

## IMMUNOLOGIC FEATURES OF SPELEOTHERAPY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The paper studies immunologic features of speleotherapy in patients during the restorative period. One hundred and twenty-eight patients suffering from chronic obstructive pulmonary disease (COPD) at the stage of an incomplete remission were examined. The patient groups of 74 men and 54 women were divided into 2 representative groups by a method of randomization.

Studies showed a pronounced reliable positive dynamics in indices of cellular and humoral links of immune status in patients with COPD after speleotherapy: an increase in concentrations of subpopulations in all the studying of lymphocytes; normalization in correlation between subpopulations CD4+ and CD8+ lymphocytes; decrease of ABL level to tissual antigen of the lungs; an increase in PhA, a number of B-lymphocytes and content of immunoglobulins G, A, M, as well as further activation and fixation of immune response.

On the whole, indices of immune status improved after a course of treatment in 97.8% patients of the main group and in 67.5% patients of the control group simultaneously with positive dynamics of clinical symptomatic. These indices have become particularly better after 6 months in post-treatment period that evidences the prolonged efficacy of ST in contrast to other methods of treatment.

ILMURAT NUROV

*Republican Specialized Scientific  
Practical Medical Center of  
Phthisiatry and Pulmonology,  
Uzbekistan*

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### Introduction

Today an involvement of immunologic mechanisms in development of chronic bronchopulmonary pathology has been proved. During the past decade mechanisms of disturbance of immunoregulation forming a ground of chronic obstructive pulmonary disease (COPD) were elucidated (Aysanov et al., 2001; Nurov et al, 2007). Medicament interventions, so far, have not provided a controlled remission of COPD and are often accompanied by adverse effects. That's why the International Programs of treatment of this disease, besides medicament therapy, certainly provide an inclusion of non-medicament therapeutic methods to potentiate synergic effect of these methods, taking into consideration an effect on different pathogenetic links of disease (Chodosh et al., 2001).

Despite physiotherapeutic methods of treatment of COPD patients are being intensively worked out, creation of new techniques by using natural and re-formatted physical factors still remains an actual problem (Zunnunov, 2000; GOLD, 2003).

Immune system is one of the first to respond to external and internal changes being an indicator of various unfavorable effects of exogenous and endogenous character. Reaction vectors of immune system to unfavorable effects are either activation or suppression of one or several links of immune process - in other words, changes of immune status of organism (Kochetkova et al., 2004). Multiple exogenous and endogenous factors have an effect on functioning of immune system; therefore, its work may be regulated by purposeful effect with substances increasing or depressing immunity (Postnikova et al., 2004).

Therapy at different pathogenetic stages of COPD remains today one of the actual problems due to an advancing course of this disease. One of the leading causes of minor

efficacy of treatment of COPD is damage of immunologic reactivity observed in these patients (Chuchalina, 2003; Ubaydullaev, 2005).

An active using of speleotherapy (ST) in treatment of COPD, which mechanisms are studied extremely insufficiently, attracts special attention (Zunnunov and Nurov, 2005).

The aim of research is to study immunologic features of speleotherapy in patients with chronic obstructive pulmonary disease.

## Material and methods

128 patients suffering from COPD at the stage of incomplete remission, of them 74 men and 54 women (the average age -  $52.5 \pm 1.5$ ) have been examined.

All the patients were divided into 2 representative groups by a method of an open randomization.

The 1st group (the main) was formed from 103 patients (60 men and 43 women aged from 30 to 60) received speleotherapy in combination with a standard basic therapy (B2-agonists, inhaled corticosteroids etc.).

The 2nd group (control) formed of 25 patients (14 men and 11 women aged from 30 to 60) received a standard basic medication therapy without speleotherapy.

Speleotherapy in a cave "Khodjaykhon" was conducted by a method of a stage adaptation, procedures were performed in 2-3 days following adaptation to climatic conditions of the pre-mountain area "Khodjaykhon", then, was allowed the 1st visit to the cave for 30 minutes, the 2nd visit - 1.0-1.5 hours, and then - from 2 to 4 hours daily. By the end of the treatment course duration of the procedure was gradually decreasing, exposure was finished in 30 minutes. Number of procedures was 18-22.

The dynamic method of clinic-meteorologic observations is the basis of clinical research. In these observations a clinical card, containing clinical and meteorologic information, was used. Filled in by admission of patients to hospital the data of their history of life were explored indicating the presence of sensibilization of a patient to climatic changes. During his stay in clinic the morning medical examination was conducted, main symptoms (cough, sputum, lack of air, throat scrape, pains in thorax, weakness, sleepiness, arthralgia etc.) were examined.

Immunologic studies were carried out in cooperation with the officials from the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan in accordance with recommendations of the Institute of Immunology of the Ministry of Public Health of the Russian Federation (Petrov et al., 1982). Methods included determinations of:

- relative and absolute number of lymphocytes, T and B lymphocytes, as well as CD4+ cells - immune-regulating T-helpers/inductors, CD8+ T-suppressors/cytotoxic lymphocytes, CD16+ cells - natural killers - by means of monoclonal antibodies (Institute of Immunology, Ministry of Public Health of Russia).
- antigen-binding lymphocytes (ABL) with different tissue antigens of the lungs - by a method of indirect rosette-formation;
- quantitative determination of neutrophils' phagocytosis activity- by ability of cells to absorb particles of latex;
- concentration of immunoglobulins IgG, IgA, IgM was determined by a method of Mancini. Examination of patients was performed before, after and 6 months after the course of treatment. Statistical processing of results has been carried out by means of the program "Statistical" for "Windows - 2000" with the help of the Student t-criterion.

## Results and discussion

Clinical analysis showed that by admission to clinic patients had complaints of cough with excretion of mucous or mucous-purulent sputum, less severe breathlessness, lack of air,

weakness. Auscultation often fixed a prolonged expiration, dry wheeze that were accompanied by marked disorders of bronchial passage based on findings of computer spirosocopy. In 74 of 128 patients obstruction in periphery parts of bronchi was registered, in 34 - on a level of central ones and in 20 patients generalized obstruction was registered. Before treatment no reliable differences of main clinical and functional indices between patients of main and control groups were presented ( $P>0.05$ ).

Positive dynamic of clinical symptoms of disease in main group was accompanied by reliable favorable shifts in immunologic status. Analysis of results of the studying of immune system of patients in control group exhibited an increased content of leucocytes after the course of treatment, but it was not reliable; it was reliable in 6 months in patients of the main group. This index was reduced reliably in both groups of patients to leukocyte index before treatment. Relative and absolute number of lymphocytes was initially within the limits of norm, and after treatment was observed their reliable increase in patients of the main group.

Before treatment relative content of T-lymphocytes was not high ( $44.9\pm 1.15\%$ ), their absolute number was within the limits of the norm ( $1150\pm 44$  mcl). The treatment significantly increased the relative and absolute number of T-lymphocytes, especially in patients treated with CT ( $49.6 \pm 1.9\%$  and  $1356 \pm 46$  ml). In 6 months after treatment this index in patients of the main group neared to the norm ( $54.3\pm 1.5\%$ ), and absolute number increased up to  $1386\pm 32$  mcl.

Investigation of lymphocyte subpopulations showed that the average value of CD4+ lymphocytes was approximately 1.5 times lower the norm ( $27.5\pm 1.1\%$ ). After the treatment there was a reliable increase in the number of CD4 + cells in patients treated with CT ( $30.5 \pm 0.7\%$ ), which in 6 months increased to the lower limit of normal ( $32.9 \pm 0.5\%$ ). Quantity of CD8+ and CD16+ lymphocytes that were initially on the lower limit of the norm ( $17.1\pm 0.1$  и  $6.2\pm 1.0$  respectively) reliably increased after treatment in the main group (up to  $18.3\pm 0.1$  and  $9.6\pm 0.6\%$  respectively), and after 6 months the growth of these indices ( $21.2\pm 0.6\%$  and  $13.4\pm 0.6\%$ ) was observed

Level of ABL to tissual antigen of the lungs before treatment was 3 times higher the norm ( $14.7\pm 0.17\%$ ), after the course of psammotherapy a reliable decrease was observed (up to  $9.4\pm 1.5\%$ ), by the 6th month after treatment it was reduced up to almost normal values ( $5.6\pm 1.5\%$ ). An average content of CD19+ lymphocytes (B-lymphocytes was within the limits of the norm ( $17.2\pm 1.5\%$ ), at the same time during the treatment it increased, and by the 6th month accounted for  $20.3\pm 0.8\%$  and  $22.7\pm 0.6\%$  in patients of both groups, as well the growth of absolute number of B-lymphocytes was observed. The level of serum immunoglobulin was reduced before treatment ( $578\pm 22$  mg%) and during the treatment it reached ( $890\pm 28$ mg%), especially in 6 months it was increasing up to normal values ( $1048\pm 32$  mg%). Performance of immunoglobulin A and immunoglobulin M, which were within normal limits during treatment significantly increased.

One of the most important functional characteristics of neutrophiles is their phagocytosis activity (PhA). Studies showed that the percentage of PhA in the blood was decreased ( $40.6\pm 1.7\%$ ). During the treatment with ST in patients of the main group their PhA increased up to  $44.4\pm 1.5\%$ , and in 6 months - up to  $48.7\pm 1.4\%$ .

Thus, results of our immunologic investigations exhibited a pronounced reliable positive dynamics of indices of cellular and humoral links of immune status in COPD patients against the background of ST: an increase in concentration of subpopulations of all the studied lymphocytes, correlation of subpopulations CD4+ and CD8+ lymphocytes, reduction of an increased level of ABL to tissual antigen of the lungs, growth of PhA, quantities of B-lymphocytes and content of immunoglobulins G, A, M, as well as further activation and fixation of immune response.

By the end of the course of the treatment indices of immune status were improved in 96.8% of patients in the main group and in 67.5% of patients of the control group simultaneously with positive dynamics of clinical symptomatic; especially these indices

were improved 6 months after the treatment, which proves a prolonged efficacy of ST in contrast to other methods of treatment.

The given investigation showed that such features of the cave “Khodjaykhon” as high concentration of breathable fine dispersion natural multi-component aerosol and negative aerosols, minimum contamination, absence of allergens and optimal temperature-humidity microclimate regime in complex have a positive effect on patients with chronic obstructive pulmonary disease.

Taking into account the mechanism of the healing effect, the speleotherapeutic procedure in the cave “Khodjaykhon” may be recommended in COPD as a part of complex treatment in the period of aggravation or as a mono-factor in the period of an incomplete remission, aimed at reducing intensity of inflammatory changes in bronchi; and perfecting clinic-immunologic potentialities of bronchi-pulmonary system as well as prolongation of remission of disease.

Thus, CT is highly effective and has long immuno-modulating effect treatment for COPD during the rehabilitation period.

## Conclusion

1. Immune status in patients with COPD is characterized by suppression of T-cell (CD3 + and CD4 +), humoral (IgG, IgA, IgM) immunity links, as well as factors of nonspecific protection (CD16 + and phagocytosis). The level of B-lymphocytes and SLA histocompatibility antigen in the lungs increases.
2. In speleoterapevticheskoy cave “Hodzkhavkon” moderate external weather gibobariva hypoxia and low bacterial sow, high concentrations of the microparticles of salt and negative air ions, stable, comfortable micro-climatic conditions in complex have highly efficient integral immunomodulatory effect in patients with COPD.
3. Highly efficient speleotherapy, which is linked to the achievement of complete remission of COPD in an extremely short time, eliminates the phenomenon of the inflammatory process.

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