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VITAMIN D STATUS IN PATIENTS WITH TUBERCULOSIS IN YAKUTIA

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Material and methods: Enzyme immunoassay (EIA) concentrations of 25-hydroxycholecalciferol (25(OH)D) were studied in 88 patients with tuberculosis. Serum levels 25(OH)D were assessed using the following criteria: optimal level 30-100 ng/mL; subnormal level 20-30 ng/mL; vitamin D deficiency -10-20 ng/mL; severe deficiency – less than 10 ng/mL. For statistical processing, Student's unpaired t-test, Mann-Whitney, and Kruskall-Wallis tests were used. Cutoff for statistical significance of differences (p) was 5%.

Results: Mean age of patients was 40,7 (16,1) years. Proportion of male patients was significantly larger (p=0.035). Levels of 25(OH)D in men were somewhat lower than in women, but the differences were statistically negligible. No statistically significant correlation was established between age and level of 25(OH)D (r=-0.037; p=0.729). Assessment of distributions of vitamin D levels against laboratory reference showed, that serum vitamin D level was optimal in 4.5% of patients, and 12.5% had subnormal levels of vitamin D (20 to 30 ng/mL). In 34% of patients, vitamin D level was graded as 'vitamin d deficiency' (10 to 19.9 ng/mL); 49% had 'severe vitamin D deficiency' (below 10 ng/mL).

Conclusions: Results of this pilot study demonstrated the presence of marked vitamin D deficiency in patients with TB. Due to absence of control group, no comparisons of vitamin D levels between TB patients and general population could be made. Considering the role of vitamin D in the induction of innate antimicrobial immune response, further investigation is needed into the causes of deficiencies, opportunities to correct deficiencies in patients with TB, role of vitamin D in therapy of TB, and a role of vitamin D receptor gene polymorphism in Yakut ethnic group.

Keywords: vitamin D, tuberculosis, 25(OH) D, calcidiol, Yakutia.

Tuberculosis (TB) is one of the most urgent and underappreciated problems in world healthcare, and, at the same time, a sociomedical problem in virtually all countries [6]. Based on WHO reports, in 2017, as much as 1 million were diagnosed with TB, and 1.3 million died of it. Russia is currently among the 22 countries with the highest TB burden [1].

TB often goes along with nutritional deficiency, including deficiency in vitamin D. Vitamin D has an important role in innate host defense mechanisms against infection, by facilitating macrophage and monocyte activation, which is of significance in disease development. In the event of host infection with M.tuberculosis, calcidiol, key circulating metabolite of vitamin D, preserves induction of the innate antimicrobial immune response, curbing the growth of tubercle bacilli [16]. Vitamin D deficiency in patients with TB is interrelated with M.tuberculosis drug sensitivity. In pre-antibiotic era, high doses of vitamin D were widely used for treating patients with TB [8].

Hence, there may be a place for vitamin D in therapy of TB, which calls for further studies.

Objective: to study the availability of vitamin D in patients with tuberculosis in Yakutia.

Material and methods: This study was conducted among 88 patients, who had been hospitalized in the Phthisiatry Research-Practice Center in 2017 to 2018, with the confirmed diagnosis of TB (51 male; 37 females). No one was under medication with vitamin D during the study period. Serum concentrations of 25-hydroxycholecalciferol (25(OH)D) were determined, using enzyme immunoassay (EIA) kit from Euroimmun, Germany. The following criteria were used to estimate serum level of 25(OH)D: optimal level 30-100 ng/mL; subnormal level 20-30 ng/mL; vitamin D deficiency -10-20 ng/mL; severe deficiency – less than 10 ng/mL.

Statistical processing was performed using IBM SPSS Statistics 22 software suite. To compare patient groups, we used unpaired t-test, Mann-Whitney, and Kruskall-Wallis tests. Cutoff for statistical significance pf differences (p) was 5%.

Results and discussion: Main characteristics of the patients studied are

Table 1

Main characteristics of patients

Indicator	Both genders n=88	Males n=51	Females n=37	p
Mean age, years	40.7 (16.1)	43.9 (13.6)	36.3 (18.2)	0.035
Tuberculosis (TB) clinical forms, n (%)				
Disseminated TB	17 (19.3)	14 (27.5)	3 (8.1)	0.023
Infiltrative TB	48 (54.5)	29 (56.9)	19 (51.4)	
Focal TB	8 (9.1)	1 (2.0)	7 (18.7)	
Tuberculoma	4 (4.5)	3 (5.9)	1 (2.7)	
Caseous pneumonia	3 (3.4)	2 (3.9)	1 (2.7)	
Thoracic lymph node TB	3 (3.4)	0 (0)	3 (8.1)	
Primary TB complex	2 (2.3)	1 (2.0)	1 (2.7)	
Other forms	3 (3.4)	1 (2.0)	2(5.4)	

Note. Data are presented as mean and standard deviation, M (SD); p - statistical significance of differences between males and females.

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summarized in Table 1. Mean age of the patients was 40,7 (16,1) years. Male proportion was significantly larger than female (p=0.035). Infiltrative or disseminated TB were the two most frequent clinical forms of TB.

In both groups, distributions of 25(OH) D levels were deviating from normal distribution, therefore quartiles were calculated, to describe measures of central tendency and scatter. Levels of 25(OH) D in men were somewhat lower than in women, but the differences were statistically negligible. Considering a generally older age of men, compared to women, rank correlation analysis was performed. No statistically significant correlation was established between age and level of 25(OH) D (r=-0.037; p=0.729).

Assessment of distributions of vitamin D levels against laboratory reference showed, that serum vitamin D level was optimal in 4.5% of patients, while 12.5% had subnormal levels of vitamin D (20 to 30 ng/mL). In 34% of patients, vitamin D level was graded as 'vitamin d deficiency' (10 to 19.9 ng/mL), and in 49% – as 'severe vitamin D deficiency' (below 10 ng/mL) (Table 2).

Currently, an estimated 1 billion people have vitamin D deficiency. The recent large-scale studies have elicited a statistically significant correlation between vitamin D deficiency and the prevalence of a number of chronic diseases, including lung diseases, and TB as one of them [5,10,12,13,15]. Some long-lasting conjectures can be found in works of classical scholars in pediatrics, linking the disturbances in vitamin D metabolism with decreased immunity: namely, Tur A.F. emphasized that rickets and infections, and TB in particular, accompany one another [3]. Sufficiency of vitamin D in patients with TB infection is an under-investigated topic, except for several studies.

A study in the Province of Castellon, Spain, included 42 patients with TB and 202 contacts. Only 20.3% of them had sufficient serum levels of 25(OH)D (≥ 30 ng/mL) [7]. Study of vitamin D levels in patients with TB in Mwanza, Tanzania, showed hypovitaminosis in 39.6% of patients, of them, vitamin D deficiency in 4.3% [9]. Study in Vietnam comprised 166 patients, and found that vitamin D deficiency in men was 35.4%, and 45.3% in women [11].

Study on the effect of mean therapeutic doses of vitamin D, administered as part of multimodality therapy for multidrug and extensively drug resistant TB in Belarus, showed that serum level of 25(OH) D was 12.3±0.3 before therapy, and 19.8±0.2 after 6 months of therapy. Mean course of vitamin D administration was 184.5±3.5 days. Patients receiving vitamin D on top of polychemotherapy displayed positive response on their x-rays and microbiological tests. Also, administration of mean therapeutic doses of vitamin D on top of chemotherapy resulted in less proportion of patients who did not convert from positive to negative (57.9%), compared to patients who received chemotherapy without vitamin D (72.7%) [4].

Similar study was conducted in London, assessing the effect of high doses of vitamin D in patients with sputum-positive TB. Vitamin D supplement reduced time to sputum conversion by 1 week (from 43.5 to 36 days). Mean time to sputum culture conversion was 36 days for intervention group, and 43.5 for placebo group [14].

Sharply decreased levels of 25(OH)D in patients with TB (compared to healthy donors) were observed in the study in Saint-Petersburg, Russia (8.2±1.4 ng/mL of calcidiol in fibrocavitary TB vs. 19.3±1.4 ng/mL in healthy donors) [2].

In Yakutia, to date, no studies have been undertaken yet exploring the effect of vitamin D on treatment of patients with TB. As it appears from the studies conducted in other cities, reduced level of vitamin D is widely observed, even in healthy people. In view of potential effect of vitamin D prescription on sputum culture conversion, and on progression of TB disease, there is a need in studies in a region of Yakutia.

Conclusions. Results of this pilot study demonstrated the presence of marked vitamin D deficiency in patients with TB. Due to absence of control group, no comparisons of vitamin D levels between TB patients and general population could be made. Considering the role of vitamin D in the induction of innate antimicrobial immune response, further investigation is needed into the causes of deficiencies, opportunities to correct deficiencies in patients with TB, role of vitamin D in therapy of TB, and a role of vitamin D receptor gene polymorphism in Yakut ethnic group.

Table 2

Serum vitamin D levels

Indicator	Both genders n=88	Males n=51	Females n=37	p
Level of 25(OH)D[2]	10.0 (9.2; 18.2)	9.8 (8.7; 13.5)	15.0 (9.3; 19.2)	0.056
Distributions of vitamin D levels, n (%)				
Optimal (30-50 ng/mL)	4 (4.5)	3 (5.9)	1 (2.7)	0.085
Subnormal level (20-29.9 ng/mL)	11 (12.5)	4 (7.8)	7 (18.9)	
Deficiency (10-19.9 ng/mL)	30 (34.1)	14 (27.5)	16 (43.2)	
Severe deficiency (0-9.9 ng/mL)	43 (48.9)	30 (58.8)	13 (35.1)	

Note. Data are presented as mean and standard deviation, M(SD); data are presented as quartiles, Me (Q1; Q3); p - statistical significance of differences between males and females.

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IMMUNOCORRECTIVE THERAPY IN COMBINED TREATMENT OF PATIENTS AFTER SIMULTANEOUS SURGERY ON THE ABDOMINAL ORGANS DURING THE EARLY POSTOPERATIVE PERIOD

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The article analyzes results of the combined treatment at 452 patients, aged 16 to 64, after the simultaneous surgery on the abdominal organs for visceroptosis, during the early postoperative period. In 280 (61.9%) of them, studies of the immune status were conducted against the background of immunocorrective therapy. Thymogen and polyoxidonium were used as immunocorrectors. The drugs were injected to patients during surgery intravenously: the thymogen by 2 ml. of 0.01% solution, the polyoxidonium-12 mg in solution. In the postoperative period, the drugs were injected intramuscularly for 8 days: the thymogen by 1 ml of 0.01% solution, the polyoxidonium 6 mg in solution. Use of the immunocorrective therapy allowed to achieve a significant improvement in the dynamics of immune indicators in patients compared to a control group. The polyoxidonium effect on immunological parameters was strongly pronounced and significantly exceeded the effect of thymogen.

Keywords: visceroptosis, simultaneous operations, immunocorrective therapy.

Combined surgical correction for visceroptosis is characterized by the postoperative period severity and treatment complication, which is due to simultaneous surgery on the abdominal organs. Research met in the scientific literature on the surgery problem of the digestive system diseases mainly raises questions on new types of surgical approaches, methods of operation, methods of hemostasis, etc., and treatment of this category of patients in the postoperative period is not fully covered, which determines the need for a deeper study of this stage of treatment.

Materials and research methods. We performed surgical treatment of 452 patients aged 16 to 64 years. 421 (93.1%) patients were operated at the age of 21 to 60 years, i.e. at the most active working age. Patients older than 60 years were admitted for surgical treatment from other medical institutions, where due to the chronic intestinal obstruction and progressive weight loss, they were examined with suspicion of colon cancer. Patients operated at the age of 20 years, as a rule, belonged to the group of patients with a form of visceroptosis, occurring with a pronounced pain syndrome, and 19 of them had daily defecation.

To treat patients with visceroptosis, we applied methods of combined surgical correction depending on variants of the pathological process, operational findings and verification with the data of a comprehensive clinical study. In this case, simultaneous surgical treatment of all changes detected in the preoperative period and requiring surgical correction is performed. Many authors indicate causal relationship and interdependence between changes in one organ and development of painful processes in another, and in this regard, they support expansion of indications for combined surgical interventions. Our experience of simultaneous operations at patients with visceroptosis confirms correctness of these assumptions.

The combined surgical treatment includes both well-known methods of operations on the gastrointestinal tract, and techniques developed in our clinic (Table 1).

1718 operations were performed at 452 patients. On average, each patient had 3-4 simultaneous operations.

Rehabilitation of patients after operations on organs of the gastrointestinal tract (GIT) has the main goal to restore the motor-evacuation function of the gastrointestinal tract that was disrupted during surgery, as well as normalization of the digestive conveyor. Especially severe postoperative disorders occur in the organs of nervous and endocrine regulation, in the process of metabolism. In the early postoperative period, combined therapy is performed aimed at stabilizing the condition of patients and preventing the development of early complications: failure of anastomosis, development of infectious complications and pneumonia.

Traumatic and operational stress have a depressing effect on the functional state of vital organs and systems in the postoperative period, and especially the immune system, which leads to an increase in the frequency of postoperative complications and fatalities. The use of immunocorrective therapy in the combined treatment of patients with various surgical pathologies allows us to improve the results of treatment, reduce frequency of postoperative complications.

In patients with visceroptosis complicated by CTS, before surgery, we observed a moderate decrease in concentration of IgA and a marked increase in IgG compared to the control group, which indicates a greater tension of the immune

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