

# **Influence of antioxidant therapy on the parameters endobronchial microcirculatory and intensity of inflammation in patient having exacerbation of COPD**

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**Abstract:** COPD is one of the main reasons of morbidity and mortality worldwide, leading to economic and social damage, and its level increases. Oxidation stress, inflammation and disturbance of endobronchial microhemocirculation are relative processes playing a key role in development and progressing of COPD. Preparation dihydroquercetin blocks free radical reactions, thereby influencing on the basic links in pathogenesis of COPD. Considerable dynamics of indices of BAL fluid demonstrates the anti-inflammatory effect of preparation dihydroquercetin. All above-stated allows to speak about dihydroquercetin as the important addition of medicamentous therapy of COPD.

**Key words:** Chronic obstructive pulmonary disease, endobronchial microhemocirculation, bronchoalveolar lavage fluid, dihydroquercetin.

COPD is one of the main reasons of morbidity and mortality in many countries, leading to economic and social damage, and its level increases. According to the number of forecasts COPD, that took the sixth place in the check-list of the reasons of death in 1990, by the year 2020 will take the third place in this register. Especially high growth of death rate from COPD is marked among women. In the developed countries the greatest expenses for public health services systems are connected with exacerbations of COPD. Presence of COPD considerably increases the general expenses for treatment of patients, especially expenses for inpatient treatment [1,6]. According to official data there are about 1 million COPD patients, while, according to the academician A.G. Chuchalin, actual quantity of these patients can exceed 11 million, i.e. only each eleventh patient with COPD gets to the statistical reporting. Thereby real prevalence rate of COPD in Russia is still unknown [5,6]. Approximately 119000 persons at the age of 25 and older have died from COPD in the USA in 2000. The prospective total costs of treatment of COPD in 2002 has made 32,1 billion dollars, among them factor costs have made 18 billion and indirect costs 14,1 [4]. So, COPD is considered to be a great social, demographic and economic problem. Lungs of COPD patients in the period of exacerbation are characterized by high concentration of neutrophils and macrophages, which promote the release of great number of free radicals. It results in so-called «oxidation stress» formation. Oxidation stress, inflammation and disturbance of endobronchial microhemocirculation are relative processes playing a key role in development and progressing of COPD [2,7,8]. The majority of available drugs cannot influence to the full on the basic pathogenetic links of mentioned disease. Inhaled glucocorticoids which to date are the most effective anti-inflammatory preparations, do not positively influence in mild and moderate COPD, but only in severe COPD they reduce frequency and intensity of exacerbations [2,3,7]. Therefore presently there is a lot of research experiments carried out in order to find out the appropriate drug capable to influence on the inflammation, and to restore endobronchial microcirculation. Preparation dihydroquercetin is known for its antioxidant activity, it blocks free radical reactions, thereby influencing on the basic links in pathogenesis of COPD.

## **Experimental**

### **Material and Reagents**

The purpose of our work was to study the changes in bronchoalveolar lavage (BAL) fluid indices and the features of endobronchial microhemocirculation that are considered to be the displays of a chronic inflammation at COPD and to find out the effects of dihydroquercetin as a part

of complex therapy on these links of pathogenesis.

10 patients (7 men and 3 women, mean age -  $57 \pm 7,7$  years, average duration of disease -  $11,8 \pm 3,1$  years, length of smoking -  $25,8 \pm 7,4$  years,  $30,43 \pm 9,5$  pack/years) having exacerbation of COPD, receiving dihydroquercetin as a part of complex therapy in accordance with GOLD [1]; daily dose made up 50 mg. 14 sex-age-matched COPD patients that got standard therapy according to the severity of disease as it was recommended by GOLD 2006 made up control group.

### Results

All patients along with standard clinicolaboratory and tool methods of examination before and after the therapy course were carried out diagnostic fiber-optic bronchoscopy (FBS) with simultaneous registration of laser Doppler flowmetry (LDF) with the use of laser analyzer of capillary blood flow LAKK-02 («LAZMA», Moscow). The following values were analyzed: microcirculation parameter (MP), average square-law deviation, variation factor, and also amplitudes of fluctuations in endothelial (AE), neurogenic (AN), myogenic (AM), respiratory (AR) and cardiac (AC) ranges. Besides, BAL fluid was got according to the S. I. Tkacheva's original technique with definition of the general indicator of cellularity, cellular-compound and index of destruction. Statistical analysis was carried out via statistical system Statistica 6.0 for Windows (Stat Soft).

After conducted therapy there was no significant difference of such indices of inflammation as peripheral blood leukocyte level, ESR. At patients receiving dihydroquercetin, these indicators have made: leukocytes  $6,9 \pm 0,514 \cdot 10^9/l$  before treatment and  $5,84 \pm 0,06 \cdot 10^9/l$  after therapy, ESR accordingly -  $13,2 \pm 3,93$  mm/h and  $6,2 \pm 1,9$  mm/h. In controls the levels of leukocytes have made  $6,25 \pm 1,65 \cdot 10^9/l$  and  $5,81 \pm 0,69 \cdot 10^9/l$  and ESR -  $12,46 \pm 3,61$  mm/h and  $6,46 \pm 1,5$  mm/h before and after the treatment respectively. Similar law was observed at studying of biochemical markers of inflammation: fibrinogen and seromuroid. In controls the levels of fibrinogen have made  $4183,85 \pm 623,4$  mg/l and  $4104,9 \pm 297,5$  mg/l, the levels of seromuroid  $0,161 \pm 0,026$  and  $0,161 \pm 0,012$  before and after the treatment respectively. In patients receiving dihydroquercetin, the levels of fibrinogen were  $4747 \pm 664$  mg/l and  $3996,3 \pm 360,8$  mg/l, the level of seromuroid were  $0,161 \pm 0,041$  and  $0,142 \pm 0,028$  before and after therapy respectively. By estimation of FBS indices bilateral diffuse purulent or mucopurulent endobronchitis before therapy was diagnosed in patients of basic and control groups. By estimation of inflammatory index (II) it was revealed that the relation of degrees of manifestation in both groups was about: 0 %, 30%, 55%, 15% respectively for 0, I, II and III degrees of manifestation respectively. However, control FBS after 10 days of treatment revealed the difference between experimental group and controls. 7% of controls showed frank (II - 3) endobronchitis, 78,6% II 1-2, and only 14,3% were characterized by normal tracheobronchial tree (II - 0). At the patients receiving dihydroquercetin, restoration of a normal picture has been registered in 60 % of cases, and in 40% corresponded II 1-2 (because of hyperemia of vascular channel). The quantity and characteristics of a secretion at all persons of experimental group after treatment were also practically normal while at patients of control group in 75 % remained mucopurulent endobronchitis.

By studying of cellular compound of BAL fluid, initial cytogram indices in both groups did not differ. Average cytoxis has made  $1,12 \pm 0,7 \cdot 10^6$  per ml/ $1,09 \pm 0,6 \cdot 10^6$  per ml, the average levels of macrophages  $35,6 \pm 4,8\%/34,2 \pm 3,7\%$ , the levels of lymphocytes  $9,43 \pm 1,5\%/9,36 \pm 2,1$  %, the levels of neutrophils  $42,7 \pm 6,3\%/45,0 \pm 7,6\%$ , an index of destruction  $65,7 \pm 5,01/68,6 \pm 4,3$  in experimental and control groups accordingly. After the course of treatment at patients received dihydroquercetin as a part of complex therapy the levels of macrophages were significantly elevated in comparison with controls ( $66,4 \pm 7,8\%/51,15 \pm 6,7\%$ ), levels of neutrophils were declined ( $5,46 \pm 5,1\%/14,8 \pm 4,3\%$ ), the same can be said about the index of destruction ( $24,6 \pm 2,918/41,3 \pm 4,56$ ).

By estimation of LDF data at patients of both groups prior to the beginning of treatment the spastic type of disorder of microcirculation was revealed. It is characterized by decrease of average values of PM by simultaneous increase in amplitude of slow fluctuations (LF) and decrease of the

amplitude of pulse fluctuations (CF), and also increase of indices of vascular resistance. After the course of treatment experimental group showed more marked 4,5-times increase of PM. This index was only 2 times higher in control group. This in combination with high-amplitude pulse waves (ACF) means significant increase of perfusion, which is typical for hyperemic type. Control patients still demonstrated indices indicating of smooth muscle elements of microvasculature.

According to the data of the veivlet-analysis, insignificant decrease of the AE indices (on the average on 78%) by getting dihydroquercetin shows reduction of endogenous muscle relaxant production (possibly, it can be connected with reduction of inflammation and intensity of smooth muscle spasm of vessels), at the same time AE of controls remained practically at the same level. At patients receiving dihydroquercetin, in comparison with control group considerable (in 3,5 times) reduction of indicators AN, AM, AR, AC (i.e. approach to normal values) was registered. It indicates the restoration of tone of arteriole and arteriolar sites of arteriovenular anastomosis.

### **Discussion and Conclusion**

Short-term application of dihydroquercetin in addition to standard therapy decreases damaging influence of free radicals on cellular membranes, allows to restore endobronchial microhemocirculation. Dynamics of BAL fluid indices shows anti-inflammatory effect of dihydroquercetin.

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## **Medical and biological study of mixture of drugs *rhodiola rosea* and *hepericum perforatum*, to increase the organism to rezistentonsti low and high temperatures**

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**Abstracts.** This work was carried out to identify the antioxidant, act-protective effect of a new mixture of drugs of *Rhodiarosea* and *Hepericum perforatum*. The entrance to the 100 research laboratory animals has been experimentally proved aktoprotektive and antioxidant effects test mixture.