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THE HYPOTYRESIS IN PATIENTS WITH CHRONIC OBSRUCTIVE PULMONARY DISEASE (COPD)

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Abstract

The processes of reparative regeneration of the bronchial epithelium are controlled by thymic factors, thyroid hormones, and cellular immunity in patients with COPD in a stage of exacerbation. It complicates by purulent necrotic of the bronchopulmonary system amid a decrease of reduce synthesis of endogenous triiodothyronine. We gave pathophysiological rationale for use of thyroid hormone replacement therapy for correction of hormone (thymalin and thyroid -) dependent functional activity of lymphocytes. We proved the clinical effectiveness of the using alternative triiodothyronine therapy as an extra-immune immunocorrector. It includes thyroid and thymalin-dependent effects in patients with COPD with low triiodothyronine syndrome in the period of exacerbation.

Key words: **COPD, thyroid, triiodothyronine, hypothyreosis, fibrinolytic activity**

Rational: The thyroid hormones have the ability to stimulate reparative regeneration, activate prokoagulantion and fibrinolytic activity (including lymphocyte-dependent) [1, 5, 6]. The synthesis and functional activity of hormones of the thyroid gland change in patients with a long course of chronic obstructive pulmonary disease (COPD), due to the exacerbation of the process, [2].

The interdependence between the level of secretion of thyroid hormones and the development and chronicization of chronic non-specific inflammatory process was revealed. The deficiency of thyroid hormones contributes both to the development and maintenance of chronic inflammation in the bronchi at bronchial asthma (BA) [3]. Also it decreases thyroxin content at the physiological level of T3 in patients with asthma over the age of 40 years [4].

The peculiarity of the influence of hormones on the course of COPD in the stage of exacerbation with low level of triiodothyronine and influence of substitution therapy comorbidity state remain insufficiently discovered.

That is why we want to prove the feasibility of conducting research in this direction.

Objective: We want to confirm the pathophysiological and clinical rationale of the using substitution therapy with thyroid hormones for the correction of hormone (thymalin and thyroid). We think that it depends on functional activity of lymphocytes in patients with COPD in the exacerbation phase in combination with purulent necrotic forms of nonspecific pathology of the bronchia-pulmonary system and low-level syndrome of triiodothyronine.

Materials and methods: We investigated 112 patients with COPD in a state of exacerbation in combination with purulent-necrotic forms of nonspecific pathology of the bronchopulmonary system.

All patients were divided into 3 groups: the 1st group included 42 people (7 patients with chronic lung abscess, 10 patients with bronchiectasis, 2 patients with cystic lung disease, 18 patients with chronic purulent bronchitis and 5 patients with cyst lung) with a physiological level of secretion of thyroid hormones; in the 2nd - 38 people (9 for chronic lung abscess, 9 for patients with bronchiectasis, 2 for patients with cystic lung disease, 13 for patients with chronic purulent bronchitis and 5 for patients with lung cyst) with a reduced level of secretion of thyroid hormone, substitution therapy with triiodothyronine to the treatment complex did not include to the preoperative period; 32 patients (4 patients with chronic lung abscess, 5 patients with bronchiectasis, 1 patient with cystic lung disease, 17 patients with chronic purulent bronchitis and 5 patients with lung cyst) to the lower level of thyroid hormone secretion up to the 3rd group the medical complex of which included substitution therapy with triiodothyronine, blood 24 healthy donors was used by means of control.

The diagnosis established on the basis of data of complex clinical-radiological examination, indicators of the function of external respiration. All patients had an exacerbation of chronic bronchitis in the period of the examination.

We determined the following parameters: levels of TSH in serum, total T4 and total T3 in serum, determination of biological activity of thymalin, fibrinolytic activity (FA) of leukocytes in blood, parameters of CD4 + and CD8 + [5]

The research material is blood and bronchoalveolar washings (BAAS), samples of the bronchial mucosa, from the biopsy sites of the bronchopulmonary tissues.

The thyroid disease after a complex examination was in all examined patients. Therefore we think that the level decrease of T3 is not as a symptom of hypothyroidism but it is as a manifestation of pseudodysfunction of the thyroid gland. It is in severe nontyreoid diseases and it characterizes by the level decrease of total and free T3 in the blood serum due to the suppression of the peripheral 5'-monoidal T4 [6]

We used Lyotironin (synthetic T3 - triiodothyronine hydrochloride) for substitution therapy at 25 micrograms 2 times a day for a course of 7-10 days. The drug does not have a "withdrawal syndrome" [5, 6]. The daily dose of the drug was about 50% among the patients with a decreased level of T3 and hypothyroidism with in substitution hormonal therapy. But the main aims of the treatment was the stimulation of reparative regeneration of bronchial tissues and decrease the imbalance of functional integration of the system of cellular immunity, the system of hemocoagulation / fibrinolysis in the period of exacerbation of COPD.

We found that the level of the thyrotropic hormone of the pituitary gland and the content of total thyroxin in the serum in patient’s 1-st, 2-nd and 3-d was on physiological norms. The level of total triiodothyronine in patients of the 1st group did not different from it in the group of healthy individuals. But it decreased by 1.2 times ($p < 0.01$, $p1 < 0.05$) in patients of the 2nd and 3rd groups.

The concentration of total thyroxin in the tissue extracts of the mucous membrane of the bronchi in patients 2nd and 3rd groups, as compared with patients in the 1st group, was decreased by 26,1-21,2% ($p < 0,05$). We registered the absence of T3 in the extracts of the tissues of the mucous membrane of the bronchi in the patients of the 2- nd and 3 rd groups. There was systemic deficiency of T3 in this group. It combined with a decrease in the concentration of T3 and T4 in the tissues of the bronchial mucosa. Thus, in patients with COPD in a state of exacerbation the content of thyroid hormones in the peripheral blood characterized the disturbance of local endocrine balance.

The significant difference in the effect of leukocytes on the fibrinolytic activity of the plasma revealed in healthy persons and patients. So we added the leukocytes to the euglobulin clot in the group of healthy people and it accelerated its lysis by 22.9 ± 1.3%. Then in the patients of the 2nd and 3rd groups the leukocytes slowed the lysis of the euglobulin clot at 3, 0 ± 0, 1% (p

<0,001) and 2, 8 ± 0, 1% (p <0,001). The fibrinolytic activity of leukocytes was lower than the physiological level of its oscillations in 4, 2 times (p <0,001) in patients of the 1st group.

Also we determined that under the influence of timalin leukocytes potentiated fibrinolytic activity in patients of the 2nd and 3rd groups: in patients of the second group +5, 1 ± 0, 2%, in of patients in the 3rd group - up to 4.9 ± 0.2% (p3 <0.001). The investigated parameter increased under the action of the thyroid hormone in the groups of patients with a low systemic level of T3: in patients of the 2nd group by 66.7% (p4 <0.001), in patients of the third group - by 57.1% (p4 <0.001)

The tissue extracts retained their inhibitory expression of surface cellular identification markers only in patients of the 2nd group at concentration of 1: 5000: the CD4 + index were reduced by 18.6% (p <0.02). In the general blood flow the level indicator of CD8+ decreased in the 1st, 2nd and 3rd groups as by 24.2% (p <0.01), 28.4% (p <0.001) and 32.7 % (p <0.001).

Thus, there was a total immunoactive influence of tissue factors. It aimed at forming a “hyper” suppressor variant of the immune imbalance.

In healthy persons receptors expressed 20.8 ± 0.5% of lymphocytes to tissue plasminogen activator. And in patients with COPD it was reduced by 50.5-47.1% (p <0.001).

We studied the processes of reparative regeneration of bronchial tissues. We found that in patients with COPD who entered to the hospital the proliferative index (PI) was reduced by 58.4-56.5% (p <0.001). And it increased by 48.3 -40.7% (p_1 <0.001) under the influence of thymalin. We found the ability of the thyroid hormone to potentiate thymalin-dependent proliferative activity. The level increased in patients with the 1st, 2nd and 3rd groups, by 28.0% (p_2 <0.001), 28.1% (p_2 <0.01) and 25.6% (p_2 <0.01). Thus, the presence of purulent-destructive processes in bronchopulmonary tissue is an essential "burden factor" for disorders of reparative regeneration of bronchial epithelium in patients with COPD.

We revealed in patients with COPD an increase in regional coagulation potential. It prevented the completion of the inflammatory process in the mucous membrane of the bronchi. And it was the basis for chronic disease and the development of pneumosclerotic changes. Thus, the time of recalcification (TP) of the culture medium in the patients reduced by 27.5-38.5% (p <0.001). And it increased by 14.5-19.5% (p_1 <0.05) under the influence of thymalin. Moreover, we did not find the significant influence of thyroxin on timalin-dependent prokoagulantnaya activity of epithelial cells in patients of the 1st group. And the investigated index increased by 12.5-12.4% (p_2 <0, 05) in patients of the 2nd and 3rd groups.

The hypercoagulation shifts at the level of bronchial tissues in patients with COPD combined with changes in local proteolytic potential. So in the patients of the 1st, 2nd and 3rd

groups the activator activity of the culture medium increased at 69.0%, 50.3% and 55.0% (p <0.001).

Timalin did a potentiating effect on the fibrinolytic activity of the culture medium only in patients of the 1st group: fibrinolytic activity (FA) increased by 11.9%, p1 <0.05. We found the dynamics of FA under the influence of thyroxin in patients of all groups. It indicated the modulating effect of the thyroid hormone on the functional activity of cells of the bronchial epithelium.

The thyroid hormones leaded to formation of a thymus-mediated "balanced" dysfunction in the system of coagulation / fibrinolysis aside of fibrinolysis. The fibrinolysis promotes the effective recanalization of bronchi and lysis of deposits of the fibrin.

Conclusions:

1. The processes of reparative regeneration of the bronchial epithelium (including its procoagulant and fibrinolytic potential) in patients with COPD in the state of exacerbation with low of endogenous triiodothyronine are under control by thymic factors (thymus induced proliferation), thyroid hormones (thyroid-mediated proliferation), and also cellular immunity (lymphocyte-mediated hormone-dependent plastic effect).

2. We gave the pathophysiological substantiation using replacement therapy of thyroid for the correction of hormone (thymalin and thyroid) -dependent functional activity of lymphocytes (including fibrinolytic and procoagulant) in patients with COPD in the stage of exerbation with the syndrome of low triiodothyronine.

3. We proved clinical efficacy of using triiodothyronine substitution therapy as extraimmune (including thyroid- and thymalin-dependent effects) immunocorrector in patients with COPD with syndrome of low triiodothyronine. It is due to stimulation of reparative regeneration of bronchial tissues and reduction of imbalance of functional integration of the system of hemocoagulation / fibrinolysis in the period exacerbation of COPD.

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