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COVID-19: WHAT DRUG CAN BE USED TO TREAT A NEW CORONAVIRUS DISEASE AND WHY -

Review article

-Inhalation of warm aerosol with solvent of pus - a new vector for the treatment of pneumonia caused by COVID-19.

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ABSTRACT

It is shown that the distinctive feature of severe pneumonia in patients infected with COVID-19 is the maximum accumulation of pus and mucus in the alveoli, and bronchioles and bronchi. Pus and mucus completely fill the lumen of the respiratory tract, so the lungs are deprived of airiness. Pus and mucus squeeze air out of the respiratory tract and disrupt gas exchange in the lungs, which causes hypoxia and hypoxic damage to brain cells. It is shown that despite this feature of the pathogenesis of coronavirus disease, its treatment still does not provide effective dissolution and removal of thick pus and mucus from the respiratory tract. Such rapid dissolution and removal of pus from the lungs was not possible until a few years ago. But these days, this is already quite real, since a new group of medicines was recently discovered, called "Solvents of pus". The review lists patents for invented medicines and methods of their use for the purpose of dissolving and removing thick and sticky pus in various purulent diseases. It is indicated that in January 2020, an aerosol was invented for the inhalation of the original pus solvent, the use of which can dramatically change the effectiveness of saving the lives of patients infected with COVID-19. A prescription for a new drug is described in detail.

Key words: Coronavirus, pneumonia, SARS-CoV-2, COVID-19, new drugs, solvents of pus.

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INTRODUCTION

It was found that the cause of death of people with pneumonia caused by COVID-19 is hypoxic damage to brain cells. In turn, the cause of hypoxia is respiratory failure caused by pneumonia.

Coronaviruses cause respiratory pathology, and the disease usually has symptoms similar to other respiratory diseases that viruses cause. In addition to fever, the disease is manifested by coughing and shortness of breath. At the same time, the most reliable diagnostic signs of the disease are detected using lung radiographs, which show invasive lesions in the lungs. Often, the condition of patients requires their hospitalization due to the danger to their lives, because often the disease is complicated by respiratory failure, hypoxia and ends in death.[1]

The virus is highly homologous to the coronavirus (CoV) that caused an outbreak of severe acute respiratory syndrome (SARS) in 2003. Thus, it was named SARS-CoV-2 by the World Health Organization (WHO) on February 11, 2020. And the associated disease was named CoV Disease-19 (COVID-19)".[1] Soon WHO warns that COVID-19 is "***public enemy number 1***" and potentially more powerful than terrorism. [2]

The outbreak of COVID-19 caused by the novel virus SARS-CoV-2 started in the end of December 2019. In less than some months, it has spread all over China and now it covers almost the entire globe.[3]

Fever is often the major and initial symptom of COVID-19, which can be accompanied by no symptom or other symptoms such as dry cough, shortness of breath, muscle ache, dizziness, headache, sore throat, rhinorrhea, chest pain, diarrhea, nausea, and vomiting. Some patients experienced dyspnea and/or hypoxemia one week after the onset of the disease.[4] In severe cases, patients quickly progressed to develop acute respiratory syndrome, septic shock, metabolic acidosis, and coagulopathy.[5-7]

An important feature of this new disease is that abnormalities in chest radiography are found in most COVID-19 patients and featured by bilateral patchy shadows or ground glass opacity in the lungs. Patients often develop an atypical pneumonia, acute lung injury, and acute respiratory distress syndrome (ARDS).[8]

The main feature of the clinical course of this disease is that цhen ARDS happens, uncontrolled inflammation, fluid accumulation, and progressive fibrosis severely compromise the gas exchange. Therefore, the worst chest radiographic findings often parallel the most severe extent of the disease.[9]

However, the world still recognizes that due to the lack of experience with the novel CoV, physicians can mainly provide supportive care to COVID-19 patients.[3] Due to the lack of effective medications, doctors use various potential treatments for COVID-19 patients: These therapies include current and potential treatments with antiviral drugs, immune suppressants, steroids, plasma from recovered patients, Chinese medicine, and psychological support. [10]

The search for medicines for coronavirus disease follows the traditional path. In particular, pharmaceutical companies are racing to develop antibodies and vaccines against the virus.[11,12]

Most researchers and doctors agree that SARS-CoV-2 mainly attacks the lungs in the beginning and probably also attacks, to a lesser degree, other organs that express ACE2, such as the gastrointestinal system and the kidneys. Nevertheless, respiratory dysfunction and failure are the major threat to the patients and the major cause of death. Thus, respiratory support is critical to relieve the symptoms and save lives and includes general oxygen therapy, high-flow oxygen, noninvasive ventilation, and invasive mechanical ventilation depending on the severity of the disease. Patients with severe respiratory symptoms have to be supported by extracorporeal membrane oxygenation (ECMO), a modified cardiopulmonary bypass technique used for the treatment of life-threatening cardiac or respiratory failure.[3]

Therefore, we can conclude that there is no effective antiviral therapy for patients with COVID-19.[3,12] Unfortunately, there are no proven effective specific treatment strategies and the risk-benefit ratio for commonly used treatments such as corticosteroids is unclear.[12] There is no doubt that COVID-19 is associated with severe disease that requires intensive care in approximately 5% of proven infections.[13] There is currently a wide mortality range, from 22% to 62% in the early Hubei province case series.[15,16] The exact cause of death is unclear at this point, with progressive hypoxia and multiorgan dysfunction being the presumed causes.[15] The principal feature of patients with severe disease is the development of ARDS: a syndrome characterized by acute onset of hypoxemic respiratory failure with bilateral infiltrates.[14]

It is possible that if the lives of patients with pneumonia caused by COVID-19 and secondary infection are threatened, the arsenal of drugs used can be expanded by another promising group of drugs that no one has yet suggested using. We are talking about a group of antiseptics designed specifically for rapid dissolution and removal of thick sticky pus.[17]

The fact is that in patients with COVID-19, respiratory failure in pneumonia develops due to the accumulation of mucus and pus in the alveoli and in the lumen of the bronchioles and bronchi. Such a complication is very clearly visible in computed tomography of the lungs in patients with COVID-19. In addition, the condition of patients can worsen obstructive bronchitis, which can often also be caused by the presence of thick pus and thick mucus in the lumen of the bronchi and bronchioles. It is shown that in such patients, it is difficult to ventilate the lungs, and patients are not able to independently remove thick pus and thick mucus from the lumen of the respiratory tract.[18]

At the same time, traditional means and methods of treatment of purulent diseases do not provide rapid dissolution and removal of thick pus.[17]

We assume that hypoxia in patients with COVID-19 is caused by filling the Airways with thick pus and thick mucus. A direct confirmation of this is the results obtained by analyzing x-ray images of patients ' lungs, performed in patients with a confirmed diagnosis of COVID-19 infection and suffering from pneumonia with severe pulmonary insufficiency. Indirect confirmation of this statement is

the low effectiveness in eliminating hypoxia with forced ventilation of the lungs with respiratory gases with oxygen in patients with COVID-19.

We also believe that the low effectiveness of treatment of patients with pneumonia caused by COVID-19 is due to the lack of "Solvents of pus" and technologies for their use in the complex therapy of pneumonia complicated by respiratory failure and hypoxia in patients with COVID-19. In our opinion, pus and mucus fill all the Airways in the lungs, remain in the lumen of the alveoli and bronchioles, do not move out and do not free the Airways for gas exchange, despite the treatment being carried out precisely because of the lack of pus solvents in the therapy of patients.

We will touch on the history of treatment of purulent diseases and the discovery of drugs-pus solvents. This is paradoxical, but official medicine and pharmacology still do not allocate a separate group of drugs that quickly dissolve thick pus.[19] Therefore, for the treatment of purulent diseases, conventional antiseptic and disinfectants are used. Mainly used solutions that have a decontaminating effect. In addition to this group of drugs, sometimes try to remove pus using warm water and plasma-substituting liquids. These medicines are used for topical use. Usually, open purulent foci and wounds are irrigated with solutions of these funds through such procedures as baths, dressings and compresses.[20]

The disinfecting activity of traditional solutions of antiseptics and disinfectants is not in doubt. However, conventional remedies and conventional technologies for their use in the treatment of purulent diseases do not provide rapid dissolution and removal of thick pus from purulent wounds and cavities.[21] Moreover, despite the repeated use of these drugs, thick pus often remains in its place for a long time.[22,23] An example of low anti-purulent effectiveness of traditional antiseptics is a very weak and slow dissolution and removal of thick pus in tuberculosis empyema of the pleura, in which traditional drugs and technologies for their use are not able to remove thick pus from the pleural cavity earlier than 6-8 months of course treatmentя.[24]

It was found out that today in the treatment of purulent diseases, decontaminating agents are used that have a detrimental effect on all forms of life, but no means are used that dissolve thick purulent masses.[25] It is shown that throughout its history, humanity has been continuously searching for effective remedies for "pus". But it was only recently that were able to open these drugs. The priority of the discovery of pus solvents belongs to Russia and is confirmed by patents for invented medicines and methods of their application, which provide emergency dissolution of thick and sticky pus, as well as sulfur plugs, tear stones and even milk curd. It turned out that the main ingredients of pus solvents are water, drinking soda (sodium hydrocarbonate) and hydrogen peroxide. This group of drugs is called "Solvents of pus". It was found that the most effective and safe pus solvents are solutions of 2-4% sodium hydrocarbonate and 0.5-3% hydrogen peroxide at a temperature of +42 °C.[25]

It is established that solvents of thick pus are warm water solutions with moderate alkaline, hyperosmotic,

oxidative and pronounced boiling activity. When locally interacting with pus, they cause alkaline saponification of protein-lipid complexes in it, and pus due to the catalase enzyme "includes" the release of oxygen gas from hydrogen peroxide in solutions, which provides solutions with a biochemical softening of thick pus, rapid introduction into the purulent mass and physical destruction of its monolithic structure due to intra-tissue cold boiling due to the rapid release of gas bubbles.[17,26,27]

It is shown that the cardinal difference between the formulation of drugs that dilute thick pus, thick mucus and sulfur plugs, from the formulation of medicines of all other pharmacological groups, is as follows. The invented pus solvents are a warm (at a temperature above +37 °C) solution of sodium hydrocarbonate (preferably a saturated solution), which contains hydrogen peroxide in a concentration of up to 3% and a gas (carbon dioxide, oxygen or inert gases such as helium and argon under excessive pressure.[25]

Here is a list of developed pus solvents and new technologies for their use in chronological order up to 2018:

«Method of treatment of long-term non-healing wounds» (RU Patent 2187287);

«Method of treatment of empyema of the pleura by N.S.Strelkov» (RU Patent 2308894);

«Multifunctional solution for epibulbar instillations» (RU Patent 2452478);

«Uterine lavage technique» (RU Patent 2327471);

«Agent for fistula sanitation in infected pancrenecrosis» (RU Patent 2455010);

«Softening agent for thick and viscous pus» (RU Patent 2360685);

«Method and means for removal of sulphur plug» (RU Patent 2468776);

«Method for peritoneal dialysis using gasified solution» (RU Patent 2336833);

«Hyper-gassed and hyper-osmotic antiseptic mixture» (RU Patent 2331441).

In addition to these inventions the following inventions were created in 2018 and 2019: *«Bleaching cleanser of dentures» (RU Patent 2659952) and «Method to use a solution for removing plaque using an irrigator» (RU Application N 2019118503.14.06.2019).*

In this case, an original solution was proposed in the form of a bleaching agent for cleaning teeth and dentures. That whitening denture cleaner is an aqueous solution heated to +37 - +42 °C, which includes 2.0-10.0 % sodium hydrocarbonate, 3 ± 0.3 % hydrogen peroxide and oxygen gas to create an overpressure of 0.2 ATM. at +8 ° C.

The original method of using this solution or solution, which includes 2.0-10.0% sodium hydrocarbonate, 2.7 – 3.3% hydrogen peroxide, water for injection and argon gas at an equilibrium pressure of 3-4 ATM, is as follows. The solution is first aerated, then immediately placed in a hermetically sealed container of a household irrigator and heated to a temperature of +43 - +65 °C.

It is shown that such a gazatted solution bleaches and cleans the surface of teeth and dentures with high speed and efficiency due to hyperthermic softening, alkaline saponification, oxidative bleaching, cavitation

loosening, flotation and suspension. The solution has the ability to quickly diffuse into the thickness of dental plaque, blood spots and pus clots, destroy inter-protein and protein-lipid bonds in them, transform hemoglobin and its remains into a soluble form, discolor the remains of blood and pus, remove them from the surface of the dental prosthesis without aggressive action on its surface and the oral mucosa.[28]

The discovery of this group of drugs suggests that pus-dissolving drugs may be effective for restoring airway patency and eliminating hypoxia in pneumonia caused by COVID-19, since it is with the help of pus-dissolving agents that thick pus and thick mucus with blood veins can be quickly dissolved and removed from the lumen of the airway bronchi to the outside. The fact is that in essence, the expulsion of purulent masses from the respiratory tract with the help of solvents of pus is an analogy to sanitizing purulent fistulas, cavities and wounds. Therefore, it is very likely that pus solvents can quickly dissolve the thick pus and thick mucus in the respiratory tract and facilitate the removal of pus and mucus outside. This will free up the airways, which will again become free for breathing gases, which will facilitate breathing, increase the delivery of oxygen to the alveoli of the lungs, and increase the efficiency of gas exchange.

In order to quickly dissolve and remove thick pus and thick mucus from the bronchioles and alveoli, and not just from the bronchi, another invention was developed. It is most suitable for the treatment of patients with pneumonia caused by COVID-19. We are talking about the following invention: "*Aerosol for inhalation in obstructive bronchitis" (RU Application N 2020100533. 09.01.2020).*

The essence of the proposed aerosol for inhalation, designed to dissolve and expectorate thick pus and thick mucus in pneumonia and obstructive purulent bronchitis in order to facilitate breathing and eliminate hypoxia in resuscitation patients, providing the size of microparticles in the range of 0.5 - 2 microns by dispersed spraying of liquids using ultrasonic, compression and jet inhalers and nebulizers, is that as medicines are used the next components at the following ratio (wt. %):

Sodium hydrocarbonate-1,2;
Hydrogen peroxide-0.3-0.5;
Lidocaine hydrochloride-0.5;
Distilled water-the rest, at a pH of 8.5, osmotic activity of 280-300 mosmol/l of water and a local temperature of + 41 - + 55 °C.

Introduction to the solution of 1.2% sodium hydrocarbonate provides the creation of an alkaline buffer solution at pH 8.5 and provide safe for patients alkaline saponification of protein and protein-lipid complexes in the lumen of the bronchi, which is the basis of dissolution of thick pus and thick mucus and subsequent facilitate expectoration them out.

The presence of lidocaine hydrochloride in the declared solution at a concentration of 0.5% is explained by the fact that this concentration value is the minimum in the officially recognized range of concentrations that provide effective terminal anesthesia of this local anesthetic.

The presence of 0.3 - 0.5% hydrogen peroxide in an aqueous solution, which

has antiseptic activity, provides sterility to the claimed agent and an antiseptic effect on the lumen of the bronchi. Therefore, the declared aerosol excludes infection during inhalation.

The stated temperature range of the aerosol for inhalation is 41-55 °C is optimal for local hyperthermia, which is necessary for maximum acceleration of the speed of chemical and physical-chemical processes in the interaction of aerosol microparticles with protein and protein-lipid complexes of pus and mucus according to the Arrhenius law. The fact that the lower range of 41 °C due to the possible presence of a temperature in a patient with fever, and the upper limit temperature of the inhaled vapor 55 °C proved safety steam in the Turkish bath Hamam at this temperature and not above it.

When inhaling hot aerosol with microparticles of 0.5 – 2 microns in size, they are very deep inside the lumen of the bronchi, regardless of their obstruction and the presence of pus and mucus, namely, up to the places of complete blockage and/or up to the alveoli. Therefore, aerosol microparticles settle on the entire surface of pus and mucus covering the trachea and bronchi throughout, and interact with these biological masses, dissolving them due to alkaline saponification and loosening them due to cold boiling due to the release of oxygen gas as a result of catalase splitting of hydrogen peroxide. The fact is that pus and blood contain the enzyme catalase. Moreover, in addition to the specified pharmacological activity, the declared aerosol has a bleaching activity, namely, the ability to discolor traces and blood spots. The discoloring activity is explained by the bleaching effect of hydrogen peroxide, which is associated with hemolysis of red blood cells and with the destruction of light-absorbing double bonds inside the colored pigments of hemoglobin and its metabolites.[28,29]

In our opinion, the developed aerosol can be used for emergency dissolution and loosening of thick masses of pus and mucus for expectorating them outwards in order to facilitate breathing, increase the lumen of the bronchi and eliminate hypoxia in resuscitation patients with pneumonia caused by COVID-19. To do this, the aerosol should be used by inhalation.

It is shown that the declared aerosol in a few seconds after the beginning of inhalation almost completely loosens and dissolves thick pus and thick mucus in the lowest parts of the bronchi and reaches the surface of the bronchial mucosa. Between the lower layer of dense biological mass and the surface of the bronchi, the claimed aerosol also causes a cold boiling process. In this case, moderate formation of oxygen gas bubbles is accompanied by the penetration of lidocaine hydrochloride deep into the bronchial mucosa, which causes terminal anesthesia, prevents the local irritating effect of the aerosol and the cold boiling process. The formation of oxygen gas bubbles between the surface of the bronchi and the lower layer of the mass of pus and/or mucus gently separates this biomass from the surface of the bronchi and provides an effective and safe expectorant effect.

Thus, COVID-19 is the cause of filling the alveoli, bronchioles and bronchi with thick pus and thick mucus. In patients

infected with coronavirus, thick pus and mucus do not expectorate, so they prevent gas exchange in the lungs, reduce the effectiveness of respiratory mixtures and initiate hypoxia. At the same time, the applied complex of medical measures does not provide for the inhalation use of medicines-solvents of thick pus and mucus. However, in recent years and months, medicines have been invented that can very quickly dissolve and remove thick pus and thick mucus from the respiratory tract. It is shown that a new group of medicines was discovered in Russia and was named "Solvents of pus".

It is expected that the most suitable solvent of pus and mucus in the respiratory tract for pneumonia caused by COVID-19 may be an aerosol that is prepared from a solution containing 2-4% sodium hydrocarbonate and 0.5-3% hydrogen peroxide (additionally, it may contain 0.5% lidocaine hydrophochloride) and is administered by inhalation at a temperature of + 41-55 °C.

Conclusion

Progressive increase in thick pus and thick mucus in the alveoli, bronchioles and bronchi, observed in patients with pneumonia caused by COVID-19, plays an important role in inhibiting gas exchange in the lungs, in the development of hypoxia and in reducing the effectiveness of traditional resuscitation measures. It is possible that the use of an aerosol for inhalation, which includes a new group of drugs, namely, a solvent of thick pus, can break this vicious circle and reduce the mortality of patients with coronavirus infection. However, in order to make this proposal completely clear, various specialists must be involved. But, the inhalation of a warm aerosol with a solvent of pus that has an antiseptic effect is a realistic goal that can be achieved in the near future, and advances in this area can reduce the danger of coronavirus infection.

The motive that led the authors to this study.

Unfortunately, the coronavirus is still invincible. Within a few months, he had conquered almost the entire planet. And the disappointing experience of fighting COVID-19 in Italy, Spain, and the United States of America made the Russian government take the likelihood of a pandemic of COVID-19 very seriously. To do this, our country followed the example of China and closed the entry of foreigners into our country, as well as restricted the entry of Russian citizens. At the same time, on April 1, 2020, most of the country's residents were sent on vacation for a week, and then all schoolchildren, students of technical schools and universities switched to distance learning. At the same time, all citizens over the age of 65 were sent to self-isolation and were issued sick leave. At the same time, on April 1, 2020, all public events were canceled, and an emergency health assessment was organized for all passengers at airports and railway stations. The health care system has been rebuilt along the lines of China. In particular, infectious diseases hospitals with the necessary equipment and medical personnel have already been prepared in each region. Finally, a ban on free movement in the country, including localities, has been issued.

In particular, a few months ago, one of the co-authors of this article had major problems with respiratory failure due to

the difficulty of expectorating pus and mucus. And there are no known medicines and methods of treatment did not improve the condition. Therefore, we decided to apply our knowledge and experience in creating new medicines and developed an aerosol for inhalation. Co-author Natalia Urakova was the first patient to test this product on herself and evaluate its effectiveness. We very much hope that our information will help scientists and patients in the fight against COVID-19.

Conflict of interest: None declared.

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