International Journal of Biomedicine 11(2) (2021) 177-180
http://dx.doi.org/10.21103/Article11(2)_CR1

CASE REPORT

INTERNATIONAL JOURNAL OF BIOMEDICINE

The Experience of Surfactant Therapy in Severe COVID-19 Pneumonia: A Case Report

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Abstract

The COVID-19 pandemic has presented challenges to finding effective treatment for lung damage. Medical researchers from different countries recognize the deficiency of pulmonary surfactant (PS) as a significant cause of the alveolar collapse, followed by microatelectasis and severe disturbances in the ventilation-perfusion relationship. Due to the pathophysiological rationale, experimental confirmations, and accumulated clinical experience, the PS preparations can be used to treat patients with severe COVID-19. The article provides a description of a case when surfactant therapy was successfully used in a patient with severe COVID-19 pneumonia.(**International Journal of Biomedicine. 2021;11(2):177-180.**)

Key Words: COVID-19 • pneumonia • pulmonary surfactant

For citation: Banin IN, Budnevsky AV, Grechkin VI, Ovsyannikov ES, Tokmachev RE, Neznamov OD, Savushkina IA. The Experience of Surfactant Therapy in Severe COVID-19 Pneumonia: A Case Report. International Journal of Biomedicine. 2021;11(2):177-180. doi:10.21103/Article11(2)_CR1

Abbreviations

ARDS, acute respiratory distress syndrome; **BP**, blood pressure, **BT**, blood test; **CT**, computed tomography; **GP,** general practitioner; **HR**, heart rate; **PS**, pulmonary surfactant; **RR**, respiratory rate.

Introduction

In 2019, SARS-CoV-2, a new RNA virus of the genus Betacoronavirus of the family Coronaviridae, was discovered. The disease caused by this virus has been designated by the World Health Organization (WHO) as Coronavirus Disease 2019 (COVID-19). The first case was officially registered in Wuhan, China, in December 2019, and on January 30, 2020, the SARS-CoV-2 outbreak was declared an emergency of international concern. Due to the rapid spread and high contagiousness, the WHO labeled COVID-19 a global pandemic on March 11, 2020. According to the WHO, by March 19, 2021, more than 120.9 million cases had been confirmed worldwide, with more than 2.67 million deaths and more than 91 million patients recovered.

Unfortunately, both etiotropic and pathogenetic pharmacotherapies did not prove their efficacy for the treatment of lung damage and other complications of the disease caused by SARS-CoV-2. This is confirmed by frequent, sometimes multidirectional changes in treatment tactics, none of which has received sufficient recognition in accordance with the provisions of evidence-based medicine. It has been found that type II alveolocytes are one of the many targets for the SARS-

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CoV-2 virus. Their deaths are accompanied by a pronounced decrease in the PS synthesis.[1] Medical researchers from different countries recognize the PS deficiency as a significant cause of alveolar collapse, followed by microatelectasis and severe disturbances in the ventilation-perfusion relationship. Besides maintaining the surface tension of alveoli, surfactant activates alveolar macrophages. This physiological mechanism prevents the spread of secondary bacterial infection.

The secondary PS deficiency in the pathogenesis of severe pneumonia and ARDS caused by influenza A/H1N1 was the reason for the experimental use of PS in complex therapy.[2] The pathogenetic substantiation of surfactant therapy for ARDS in influenza A/H1N1 was the reason for attempts at clinical use of various PS preparations during the 2009-2010 epidemic. In these small studies, positive results were obtained: the use of PS preparations improved gas exchange even in patients with critical hypoxemia and allowed avoidance of extracorporeal membrane oxygenation.[3] PS preparations can be used in different medicinal forms: an aerosol through an inhaler or intrabronchially by an endoscope. These preparations work as the patient's own surfactant, which is not produced in an appropriate amount due to damage to type II alveolocytes.

The pathophysiological rationale, experimental confirmations, and accumulated clinical experience served as the basis for an attempt to use PS preparations in the treatment of patients with severe COVID-19. During the COVID-19 pandemic, PS preparations were used to treat patients with severe COVID-19 in the Almazov National Medical Research Centre, the Federal Research and Clinical Center of Physical-Chemical Medicine of the Federal Medical Biological Agency, the I.M. Sechenov First Moscow State Medical University Hospital, and the Perinatal Medical Centre in Tyumen.[4] The analysis of 120 cases of the use of PS preparations showed a decrease in mortality from 80% to 14.3% among patients with severe COVID-19.[5]

Voronezh Clinical Emergency Hospital #1 has been working in the context of the COVID-19 pandemic since March 2020. Clinical experience in the diagnosis and treatment of patients with COVID-19 has been accumulated during this period. We present our experience of using a PS preparation in the treatment of a patient with COVID-19.

Case Presentation

A 47-year-old man, on May 25, 2020, felt sudden nasal congestion and a mild sore throat. During the first day, the symptoms were relieved by the use of a vasoconstrictor and herbal lozenges to reduce the sore throat. He did not seek medical attention. However, five days later (May 30), he felt worse: weakness, a rare unproductive cough, and a feeling of heaviness in the chest appeared; the body temperature increased up to 37.8°C (100.04°F).

Anamnesis vitae

The patient has an active lifestyle, being an amateur athlete who regularly trains at least 2 times a week, undergoes an examination by a GP on a yearly basis. Bad habits and chronic diseases were not registered. The patient denies having any allergic, oncological, or other chronic diseases. According to data from the patient's medical record, BP–125/75 mmHg, HR–56-58 bpm, RR–14-16 rpm, SpO_2–99-100%.

On June 1, 2020, the patient visited a GP. He was prescribed outpatient treatment according to a document developed by an interdisciplinary working group of experts based on Russian and foreign clinical experience – temporary guidelines "Prevention, diagnosis, and treatment of new coronavirus infection (COVID-19)," version 6, relevant at the time of seeking medical help. Standard laboratory tests were performed: clinical BT, biochemical BT, PCR tests for SARS-CoV-2. A positive result of the PCR test was obtained on June 6, 2020. According to the recommendations given by the GP, the patient was taking umifenovir 200 mg 4 times a day, josamycin 500 mg twice a day, ambroxol 30 mg 3 times a day, paracetamol 500 mg.

On June 6, 2020, the patient deteriorated. Exertional dyspnea, weakness, fever, and sweating intensified, the duration of attacks of unproductive paroxysmal cough increased, and therefore he called a specialized ambulance team and was delivered to the Voronezh City Clinical Emergency Hospital #1 with a referral diagnosis of "Coronavirus disease verified by PCR test. Severe community-acquired pneumonia."

Clinical Findings and Diagnostic Assessment

The patient's general condition upon admission to the hospital was characterized as severe. He showed signs of inhibited consciousness and his answers to questions were monosyllabic. The body temperature was 37.8°C (100.04°F).

The results of external examination are the following: the patient had moist and pale skin, cyanosis of the lips. No visible changes of the chest. There was a slight soreness of the intercostal muscles on palpation. RR–28 rpm. Vesicular breathing, weakened; no wheezing in the lungs. No visible changes of the heart area. The apical impulse was in the fifth intercostal space, 1.5 cm medially to the left mid-clavicular line. HR–110 bpm, BP–110/70 mmHg. Heart sounds were muffled, rhythmic. The tongue was dry; the abdomen had a normal shape and was soft and painless on palpation. The liver was not enlarged. Respiratory function was reduced. SpO_2 was 92%-93% breathing with atmospheric air. Laboratory study results are presented in Table 1 (June 7, 2020).

On June 6, 2020, a CT of the chest showed polysegmental pneumonia typical for COVID-19 in both lungs parenchyma, multiple zones of ground-glass opacity merging with each other of peribronchial and subpleural locations. There were more than 3 zones with a maximum diameter of over 5 cm. Lung lesion was about 70%.

Treatment

The patient received hydroxychloroquine 400mg twice on the first day, followed by 200 mg twice a day for the next 6 days, azithromycin 500 mg intravenously for 7 days, direct-acting anticoagulants (Enoxaparin 40 mg a day subcutaneously), and oxygen therapy. Over the next 4 days, despite the ongoing therapy, the patient's condition worsened: dyspnea increased and SpO_2 decreased to 88% in spite of the continuous humidified oxygen therapy. Non-invasive

ventilation in prone positioning was initiated in order to relieve respiratory failure. Considering progressive respiratory failure, therapy was amplified by lopinavir+ritonavir (400mg+100mg) twice a day, interferon beta-1b according to the scheme; methylprednisolone 1000mg for 3 days; ampicillin+sulbactam 3.0g twice a day intravenously followed by meropenem 1.0g three times a day; dalteparin sodium 5000 IU subcutaneously; parenteral nutrition based on combinations of dextrose, potassium chloride, calcium chloride, magnesium chloride, sodium chloride, and malic acid; ascorbic acid 10.0g a day intravenously. However, this therapy was not effective. Dyspnea increased, laboratory parameters reflecting the progression of the systemic inflammatory response were getting worse (high levels of C-reactive protein, ferritin, lactate dehydrogenase by July 13, 2020). Considering these facts and the increased risk of ARDS development, it was decided to add tocilizumab 400 mg by a single intravenous drip infusion.

Table 1.

Dynamics of laboratory and instrumental tests

Parameters	06.07.20	07.13.20	07.18.20	09.03.20
Erythrocytes, $\times10^{12}$/l	5.49	4.8	4.6	3.2
Haemoglobin, mg/l	154	139	134	120
Leukocytes, $\times10^{9}$/l	2.8	11.5	8.9	6.8
Band neutrophils, %	7	10	6	2
Segmented neutrophils, %	68	70	68	64
Lymphocytes, %	21	16	19	25
Eosinophils, %	1	0	0	1
Monocytes, %	3	4	7	8
Thrombocytes, $\times10^{9}$/l	162	150	147	280
CRP, mg/l	197	207	35	10
Ferritin, μg/l	755	1308	1100	255
LDH, U/l	310	360	280	200
SpO2, %	92-93	80-82	83-85	95-96

CRP – C-reactive protein, LDH – lactate dehydrogenase, SpO_2 – oxygen saturation

In the following days, a weak positive change in the patient's condition was noted: normalization of body temperature, a slight decrease in levels of CRP and LDH. However, the low level of oxygen saturation remained for a long time, causing the prolongation of non-invasive ventilation for 76 days. A significant improvement in the patient's condition (dyspnea decreased, SpO_2 increased to 95%-96%) was achieved by double endoscopic endobronchial injection of PS preparation (Poractant Alfa 1.5 ml [120 mg]) into both lungs within 2 days.

Subsequently, stable positive clinical and laboratory dynamics were observed (Table 1). Size reduction of the consolidation areas and ground-glass opacity zones was noted after repeating the CT of the chest on August 31, 2020. There were 2 zones with a maximum diameter over 1.5 cm; lung lesion was under 10%. Subpleural areas of pulmonary fibrosis were found in both lungs. The patient was discharged on the 91st day with two negative SARS-CoV-2 PCR test results.

Discussion

At this moment, the preventive prescription of etiotropic and pathogenetic therapy, until the development of a complete symptom complex and life-threatening conditions, is the main approach, which is based on our one-year experience in managing patients with COVID-19. Several medicines are used in the treatment of COVID-19: favipiravir, remdesivir, umifenovir, interferon-alpha. Clinical studies of the efficacy and safety of targeted drugs in patients with severe or critical COVID-19 are also ongoing. Macrophage activation syndrome (MAS), a form of secondary hemophagocytic lymphohistiocytosis, in COVID-19 is a result of massive uncontrolled activation of the immune system provoked by acute viral infection. Considering this fact, patients should be given immunosuppressive therapy along with symptomatic and etiotropic therapy in the majority of cases to suppress the hyperactivation of the immune system.

However, the lack of effective etiotropic and pathogenetic pharmacotherapy of diseases caused by the SARS-CoV-2 virus led the world medical scientific community to search for ways of treatment using medicines that had previously demonstrated their pathogenetic efficiency. Thus, it is known from previous studies that surfactant therapy for ARDS in influenza A/H1N1 improved gas exchange in patients with hypoxemia. In connection with the damage to type II alveolocytes caused by the SARS-CoV-2 virus and a pronounced decrease of PS synthesis, surfactant therapy can be one of the pathogenetically justified ways of treating COVID-19 patients. The administration of PS preparations is likely to reduce the risk of alveolar collapse and disturbances in the ventilation-perfusion relations, and it also prevents the spread of secondary bacterial infection, which decreases the chance of long-course antibiotic therapy.

Conclusion

This clinical case clearly demonstrates that the therapy for patients with COVID-19 is an extremely complex, dynamically changing process. The management of such patients requires constant monitoring, timely laboratory testing, and an adequate response from medical personnel. The surfactant therapy used to treat the patient with severe SARS-CoV-2-virus-induced pneumonia made it possible to stabilize his condition, improve the ventilation-perfusion ratio, and avoid switching to invasive ventilation. Thus, the presence of secondary PS deficiency in the COVID-19 pathogenesis, as well as surfactant therapy for the disease, is an urgent topic for further research.

Competing Interests

The authors declare that they have no competing interests.

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