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ORIGINAL ARTICLE

APPLICATION OF HALOINHALATIONS AT THE SANATORIUM-RESORT STAGE OF REHABILITATION OF PATIENTS AFTER COVID-19

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ABSTRACT

Background. After suffering from COVID-19, a large number of patients need respiratory rehabilitation. One of the methods of rehabilitation is inhalation with salt aerosols.

Objective. Our work aimed to study the effectiveness of inhalations of a dry aerosol of salt precipitated from the mineral water of the "Teplitsa multidisciplinary sanatorium", Transcarpathian region of Ukraine.

Material and Methods. 30 male patients were examined after suffering from COVID-19. We formed two groups of patients, control and main, 15 people each. Patients in the control group received inhalation with a dry aerosol of table salt of the "Aero-M-sol". In contrast, patients in the main group received a course of inhalations with a dry aerosol of salt precipitated from the mineral water.

Results and discussion. Under the influence of the rehabilitation complex in both groups, there is a performance improvement but significant changes are observed only in patients of the main group. The indicator Forced Vital Capacity1 increased to the greatest extent, which after rehabilitation is significantly higher than in the control group ($p<0.05$). As a result, the Tiffeneau index significantly increases in the main group compared to the control group, reaching normal values. The main effect is associated with a decrease in obstructive complications of the respiratory tract as a result of a decrease in inflammation. The use of iodine-bromine brines (as in our case) for inhalation in the treatment of respiratory diseases has been proven to be effective, with systemic effects in the form of decreased IgE and increased IgA in the blood serum having been noticed.

Conclusions. The use of haloinhalations with MW salts in the rehabilitation of patients after suffering from COVID-19 disease significantly improves the clinical condition of convalescents.

Keywords: *COVID-19, rehabilitation, inhalation, mineral waters*

INTRODUCTION

After suffering from the coronavirus disease COVID-19, many patients develop respiratory dysfunction associated with restrictive lung changes and inflammatory obstructive changes in the bronchi. Also, bronchial hyperreactivity is primarely associated with reduced inorganic substances in the airways [1].

These violations necessitate directed respiratory rehabilitation [2, 3]. One of the physiotherapeutic techniques that increases the effectiveness of the basic treatment of respiratory pathologies is halotherapy, inhalation with a dry salt aerosol [4, 5, 6].

Halotherapy has been found to positively affect patients suffering from chronic respiratory diseases, improving mucociliary clearance and lung function in common chronic respiratory diseases, as well as quality of life.

There are currently no formal guidelines for using halotherapy in the form of salt chambers (halo chambers) or dry powder inhalers, but there is evidence for its use as a possible adjuvant therapy [7].

Based on these data, some researchers propose to include halotherapy in the rehabilitation complex for patients who have suffered from COVID-19 [8].

Usually, for halotherapy, dry dispersed NaCl aerosol is used. The features of its action are the improvement of the condition of the ciliated epithelium, the normalization of bronchial patency, the progress of the drainage function of the bronchi, the reduction of edema of the bronchial mucosa, the pronounced desensitizing effect of the immunosuppressive action (decrease in eosinophilia, circulating immune

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complexes). The role of histamine in the activation of bronchoconstriction has been shown by many [9, 10]. In this regard, the results of studies showing that histamine mediates the respiratory tract reaction to isotonic NaCl solution are exciting [11, 12].

When studying the absorption of dry NaCl aerosol in the respiratory organs, it was found that the degree of retention of particles of the same dispersion is higher in dry aerosol. In this regard, the use of a highly dispersed aerosol makes it possible to use low doses and reduce the likelihood of unwanted side reactions [13, 14]. Possible short-term side effects after halotherapy are dizziness, headache, cough, nasal discharge, and a slight increase in body temperature.

Recently, there has been an increasing interest in using various mineral waters (MW) for inhalation, especially in the form of evaporated salts [15, 16].

When inhaled, the salt composition of mineral water, enters the cavity of the upper respiratory tract and lungs in the form of a fine aerosol. It directly affects the mucous membrane of the respiratory tract. As a result of MW salt dispersion, its contact with mucous membranes increases, the absorption of chemical components is accelerated, and the condition of the external respiration improves. In the aerosol coagulation zone in the trachea and bronchi, the motor activity of the ciliated epithelium increases, and the viscosity of the bronchial secretion decreases, which increases mucociliary clearance and airway clearance in patients with obstructive disorders of the respiratory system, including those caused by coronavirus infection [17].

The extensive absorption surface of the mucous membrane of the respiratory tract during haloinhalation causes not only a direct effect of the biologically active components of MW on the upper and lower respiratory tract and lungs, but also indirectly on the entire body [18].

Features of the action of different types of MW are associated with the presence of ions of various elements and gas composition, which determines their differentiated use.

The work aims to study the effectiveness of halotherapy with mineral water salts in rehabilitating patients with COVID-19.

MATERIALS AND METHODS

30 male patients were examined after suffering from COVID-19. The average period of convalescence after suffering a disease was (2.6±1.6) months. Rehabilitation was carried out in the «Multiprofile sanatorium Teplitsa» of the Transcarpathian region of Ukraine.

Inclusion criteria: confirmed clinical diagnosis of COVID-19 in history, radiographically or tomographically confirmed pneumonia of different localization, age from 50 to 60 years, normal body weight (BMI – 20-25 kg/m²).

Exclusion criteria: history of tuberculosis or other chronic infectious and non-infectious respiratory diseases, confirmed presence of COPD, presence of neoplasms, time from clinical recovery from COVID-19 of more than 4 months, overweight, obesity (BMI>25 kg/m²).

We formed 2 groups of patients.

Group 1 (control) – 15 people. The mean age was 58.7±3.3 years. Patients in this group received a basic rehabilitation complex. It included massage, physical rehabilitation in the form of group sessions of therapeutic physical exercises, and ultrasound exposure to the chest area (for a course of 10 procedures). A course of inhalation with a dry aerosol of environmentally friendly table salt was added to the basic rehabilitation complex. The chemical composition of this salt was as follows:

- Sodium chloride – 97.7%
- Calcium ion – 0.60%
- Magnesium ion – 0.10%
- Sulfate ion – 1.30%
- Iron oxide – 0.10%
- Sodium sulfate – 0.20%.

The dispersity of the aerosol was at least 80% of particles no larger than 5 microns in size; the procedure duration is 5 minutes, daily for the course No. 10 inhalations.

Group 2 (main) – 15 people. The mean age was 57.7±3.1 years. To this group of patients, a course of inhalations with a dry aerosol of salt evaporated from the MW of the Teplitsa deposit (Multipurpose sanatorium Teplitsa, Transcarpathian region, Ukraine) was added to the basic medical rehabilitation complex for this group of patients. The chemical composition of this salt was as follows:

- Sodium and potassium – 12.83 g/l,
- Chloride – 20.15 g/l,
- Bromine – 7.20 mg/l,
- Iodine – 0.75 mg/l,
- Metasilicic acid – 7.41 mg/l.

Inhalations with dry aerosols were dispensed by the Haloinhalator Galoneb apparatus (GISA-01), Ukraine. The dispersion of aerosols was not less than 80% of the particles, no larger than 5 microns; the procedure duration was 5 minutes daily for a course of No. 10 inhalations.

All patients underwent a comprehensive examination before the start of the rehabilitation course and after its completion. The complex of examinations included clinical methods, functional studies, complete blood count, and biochemical blood tests (total protein content, bilirubin and its fractions, creatinine, glucose and C-reactive protein) by standard laboratory methods.

When examining the function of external respiration using a computer spirograph «Cardio-Spiro», Ukraine, the vital capacity of the lungs (VC), the forced vital capacity of the lungs (FVC), forced expiratory volume per one second (FEV1), and the Tiffeneau index were evaluated. The due VC values were calculated according to Anthony's formula.

To assess physical performance, Six-Minute Walk Test (6MWT) was used [19].

Statistical processing of the obtained data was carried out using the XLSTAT 2021 program. To assess the significance of differences between the samples, the φ* – criterion, Fisher's angular transformation, was used. The Student's method for related samples was used o assess the significance of differences in groups before and after rehabilitation; The Student's method for unrelated samples was used to determine intergroup differences. Differences $p<0.05$ were considered significant.

The study was a prospective, explorative and observational trial. This trial was performed in accordance with the Declaration of Helsinki; it was approved by the Commission on Bioethics of the "Ukrainian Research Institute of Medical Rehabilitation and Resort Therapy of the Ministry of Health of Ukraine", No. 8 of 15.08.2022.

All patients provided written informed consent before inclusion in the study.

RESULTS AND DISCUSSION

Anthropometric parameters of the examined patients are presented in Table 1. The average BMI in patients of both groups was at the upper limit of normal.

Before treatment, patients in both groups complained of fatigue, cough, shortness of breath, headache, and decreased physical activity (Table 2). As seen from Table 2, as a result of treatment in both groups, there was a decrease in the frequency of clinical symptoms. However, if significant changes were recorded only in the control group in four indicators, then in the main group, the frequency of all indicators significantly decreased. In addition, the frequency of manifestation of five symptoms out of six observed after the end of treatment was significantly lower in the main group than in the control group. The only indicator for which there was no significant difference between groups was headache.

The spirographic parameters of the subjects are presented in Table 3. Before the start of rehabilitation, the vital capacity of the lungs in patients of both groups was at the lower limit of the norm (concerning the predicted one). The values of the forced vital capacity and especially the forced vital capacity for 1 second, are significantly below the norm ERS. This is also evidenced by the extremely low value of Tiffeneau index – 57.1% for both groups, with a norm of no less than 75.0% [20]. The value of this index clearly indicates the presence of obstructive respiratory failure in patients. This condition may be associated with spasms or swelling of the bronchial mucosa, which makes it difficult for free air circulation.

Under the influence of the rehabilitation complex in both groups, there is a performance improvement. However, significant changes are observed only

Table 1. Anthropometric parameters, M±m

Indicators	Control group n=15	Main group n=15	p
Height, m	1.71±0.73	1.72±0.67	>0.05
Weight, kg	83±4.8	85±4.3	>0.05
BMI, kg/m²	24.3±2.1	24.7±1.9	>0.05

p – reliability between indicators in the main and control groups after the course of treatment

Table 2. Changes of clinical signs before and after rehabilitation, n, (%)

Clinical manifestations	Control group n=15		Main group n=15		p
	Before treatment	After treatment	Before treatment	After treatment	
Cough	13 (87)	8 (53)*	14 (93)	4 (27)*	<0.05
Dyspnea	11 (73)	7 (47)	12 (80)	5 (33)*	<0.05
Fatigue	12 (80)	7 (47)*	12 (80)	4 (27)*	<0.05
Headache	7 (47)	4 (27)*	9 (60)	4 (27)*	>0.05
Sleep disturbance	6 (40)	4 (27)	6 (40)	0*	<0.05
Irritation	6 (40)	2 (13)*	6 (40)	0*	<0.05

* – reliability of changes between indicators in the group before and after the course of treatment (p<0.05);
p – reliability between indicators in the main and control groups after the course of treatment (p<0.05)

in patients of the main group. The indicator FEV1 increased to the greatest extent, which after rehabilitation is significantly higher than in the control group ($p<0.05$). As a result, the Tiffeneau index significantly increases in the main group compared to the control group, reaching normal values.

As a consequence of improved respiratory performance, there was an increase in the distance that patients walked in the Six-Minute Walk Test (Table 4). The initial values of 6-minutes walking distance (6MWD) were reduced in both groups, which indicates a decrease in the patients' physical fitness. The recorded 6MWD values are typical for patients with interstitial lung diseases (250-275 m). After treatment, statistically significant changes were recorded in both groups. However, the increase in distance in the main group is much more powerful and significantly higher than in the control group.

It should be noted that the value of pulse oximetry in both groups before the start of rehabilitation was within the normal range and slightly increased after (Table 5).

The study of peripheral blood confirms the oximetry data. As seen from Table 6, even before the start of rehabilitation, the patients had no pathological changes in the red blood - the number of erythrocytes and the hemoglobin content were close to the upper limit of the physiological norm. An increase in these characteristics during the rehabilitation period is noted in patients of both groups but is not statistically significant.

As for the indicators of white blood, the percentage of leukocytes before the start of rehabilitation did not exceed the reference values in both groups and subsequently decreased slightly. The ratio of neutrophils and lymphocytes in both groups changed in the same direction but to a different extent. There was a decrease in the percentage contribution of neutrophils, especially stab. Their reduction was significant in both groups; however, in the main group, it was statistically significantly more potent than in the control group ($p<0.05$). There was also a decrease in the contribution of segmented neutrophils in both groups, but it was insignificant.

On the contrary, the percentage of lymphocytes increased, and in the main group, it was statistically significant. As a result, there was a decrease in the Krebs index, which was significantly lower in the main group ($p<0.05$). This phenomenon can be interpreted as a decrease in the level of inflammation preserved after suffering from COVID-19 [21, 22, 23].

Also, in the main group, the number of eosinophils significantly increases, which can be explained by an

Table 3. Changes of spirography indicators before and after rehabilitation, M±m

Indicators	Control group n=15		Main group n=15		p
	Before treatment	After treatment	Before treatment	After treatment	
VC, l	2.8±0.2	3.1±0.3	2.8±0.1	3.3±0.2*	>0.05
VC\VC predicted, %	75.7±4.9	83.8±5.3	75.7±4.8	89.2±5.5*	>0.05
FVC, l	2.6±0.2	2.8±0.3	2.5±0.2	3.1±0.2*	>0.05
FEV1, l/s	1.6±0.1	1.9±0.2	1.6±0.2	2.5±0.2*	<0.05
Tiffeneau index, %	57.1±4.7	61.3±4.9	57.1±4.8	75.8±5.1*	<0.05

* – reliability of changes between indicators in the group before and after the course of treatment ($p<0.05$);
p – reliability between indicators in the main and control groups after the course of treatment ($p<0.05$)

Table 4. Changes of Six-Minute Walk Test, M±m

Indicator	Control group n=15		Main group n=15		p
	Before treatment	After treatment	Before treatment	After treatment	
6MWD, m	275±14.0	326.0±10.4*	288±10.7	362.7±11.6*	<0.05

* – reliability of changes between indicators in the group before and after the course of treatment ($p<0.05$);
p – reliability between indicators in the main and control groups after the course of treatment ($p<0.05$)

Table 5. Changes of pulse oximetry, M±m

Indicator	Control group n=15		Main group n=15		p
	Before treatment	After treatment	Before treatment	After treatment	
SpO_2, %	96.9±0.5	97.8±0.2	96.7±0.3	98.1±0.2	>0.05

p – reliability between indicators in the main and control groups after the course of treatment

Table 6. Changes of indicators of peripheral blood, M±m

Indicators	Control group n=15		Main group n=15		p
	Before treatment	After treatment	Before treatment	After treatment	
Erythrocytes, 10^{12}/l	4.7±0.2	4.8±0.4	4.7±0.1	4.9±0.1	>0.05
Hemoglobin, g/l	140.5±4.0	141.0±4.0	139.7±5.5	141.2±3.2	>0.05
Leukocytes, 10^9/l	7.3±0.7	6.9±0.6	7.1±0.5	6.7±0.6	>0.05
Band neutrophils, %	4.9±0.6	3.6±0.5*	5.1±0.6	2.7±0.5*	<0.05
Segmented neutrophils, %	58.0±6.0	56.2±4.2	57.0±3.0	54.1±2.4	>0.05
Lymphocytes, %	27.8±3.2	31.5±2.2	28.4±3.1	35.0±2.0*	>0.05
Krebs index, c.o.	2.25±0.7	1.88±0.6*	2.21±0.8	1.63±0.6*	<0.05
Eosinophils, %	2.1±0.8	3.6±0.7	2.2±0.7	3.9±0.8*	>0.05
Monocytes, %	5.6±1.2	5.9±1.0	5.3±0.6	5.1±1.1	>0.05
Basophils, %	0±	0±	0±	0±	>0.05
Platelets, 10^9/l	271.2± 41.7	276.2±40.8	288.2±24.9	291.5±17.9	>0.05

* – reliability of changes between indicators in the group before and after the course of treatment ($p<0.05$);
p – reliability between indicators in the main and control groups after the course of treatment ($p<0.05$)

Table 7. Changes of metabolic indicators, M±m

Indicators	Control group n=15		Main group n=15	
	Before treatment	After treatment	Before treatment	After treatment
Total bilirubin, µmol/l	11.7±2.1	11.2±1.9	12.2±1.9	10.8±1.5
Direct (bound) bilirubin, µmol/l	4.0±0.7	3.9±0.5	4.2±0.5	3.8±0.4
Indirect bilirubin (free), mmol/l	7.7±1.4	7.4±1.4	7.9±1.4	7.0±1.1
Creatinine, µmol/l	79.1±6.7	75.3±5.3	79.9±3.6	71.8±2.9
Total protein, g/l	72.5±5.9	71.2±4.2	71.1±5.2	71.2±4.6
C-reactive protein, mg/l	2.2±0.8	0.9±0.2	2.1±0.7	0.5±0.1*
Fibrinogen, g/l	3.8±0.4	3.5±0.4	4.1±0.6	3.5±0.7
Glucose, mmol/l	5.5±0.1	5.5±0.1	5.9±0.8	6.1±1.2

* – reliability of changes between indicators in the group before and after the course of treatment ($p<0.05$)

allergic-like reaction to the active components of the mineral salt.

The level of monocytes was at the upper limit in both groups of patients and practically did not change. Since the function of these cells is associated with specific phagocytosis (mainly with the elimination of the remains of destroyed cells), it can be assumed that the examined patients continue to utilize cells affected by coronavirus infection.

The values of metabolic parameters in both groups were within the normal range and did not significantly change during the rehabilitation period. The only exception is the C-reactive protein, the value of which significantly decreased in the main group, which indicates the attenuation of residual inflammatory manifestations after COVID-19 (Table 7).

Thus, we see that the main respiratory complications after COVID-19 are associated with airway obstruction. One of the most common manifestations of respiratory tract diseases is allergic reactions, namely: runny nose, itching, cough, shortness of breath, and swelling of the mucous membranes. Respiratory tract infections, particularly those caused by COVID-19, are complicated by immune sensitization involving the lung immune response. Experimental studies have shown that halotherapy reduces the infiltration of inflammatory cells into the lungs and airway mucosa. It also relieved oxidative stress in the lung tissue. Halotherapy relieves chronic obstructive pulmonary disease by alleviating NLRP3 inflammasome-mediated pyroptosis [24].

Our study has several limitations. The main ones are:

- the small sample size,
- the sex and age of the patients,
- the time since the illness,
- the chosen regimen for the procedures.

Changing these parameters will provide additional information on the impact of halotherapy with mineral water salts on the rehabilitation of patients after COVID-19.

CONCLUSIONS

The use of haloinhalations with MW salts in the rehabilitation of patients after suffering from COVID-19 disease significantly improves the clinical condition of convalescents. The main effect is associated with a decrease in obstructive complications of the respiratory tract as a result of a decrease in inflammation.

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Disclosure conflict of interest

The authors declare that they have no conflicts of interest concerning this article.

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