THE INFLUENCE OF RATIONAL COMBINATION THERAPY ON THE QUALITY OF LIFE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE*

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Introduction. Chronic obstructive pulmonary disease (COPD) remains one of the major health problems nowadays. The aim of the research was to increase the treatment efficiency for COPD group B patients by using antibiotics, mucolytics, topical nebulizer therapy and halotherapy sessions in combination therapy. The study enrolled 70 COPD group B patients, the average age of patients was 59.6±2.2 years. The diagnosis was made in accordance with the Order of the Ministry of Public Health of Ukraine as of June 27, 2013 № 555. Patients were divided into two groups. Patients of the first group (control, n=35) received basic therapy - azitrox 500 mg once daily, acetylcysteine 200 mg - 2 times daily and combination bronchodilator therapy in the form of dose inhaler containing fenoterol hydrobromide 50 mcg and ipratropium bromide 20 mcg (Budeson) - 2 times a day [8]. In addition to basic therapy, patients of the second group (main group, n=35) in addition to basic therapy were prescribed double nebulizer therapy with the compressor nebulizer NEB-10 "Microlife" 2 times a day containing combined broncholytic agent fenoterol hydrobromide with ipratropium bromide (2 Freimid) diluted in 2 ml of saline; solution of budesonide (Pulmicort) nebulized 2 x 0.5 ml mg/ml = 1.0 mg, dissolved in 2 ml of saline - 2 times a day №7, and additionally, starting on day 4, halotherapy sessions. Thus, the proposed combined therapy of COPD group B patients is more advanced and rational, it improves the effectiveness of basic medical therapy by optimizing the recovery and rehabilitation process, which has a positive effect on the improvement of the seven components of QOL, it is well tolerated and does not cause side effects.

Key words: Chronic obstructive pulmonary disease, patients' quality of life.

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moderate; 21-30 - expressed; 31 - very serious. The impact of COPD on QOL is closely linked to the onset of anxiety and depression [4].

It is known that clinical presentation and prognosis of the disease are negatively affected by disorders of psychological status that develop with COPD [1]. Contemporary scientists found that the neuro-vegetative and acquired psychological disorders are significant components of the pathogenetic complex, which determine development, course and prognosis of COPD. Therefore, it seems logical that treating patients with COPD should have an integrated approach, and include not only the treatment of the underlying disease, but mandatory correction of associated disorders, including the psycho-emotional sphere [1].

Clinical practice convincingly shows that successful treatment of respiratory diseases depends not only on the correct choice of medicines, but also on the delivery mode of the respiratory drugs. Therefore, recently, in the management protocols of pulmonary patients, one of the important places is given to the topical nebulizer therapy. Properly selected nebulizer therapy, prescribed on time, is associated with a significant increase in the effectiveness of treatment and rehabilitation of such patients, and a reduction in the overall cost of treatment. Thus, it is known that in oral administration of any drug, therapeutic action occurs much later due to the time of passage through the digestive tract and absorption, elimination in the circulatory system, active metabolism in the liver, reaching the "focus morbi" in the altered form. Nebulizer and inhalation drug administration promotes a rapid delivery of high therapeutic concentrations directly to the sited of lesion, minimizing systemic impact and side effects, which is especially important for treating chronic respiratory diseases, including COPD.

Nowadays, non-drug treatment methods play an important role in the therapy and rehabilitation of patients with chronic respiratory diseases. Halotherapy is a treatment and rehabilitation method, based on using artificially created microclimate of salt caves using natural environmental factors [2]. The main active curative factor of halotherapy is an inhalable aerosol that consists of negatively charged sodium chloride air ions, simulating the microclimate of natural salt mines. When the inhalable aerosol fraction hits the terminal part of the bronchial tree, the activation of the drainage function of bronchi and increase in the amount of easily detachable sputum take place due to the osmotic effect. On the one hand, it contributes to the elimination of one of the components of bronchial obstruction, and on the other - the repairable sodium chloride aerosol exerts anti-inflammatory and immunomodulatory effects, which significantly improves the effectiveness of basic medical therapy. All this contributes to a positive regression of clinical symptoms in COPD patients who achieved remission and consolidation [8].

The aim of the research was to increase the treatment efficiency for COPD group B patients by using antibiotics, mucolytics, topical nebulizer therapy and halotherapy sessions in combination therapy.

**Materials and methods**

The study enrolled 70 COPD group B patients, the average age of patients was 59.6±2.2 years. The diagnosis was made in accordance with the Order of the Ministry of Public Health of Ukraine as of June 27, 2013 № 555 "On Approval and Implementation of Medical and Technological Documents on Standardization of Medical Assistance in Chronic Obstructive Pulmonary Disease" [7]. Based on the results of a comprehensive examination, which included evaluation of clinical symptoms of the disease (cough with sputum, shortness of breath, fever, dry wheezing during auscultation of the lungs), general clinical laboratory and instrumental research methods (blood, urine, sputum, chest radiography, spirometry with bronchodilation test were applied. All patients received therapy in accordance with the Order of the Ministry of Public Health of Ukraine of 2013 №555 [7]. Evidence-based clinical guidelines for Chronic Obstructive Pulmonary Disease [3]. COPD symptom severity was assessed using the questionnaires - the Modified Scale for Shortness of breath (MMDR) and the "COPD assessment Test" (CAT) [7]. The quality of life of patients was studied using a "COPD assessment Test" questionnaire, consisting of 8 questions which significantly characterize the disease, and includes the following symptoms and sensations: cough, sputum, shortness of breath, tightness in the chest, activity at home, confidence away from home, sleep quality, energy / fatigue. Each answer was evaluated based on a 5-point system. The interpretation of the test results was evaluated according to the following scheme: 0-10 points indicates a slight impact on the patient's QOL, 11-20 points - moderate, 21-30 points - strong, 31-40 points - extremely strong influence [4, 7].

Psycho-emotional status of COPD patients was assessed using Ch.D. Spielberger- Yu.L. Khanin questionnaire. The result was rated according to the following scheme: up to 30 points - low anxiety; 31-45 - moderate anxiety; 46 and more - high anxiety [6]. The test is a reliable way to self-assess the level of anxiety at the moment (reactive anxiety as a condition) and personal anxiety as a stable characteristic of a person.

The reliability of the obtained results was determined using the Student t-test. The differences were considered plausible when the probability of an error was p<0.05 (as accepted in medical biological studies).

Patients were divided into two groups. Patients of the first group (control, n=35) received basic therapy - azitrox 500 mg 1 time per day, acetylcysteine 200 mg - 2 times daily and combination bronchodilator therapy in the form of dose inhaler containing fenoterol hydrobromide 50 mcg and ipratropium bromide 20 mcg (berodual H) - 2 times a day, anti-inflammatory therapy in the form of the turbulizer budesonide (pulmicort) 100 mcg twice a day for 7 days.

Patients of the second group (the main group, n=35) in addition to the basic therapy were prescribed double nebulizer therapy with the compressor nebulizer NEB-10 "Microlife" 2 times a day containing combined broncholytic agent fenoterol hydrobromide with ipratropium bromide (2 Freimind) diluted in 2 ml of saline, solution of budesonide (Pulmicort) nebulized 2 x 0.5 ml mg / mL=1.0 mg, dissolved in 2 ml of saline - 2 times a day №7; and additionally, stating on day 4, halotherapy sessions using the "IONNA" halogenator mode (ionizer 30±50% power, air flow volume 15 ± 20m3/h, chamber temperature 40±50°C, duration 40±60 min.) once a day №10.

Frewrey Combi is a combination drug that contains two active broncholytic ingredients: 1 ml solution contains: 0.5 mg fenoterol hydrobromide, which is a beta adrenomimetic and 0.25 mg ipratropium bromide, which has an anticholinergic effect.
Budesonide is a corticosteroid, which has an anti-inflammatory effect, and the lower frequency and severity of side effects than oral corticosteroids.

Results and discussion

The effectiveness of therapy was evaluated by the dynamics of reduction of clinical symptoms of the disease, assessed by the laboratory, instrumental and functional study methods.

According to the assessment of quality of life of COPD group B patients using the CAT questionnaire, there was a significant decrease in the total amount of points under the influence of therapy in patients in both groups. However, we marked significant differences between the main and control group (p<0.05) after treatment. Thus, in patients of the main group, an average CAT score before treatment was 21.03±1.9 points, which confirms a fairly strong negative impact on QOL of COPD patients of this group. After treatment, the integral score was 9.15±0.7 points (p<0.05), i.e., it decreased by 57.7%. In patients of the control group, an average CAT score before treatment was 20.77±2.1 points, and after treatment – 7.9±0.9 points (p<0.05), i.e., it decreased by 66.6%, indicating the improvement of patients’ quality of life.

The data show that the proposed combination therapy significantly improves the clinical course of COPD, due to the reduction of both subjective and objective symptoms, as well as significant changes in key integral parameters of external respiration.

Psycho-emotional status of COPD patients was assessed using Ch.D. Spielberger- Yu.L. Khanin questionnaire. The results of patients’ survey showed that a higher level of reactive anxiety (RA) was determined in COPD patients, which changed during treatment. Thus, after a course of treatment, there was a significant reduction of RT, but more prominent in the patients of the main group (p<0.05). Hence, in patients, who received the combination therapy along with halotherapy course, the average RA after treatment was 33.4 ± 1.9 points, and before the treatment – 51.1±2.1 (p<0.05), whereas in patients of the control group the level of RA was 49.6±1.6 and 39.8±1.7 points, respectively (p<0.05) (Fig.1).

Thus, a comparative analysis of the research findings indicates that including halotherapy in the comprehensive therapy potentiates the effects of truly faster regression of clinical symptoms and improvement in airway conductance, contributes to the stabilization of the psycho-emotional sphere of patients, promotes growth of all components of QOL.

The analysis of the results of patients’ examination at the Modified Borg Dyspnoea Scale (mBORG) showed that the average total score before treatment in patients of the main group was 2.4±0.6 points, and after treatment it decreased significantly - by 0.9±0.3 points (p<0.05), whereas in patients in the control group before treatment the total score was 2.2±0.64, and after treatment it was 1.1±0.4 points (p<0.05), i.e., not a significant decrease.

After the treatment, the positive clinical and functional dynamics of the patients’ condition was noted. Thus, we observed an increase in FEV1, FEV1 /FVC in patients in both groups, indicating a decrease in the degree of bronchial obstruction. However, a significant improvement in bronchial obstruction was detected in patients in the main group who received topical nebulizer therapy with sequential administration of fenoterol hydrobromide solution with ipratropium bromide, budesonide, and halotherapy in addition to the halotherapy. Thus, there was a significant increase in forced expiratory volume in 1second (FEV1) by 9.3% (p<0.05) and FEV1/FVC by 7, 6 % (p<0.05) in the patients of the main group after treatment. Whereas in patients of the control group, these informative indicators of bronchial obstruction did not change significantly. The results are shown in Table 1.

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| Indicator, units of measurement | Control group (n=35) | Main group (n=35) |
|---------------------------------|---------------------|------------------|
| FVC, %                          | Before treatment    | 71.2 ± 1.5        | 74.2 ± 1.25*      |
|                                 | After treatment     | 75.1 ± 1.6        | 73.2 ± 1.76       |
| FEV1, %                         | Before treatment    | 70.12 ± 1.7       | 76.9 ± 1.64*      |
|                                 | After treatment     | 74.8 ± 1.9        | 74.8 ± 1.66       |
| MEF25, %                        | Before treatment    | 53.9 ± 1.63       | 54.4 ± 1.66       |
|                                 | After treatment     | 56.6 ± 1.82       | 51.9 ± 1.42       |
| MEF50, %                        | Before treatment    | 50.2 ± 1.4        | 52.4 ± 1.7        |
|                                 | After treatment     | 53.6 ± 1.33       | 51.9 ± 1.42       |
| MEF75, %                        | Before treatment    | 46.9 ± 2.1        | 45.9 ± 1.9        |
|                                 | After treatment     | 49.7 ± 1.86       | 50.8 ± 1.7        |
| FEV1 /FVC, %                    | Before treatment    | 69.1 ± 1.83       | 68.6 ± 1.4        |
|                                 | After treatment     | 73.2 ± 1.76       | 74.2 ± 1.25*      |

Notes: * - the differences are significant before and after treatment (p<0.05).

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|                                 | After treatment     | 73.2 ± 1.76       | 74.2 ± 1.25*      |

Notes: * - the differences are significant before and after treatment (p<0.05).
Then, in patients treated with combination therapy, the walking distance increased from 436.4±10.2 - before treatment, to 471.2±12.7 m after treatment (p<0.05), which has positive effect on QOL.

| The group of patients | 6 MWD (m) | CaO₂ % |
|-----------------------|-----------|---------|
| Control group (n=35)  | Before treatment | 422.6±12.5 | 94.6±0.91 | 96.5±0.56 |
| n=35                  | After treatment  | 456.2±14.3 | 94.8±0.8  | 97.2±0.68 |
| Main group (n=35)     | Before treatment | 436.4±10.2 | 94.8±0.8  | 97.2±0.68 |
|                      | After treatment  | 471.2±12.8 | 94.8±0.8  | 97.2±0.68 |

*p (p<0.05) - the differences are significant before and after treatment.

The dynamic retrospective study of patients of both groups showed that in 77% of patients who received the proposed combination treatment, have not had any relapses during the year. However, annual remissions were observed only in 43% of patients of the control group (p<0.05).

Thus, the results of the research indicate that adding topical nebulizer delivery of respirable fraction of the aerosol containing combined pathogenetic medical factors, including admixture of fenoterol hydrobromide, ipratropium bromide and budesonide, combined with the halotherapy to basic treatment of COPD group B patients, significantly improves the results of basic treatment by creating a sufficient concentration of aerosol at the site of bronchial tree lesions and osmotic effect, which significantly increases regression of the clinical symptoms due to improvements in airway conductance and stabilization of associated psycho-emotional sphere disorders. When the inhalable aerosol fraction hits the terminal part of the bronchial tree, the activation of the drainage function of bronchi and increase in the amount of easily detachable sputum take place due to the osmotic effect.

Thus, the proposed combined therapy of COPD group B patients is more advanced and rational, it improves the effectiveness of basic medical therapy by optimizing the recovery and rehabilitation process, which has a positive effect on the improvement of the seven components of QOL, is well tolerated and does not cause side effects.

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