

Research article

# Haloaerosoltherapy and complex recovery treatment based on it as methods of physical rehabilitation for patients with chronic obstructive pulmonary disease

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**Abstract:** Rehabilitation programs for patients with COPD are based on physical exercises usage, but accounting low tolerance to physical activity, this is not always a real task. **The aim** is to study the effect of haloaerosoltherapy (HAT) and complex rehabilitation treatment based on it on functional recovery of COPD patients. **Materials and methods:** 133 patients with COPD (GOLD II-III) beyond acute period were examined. Bronchial obstruction, intensity of clinical manifestations, disturbances of cardiovascular system were investigated. The 6-minute walk test was conducted. **Results:** Before treatment, it has been shown that exercise tolerance significantly depended on severity of bronchial obstruction, intensity of clinical manifestations and degree of cardiovascular risk. Treatment was carried out according to three treatment complexes (TC). TC-1 was based on HAT usage with certain concentration and dispersion of aerosol, 18-20 seances per course. In TC-2, singlet oxygen therapy was included, in TC-3 mineral water was administered as drinking use and inhalation. After course of treatment, walking distance covered in 6 minutes has been increased in patients of all groups. When using complex treatment, these changes were more pronounced. **Conclusions:** HAT with appropriate dispersion and concentration of haloaerosol promotes increasing tolerance to physical activity and may be used as a stage of physical rehabilitation with possible subsequent therapeutic physical exercises. Notably pronounced positive dynamics of studied data was noted in COPD patients convalescents after COVID-19.

**Key words:** COPD, physical rehabilitation, haloaerosoltherapy, COVID-19 convalescents.

## 1. Introduction

Stabilization of the pathological process and maximal possible functional recovery of the organism is the leading aim in the management of patients with chronic diseases, including bronchopulmonary system. Chronic obstructive pulmonary disease (COPD) is currently considered as multicomponent pathology that begins in the bronchopulmonary system, but is subsequently accompanied by a number of systemic extrapulmonary manifestations [1,2]. Among them – involvement of the cardiovascular system, metabolic disorders, weakness and atrophy of muscle tissue and some others, which together with changes in the bronchopulmonary system, lead to significant functional disturbances of the organism. The main clinical manifestation of these functional disorders is decreased exercise tolerance, which significantly reduces the patients' "quality of life" and leads to disability [1, 2, 3]. Therefore, the development of physical rehabilitation methods for patients with COPD is a very actual problem [4].

According to international recommendations rehabilitation must begin immediately after the stabilization of the patient's condition and the individual rehabilitation program should change according to the dynamics of the functional state of the patient [5]. Rehabilitation of patients with COPD involves a multidisciplinary team and the using the complex of non-pharmacological methods [6]. Taking into account the negative influence of systemic inflammation of low intensity on the muscle tissue, as well as limited physical activity of these patients due to existing bronchial obstruction, the basis for rehabilitation programs are sets of various physical therapeutic exercises [7].

Psychotherapy and nutritional advices are also an important part of the respiratory rehabilitation programs, particularly for individuals suffering from obesity or loss of weight and muscle tissue [8, 9]. Some programs also include occupational therapy [10]. However, these recommendations play only a supporting role.

It has been proven that physical training directly improves the tolerance to physical activity, namely, it reduces dyspnea and the respiratory rate during exercise of a certain intensity. However, not all patients with COPD can follow the recommendations regarding the duration and intensity of training. There are data that 50% of these patients do not want to participate in long-term rehabilitation programs [5], which can last up to 6 months or more [11]. In addition, increasing physical activity may be an unrealistic goal for patients with very reduced exercise tolerance [12]. The conducted investigations proved that the initial functional state of the organism is of great importance for the success of rehabilitation programs based on physical training. If initial functional state is insufficient, physical training is ineffective [12].

In this regard, the question arises for studying the influence of other types of non-pharmacological recovery treatment on the functional state of patients with COPD, role of these methods in increasing the tolerance to physical activity and the expediency of their usage in rehabilitation programs. Haloaerosoltherapy (HAT) should be mentioned among such non-medicinal methods that can significantly influence the course of COPD within a relatively short duration of treatment (20-24 days).

HAT is based on the usage of dry rock salt aerosol media with certain parameters of concentration and dispersion in a form of group inhalations. The necessary therapeutic concentration of rock salt aerosol (haloaerosol) is possible to achieve with the help of special devices – halogenerators. As a result of the hyperosmolar effect of haloaerosol with appropriate concentration positive changes are received – improvement of rheological properties of sputum, stimulation of ciliated epithelium, which causes an increase of the bronchi drainage function [13, 14]. Haloaerosol also has a bactericidal effect, which provides sanitation of the bronchial tree and, alongside with the improvement of the bronchi drainage function, leads to the reduction of the local inflammatory process activity and a decrease in bronchial obstruction. This makes it possible to relieve coughing, reduce dyspnea intensity, improve lungs ventilation and therefore increase the ability to perform physical exercises. In addition, it has been proven that the course of HAT treatment helps to reduce the activity of systemic inflammation, the intensity of oxidant stress and has an indirect immunomodulative effect [13-15].

**The aim of the work** was to study the influence of HAT and complex rehabilitation treatment based on this method on the functional recovery of COPD patients and to substantiate the expediency of its use as a stage of physical rehabilitation for these patients.

## 2. Materials and methods

The study involved 133 COPD patients (GOLD II-III) beyond the acute period, aged from 41 to 72 years. The average age of patients was  $60,3 \pm 1,71$  years, and duration of the disease –  $14,2 \pm 0,89$  years. Among the examined 64,7 % (86 patients) were male and 35,3 % (47 patients) were female.

According to GOLD recommendations the diagnosis was based on relevant clinical and anamnestic data (using COPD Assessment Test – CAT) and spirometric examination

with a pharmacological test for bronchial obstruction reversibility [1].

It is generally accepted that CAT characterizes the intensity of clinical manifestations of COPD. According to the sum of CAT points three groups of patients were distinguished:

- 16 patients with CAT less than 10 points, which indicates a low level of COPD symptoms;
- CAT within the range of 10-19 points (symptoms are moderate) occurred in 95 patients;
- high level of COPD symptoms (CAT  $\geq$  20 points) was observed in 22 patients.

Evaluating ventilation function, the main attention was paid to forced expiratory volume in the first second (FEV<sub>1</sub>) as an integral indicator of bronchial obstruction and to the ratio of FEV<sub>1</sub> to the forced vital capacity of the lungs (FEV<sub>1</sub>/FVC), which is one of the main criteria for the diagnosis. According to the level of FEV<sub>1</sub>, two groups of patients were distinguished: 81 patients with value of FEV<sub>1</sub> within 50-70% of the normal and 52 patients with FEV<sub>1</sub> within 30-49%.

Accounting that COPD is currently considered as a systemic pathological process, the presence of comorbid pathology was also assessed. The pathology of the cardiovascular system was most often observed, namely, arterial hypertension (AH) was registered in 45,9% of the examined and chronic ischemic heart disease (CIHD) - in 26,3% of patients. Considering this, the general cardiovascular risk was also assessed based on the usage of SCORE scale, which makes it possible to estimate the probability of fatal cardiovascular complications developing in the next 10 years of patients' life. Presence of associated pathology and lipid profile data were also taken into account [16].

These data allowed to distinguish 2 groups of patients according to the degree of cardiovascular risk (CVR):

- 57 patients with low and moderate risk;
- 76 patients with high and very high risk.

To evaluate the general functional state of the organism, a Six-Minute Walk Test (6MWT) was performed, which is most often used for assessment of physical exercise tolerance [17]. The walking distance was measured, before and after the test the severity of dyspnea was evaluated according to the *Borg* scale, heart rate (HR) was calculated and the blood saturation level (SpO<sub>2</sub>) was registered using a pulseoximeter.

Subsequently, 113 examined patients underwent a course of recovery treatment according to three treatment complexes (TC). The treatment included appropriate treatment regimen, diet, the necessary basic broncholytic and anti-inflammatory therapy according to the severity of the disease and a physiotherapeutic complex.

According to TC-1 the main method of treatment was the use of HAT, which was carried out with the help of halogenerators of a new type, which makes it possible to generate haloaerosols of given concentration and dispersion. The HAT course included a period of adaptation – 2-3 days, during which the duration of procedures gradually increase from 15 to 60 min (15 min, 30 min, 45 min, 60 min) and the main treatment period, which included daily, except Sundays, HAT seances lasted for 60 min each, 18-20 seances per course of treatment. The initial haloaerosol concentration during HAT seances was 40-50 mg/m<sup>3</sup>, aerosol particles up to 6 microns in size accounted 70%-75%. Control of aerosol concentration and dispersion was carried out using a special laser-optical system. The TC-1 was prescribed for 30 COPD patients who had no previous COVID-19.

In case of TC-2 the HAT course, which was also carried out according to the described above method, was supplemented with singlet oxygen therapy (SOT) in the form of inhalations lasting for 15 minutes and 100-150 ml of activated water intake, 12 procedures of SOT per course. SOT was prescribed in order to reduce oxidant stress, which is one of the leading links in the pathogenesis of COPD and its comorbid manifestations. This complex was administered to 62 patients, including 23 patients with COPD (TC-2A) and 39 COPD patients convalescents after COVID-19 (TC-2B).

TC-3 included conducting HAT according to the standard method as in TC-1 and

low-mineralized hydrocarbonate siliceous mineral water (MW) "Shayanska" drinking intake three times daily during the entire course of treatment and inhalations of the same water, overall 15 procedures. The treatment involved drinking of degassed MW of room temperature (up to 75-100 ml per single dose), 20-30 minutes before breakfast and 1 hour after each meal (total volume of water is no more than 500 ml per day). Inhalations were carried out 30-60 minutes after HAT seance, duration of each procedure was 15 minutes. The expediency of this MW intake is based on the systemic alkalinizing and acid-neutralizing properties due to the predominance of hydrocarbonates in the composition of "Shayanska" MW and its favorable influence on the excretory systems function of the organism [18]. TC-3 was prescribed for 21 COPD patients convalescence after COVID-19.

The combination of the local effect of haloaerosol, which has sanogenic (antibacterial and mucolytic) and anti-inflammatory effects [12, 13], with these additional influences is aimed at increasing the effectiveness of complex recovery treatment by improving antioxidant protection and correcting metabolic disorders.

### 3. Results and discussion

Before the course of rehabilitation treatment all examined patients with COPD were beyond the acute period, but had certain clinical manifestations that confirmed the correctness of the diagnoses and reflected the peculiarities of the disease. In general, the sum of CAT points in the examined COPD patients reached  $14,6 \pm 0,47$ , which indicates a moderate impact of COPD symptoms on the health and daily life of patients, and  $FEV_1$  was at the level of  $52,8 \pm 1,13\%$  (table 1). At the same time, the severity of resting dyspnea according to the Borg scale was  $2,48 \pm 0,07$  points.

**Table 1.** Clinical characteristics of COPD patients depending on the  $FEV_1$  level

Data, units	COPD patients (n=133)	FEV <sub>1</sub> , %		p'
		50-70 (n=81)	30-49 (n=52)	
Sex:				
- male, %, (n)	64,7 (86)	56,8 (46)	71,2 (37)	<0,1
- female, %, (n)	35,3 (47)	43,2 (35)	28,8 (15)	<0,1
Age of patients, years	$60,3 \pm 0,71$	$58,5 \pm 0,93$	$62,4 \pm 1,01$	<0,01
FEV <sub>1</sub> , %	$52,8 \pm 1,13$	$61,7 \pm 0,75$	$39,0 \pm 0,94$	<0,001
CAT, points	$14,6 \pm 0,47$	$12,4 \pm 0,46$	$17,9 \pm 0,79$	<0,001
SCORE scale, %	$5,94 \pm 0,43$	$4,34 \pm 0,43$	$8,30 \pm 0,74$	<0,001
CVR:				
- low and moderate, % (n)	42,9 (57)	55,6 (45)	23,1 (12)	<0,001
- high and very high, % (n)	57,1 (76)	44,4 (36)	76,9 (40)	<0,001
AH, % (n)	45,9 (61)	44,4 (36)	48,1 (25)	-
CIHD, % (n)	26,3 (35)	18,5 (15)	38,5(20)	<0,02
resting heart rate, beats/min	$76,2 \pm 0,84$	$74,6 \pm 1,09$	$78,4 \pm 1,23$	<0,05
6MWT, m	$428,5 \pm 4,64$	$436,6 \pm 6,23$	$414,7 \pm 6,77$	<0,05
resting SpO <sub>2</sub> , %	$96,1 \pm 0,12$	$96,6 \pm 0,14$	$95,3 \pm 0,18$	<0,001
resting dyspnea, points	$2,48 \pm 0,07$	$2,17 \pm 0,07$	$2,96 \pm 0,12$	<0,001

Notes here and in tables 2-3 below: p' is the significance of data difference between patients' groups.

The state of cardiovascular system which, in particular, can be assessed using the SCORE scale, is of great importance in evaluation of the pathological process severity in the organism as a whole. The average SCORE value in general among all patients reached

5,94±0,43%, which indicates a predisposition to a high CVR of fatal events in the next 10 years and confirms the mutual encumbrance of these pathological processes.

Analyzing clinical data in relation to the FEV<sub>1</sub> value, as an integral index of bronchial obstruction (table 1), it was noted that the average age of patients with severe obstruction (FEV<sub>1</sub> 30-49%) was statistically higher, but the difference of 4 years was not enough to explain a significant increase in bronchial obstruction, a reliable elevation of CAT (p<0,001) and SCORE value (p<0,001), which reflects both the increase in the intensity of COPD symptoms and the severity of CVR. It was marked that among patients with severe bronchial obstruction in comparison with moderate one, frequency of high CVR increased in 1,7 times (p<0,001) and the occurrence of CIHD raised in 2,1 times (p<0,02).

When examining these two groups of patients, it was also found that severe bronchial obstruction was accompanied with higher data of resting dyspnea according to the Borg scale (p<0,001), which was associated with an increase in resting heart rate (p<0,05) and worsening of blood saturation (p<0,001). These changes ultimately led to reduction in the distance the patient walked for 6 minutes to 414,7±6,77 m versus 436,6±6,23 m at patients with FEV<sub>1</sub> 50-70% (p<0,05) (table 1).

Analyzing clinical data depending on the level of the CAT sum (table 2), it was found that as the intensity of COPD symptoms increased, bronchial obstruction reliably intensified from FEV<sub>1</sub> 62,7±2,31% at CAT<10 points to FEV<sub>1</sub> 44,0±2,51% at CAT ≥ 20 points. It was naturally accompanied by an increase in resting dyspnea, a decrease in blood saturation, intensification of resting heart rate, and reduction in the walking distance during the 6-minute test. In particular, patients with a stable course of COPD (CAT<10 points) walked 441,1±12,5 m in 6 minutes, while patients with CAT≥20 points walked only 395,5±10,8 m (p<0,01).

**Table 2.** Clinical characteristics of COPD patients depending on CAT values

Data, units	CAT, points		
	< 10 (n=16)	10-19 (n=95)	≥ 20 (n=22)
Sex:			
- male, %, (n)	43,7 (7)	68,4 (65)	63,6 (14)
- female %, (n)	56,3 (9)	31,6 (30)	36,4 (8)
Age of patients, years	57,1±1,96	60,4±0,85	61,0±1,72
p'	p <sub>1-2</sub> <0,2		p <sub>1-3</sub> <0,2
FEV <sub>1</sub> ,%	62,7±2,31	53,4±1,28	44,0±2,51
p'	p <sub>1-2</sub> <0,001	p <sub>2-3</sub> <0,01	p <sub>1-3</sub> <0,001
CAT, points	7,06±0,40	13,7±0,30	23,6±0,86
SCORE scale, %	3,06±0,70	6,26±0,53	6,51±0,94
p'	p <sub>1-2</sub> <0,001		p <sub>1-3</sub> <0,001
CVR:			
- low and moderate, % (n)	81,3 (13)	38,9 (37)	31,8 (7)
p'	p <sub>1-2</sub> <0,001	-	p <sub>1-3</sub> <0,01
- high and very high, % (n)	18,7 (3)	61,1 (58)	68,2(15)
p'	p <sub>1-2</sub> <0,001	-	p <sub>1-3</sub> <0,01
AH, % (n)	31,3 (5)	47,4 (45)	50,0 (11)
p'	p <sub>1-2</sub> <0,3		p <sub>1-3</sub> <0,3
CIHD, % (n)	12,5 (2)	23,2 (22)	50,0 (11)
p'	p <sub>1-2</sub> <0,3		p <sub>1-3</sub> <0,05
resting heart rate, beats/min	74,6±2,19	75,2±0,96	81,5±2,16
p'		p <sub>2-3</sub> <0,02	p <sub>1-3</sub> <0,05
6MWT, m	441,1±12,5	431,6±5,37	395,5±10,8
p'		p <sub>2-3</sub> <0,01	p <sub>1-3</sub> <0,01
resting SpO <sub>2</sub> , %	97,4±0,34	96,9±0,16	95,4±0,52
p'	p <sub>1-2</sub> <0,2	p <sub>2-3</sub> <0,02	p <sub>1-3</sub> <0,01
resting dyspnea, points	2,00±0,09	2,41±0,08	3,14±0,21
p'	p <sub>1-2</sub> <0,001	p <sub>2-3</sub> <0,01	p <sub>1-3</sub> <0,00 1

An increase in the total CAT score  $\geq 10$  points was accompanied by a simultaneous elevation of SCORE value ( $p < 0,001$ ) and the frequency of high CVR in 3,3 and 3,4 times, respectively (table 2).

Thus, the obtained data confirm high diagnostic significance of FEV<sub>1</sub> control and assessment of COPD severity according to CAT as for the adequate interpretation of the treatment effectiveness and so for the prognosis of the pathological process as a whole.

A similar situation is observed in relation to the analysis of the investigated clinical data depending on the CVR severity (table 3). It should be noted that patients with high and very high cardiovascular risk were older than those with low and moderate CVR by an average of 8 years ( $p < 0,001$ ), which may be important in the development of comorbid pathology and influenced the general functional state of the organism. According to most data, a significant difference was noted between these groups, including FEV<sub>1</sub> and CAT. At patients with high and very high CVR a significant appropriate increase in the frequency of comorbid pathology should also be noted, especially in relation to the clinical manifestations of CIHD and arterial hypertension (in 24,8 times and 2,3 times, respectively) (table 3).

It should also be marked that patients with high and very high CVR covered a shorter distance in six minutes in comparison with patients with low and moderate CVR ( $420,4 \pm 5,83$  m vs  $440,8 \pm 8,03$  m;  $p < 0,05$ ) and had a greater degree of resting dyspnea. Only the blood saturation data revealed no difference in groups of patients with different level of CVR.

**Table 3.** Characteristics of COPD patients depending on the cardiovascular risk level

Data, units	Cardiovascular risk		
	Low and moderate (n=57)	High and very high (n=76)	p'
Sex:			
- male, %, (n)	45,6 (26)	78,9 (60)	<0,001
- female %, (n)	54,4 (31)	21,1 (16)	<0,001
Age of patients, years	55,7 $\pm$ 1,09	63,3 $\pm$ 0,75	<0,001
FEV <sub>1</sub> , %	57,4 $\pm$ 1,47	49,3 $\pm$ 1,52	<0,001
CAT, points	13,3 $\pm$ 0,69	15,5 $\pm$ 0,63	<0,05
SCORE scale, %	2,69 $\pm$ 0,20	8,33 $\pm$ 0,59	<0,001
AH, % (n)	26,3 (15)	60,5 (46)	<0,001
CIHD, % (n)	1,8 (1)	44,7(34)	<0,001
resting heart rate, beats/min	73,8 $\pm$ 1,14	77,7 $\pm$ 1,10	<0,02
6MWT, m	440,8 $\pm$ 8,03	420,4 $\pm$ 5,83	<0,05
resting SpO <sub>2</sub> , %	96,3 $\pm$ 0,20	96,0 $\pm$ 0,14	-
resting dyspnea, points	2,25 $\pm$ 0,09	2,66 $\pm$ 0,10	<0,01

Thus, functional reserves of COPD patients depend both on the severity of bronchial obstruction and the intensity of clinical manifestations assessed by CAT, as well as on the presence of cardiovascular comorbid pathology and the degree of CVR.

Therefore, the question arises about the development of rehabilitation programs that would not only influence the disturbances of the bronchopulmonary system, but also, at least indirectly affecting metabolic processes and contributes to the stabilization of the cardiovascular system function.

Under the influence of treatment positive dynamics of clinical symptoms was observed, which was confirmed by such integral indices of the patient's clinical condition as the level of CAT, severity of dyspnea according to the Borg scale and increase in the walking distance covered by patients in six minutes (table 4).

**Table 4.** Dynamics of clinical data in COPD patients under the influence of various TC

Data, units	TC-1 (n=30)	TC-2 (n=62)	TC-3 (n=21)
CAT, points	<u>17,0±1,29</u> 10,4±0,78	<u>13,3±0,59</u> 6,08±0,50	<u>14,9±1,27</u> 7,95±1,26
p	<0,001	<0,001	<0,001
resting dyspnea, points	<u>2,43±0,10</u> 2,00±0,14	<u>2,32±0,10</u> 1,48±0,10	<u>2,81±0,30</u> 1,67±0,27
p	<0,02	<0,001	<0,01
Δ, points	0,41±0,09	0,85±0,07	1,14±0,21
p'	p <sub>1-2</sub> <0,001	p <sub>2-3</sub> <0,2	p <sub>1-3</sub> <0,01
6MWT, m	<u>437,6±8,04</u> 459,0±8,01	<u>430,0±7,48</u> 458,8±7,87	<u>404,1±13,0</u> 433,3±12,5
p	<0,1	<0,01	<0,2
distance elevation, m	21,5±4,19	29,3±3,24	29,2±4,27
dyspnea after 6MWT, points	<u>3,37±0,12</u> 2,72±0,16	<u>3,33±0,12</u> 2,36±0,12	<u>3,72±0,32</u> 2,72±0,27
p	<0,01	<0,001	<0,05
Δ, points	0,62±0,13	1,03±0,08	1,00±0,18
p'	p <sub>1-2</sub> <0,02	-	p <sub>1-3</sub> <0,1
resting heart rate, beats/min	<u>76,3±1,67</u> 74,2±2,06	<u>75,6±1,31</u> 70,9±1,18	<u>78,7±2,14</u> 73,0±1,78
p	-	<0,01	<0,05
heart rate after 6MWT, beats/min	<u>81,9±1,75</u> 78,8±1,73	<u>86,3±1,53</u> 80,7±1,31	<u>86,6±2,10</u> 82,0±2,54
p	<0,3	<0,01	<0,2
resting SpO <sub>2</sub> , %	<u>96,3±0,28</u> 97,2±0,21	<u>96,0±0,18</u> 97,1±0,14	<u>96,1±0,23</u> 97,1±0,22
p	<0,02	<0,001	<0,01
SCORE, %	<u>7,27 ±0,96</u> 5,53±0,69	<u>5,36 ±0,57</u> 4,32±0,43	<u>5,01 ±0,90</u> 3,87±0,67
p	<0,2	<0,2	-
FEV <sub>1</sub> , %	<u>49,2±2,46</u> 56,4±2,55	<u>55,5±1,53</u> 63,8±1,81	<u>53,8±2,85</u> 61,5±3,45
p	<0,05	<0,001	<0,1

Notes: in the numerator – data before treatment; in the denominator – data after treatment; p – significance of the difference between data before and after treatment; p' – significance of the data difference between groups of patients; Δ is the difference of data values.

In particular, before treatment in the patients of all groups the average value of CAT was more than 10 points (ranging from 13,3 to 17,0 points), which indicates a moderate impact of COPD symptoms on the health and daily life of patients. Under the influence of HAT (TC-1) the level of CAT decreased to 10,4±0,78 points (p<0,001). So patients almost reached the minimum level of clinical manifestations of the disease. When using TC-2 (with additional prescription of SOT) and TC-3 (with the additional administration of mineral water per os and by inhalation) the level of CAT decreased to 6,08±0,50 points (p<0,001) and 7,95±1,26 points (p<0,001) respectively, which corresponds to a stable course of the disease with a low impact of COPD symptoms on the health and daily life of patients. It should be noted that CAT value in patients treated according to TC-1, TC-2 and TC-3 decreased by 38,8%; 54,3% and 46,6% respectively, which confirms the high efficiency of the treatment in general (table 4).

Two subgroups of patients were distinguished among the patients who received TC-2: COPD patients who did not undergo coronavirus infection (23 patients – group TC-2A) and COPD patients convalescents after COVID-19 (39 patients – group TC-2B). In the

group TC-2A, the total CAT score decreased by 40,1% (from  $15,4 \pm 1,24$  points to  $9,23 \pm 0,84$  points;  $p < 0,001$ ), and in convalescents after COVID-19, this dynamic was even more significant - by 64,0% (from  $12,2 \pm 0,50$  points to  $4,31 \pm 0,42$  points;  $p < 0,001$ ). This fact confirms the necessity and expediency of rehabilitation treatment immediately after the acute period of COVID-19.

At the same time, patients noted a significant decrease in resting dyspnea (table 4). However, at patients using complex treatment, this reduction was more significant, especially when using singlet-oxygen therapy. In particular, resting dyspnea decreased by  $0,85 \pm 0,07$  points after TC-2 compared with  $0,41 \pm 0,09$  points in patients treated according to TC-1 ( $p < 0,001$ ). This made it possible for patients to walk a greater distance in 6 minutes, which indicates a certain increase in tolerance to physical activity. On average, the walking distance during the 6-minute walk test increased by 21,5-29,3 meters for all patients (table 4). However, only when using TC-2, this increase was statistically significant, at the same time in case of TC-1 and TC-3 it had only the character of a tendency.

In addition, it should be noted that when analyzing the effectiveness of TC-2 according to subgroups (TC-2A and TC-2B), it was found that the increase in the walking distance was statistically significant only in COPD patients convalescents after COVID-19 (TC-2B). In this group the elevation of the walking distance was  $34,1 \pm 4,60$  m. At the same time, in COPD patients without previous COVID-19 (TC-2A), the growth of the walking distance has only a trend and reached  $21,1 \pm 3,42$  m, which is significantly less than in the group TC-2B ( $p < 0,05$ ). This fact once again confirms the necessity for recovery treatment immediately after the acute period of COVID-19.

In general, it should be taken into account that the examination of patients was conducted with an interval of 20 days, which is a very short period for achieving reliable changes of 6MWT. Even the testified trend in such a short period of time is proof of the treatment effectiveness.

Particularly important is the fact that the severity of dyspnea after 6MWT, compared to that one before treatment, significantly decreased in all TC (table 4). This unequivocally confirms the increase of tolerance to physical activity and is a very important argument that testifies the effectiveness of rehabilitation treatment in COPD patients. However, it should be noted that, as in the previous case of assessment of resting dyspnea, this reduction was more significant when using TC-2.

The resting heart rate, which was determined before 6MWT, did not change significantly during the treatment in patients who received TC-1, but decreased after TC-2 and TC-3 that also, to some extent, may indicate the stabilization of patients' condition in general (table 4).

Special attention should be paid to changes in heart rate before and after treatment, which was calculated after 6MWT (table 4). After TC-1 and TC-3, the heart rate determined after 6MWT had only a tendency to decrease, compared to that one before treatment. When using TC-2 it decreased significantly, which confirms the more favorable effect of complex treatment using SOT on the clinical course of the disease.

The positive effect of recovery treatment on the course of the pathological process was also confirmed by a significant improvement in blood saturation at patients treated with all three TC without any difference between them (table 4). This is a very good prognostic indicator, especially in COPD patients convalescents after COVID-19, since blood saturation is one of the main homeostatic constants of human organism, which determines the level of its vital activity.

Changes in the SCORE value were also evaluated (table 4), although it is impossible to achieve in 20-23 days significant improvement in the prevention of fatal cardiovascular changes. However, when TC-1 and TC-2 were used, a tendency towards a decrease in the value of SCORE was noted, which is probably related to the improvement of biochemical data, in particular, a decrease in blood cholesterol level. The decrease in the SCORE value took place under the influence of all TC by 23,9%, 19,4% and 22,8%, respectively. This



probably is associated with decrease in inflammatory activity and intensity of oxidant stress, which results in indirect influence on lipid metabolism.

Results of clinical observations have been also confirmed by changes in ventilation data, in particular, FEV<sub>1</sub>, which reliably increased at the end of treatment without a significant difference between TC (table 4). This positive dynamics allows to count that the basis for positive changes in COPD course is the HAT usage due to its local effect on the tracheobronchial tree. At the same time, it should be noted that when using TC-1, FEV<sub>1</sub> increased in average by 7,2%, after TC-2 FEV<sub>1</sub> elevated by 8,3% and applying TC-3 – by 7,7%.

Thus, clinical and functional data indicate high effectiveness of recovery treatment in COPD patients based on HAT, especially with the additional usage of SOT, which is probably related to its effect on oxidative stress.

#### 4. Conclusions

1. HAT with the appropriate dispersion and concentration of the haloaerosol, which ensures its' sanative and anti-inflammatory effects, related reduction of bronchial obstruction and stabilization the disease' course as a whole, leads to an increase in tolerance to physical activity and can be used as a stage of physical rehabilitation with the possible subsequent including therapeutic physical exercises.

2. HAT may be supplemented by other physiotherapeutic methods that enhance the influence on certain pathogenetic mechanisms of COPD and can contribute to the stabilization of the diseases' process, promote the recovery of the functional state of COPD patients, which is accompanied by increasing of tolerance to physical activity.

3. Taking into account the pronounced positive dynamics of the investigated data in COPD patients convalescents after COVID-19, the usage of HAT can be recommended for this contingent of patients immediately after the acute period of the disease.

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