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 a 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 (beclometasone 100 mcg twice a day for 7 days. Patients of the second group (main group, n=35) additionally, starting on day 4, halotherapy sessions. Thus, the proposed combined therapy of COPD group B patients contains 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.

Chronic obstructive pulmonary disease (COPD) remains one of the major health problems nowadays [8,11]. Today, according to experts of the World Health Organization, COPD is one of the leading causes of death in the adult population. In the global structure of causes of death, COPD ranks fourth in the age group above the age of 45 and is the only disease whose portion in mortality is increasing. This results in increases in morbidity and mortality rates. It is known that the influence of reduction of bronchial patency on the development of coronary catastrophes is compared to hypercholesterolemia [9]. Therefore, improving the methods and approaches to COPD treatment is particularly important [10].

COPD is characterized by a multifaceted impact on a patient's life, changing not only physical activity but also the quality of life (QOL). For the quantitative assessment of the patient's well-being, integrated tests (questionnaires) are becoming increasingly important, allowing us to more accurately reveal the course of the disease - the dynamics of the condition even over a short period of time. The sum of the CAT points indicates how COPD affects the patient's QOL: 0-10 points - insignificant impact; 11-20 -

moderate; 21-30 - expressed; 31 - very serious. The im-

pact 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 psy-

chological status that develop with COPD [1]. Contempo-

rory scientists found that the neuro-vegetative and

acquired psychological disorders are significant compo-

nents of the pathogenetic complex, which determine de-

velopment, 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 cor-

rection 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

to 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 effective-

ness 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 de-

livery of high therapeutic concentrations directly to the

site of lesion, minimizing systemic impact and side ef-

fects, which is especially important for treating chronic

respiratory diseases, including COPD.

Nowadays, non-drug treatment methods play an im-

portant role in the therapy and rehabilitation of patients

with chronic respiratory diseases. Halotherapy is a trea-

tment and rehabilitation method, based on using artificially

created microclimate of salt caves using natural environ-

mental factors [2]. The main activatory factor of halotherapy is an inhalable aerosol that consists of nega-

tively charged sodium chloride air ions, simulating the microclimate of natural salt mines. When the inhala-

table 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 con-

tributes 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 treat-

ment efficiency for COPD group B patients by using anti-

biotics, 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±2.2 years. The diagno-

sis was made in accordance with the Order of the Minis-

try 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 examina-
tion, which included evaluation of clinical symptoms of the disease (cough with sputum, shortness of breath, fe-

ver, dry wheezing during auscultation of the lungs), gen-

eral clinical laboratory and instrumental research meth-

ods (blood, urine, sputum, chest radiography, spirometry

with bronchodilation test) were applied. All patients re-

ceived therapy in accordance with the Order of the Minis-
try of Public Health of Ukraine of 2013 №555 [7]. Evi-
dence-based clinical guidelines for Chronic Obstructive Pulmonary Disease [3]. COPD symptom severity was as-

dessed 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, consist-
ing of 8 questions which significantly characterize the
disease, and includes the following symptoms and sen-
sations: cough, sputum, shortness of breath, tightness in

the chest, activity at home, confidence away from home, sleep quality, energy / fatigue. Each answer was evalu-

ated 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 pa-

tient'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 as-

sessed using Ch.D. Spielberger- Yu.L. Khanin question-

naire. The result was rated according to the following

scale: up to 30 points - low anxiety; 31-45 - moderate

anxiety; 46 and more - high anxiety [6]. The test is a reli-

able way to self-assess the level of anxiety at the mo-

ment (reactive anxiety as a condition) and personal anxi-

ety 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 turbu-

haler 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 bron-

cholytic 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.

Frewerey Combi is a combination drug that contains

two active broncholytic ingredients: 1 ml solution con-

tains: 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 5.1±0.7 points (\(p<0.05\)), i.e., it decreased by 75.7%.

In patients of the control group, an average CAT score before treatment was 20.77±1.9 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 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.

![Table 1](image)

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.

10 days after the beginning of the therapy, we observed the dynamics of exercise tolerance in patients of both groups [5]. The obtained results are presented in Table 2.

After treatment, patients in both groups experienced an increase in exercise tolerance, but in the control group, the increase in walking distance was not significant. Thus, before treatment the walking distance was 422.6±12.5m, after treatment – 456.2±14.3m. (\(p<0.05\)).

![Figure 1](image)
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.

<table>
<thead>
<tr>
<th>The group of patients</th>
<th>6 MWD (m)</th>
<th>CaO₂ %</th>
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<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Control group (n = 35)</td>
<td>422.6±12.5</td>
<td>456.2±14.3</td>
</tr>
<tr>
<td>Main group (n = 35)</td>
<td>436.4±10.2</td>
<td>471.2±12.8 *</td>
</tr>
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*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.

References
7. Order of the Ministry of Health of Ukraine of June 27, 2013 № 555 "On Approval and Implementation of Medical and Technological Documents on Standardization of Medical Assistance in Chronic Obstructive Pulmonary Disease" p.164

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