TB+SH+Se (n=30) Abs. (%)	TB+SH (n=30) Abs.(%)	TB/HIV+HS+Se (n=30) Abs. (%)	TB/HIV+SH (n=30) Abs. (%)	MDRTB+SH+Se (n=30) Abs. (%)	MDRTB+SH (n=30) Abs. (%)
Stopping of bacilli excretion	26 (86.66)	24 (80)*	20 (66.66)	14 (46.66)*	15 (50.0)	17(56.66) *
Healing of cavities	15 (50)	11 (40.0)*	13 (43.33)	10 (33.33)*	10 (33.33)	7 (23.33) *

Note. * – Significant difference between the indicators of the observation and comparison groups* (p≤0.05).

Conclusions

1. In patients with tuberculosis with a pathological structure of the thyroid gland, subclinical hypothyroidism is observed with further aggravation of the hypofunction of this organ against the background of anti-tuberculosis chemotherapy.

2. The inclusion of sodium selenite in the complex therapy of tuberculosis patients of various groups, when combined with thyroid pathology, leads to the restoration of thyroid function and has a protective effect against the thyrotoxic effect of anti-tuberculosis chemotherapy drugs.

3. The participation of sodium selenite in the intensive phase of treatment of patients with tuberculosis when combined with thyroid pathology leads in average to an increase in abacillation by 6.66 %-20 % and healing of destruction in average by 10 % when compared with the control.

4. Sodium selenite can be recommended as an accompanying drug during chemotherapy for tuberculosis patients with subclinical hypothyroidism.

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ВПЛИВ СЕЛЕНУ НА ВІДНОВЛЕННЯ ФУНКЦІЇ ЩИТОПОДІБНОЇ ЗАЛОЗИ ТА РЕЗУЛЬТАТИ ПРОТИТУБЕРКУЛЬОЗНОЇ ХІМІОТЕРАПІЇ ПРИ ТИРЕОЇДНІЙ ДИСФУНКЦІЇ

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РЕЗЮМЕ. Вивчали вплив селену на тиреоїдний статус і результати хіміотерапії 180 хворих на туберкульоз із патологічними структурними змінами щитоподібної залози. У цієї категорії пацієнтів діагностовано субклінічний гіпотиреоз. На тлі протитуберкульозної хіміотерапії прогресував субклінічний гіпотиреоз. Призначення селеніту натрію відновлювало функцію щитоподібної залози з підвищенням у крові рівня вільного тироксину та зниженням активності тиреотропного гормону, а також оптимізувало результати хіміотерапії, збільшуючи відсоток хворих на туберкульоз із припиненням бактеріовиділення та загоєнням каверн у легенях. Тому селеніт натрію рекомендували як супутній препарат при протитуберкульозній хіміотерапії.

Ключові слова: туберкульоз, щитоподібна залоза, селен, результати хіміотерапії.

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