



Review Article

COVID-19: Cause of death and medications

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ABSTRACT

It is shown that in patients with severe pneumonia with COVID-19, the lungs lose their airiness, as pus and mucus completely fill the lumen of their Airways. Gas exchange in the lungs stops. This is the cause of hypoxia and death of patients with a new coronavirus disease. Since it is not yet possible to quickly restore the airiness of the lungs of patients with severe acute respiratory distress (SARS), many die if extracorporeal membrane oxygenation (ECMO) is not used. It is shown that this procedure is very complex and expensive, so it is not available to everyone. In addition, ECMO may not always be applied in a timely manner. As an alternative to ECMO, an easy, cheap and publicly available method of extrapulmonary oxygenation is offered using a solution of hydrogen peroxide, which can be administered internally as a beverage carbonated with oxygen, and in the form of injections in the "right place". In the review of the listed patents invented drugs and their formulations. The role of all ingredients is described in detail.

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1. Introduction

A new coronavirus disease (COVID-19) has been shown to be life-threatening to patients due to an unusual pneumonia that makes the lungs airless.¹ Computed tomography of the lungs reveals that in patients with coronavirus pneumonia, the lungs look like "frosted glass".² Therefore, the bilateral distribution of ground glass opacities (GGO) with or without consolidation in the posterior and peripheral lungs is pinned by the COVID-19 diagnostic symptom.¹ In turn, an airless lung becomes an obstacle to gas exchange and causes hypoxia.³ Besides it, cause of hypoxia in patients with COVID-19 is bronchial inflammation and bronchial obstruction.⁴ The fact is that with atypical pneumonia and obstructive bronchitis, mucus and pus displace air from the alveoli, bronchioles and bronchi. Therefore, the lungs of a patient with COVID-19 lose their airiness and patients develop severe acute respiratory syndrome (SARS) - that

is the clinical essence of a new infectious disease.^{4,5} At the same time, hypoxia in patients is not eliminated even with artificial ventilation of their lungs with respiratory gases with oxygen. Today it is generally accepted that only extracorporeal membrane oxygenation (ECMO) and a modified method of artificial blood circulation can save the life of patients with severe SARS.⁶

However it was recently proposed for the first time previously it was proposed to restore the airiness of the lungs in patients with the new coronavirus disease COVID-19 by inhaling an aerosol with hydrogen peroxide and sodium hydrocarbonate.⁷ It has been shown that this antiseptic is a drug from a new group of drugs called "Solvents of pus".⁸ And this aerosol is able to quickly dissolve thick pus and thick mucus in the respiratory tract at obstructive bronchitis. But this drug and its method of application have not yet passed clinical trials and are not included in the standard treatment of pneumonia and obstructive bronchitis caused by the new coronavirus

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disease COVID-19.

In these conditions, there is only one permitted method to eliminate hypoxia and save patient from death at COVID-19 - this is extrapulmonary (extracorporeal) blood oxygenation. However, traditional extracorporeal blood oxygenation is a very complex and expensive procedure. The fact is that to save the life of such a patient, this procedure must be applied around the clock for 5-7 days. At the same time, ECMO costs from 5,000 to 10,000 dollars per day.⁹ It was shown a large variation in the common cost of ECMO over multiple cost categories (e.g., range of total in-hospital costs of treatment: USD 42,554-537,554 [in 2013 values]).

So extracorporeal blood oxygenation can not be performed for all patients. In this regard, in situations where extracorporeal blood oxygenation cannot be applied, and hypoxia really threatens the life of the patient with pneumonia and obstructive bronchitis caused by COVID-19, we suggest using another method of blood oxygenation. We are talking about a new way to saturate the blood with oxygen without gas of oxygen, namely, using hydrogen peroxide.¹⁰⁻¹²

In our opinion, it is time to expand the arsenal of extrapulmonary blood oxygenation. In particular, an alternative method of blood oxygenation is absolutely necessary for situations where it is urgently necessary to prolong the life of a patient with hypoxia for several tens of minutes, but it is not possible to urgently connect the patient to ECMO. Such alternative method of blood oxygenation in critically period of time will allow to deliver the patient alive to a special surgical department, where can then use standard oxygenation procedure ECMO. To do this, it is very important that this alternative method is very simple, cheap, and publicly available.

It is assumed that the basis of an alternative method of extrapulmonary blood oxygenation in people when saving their lives in critical situations may lie in the introduction of a solution of hydrogen peroxide inside or by injection in the "right place".^{13,14} It is shown, that hydrogen peroxide can compete with oxygen gas during resuscitation in critical situations.¹⁵

The role of hydrogen peroxide at hypoxia was first shown in experiments with aquarium fish, which we were used to study the dynamics of their motor activity in acute hypoxia in order to identify analogies with the dynamics of fetuses motor activity in pregnant women at acute intrauterine hypoxia.^{10,11,16} As a result of these studies, it was found for the first time that the dynamics of motor activity of adult aquarium fish and fetuses of pregnant women in the second half of pregnancy in conditions of acute hypoxia are similar to each other. The results showed that the known antihypoxants do not prolong the life of fish in acute hypoxia, and hydrogen peroxide at a dose of 0.2 ml/kg of fish weight, introduced once into the water in which the fish swims, extends the period of keeping fish alive in hypoxia

by an average of 2.0 times, similar to a decrease in water temperature by 10 °C.

In parallel series of experiments, it was found that repeated periodic introduction of hydrogen peroxide in a "therapeutic dose" in water with aquarium fish that experience hypoxia, several times extends the life of fish without atmospheric air entering this water. At the same time, increasing the dose of peroxide in the water to excessive values kills fish.^{11,15} These results about the fantastic efficiency of hydrogen peroxide in hypoxia formed the basis of the invention «Method of maintenance of live fish during transportation and storage» (RU Patent. 2563151).¹⁷

Then experiments using hydrogen peroxide to save the life of aquarium fish in acute hypoxia were continued, but in these experiments, a solution of hydrogen peroxide was introduced not into the water in which the fish swim, but into the stomach cavity of the fish or intramuscularly (inside the skeletal muscle of the tail). The results showed that preliminary intragastric administration of hydrogen peroxide can be used for extrapulmonary oxygenation of fish blood in conditions of acute hypoxia!^{13,18}

After that, the parameters of the Stange functional test were monitored in adult healthy volunteers. In the first series, they drank drinking water half an hour before the test, and in the second series, half an hour before the test, they drank a similar volume of a solution of hydrogen peroxide, an oxygen-rich gas at an excess pressure of 0.2 ATM. It turned out that hydrogen peroxide with gas oxygen increases the values of the Stange functional test by 10%. The obtained results allowed us to conclude that the introduction of a solution of hydrogen peroxide with gaseous oxygen into the human stomach at excessive pressure can become an independent method of treating respiratory failure and / or saving people's lives in hypoxia. This method of oxygenating the blood has been called "intragastric blood oxygenation".¹³

Around the same time period, experiments were conducted with donor blood, which was injected with a solution of hydrogen peroxide without oxygen gas. The results showed that hydrogen peroxide can saturate the blood with oxygen. Such research was continued and soon an invention was created «E.M. Soikher's hyperoxygenated agent for venous oxygen saturation» (RU Patent 2538662). According to this patent, a solution of 0.85% sodium chloride, 0.1% sodium bicarbonate and 0.05-0.29% hydrogen peroxide was proposed for injection into donor blood (which is venous and therefore devoid of oxygen) in order to saturate its red blood cells with oxygen and turn venous blood into arterial blood without introducing oxygen gas into the blood.¹²

Thus, in 2015, Russia patented the first liquid drug, which is a solution of hydrogen peroxide, which effectively replaces the gas oxygen. For the first time, it was shown that the blood of fish and humans can be oxygenated by

injection into the muscle or blood, or by entered into the stomach. That is, for the first time, alternative methods of extrapulmonary blood oxygenation were convincingly demonstrated. The antihypoxic effect of hydrogen peroxide was explained by formation of oxyhemoglobin in red blood cells of venous blood.¹⁹

In 2016, the Russian Federation issued a patent for «Agent for increasing resistance to hypoxia» (RU Patent. 2604129).²⁰ This agent is a drink from drinking water, which contains 0.3-0.5% hydrogen peroxide and oxygen gas at an excess pressure of 0.2 ATM at a temperature of +8 °C. After ingestion, it increases the body's resistance to hypoxia in conditions of respiratory failure due to additional involvement in gas exchange of the gastric mucosa and intragastric oxygen supply to the blood.

And in 2016, the Russian Federation issued a patent for another invention, namely “Lympho-substitute for local maintaining viability of organs and tissues in hypoxia and ischemia” (RU Patent 2586292).²¹ Invention refers to medicine and pharmacy and is intended for emergency provision of organs and tissues with oxygen and glucose to preserve their viability under conditions of hypoxia and ischemia. Lympho-substituent agent for interstitial injections includes (wt%):

Sodium chloride – 0.88

Glucose - 0.06-0.1

Hydrogen peroxide - 0.01-0.02

Bidistilled water for injection at a pH of 7.4 - remaining part with osmotic activity 280 mosmole/l of water.

It is shown that the developed lympho-substitute can be used for emergency local energy supply of organs and tissues in hypoxia and ischemia by injection in conditions where it is otherwise impossible to ensure the delivery of oxygen and glucose to these parts of our body. In particular, in hypoxia resulting from massive blood loss and hemorrhagic shock, the solution is administered by intravenous or intraarterial injection into venous or arterial blood (respectively) for blood plasma oxygenation and acts as a plasma-substituting fluid; in case of brain hypoxia resulting from injury to the carotid arteries and the skull, the solution is injected into the cerebral cortex by intracranial injection and/or into the ventricles of the brain by intraventricular injection through traumatic cracks, gunshot injuries and trepanation holes in the skull; in case of myocardial ischemia resulting from thrombosis and/or atherosclerosis of the coronary arteries, the solution is introduced by intracardial injection directly into the ischemic area of the heart muscle etc.¹⁴

Then in 2017, the Russian Federation issued a patent for “Means for physical endurance increase” (RU Patent. 2634271).²¹ This agent is intended for a backup increase in resistance to physical work at the limit of physiological capabilities. The agent is a drink made from drinking water that contains:

Glucose - 7%

Hydrogen peroxide - 3%

Gas oxygen at create excess pressure 0,2 AM at +8°C.

It is shown that when taken orally, this drink provides the supply of water, oxygen and glucose to the blood, has a detoxifying effect, prevents dehydration, hypoxia, hypoglycemia, promotes the release of carbon dioxide and lactic acid from the circulating blood to the stomach and intestines, provides the cells of the cerebral cortex and skeletal muscles with oxygen and glucose, increases physical endurance and optimizes the conscious performance of intensive physical work when the adaptation reserves are depleted.

Finally, in 2018, the Russian Federation issued a patent for an “Energy drink” (RU Patent 2639493).²² This energy drink is sterile, it is prepared on water for injection and is intended for introduction into the stomach of children. The ingredients are contained in it at the following ratio of components, (mac. %):

Glucose - 7

Ethyl alcohol - 0,7

Hydrogen peroxide - 0,3-0,5

Citric acid - before reaching pH 4,0±0,5

Oxygen gas - under excessive pressure 0,2 AM at +8 °C

Water for injection - remaining part.

It is shown that the developed energy drink can be introduced inside as a food, energy-providing, antihypoxic, plasma-substituting, warming, detoxifying and tonic. The fact is that the presence of 7% glucose in it corresponds to the maximum glucose content in normal milk and ensures the supply of a natural amount of glucose to the body, which eliminates glucose poisoning and the development of hyperglycemic coma. The presence of 0.7% ethyl alcohol corresponds to the normal composition of sour milk and kefir. This excludes the development of alcohol intoxication, but provides a warming effect and an increase in the child's body temperature when hypothermia. And the presence of 0.3-0.5% hydrogen peroxide provides effective blood oxygenation in the portal vein pool without gas embolism of the veins and eliminates the formation of foam inside the stomach.

In turn, carbonation of the solution with oxygen gas at an excess pressure of 0.2 ATM at +8° C corresponds to an effective and safe level of industrial carbonation of food beverages. At the same time, oxygen gas increases intragastric blood oxygenation.

2. Conclusion

Patients with the new coronavirus disease covid-19 often develop atypical pneumonia, in which the lungs lose their airiness. In this case, the Airways are filled with pus and mucus, so the gas exchange in the lungs is reduced to critical values. Hypoxia develops. In these conditions, traditional resuscitation measures become ineffective. Only

extracorporeal membrane oxygenation can save people's lives. However, this procedure is very expensive and complex. It cannot be applied to everyone in need. In this regard, as an alternative, it is proposed to draw the attention of researchers to the possibility of extrapulmonary oxygenation using a solution of hydrogen peroxide, which can be introduced into the stomach and/or in the form of injections in the "right place". It is assumed that this method can prolong the life of patients with SARS, buy time to attract additional opportunities and transport the patient to a specialized Department for the purpose of applying ECMO, which will reduce the mortality of patients with coronavirus infection. However, in order to make this proposal fully clear and develop publicly available effective methods of extrapulmonary oxygenation, it is necessary to involve specialists of various specialties. But the use of a solution of hydrogen peroxide for resorptive action in order to combat hypoxia is really way of fight against mortality from coronavirus disease.

3. Conflict of Interest

None.

4. Source of Funding

None.

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