European Journal of Clinical and Biomedical Sciences
2022; 8(1): 9-14
http://www.sciencepublishinggroup.com/j/ejcbs
doi: 10.11648/j.ejcbs.20220801.12
ISSN: 2575-4998 (Print); ISSN: 2575-5005 (Online)

Helium Physicochemical "Recruitment" of Pulmonary Alveols in Prevention of Alveolar Collapse and Prevention of Acute Respiratory Distress in Patients with COVID-19

Svistov Alexander Sergeevich[1, *], I. G. Mosyagin[2], Simakina Olga Evgenievna[3]

[1]Sergey Mironovich Kirov Military Medical Academy, St. Petersburg, Russia

[2]Main Command of the Navy, St. Petersburg, Russia

[3]Institute of Experimental Medicine, St. Petersburg, Russia

Email address:

pr.svistov@gmail.com (S. A. Sergeevich), r154ao@gmail.com (S. O. Evgenievna)

[*]Corresponding author

To cite this article:

Svistov Alexander Sergeevich, I. G. Mosyagin, Simakina Olga Evgenievna. Helium Physicochemical "Recruitment" of Pulmonary Alveols in Prevention of Alveolar Collapse and Prevention of Acute Respiratory Distress in Patients with COVID-19. *European Journal of Clinical and Biomedical Sciences.* Vol. 8, No. 1, 2022, pp. 9-14. doi: 10.11648/j.ejcbs.20220801.12

Received: December 18, 2021; **Accepted**: January 18, 2021; **Published**: March 23, 2022

Abstract: *Purpose*. Show value warmed up to 95°C. With helium (as part of thermogeliox) in reducing the surface tension water, including liquid and cellular fraction of blood, which normalizes the movement of erythrocytes in the capillaries and preserves the physiological function of the alveolar-capillary space, improving gas exchange in the alveoli. Materials and methods. The data of dynamics of complaints, anamnesis, clinical symptoms, results of laboratory and instrumental studies, results of pathological, pathomorphological and histological manifestations of severe coronavirus pneumonia (CVP) complicated by acute respiratory distress syndrome (ARDS) were analyzed. *Results and its discussion*. In the complex treatment of severe coronavirus infection (CVI), it is proposed to use the modern innovative medical technology "CIMT", which includes the modern device "Ingalit B2–01", inhaling regulated heated to 90–100 C respiratory gas mixture - thermogeliox, consisting of oxygen 20-30% and helium 70-80%, alternating with inhalation of the lungs surfactant with a nebulizer. It is advisable to inject the anticoagulant under the skin. It has been shown that the development of ARDS in CEP is associated with acute coronavirus alveolitis. A quick positive systemic therapeutic effect is the prevention of ARDS in patients with severe CEP when using our proposed "SIMT" is due to a number of physicochemical and physiological effects of thermal helium.

Keywords: Marine Medicine, COVID-19, Coronavirus Infection, Coronavirus Alveolitis, Alveolar Collapse, Modern Innovative Medical Technologies, Helium "Recruitment" of Pulmonary Alveoli

1. Introduction

Humanity is faced with a pandemic of COVID-19 coronavirus infection, a severe acute respiratory disease caused by the SARS-2019-nCoV2 coronavirus, often in the form of severe viral pneumonia, which is complicated by acute respiratory distress syndrome (ARDS) and respiratory failure with a high risk of death. The disease is caused by a new, constantly mutating virus against which humans have no acquired immunity. People of all ages are susceptible to infection. In about 15% of cases, the disease proceeds in a severe form with the use of oxygen therapy, in another 5% the condition of patients is critical. [1, 21].

According to the latest information from official online sources, as of October 12, 2020, the novel coronavirus COVID-19 continues to spread around the world1.

In many states of different continents of the world, the number of infected continues to grow2. In a number of countries, such as the USA, Brazil, India, Great Britain, Spain, Italy, etc., they talk about the second wave of CVI mutating coronavirus. Quarantine measures are re-introduced.

The current statistics on coronavirus as of 10/12/2020 (worldwide) according to Worl-dometers3 is presented in the table.

The dangerous coronavirus disease COVID-19 has affected

212 countries and territories around the world. Also, cases of the disease were recorded on two international cruise ships. In connection with the emergence of such a grave situation in March 2020, the World Health Organization declared the outbreak of coronavirus a global epidemic.

Target: show the value of helium heated to 95°C (as part of thermogeliox) in reducing the surface tension of water, including the liquid and cellular fraction of blood, which normalizes the movement of erythrocytes in capillaries and preserves the physiological function of the alveolar-capillary space, improving gas exchange in alveoli.

2. Materials and Methods

The data of dynamics of complaints, anamnesis, clinical symptoms, results of laboratory and instrumental studies, results of pathological, pathomorphological and histological manifestations of severe coronavirus pneumonia (CVP) complicated by acute respiratory distress syndrome (ARDS) were analyzed.

Table 1. *Coronavirus statistics.*

Indicator	Number of people, abs.
Total infections	37 806 667
Deaths	1 082 239
Recovered	28 384 322
They are sick now	8 340 106
Serious and critical cases and those currently ill	68 834

https://xn-80aesfpebagmfblc0a.xn-p1ai/(date of access: 12.10.2020).

https://www.bbc.com/russian/news-53365908 (date of access: 12.10.2020).

https://www.worldometers.info/coronavirus/(date accessed: 10/12/2020).

The virus is not well understood, there are no specific antiviral agents for the treatment or prevention of CVI, and there is no evidence of effective immunomodulatory treatment ([2], p. 1499-1500). Antibiotics against viruses are ineffective and are not used in treatment. However, they can be prescribed for prophylaxis and in case of detection of bacterial secondary infection ([3], p. 8-18). The most common and dangerous complication of acute coronavirus pneumonia is ARDS. It complicates the course from 15 to 33% of CVI ([4], p. 1334-1349).

Progressive respiratory failure is the leading cause of death in the SARS-CoV-2 pandemic. Despite the high interest in the pathophysiology of the disease, there is relatively little information on morphological and molecular changes in the lungs of patients who die from CVI.

The lack of new effective antivirals and other approved drugs for combating coronavirus leads to the use (off-label) of unlicensed treatments, i.e. use not according to instructions, but for a new purpose. Active scientific and clinical searches for new effective drug molecules, vaccines against coronavirus, new effective methods and methods of treatment are underway in the world. Our first clinical experience in the treatment of severe CEP using.

In April 2020, “CIMT” in 18 patients of the Republican Clinical Hospital of Syktyvkar showed that the heliox heated to 95°C acts rather quickly. After 15–20 minutes of inhalation, the patients noted an improvement in their physical condition, expressed in a decrease in shortness of breath, general weakness, pain in the throat and behind the breastbone, and cough. Clinical improvement occurred during the first inhalation (systemic effect) and persisted, gradually decreasing until the next procedure (aftereffect). The gas composition of the blood improved.

The therapeutic effect of modern "SIMT" at CVI is associated with the systemic effect of thermo-heliox on the patient's body. The experience gained in the treatment of CVI both in the hospital and on an outpatient basis and at home allowed us to improve the technology for the treatment of CVJ, which consists in alternating inhalations of Heliox heated to 95°C with the device "Ingalit B2-01" and pulmonary surfactant through a nebulizer, since simultaneous inhalation of Heliox and a surfactant warmed up to 95°C will cause a significant decrease in the heating temperature of Heliox, as well as disruption of the structure and function of the protein-lipid-polysaccharide complex of the pulmonary surfactant. An anticoagulant (Fraxiparine) is more effective when injected under the skin.

The pathogenesis of COVID-19 is not yet well understood. The opinions of scientists are contradictory; the universality of lung damage is emphasized, regardless of the primary damaging factor leading to ARDS ([5], p. 720-727). This indicates the absence of reliable, verified, repeatedly confirmed by the international scientific and clinical medical community of the mechanisms of systemic viral damage to the patient's body, both at the level of cellular biochemical processes, and at the organ and systemic levels. A number of scientists emphasize the importance of the universality of lung damage, regardless of the primary damaging factor leading to ARDS ([6], p. 435). The initial stage of the process is the activation of alveolar macrophages with the release of pro-inflammatory components, which includes a group of interleukins, including IL-6, -8, TNF-(tumor necrosis factor-alpha), a group of chemoattractants that stimulate the movement of neutrophils ([7], p. 377-394) from the blood through the endothelium and alveolar epithelium. This movement is facilitated by a systemic inflammatory response and an increase in vascular permeability ([8], p. 1137).

Another group of researchers believes that the level of IL-6, a key mediator for the cytokine release syndrome, is orders of magnitude lower than in severe cases of COVID-19. At the same time, the “cytokine storm” syndrome in the case of COVID-19 is quite unique, since the levels of ferritins and IL-6, although increased, are lower in comparison with other “cytokine storm” syndromes, and the lungs are primarily affected by kah ARDS. The syndrome of systemic inflammation is clearly different from other syndromes, and the consideration of the inflammatory process as a result of a “cytokine storm” may turn out to be incorrect ([9], p. 1152).

Some scholars believe that the lungs are not affected as a

result of a “cytokine storm”, but as a result of a direct viral cytopathic effect with damage to pneumocytes, which implies a direct cytopathic effect of the virus, and not an excessive inflammatory response. Corticosteroids could reduce inflammation, reducing subsequent lung damage. They have been used to treat infections with SARS-CoV and MERS-CoV, but studies have shown that they did not reduce mortality. The key mechanisms of multiple organ damage caused by SARS-CoV-2 infection are believed to be directly viral cytotoxicity. Viral particles can directly infect tissues and organs outside the lungs, however, the mechanism of the spread of SARS-CoV-2 in the body remains unclear ([10], p. 681-687).

The pathological picture, like most studies of CVI (COVID-19), is interpreted ambiguously by the scientific and clinical community.

Chinese doctors were the first to perform an autopsy of those who died from CVI, who described the pathological process in the lungs during COVID-2019. It turned out that the changes revealed in the lungs during CVI corresponded to those in pneumonia caused by the SARS and MERS viruses.

Pathomorphological features of lung involvement with viruses A H1N1, SARS-CoV1, SARS-CoV2 have a similar picture. Mainly in the exudative (early) stage, intraalveolar edema, accumulations fibrin, in a significant part of the cavities of the alveoli accumulation of erythrocytes, signs of interstitial inflammation. In the cells of the epithelium of the trachea and bronchi, viral particles can be found ([10], p. 681-687).

In a study conducted by German scientists with the support of the American National In- stitutes of Health, European Research Council Consolidator, the morphological and molecular changes in the lung parenchyma were compared in patients who died from COVID-19 and influenza A H1N1 in 2009. who died from ODN associated with COVID-19 or influenza A (H1N1), histologically the lung parenchyma looked like diffuse damage to the alveoli with perivascular infiltration of T cells. The lungs of those who died from CEP COVID-19 were characterized by pronounced endothelial damage. Histological analysis of pulmonary vessels in patients with COVID-19 showed widespread thrombosis with microangiopathy. Endothelial damage as a result of infection is accompanied by a local increase in von Willebrand factor and endotheliitis, which, in turn, leads to excessive production of thrombin, suppression of fibrinolysis and activation of the complement cascade and ultimately leads to the emergence of microthrombi and microcirculation disorders ([11], p. 906-918).

Summing up the results of the pathological examination.

According to the followings in China, Russia, Germany and other countries, it should be said that a similar morphological picture is described of lung damage by viruses A H1N1, SARS-Cov1, SARS-CoV2. In other words, infections caused by A H1N1, SARS-Cov1, COVID-19 viruses have a similar, if not uniform, pathogenesis.

It is believed that ARDS is characterized by diffuse alveolar damage ([12], p. 13-16). According to the modern concept, the term “diffuse alveolar injury” (DAP) is understood as a similar response of the lungs in acute injury of the airways of various etiologies. It is based on necrosis of endothelial, epithelial cells and alveolar interstitium, leading to collapse (collapse) of the alveoli. In addition, this condition is characterized by a decrease in pulmonary compliance (the usual requirement for mechanical ventilation) and hypoxemia, requires intensive therapy and various techniques of mechanical ventilation ([13], p. 61–78).

The causes of DAP as trauma (damage) can be aerosols of ammonia, nitrogen dioxide, herbicides, oxygen, zinc chloride, hydrogen sulfide, chemical warfare agents, phosgene and a number of drugs - amiodarone, nitrofurans, penicylamides, gold preparations, heroin and aero- sols - kerosene, herbicides, denatured rapeseed oil, etc.; radiation; surgical conditions - shocks: traumatic, hemorrhagic, neurogenic, cardiogenic, sepsis, acute massive aspiration, acute pancreatitis; burns of the lungs with poisoning by combustion products; transfusion therapy, air embolism; drowning; unknown reasons and many others ([13], p. 61–78; 14, p. 1334-1349). From the point of view of an incomplete list of etiological causes of development, the diagnosis of DAP corresponds to traumatic injury.

From the point of view of severe viral pneumonia, the cause of rapid progression, development of ARDS is an acute viral alveolitis. Viral pneumonia is an infection of the alveoli, due to which the alveolar space becomes clogged with a fluid consisting of exudate, desquamated cells and activated macrophages, which leads to disruption of gas exchange in the alveolar-capillary apparatus. The process of oxygen consumption from the hemoglobin of erythrocytes is disturbed, and carbon dioxide accumulates in the body ([14], p. 957).

According to most pathologists, pathomorphologists, histologists, pathomorphological ARDS corresponds to diffuse alveolar damage. However, first, the term “diffuse alveolar injury” is an unfortunate abbreviation, since the term “injury” is synonymous with the term “injury”. Violation of the anatomical integrity of tissues or organs resulting in a disorder of their functions.

Secondly, inflammation is a complex, local and general pathological process that arises in response to damage or the action of a pathogenic stimulus and manifests itself in reactions aimed at eliminating products, and, if possible, agents of damage and leading to maximum recovery in the area of inflammation. Inflammation is a protective and adaptive process.

The alveoli is a vesicle that opens into the lumen of the respiratory bronchioles. The alveoli carry out gas exchange with the pulmonary capillaries. Type 2 alveolocytes produce surfactant. The inner surface of the alveoli is covered with surfactant (C) - a surface-active complex of phospholipids, proteins and polysaccharides, which plays a major role in maintaining the architectonics of the alveolar-capillary bed and normal gas exchange. It is able to reduce the surface tension at the air/liquid interface from 72 mN to 20 mN, more than 3 times. The area of the alveolar-capillary surface is from 100 to 150 square meters.

In patients with ARDS, the lungs consist of an aeration surface and an alveolar collapse surface, which lead to intrapulmonary shunting and hypoxemia. Mechanical ventilation can increase the area of collapsed alveoli and potentially lead to atelectasis and lung damage. Standard ventilation volumes are 10-15 ml/kg. In ARDS, only the unaffected area of the lungs functions, that is, the lung capacity is reduced; therefore, large volumes of mechanical ventilation can cause lung damage combined into the concept of ventilator-associated lung injury ([15], p. 294-323).

An active scientific and clinical search for new effective methods, techniques and technologies both for the direct treatment of severe coronavirus infection and for prophylaxis is underway in the world. These include non-invasive ventilation of the lungs, high-flow oxygenation (gas flow rate up to 60 l/min), pronposition, recruitment of collapsed alveoli, hyperbaric oxygenation, etc.

Among the existing non-drug antiviral methods, techniques and technologies, our proposed innovative medical technology, the essence of which is described at the beginning of this article, has proven itself well. The use of this technology, based on the physicochemical properties of hot helium, makes it possible to physiologically recruit the pulmonary alveoli. This technology, in contrast to the recruitment of alveoli using a ventilator, is physiological, non-traumatic, does not cause complications (ventilator-associated lung injury) and solves two main tasks in the fight against CVI. These tasks are to block the replication of the COVID-19 virus and to destroy it.

The rapid therapeutic effect of helium in the composition of Thermogeliox (during the first inhalations) is more reliably associated with a decrease in alveolar edema, a decrease in the severity and area of alveolar inflammation, a decrease in the volume and viscosity of the fluid in the alveoli, which maintained normal gas exchange. These physiological features of helium are realized due to its unique physicochemical properties. Helium is a good penetrant, it has extremely high penetrating power and low density, moderate viscosity and high heat capacity, low solubility in fats and water. Due to the low density of helium, the movement of the Heliox flow will be laminar or less turbulent, and due to this, the alveoli will receive more air (oxygen). Carbon dioxide diffuses faster in the helium mixture, which means that it will be more actively removed from the alveoli. Helium in the heated oxygen-helium mixture increases the volumetric velocity of the gas mixture.

Despite the use of heated heliox in the complex treatment of diseases of the bronchopulmonary system for more than 10 years, active use in medical institutions of the Ministry of Health of Russia and the Ministry of Defense of Russia, this modern medical technology is not widely used in medical institutions. Thermogeliox, heated to 40°C, was used in the treatment of community-acquired pneumonia, chronic obstructive pulmonary disease and other pulmonary diseases ([16], p. 38–41). For blockade of replication and direct destruction of the SARS-CoV-2 virus, we use heliox heated to 90–95°C.

Surface tension (ST) is a thermodynamic characteristic of the interface between two phases in equilibrium. Force (mechanical) definition: surface tension is a force acting per unit length of a line that bounds the surface of a liquid. The surface tension at the liquid/gas interface increases with an increase in the interaction between liquid molecules ([17], p. 3-8).

In addition, it is necessary to take into account the physiological effects that changes in the PN of fluids in general and extra- and intracellular water have on the body in particular. These include dispersion (grinding, spraying) of solids and liquids into small particles or droplets, coalescence (coalescence of droplets or bubbles), coagulation (aggregation of dispersed phase particles). All of these phenomena are important for clinical medicine. Capillary phenomena are also explained by surface tension. Changes in surface tension forces affect phagocytosis (capture by cells of neighboring particles), pinocytosis (capture by the cell surface of fluid containing substances in it), and hence the dynamics of their excretion from the body. The phenomenon of adhesion (wetting) is of great importance. The magnitude of the surface tension is of diagnostic value in clinical practice. Usually, the surface tension of biological fluids is compared with water. Water has a high surface tension (72.5 mN/m) and a high viscosity (0.7 mPa). Water is a good solvent. In a living cell and in the intercellular space, solutions of various substances in water enter into interaction ([17], p. 3-8).

The surface tension of all fluids (extra- and intracellular water) decreases with increasing temperature ([18], p. 2528-2530; 19, p. 24-28). In addition, thermogeliox reduces the PN and viscosity of liquid and cellular blood fractions, and, accordingly, normalizes local and systemic blood flow in all organs and tissues of a patient with SARS-CoV-2. The surface tension of erythrocyte membranes and their suspensions is one of the most important components that determine the rheological properties of blood. Changes in the structure of cell membranes affect these interactions and is reflected in the surface tension of the suspension of erythrocytes. If the temperature and pH of the blood increase, this further affects the value of the surface tension, viscosity and fluidity of the blood ([20], p. 28-30).

With an increase in water temperature, its surface tension decreases, one Khadartsev A. A., Kireev S. S., Ivanov D. V. Possibilities of helium-oxygen therapy for pneumonia in coronavirus infection (literature review)//Bulletin of new medical technologies. Electronic edition. 2020. No. 3 [Khadartsev AA, Kireev SS, Ivanov DV Possibilities of helium-oxygen therapy for pneumonia in coronavirus infection (literature review). Journal of new medical technologies, eEdition, 2020, No. 3. doi: 10.24411/2075-4094-2020-16644 (In Russ.)]. The viscosity is. When the water temperature rises from 0 to 70°C, the surface tension of water decreases by 1.2 times. When the water temperature rises to 100°C, the surface tension of water decreases by 1.3 times.

In 2014, we conducted a study of microcirculation in healthy volunteers under conditions of hypoxic and hypercapnic exposure. The hemodynamic characteristics of

blood flow in the microvasculature and tissue blood flow were assessed. In healthy individuals in a hypoxic chamber filled with a respiratory gas mixture with a reduced concentration of oxygen and nitrogen, the addition of an inert gas argon to the respiratory mixture accelerated tissue microcirculation under conditions of hypoxia ([21], p. 13-16). Since argon and helium are inert gases, the results obtained can be extrapolated to oxygen-helium breathing mixtures.

3. Conclusion

We propose to differentiate the diagnosis of "diffuse alveolar damage" according to the etiological principle into surgical, toxicological, radiation, etc., and the defeat of the alveoli in severe viral diseases, such as acute viral infections, to formulate "acute diffuse viral alveolitis". Since the cause of damage to the alveolar apparatus in COVID-19 and other severe viral diseases is diffuse inflammation of all parts of the lungs, including the bronchi, parenchyma, and alveolar-capillary structure. In the complex treatment of severe coronavirus infection (CVI), we propose to use modern innovative medical technology, including the modern device "Ingalit B2-01", inhalation, adjustable heated to 90–100°C, respiratory gas mixture - thermogeliox (consisting of 20–30% oxygen and 70–80% helium), alternating with inhalation of pulmonary surfactant. It is advisable to inject the anticoagulant under the skin. There is a high probability that the simultaneous inhalation of Heliox and a surfactant warmed up to 95°C will inevitably cause a significant decrease in the temperature of the heating of heliox and disruption of the structure and function of the protein-lipid-polysaccharide complex of the pulmonary surfactant.

The use of this technology, based on the physicochemical properties of hot helium, allowing the physiological implementation of the "recruitment" of the pulmonary alveoli. This technology, in contrast to the recruitment of alveoli using a ventilator, is physiological, not traumatic, and does not cause complications.

One of the main mechanisms of blockade of replication and direct destruction of the SARS-CoV-2 virus by heliox heated to 95°C is a decrease in the surface tension of extra- and intracellular water, which leads to structural disruption and direct denaturation of viral envelope proteins, corona S-protein, capsid and ribosomes.

In addition, thermal heliox improves capillary blood flow and tissue microcirculation, which prevents hemic and histotoxic hypoxia and the development of acute respiratory failure, reduces the inflammatory process in the alveoli, maintains and accelerates blood flow in the alveolar-capillary space, preserving the function normal gas exchange.

The technology we offer for the prevention and treatment of CVI is technically simple to operate and quite effective. It is necessary to take into account the speed of deployment of devices in hospital and field conditions, the breadth of coverage of patients with one device. In addition, we can recommend using this technology for the prevention and treatment of massive outbreaks of coronavirus infection and seasonal influenza in large groups.

The proposed modern innovative medical technology is multifunctional, created at the intersection of physics, chemistry, physiology and medicine. The multifunctionality of the technology is that it can be used in the treatment of bronchopulmonary diseases, acute viral infections, as well as in primary hypothermia, thermal burns of the lungs and prevention of ARDS of various etiologies.

Conflict of Interest

Authors declared no conflict of interest.

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Biography

Svistov Alexander Sergeevich - Doctor of Medical Sciences, Professor, Honored Doctor of the Russian Federation, Senior Lecturer of the I Department of Advanced Training for Doctors of the Federal State Budgetary Military Educational Institution of Higher Education “Military Medical Academy named after S. M. Kirov ”of the Ministry of Defense of the Russian Federation; 194044, St. Petersburg, st. Academician Lebedev, 6; e-mail: pr.svistov@gmail.com; Mosyagin Igor Gennadievich - Doctor of Medical Sciences, Professor, Head of the Medical Service of the Main Command of the Navy; 190195, St. Petersburg, Admiralteisky proezd, 1.

Simakina Olga Evgenievna - Candidate of Biological Sciences, Researcher, Laboratory of Chronic Viral Infections, Department of Environmental Physiology, Federal State Budgetary Scientific Institution "Institute of Experimental Medicine", 197376, St. Petersburg, st. Academician Pavlova, 12.