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The research of the exhaled breath condensate to evaluate the local homeostasis in patients with pulmonary tuberculosis

Abstract: The research of the exhaled breath condensate (EBC) is important in the study of a number of indicators that characterize the local homeostasis of the respiratory system. The aim of the research was to study the direction and the degree of the changes in the EBC LC-spectra of the patients with tuberculosis according to the clinical nature of the tuberculous process established certain patterns of metabolic changes of a local nature. The noninvasiveness of the laser correlation spectroscopy (LCS) method, the high sensitivity and speed of the native material research opens up the possibility of using it in phthisiology.

Keywords: exhaled breath condensate, tuberculosis, laser correlation spectroscopy.

Introduction

The exhaled breath condensate (EBC) attracts attention as an object of study in various diseases, especially diseases of the respiratory system, because it gives an opportunity to assess the status of various physiological functions[1], the degree and direction of metabolic processes[2], etc. The EBC covers the airways and therefore contains the markers of inflammation (cytokines, prostaglandins, leukotrienes). The study of those and the other local markers of oxidative stress and inflammation is more specific as compared to other serological markers[3].

It should be noted that the study of specific biological markers and other components require the use of expensive methods. At the same time, a number of studies shows the high sensitivity of the method of laser correlation spectroscopy[4] (LCS) of the EBC in the integrated assessment of the local metabolic disturbances[5].

The purpose of this study was to examine the direction and degree of changes in LC-spectra of the TB patients' EBC according to the clinical nature of tuberculous process.

Materials and methods

The study group comprised of 143 patients with tuberculosis (TB) admitted for TB treatment in Odessa hospital. The comparison group consisted of 80 healthy men and women aged 25 to 40 years, during which the clinical examination did not reveal any abnormalities in health. EBC was prepared using A. N. Komlevoy's method[6].

The received EBC was stored at –20 °C. The biophysical properties EBC were evaluated using the LCS-03 LC-spectrometer (St. Petersburg's Institute of Nuclear Physics). The individual LC-spectrum, which is a distribution of the particles with the particular hydrodynamic radius, is displayed on the computer screen in a bar chart. From the individual LC-spectra there were obtained averaged EBC LC-spectra of the particular group (Fig. 1).

This approach allows to provide not only high quality, but also the quantitative characteristic of the EBC[7]. In addition, the individual spectra of the EBC LC-spectra were analyzed with the semiotic classifier[8].

The classifier for EBC defines four discrete zones[9]. According to the direction of the metabolic shifts there are four main groups of LC-spectra, given the nature of the structure: normologic, catabolic, anabolic and mixed (Fig. 2).

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[1] Bazhora Yu. I., Noskin LA Laser correlation spectroscopy in medicine. – Odessa: «Druk», 2002.

[2] Dobryih VA, Mun IE Problems of studying the exhaled breath condensate in respiratory diseases//Problems of tuberculosis and lung diseases. – 2005. – N 3. – S. 33–35.

[3] W. Lee, PS Thomas. Oxidative stress in COPD and its measurement through exhaled breath condensate//CTS Journal. – 2. – V.2. – N 2. – P. 150–155

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[6] Komlevoy O. M., Bazhora Yu. I. Laser correlation spectroscopy of the exhaled breath condensate//Integrativna antropologiya. – 2010. – N 1. – S. 35–38.

[7] Molecular – genetical and biophysical research methods in medicine/Bazhora Yu. I., Kresyun VI, Zaporozhan VN – K .: Zdorov'ya, 1996.

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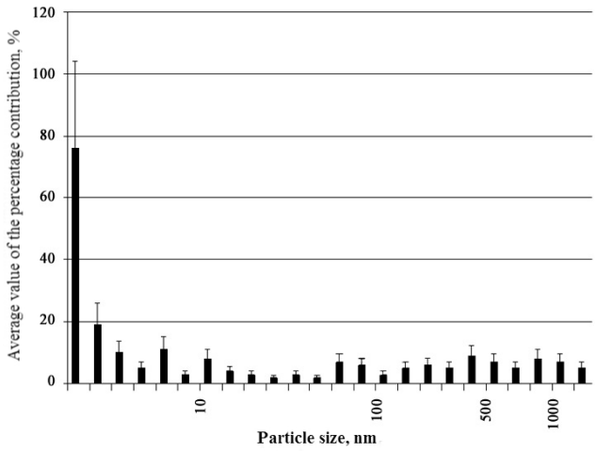

Fig. 1. – LC-averaged spectrum of healthy individuals EBC

Results and discussion

In 91.25% of healthy individuals there is the normologic LC-spectrum, four patients had the anabolic LC-spectrum and three of them — the mixed type of the LC-spectrum. And all the seven patients had initial stage of shift. These data fit in the range of deviations noted in other studies[1]. Patients with tuberculosis revealed significant metabolic changes.

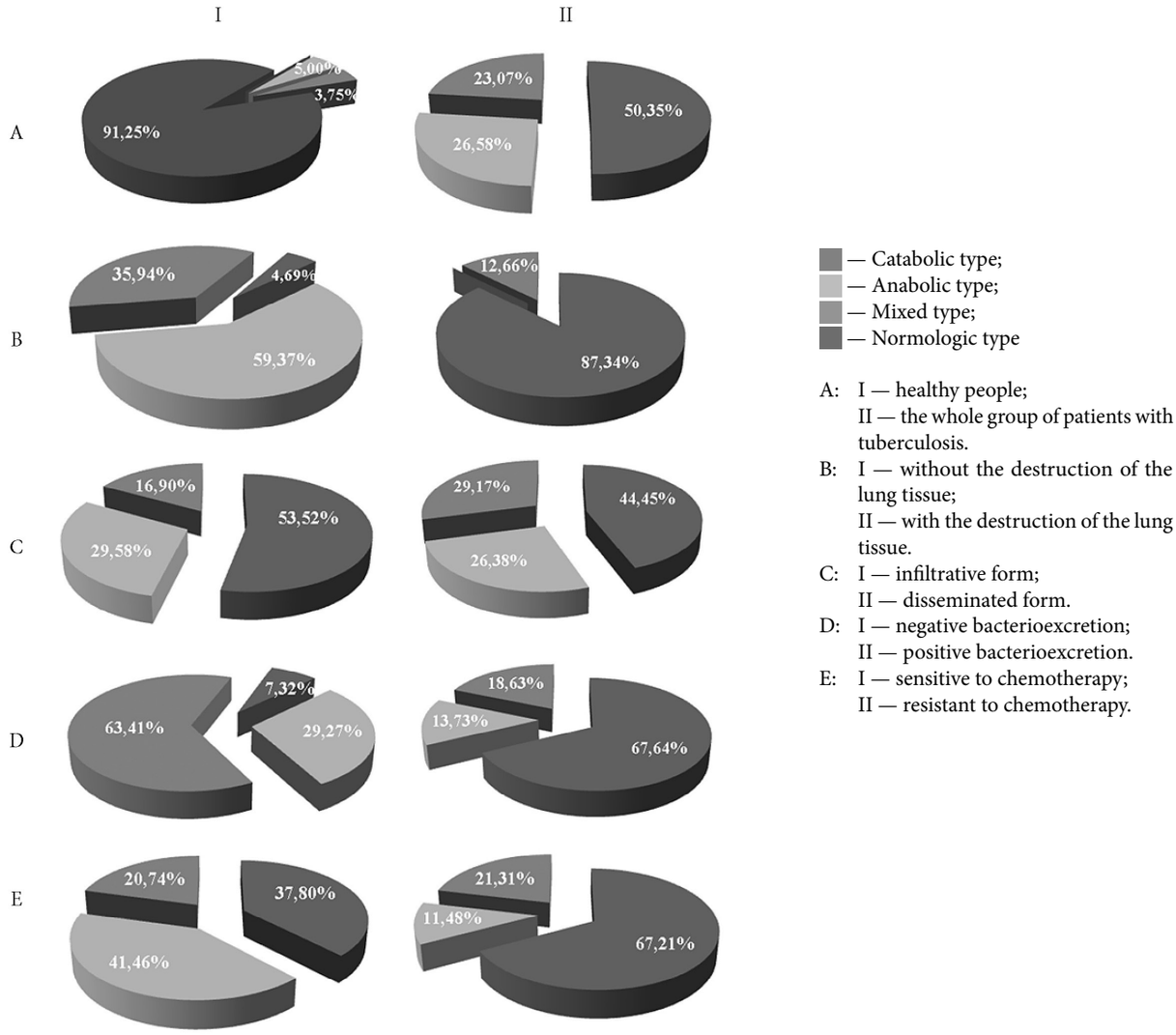

Fig. 2. – The incidence of different types of the direction of metabolic changes in patients with TB according to the EBC LC-spectroscopy

[1] Sazonets OI The diagnostical meaning of the laser correlation spectroscopy of the biological fluids in the patients with bronchial asthma.//PhD thesis abstract. SPb, 2001.

Significant difference is found in various types of metabolic changes in TB patients: half of the patients (50.35%) ($20.87<\chi^2<17.08$, $p<0.001$) have the catabolic type LC-spectrum: 50 patients had the severe degree, 22 had the moderate degree. In 26.58% of patients there was the anabolic type, 23.07% — the mixed type of shift. In both the first and second cases, they had the high and the moderate degree. Thus, in patients with tuberculosis, according to EBC LC-spectroscopy there are various types of metabolic changes that have the severe shift degree. And the prevalence of the metabolic type of shift can be explained by an increased globulin fraction in patients with tuberculosis, especially in the chronic process.

Given the variety directional shifts identified, we analyzed the results of EBC LC-spectroscopy taking into account peculiarities of tuberculosis process in the patients examined. Thus, in patients without lung tissue destruction (n=64) there was the ambiguity of metabolic disorders: 38 (59.37%) had the anabolic type, 35.94% had the mixed type, and only 4.69% had the catabolic type. As in the total group of the patients, the degree of the shift was moderate to severe. Perhaps this might be due to the active process of the formation of specific inflammation foci involving a large number of different cells of the immune system, resulting in production of inflammatory cytokines and chemokines in response to the release of a number of lipids, glycolipids and lipoproteins by *M. tuberculosis*, which leads to the accumulation of medium and large molecular complexes in the respiratory tract surface fluid. In the case of destructive processes in the lung tissue the catabolic LC-spectra with a severe shift degree were expected to be dominant: 69 (87.34%) patients ($\chi^2=47.34$, $p<0,001$). Both groups had the LC-spectra of the mixed type, predominantly in patients without lung tissue destruction (35.94%). This direction of the metabolic abnormalities may be associated with both the localization of foci of the specific inflammation and the degree of the involvement of the mucous membrane of the bronchial tree in response to tuberculous process.

When comparing the EBC LC-spectra in patients with infiltrative and disseminative forms of TB the prevalence of catabolic type deviations was found. The anabolic type occurs in about equal proportions, and the mixed one goes more often with disseminated form. The patients in this group also predominantly expressed the severe degree of impairment (73.81%). These changes in the composition of the macromolecular EBC can be linked to the degree of involvement of the lung tissue in the development of various forms of tuberculosis process.

Roughly the same pattern of distribution of LC-spectra according to the direction and the degree of metabolic changes was observed in the groups of patients with and without the bacterioexcretion. The predominance of the catabolic changes mainly with a high degree of severity was identified for 69 patients (87.34%) ($\chi^2=88.13$, $p<0,001$) with the bacterioexcretion.

Certain patterns are revealed in the groups of patients who are sensitive and resistant to specific chemotherapy. The catabolic changes in the LC-spectra prevailed in the resistant group, whereas the group of patients sensitive to chemotherapy had all the directional shifts at different rates. The same was the ratio of the LC-spectra of the violations' severity. This is understandable due to the fact that the resistance to anti-TB treatment does not contribute to the regression of the tuberculosis process and thereby prevents the immune system of such patients from stabilizing the disruption of homeostasis in the tissues of the respiratory system at a certain level.

Conclusions

The study of the EBC using the LCS revealed certain patterns of metabolic changes of the local homeostasis in patients with tuberculosis. They are correlate with the nature of the clinical course of the tuberculous process. The complex sequential pathogenetic processes occurs in lung tissue (violation of intracellular metabolism of macrophages and T-lymphocytes leads to damage to cellular structures and induces of the process of the immune system cells apoptosis, which in turn leads to the formation of secondary immunodeficiency, the development of inflammation and necrosis of the cells of the lung tissue) that result into contribution rise of the low-molecular fractions EBC recorded as catabolic (degenerative and intoxication) changes in the lungs in case of tuberculous lesions. The noninvasiveness of this method and the possibility of studying the native biological samples gives the LCS a number of advantages compared with biochemical methods of research.

Further research in this field allow us to study the possibility of using the LCS method in the formation of the patient particular phenotype portrait based on the estimation of the pattern of local homeostasis changes in the lung tissue of patients with tuberculosis for predicting the course of tuberculous process and the effectiveness of its treatment.

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