ORIGINAL ARTICLE

THE EXPERIENCE OF TREATMENT THE PATIENTS WITH COMPLICATED VIRAL RESPIRATORY TRACT INFECTIONS: ROLE OF HIGH-CONCENTRATED OXYGEN INHALATIONS ADDING CAMOMILE OIL

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ABSTRACT

The aim: To study the clinical manifestations, capillary blood saturation, frequency of respiratory failure in patients with complicated forms of acute respiratory viral infections (ARVI).

Materials and methods: The study included 70 patients with ARVI (mean age was 46.5±9.2 years). Patients observed were randomized into 2 groups. In group 1 (n=30), the only basic therapy was prescribed. In group 2 in addition to the basic therapy the inhalations with high concentrated oxygen with Camomile Oil were used.

Results: It is proved that the use of highly concentrated oxygen with camomile oil in the inhalation treatment regimen significantly reduces the duration of local respiratory symptoms ($p<0.001$) and symptoms of general intoxication ($p<0.001$), prolonged hospital stay decreases by an average of 5 days ($p<0.001$).

The relief of symptoms of RF in group 2 was noted for 10 days of hospitalization with an increase in capillary blood saturation (SatO2,%) to 95.2±2.91. Absolute therapeutic efficacy (absolute efficacy) of the correction of RF during complex treatment with the addition of highly concentrated oxygen was 88.0% versus 57.0% in group 1. Relative efficacy (RE) – 0.65 [0.46-0.90], odds ratio (OR) – 0.19 [0.06-0.61], $p<0.05$.

The positive effect of highly concentrated oxygen for local immunity state – the level of secretory immunoglobulin A ($p<0.001$) and lysozyme ($p<0.001$) was established.

Conclusions: High-concentrated oxygen inhalations adding camomile oil is effective in complex treatment at patients with complicated forms of acute respiratory viral infections.

KEY WORDS: acute respiratory viral infections, complications, oxygen inhalation

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INTRODUCTION

ARVI is a large etiologically diverse group of infectious diseases that occur with damage of the upper and lower respiratory tract (airways and airways), which have a certain similarity of pathological mechanisms and clinical symptoms. ARVI may result in severe disease [1] and can be transmitted among human populations in a short period of time via droplets, aerosols, contact with abiotic surfaces, and even fecal matter [2].

According to studies, more than half of patients admitted for treatment in a hospital with complications of acute respiratory viral infections have hypoxemia and an increase in the partial pressure of blood carbon dioxide (pCO2) above 45 mm Hg at the time of the initial examination. 20 % of patients with hospitalization due to exacerbation of the disease have respiratory acidosis [3, 4]. Aerosols commonly consist of fine solids or liquid particles that are suspended in air or gas. Aerosol therapy is generally used in critical pulmonary treatment [5]. There are several advantages that make aerosol drug delivery a preferred route of administration over various other types of dosage forms [6].

Hypoxemia can cause a thickening of the intima-media complex of blood vessels due to the development of endothelial and vascular smooth muscle cells hypertrophy and hyperplasia, which is currently considered as a marker of cardiovascular risk [7]. However, complications after the flu occur not only in people at risk, but also in young patients without concomitant health problems. The normal response to hypercapnia is an increase in respiratory drive and minute volume ventilation [8]. Hypoxemia itself rather plays a limited role in the sensation of breathlessness experienced by patients with cardiopulmonary disease on the opposite of hypercapnia that creates per se dyspnea. In healthy subjects, the respiratory drive shifts minimally in mild hypoxemia (PaO 2 60 – 65 mmHg), such as resulting from stays at high altitude or experimental hypoxic chambers [9].

The treatment of ARVI in present remains relevant. There are frequent cases of polypharmacy, unreasonable prescription of drugs, especially antibiotics, antipyretic drugs, etc. Difficulties also lie in the fact that in the debut of the disease it is rather difficult to establish the etiological factor. Therefore, the doctor has to apply mainly

symptomatic therapy, since specific treatment for many acute respiratory viral infections has not been developed. Natural products are an excellent starting point for drug discovery. Medicinal plant extracts and related products, have long been used to treat a wide range of infections including viral infection, and their purified phytoconstituents are an excellent precursor for new antiviral drugs [10].

Nowdays, the question of the effectiveness of inhalation of highly concentrated oxygen, in particular, the use of pocket spray in these patients, is not sufficiently studied.

THE AIM

The aim – to study the features of the clinical manifestations of complicated forms of ARVI, capillary blood saturation and the frequency of RF in patients admitted to the hospital, as well as the effectiveness of highly concentrated oxygen inhalations with the addition of camomile aroma oil in the form of portable sprays.

MATERIALS AND METHODS

The study included 70 patients with acute respiratory viral infections. The average age is 46.5±9.2 years. The ratio of men to women was 60% to 40% (accordingly 42 men and 28 women). All patients signed an informed consent to participate in the study. Exclusion criteria were the presence of chronic respiratory diseases, blood diseases, heart failure with functional classes III-IV, surgical pulmonary or abdominal diseases at the time of inclusion, neurological pathology that affects chest excursion. The diagnosis was set by the applying of clinical, medical, epidemiological and laboratory data.

All observed subjects underwent laboratory and instrumental studies, including a general urinalysis, clinical and biochemical blood tests, chest X-ray, electrocardiography (ECG), pulse oximetry (PO) (an indicator of saturation at rest without oxygen support). The level of sIgA was determined in swabs of the oropharynx by the enzyme-linked immunosorbent assay. The concentration of saliva lysozyme was studied by the immune diffusion reaction method.

Symptomatic therapy of all patients was carried out according to the Protocol for the diagnosis and treatment of infectious diseases (The Order of the Ministry of Health of Ukraine No. 354). Observed were randomized into 2 groups. In group 1 (n = 30), only basic therapy was prescribed. In group 2 in addition to the basic therapy were used inhalations with high concentrated oxygen with Camomile oil (Tesla's Secret by Eco Medical Europe Ltd Oxygen Breathing Mixture Sea Minerals Camomile, group 2, n=40). Oxygen inhalations in group 2 were carried out every 1-1.5 hours for 3 deep inspirations or, as necessary, more often with pronounced subjective signs of respiratory failure (shortness of breath). Both groups are based uniformly by age, gender and initial clinical manifestations, which allows a comparative assessment of the observation results and determine the reliability of the results, table I.

For statistical analysis results we used Statistica for Windows Version 10.0 (Stat Soft inc., USA). Parameters are presented in the form M±m, where M is the Mean, m is standard deviation. In the analysis of categorical group data, the criterion Pearson $\chi 2$ with Yates correction was used. The assessment of the probability of the therapeutic effect was performed taking into account the absolute (AE) and relative (RE) efficacy, as well as the odds ratio (OR), with the calculation of confidence intervals and the reliability criterion for RR and OR. At the case of $p<0.05$, differences were statistically significant.

RESULTS

At virological research of nasopharynx's swabs at 21 patients (30%) antigens of a parainfluenza, at 20 (28.6%) an adenovirus, at 16 (22,8%) a respiratory syncytial virus, at 13 (18.6%) – a rhinovirus are allocated. According to the anamnesis, the main clinical symptoms at the beginning of the disease were signs of nasopharyngitis in 17 patients (24.3%), nasopharyngotracheitis – in 22 (31.4%), nasopharyngotracheobronchitis – in 20 (28.6%), laryngotracheitis – in 11 (15.7%) people. At the time of admission to the hospital, the course of the disease was complicated by the appearance of cough with mucous sputum (70 people, 100%), shortness of breath (70 people, 100%). Objectively, according to the auscultatory and radiological picture, all patients observed signs of interstitial pneumonia (70 people, 100%).

The distribution of the main respiratory symptoms in patients of the study groups is presented in table II.

Symptoms of general intoxication were presented in fever, headache, lethargy, myalgia, and decreased appetite. The distribution of symptoms between the groups is presented in table III.

Capillary blood saturation (SatO2,%) according to pulse oximetry was 87.4±3.2% in group 1 and 86.9±4.5% in group 2.

In the general cohort of patients, the phenomena of RF, assessed by the level of blood oxygen saturation (SpO2<95%), were detected in 80% (n=56) of the subjects. In this case, RF I degree (SpO2 at the level of 90–94%) was determined in 42.9% (n=30) of patients, RF II degree (SpO2 at the level of 75–89%) – in 31.4% (n=26) patients. The distribution of patients by severity of RF is presented in table IV.

The mean heart rate (HR) was 112.2±18.7 beats/min and 115.8±17.9 in groups 1 and 2 accordingly. Respiration rate (RR) reached 22.8±4.2 and 23.1±3.9, respectively.

There was a negative regression relationship between capillary blood saturation, RR ($r=-0.31$, $p<0.05$), HR ($r=-0.31$, $p<0.05$), Fig. 1 (a), 1 (b).

On the background of the treatment, all patients showed positive dynamics and a reduction in symptoms of general intoxication. The use in the treatment of inhalations of highly concentrated oxygen with the addition of

Table I. Clinical characteristics of patient groups

Index	Group 1 n=30	Group 2 n=40	p
Age	45.4±9.8	46.9±10.2	>0.05
Men	18 (60%)	24 (60%)	>0.05
Women	12 (40%)	16 (40%)	>0.05
Hypertension	8 (26.7%)	10 (25.0%)	>0.05
Diabetes mellitus 2	4 (13.3%)	6 (15.0%)	>0.05

Table II. Distribution of respiratory symptoms in the studied groups

Symptoms	Group 1 n=30		Group 2 n=40		p
	Count	%	Count	%	
Hyperemia of the pharynx	27	90%	35	87.5%	0,74
Hoarseness of voice	18	60%	24	60%	1.0
Rhinitis	25	83,3%	34	85%	0.85
Cough	30	100%	40	100%	1.0
Heavy breathing	30	100%	40	100%	1.0

Table III. Symptoms of intoxication in the studied groups

Symptoms	Group 1 n=30		Group 2 n=40		p
	Count	%	Count	%	
Fever	30	100%	40	100%	1.0
Headache	30	100%	40	100%	1.0
Adynamia	20	66.7%	27	67.5%	0.94
Myalgia	18	60%	23	57.5%	0.83
Decreased appetite	26	86.7%	34	85%	0.84

Table IV. Distribution of patients of the studied groups by the degree of RF

Degree	Group 1 n=30		Group 2 n=40		p
	Count	%	Count	%	
RF I	13	43.3%	17	42.5%	0.95
RF II	11	36.7%	15	37.5	0.95

camomile oil, significantly reduced the duration of local respiratory symptoms: pharyngeal hyperemia by 1.7 days (37.8%), hoarseness – by 1.1 days (52.4%), rhinitis – by 1.6 days (27.6%), cough – by 7.6 days (45.3%), heavy breathing – by 4.1 days (48.8%), p<0.001, table V.

In addition, a decrease in the duration of symptoms of general intoxication and fever was noted when inhalations of highly concentrated oxygen with camomile oil were added to the treatment regimen: fever – by 1.81 days (32.3%), headache – by 0.7 days (20.1%), adynamia – by 3.49 days (47.7%), myalgia – by 2.96 days (51.2%), decreased appetite – by 2.89 days (30.4%), p<0.001, table VI.

The average bed-stay of patients in group 1 was 14.5±4.7 days, whereas when complex inhalations were included in the complex treatment with the addition of camomile aromatic oil in group 2, this indicator was recorded within 9.5±2.49 days (p <0.001).

The dynamics of changes in the levels of capillary blood saturation (SatO2,%) according to pulse oximetry in the observation groups after 10 days of treatment is shown in Figure 2. The increase in saturation reached 91.4±3.19% in group 1 and approached 95.2±2.91% in group 2.

The probability of releife of signs of respiratory failure 7 days after the start of therapy is presented in table VII.

It should be emphasized that the absolute therapeutic effectiveness (absolute efficacy) of the correction of RF during complex treatment with the addition of highly concentrated oxygen inhalations was 88.0% versus 57.0% in group 1. Relative efficacy (relative efficacy) was 0.65 [0.46-0.90], with Odds Ratio (OR) – 0.19 [0.06-0.61]; p<0.05.

In addition, the presence of a positive effect of inhalation of highly concentrated oxygen with the addition of camomile oil on the state of local immunity with a significant increase in the level of secretory immunoglobulin A (p <0.001) in saliva and lysozyme level (p <0.001) was established, table VIII.

However, in both groups the increase in sIgA and lysozyme secretion in saliva was significant, with the addition

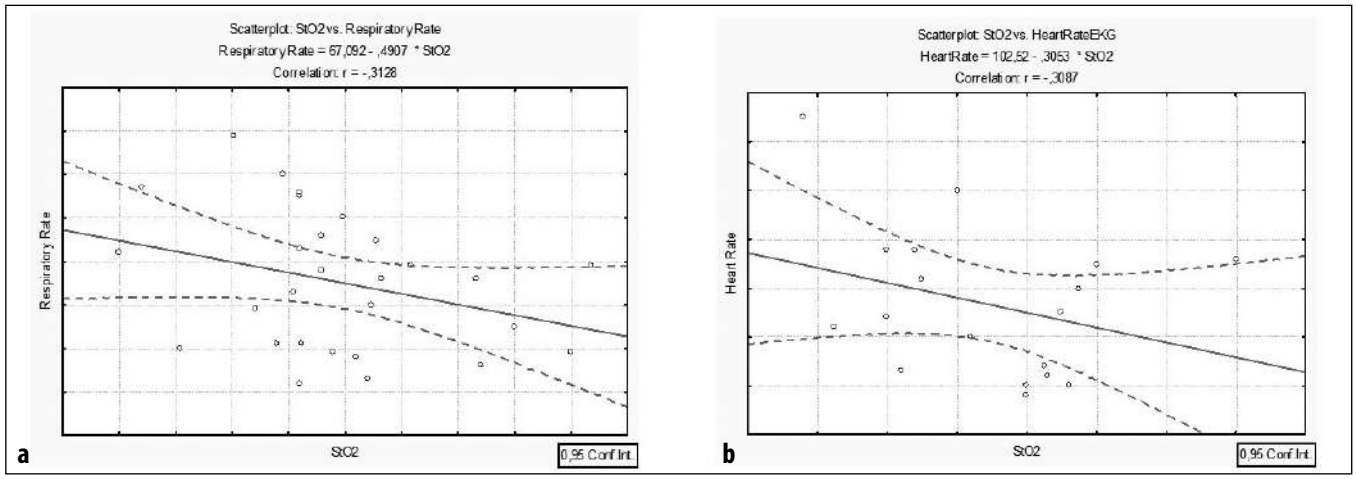

Fig. 1. (a). Regression between RR and StO2 in capillary blood at the patients with viral pneumonias, (b). Regression between HR and StO2 in capillary blood at the patients with viral pneumonias.

Table V. Duration of respiratory symptoms in the studied groups

Symptoms	Group 1 n=30	Group 2 n=40	*p*
Hyperemia of the pharynx	6.2±1.9	4.5±1.2	<0.001
Hoarseness of voice	3.2±0.91	2.1±0.71	<0.001
Rhinitis	5.8±1.10	4.2±0.70	<0.001
Cough	16.8±3.41	9.2±2.12	<0.001
Heavy breathing	12.5±3.47	8.4±2.94	<0.001

Note:
p – it is the reliability of the difference between groups.

Table VI. The duration of intoxication symptoms in the studied groups

Symptoms	Group 1 n=30	Group 2 n=40	*p*
Fever	7.42±1.95	5.61±2.11	<0,001
Headache	4.18±0.94	3.48±0.62	<0,001
Adynamia	10.8±1.23	7.31±2.18	<0,001
Myalgia	8.74±1.98	5.78±0.56	<0,001
Decreased appetite	12.4±3.12	9.51±2.34	<0,001

Note:
p – it is the reliability of the difference between groups.

Table VII. The effectiveness of the relief of RF when used to the complex treatment of inhalation of highly concentrated oxygen with the addition of camomile aroma oil

Parameters	AE, %	RE[CI%95]	OR[CI%95]
Group 1	57.0	0.65 [0.46-0.90] p<0.05	0.19 [0.06-0.61] p<0.05
Group 2	88.0		

of highly concentrated oxygen inhalations, this indicator was 13.6% and 55.8% higher than in group 1.

DISCUSSION

Respiratory failure is the most common mechanism of death in acute respiratory infections [11], incliding COVID-19 [12]. Its onset is typically during the second week of illness, with a median time of ICU admission of 10 to 12 days. Hypoxemic respiratory failure occurs in 10% to 20% of patients develops in 3% to 5% [13]. Risk factors for acute respiratory distress syndrome are age 65 years or older, cardiovascular disease, diabetes mellitus, and hypertension [13].

Early identification of progressive respiratory failure is needed to escalate the level of care and apply important interventions such as high-concentrated oxygen and other supportive measurements. So, Ruiling Zhang et al. present the case of severe influenza A (H1N1) which was controlled by the treatments of anti-infection and

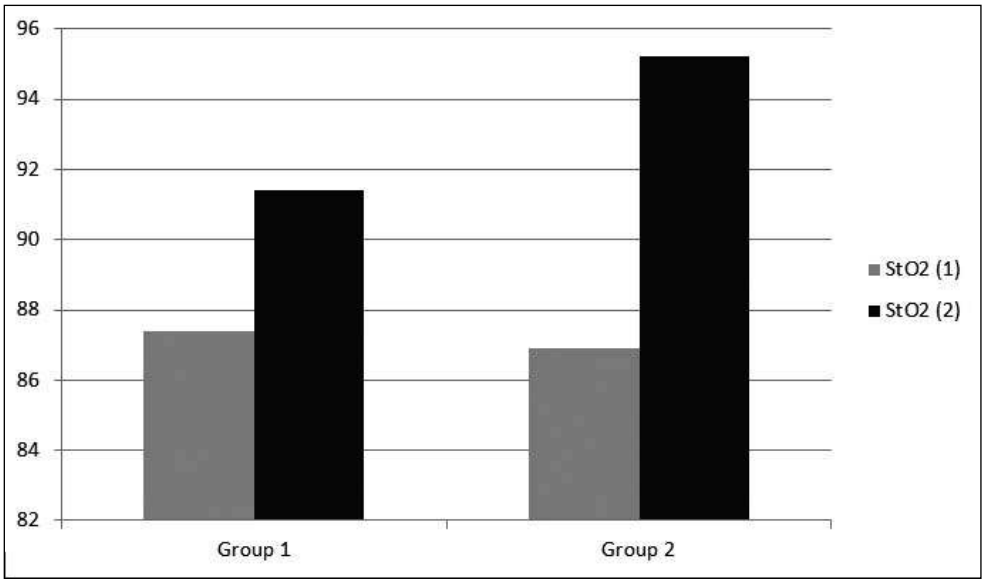

Fig. 2. The changes of capillary blood saturation indices in groups of patients with complications of ARVI

Table VIII. Dynamics of indicators' changes of local immunity in observation groups

Parameters	sIgA, gr/l		Lysozyme, gr/l	
	Initial	In observation	Initial	In observation
Group 1	0.66±0.13	0.81±0.14[1]	0.029±0.005	0.043±0.005[1]
Group 2	0.63±0.13	0.92±0.12[1,2]	0.032±0.006	0.067±0.004[1,2]

Note:
[1] – reliability of the difference in indicators in the dynamics of treatment;
[2] – reliability of the difference in indicators between groups.

oxygen therapy [14]. Min Jeong Jang et al. published the study, demonstrated role of oxygen therapy in respiratory syncytial virus infection and its protective role [15]. At the other, multicentre, randomised trial, was presented oxygen therapy at the young patients with pneumonia, lower respiratory tract infections, asthma or bronchiolitis. Non-invasive high-concentrated oxygen therapy has been used by clinicians to prevent escalation of care. Also, early non-invasive oxygen therapy therapy reduceds hospital length of stay and if this is cost-effective compared with standard treatment [16].

In earlier, double-blind, randomized study, was presented high efficacy of high concentrated oxygen for prevention of respiratory complications [17]. The authors used oxygen inhalation in patients with complicated acute respiratory viral infections in 73% of cases received a good effect, and the best results were in patients with acute respiratory failure on the background of acute respiratory viral infections. Similar results were obtained in our own study.

Sinha I.P. et al presented the study, included patients suffering from severe viral bronchiolitis, whom half of them received in addition to standard therapy the inhalation of highly concentrated oxygen. In the oxygen support group, the severity of bronchial obstruction was significantly lower; HR, RR, and the duration of hospital stay were also reduced [18]. Our study also noted an improvement in hemodynamics, a decrease in HR and RR, we have found the diminishing of terms in hospital stay when using inhaled highly concentrated oxygen with the addition of camomile aroma oil.

Greenblatt E.E. et al. [19], showed that the addition of concentrated oxygen inhalations to the standard treatment of severe asthma exacerbation with the development of respiratory acidosis leads to the resolution of acidosis and hypercapnia. The authors demonstrated a decrease in the severity of shortness of breath. Concentrated oxygen, reaching the respiratory part of the lungs, improves microcirculation with an increase in the number of leukocytes and an increase in their phagocytic activity. It should be noted that the study of Ramanathan G. et al. [20] showed the anti-inflammatory effect of oxygen and reduction of oxidative stress.

At the same time, in our own study it was found that 80% of patients hospitalized due to complications of acute respiratory viral infections have acute respiratory failure, and therefore need oxygen support. An alternative method of combined treatment with the inclusion of oxygen support can be the use of pocket cans of highly concentrated oxygen. In addition, the use of camomile aroma oil helps to optimize local immune defense in ARVI.

Despite a some arsenal of highly effective and safe antiviral drugs and antibacterial agents, clinical practice indicates that everywhere there are complications

of acute respiratory viral infections and worsening outcomes of community-acquired pneumonia. In 10% of cases in hospitalized patients, the disease acquires a life-threatening course. The use of non-drug treatment often can significantly increase the effectiveness of drug therapy. The physiological effects of pure oxygen, such as bronchodilatation, improved ventilation and perfusion of the lungs suggest that it may be an effective means of non-drug treatment of patients with complicated course of acute viral respiratory infections.

CONCLUSIONS

1. In virologic studies of nasopharyngeal swabs in patients with complicated forms of ARVI parainfluenza antigens were isolated in 30% of cases, adenovirus in 28.6%, respiratory syncytial virus in 22.8%, and rhinovirus in 18.6%.
2. Phenomenon of RF by the level of capillary blood saturation was detected in 80% of the examined: RF I-st degree was determined in 42.9% of patients, II degree I – in 31.4% of patients. A negative regression relationship was found between saturation of capillary blood, RR ($r=-0.31$; $p<0.05$) and HR ($r=-0.31$; $p<0.05$).
3. The use of highly concentrated oxygen with camomile oil in the inhalation treatment regimen significantly reduced the duration of local respiratory symptoms ($p<0.001$) and symptoms of general intoxication ($p<0.001$). With the inclusion of highly concentrated oxygen in the addition with of camomile aromatic oil in the complex treatment, the average long-term duration in the hospital decreased by an average of 5 days ($p<0.001$). Over 10 days of hospitalization, an increase in capillary blood saturation (SatO2,%) up to 95.2±2.91% in patients with I and II degrees of respiratory failure was noted in the same group.
4. The absolute therapeutic efficacy of the correction of respiratory failure during complex treatment with the addition of highly concentrated oxygen inhalations was 88.0% versus 57.0% in group 1. RE was 0.65 [0.46-0.90], OR = 0.19 [0.06-0.61], $p<0.05$.
5. A positive effect of inhalation of highly concentrated oxygen with the addition of camomile oil on the state of local immunity with a significant increase in the level of secretory immunoglobulin A ($p<0.001$) in saliva and lysozyme a level ($p<0.001$) was also noted.

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The Authors declare no conflict of interest.

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