Looking for effective ways to treat COVID-19 patients.
Perspectives of using a medical device of low-intensity VHF-UHF therapy BIOL in complex treatment.

(analytical background document)

In the current pandemic associated with the spread of the SARS-CoV-2 virus, there is an urgent need to help patients with COVID-19, both during treatment and during the next recovering period. According to the latest statement of Infectious Diseases Society of America (IDSA), there is currently insufficient evidence to recommend any particular medication or therapeutic methods for the treatment of COVID-19[1]. During epidemics like the current COVID-19 pandemic, when there are no clinically proven treatments, the tendency is to use drugs based on in vitro antiviral activity, or on anti-inflammatory effects or based on limited observational studies. Although there were also the cases that the medications supposed to be effective based on in vitro studies and observational studies for other diseases were later proven to be ineffective in clinical trials for the new cases.[2]

One of the critical and unresolved problems associated with the impact of the SARS-CoV-2 virus on the human body is the formation of fibrous tissues, primarily in the lungs, but other organs can be supposedly affected too. According to the statement of the Pulmonary Fibrosis Foundation of the USA, patients who are infected with COVID-19 may develop pneumonia and progress to severe respiratory failure, termed Acute Respiratory Distress Syndrome (ARDS), which requires life support with a mechanical ventilator. In a subset of those COVID-19 ARDS survivors, lung fibrosis develops. Unlike pulmonary fibrosis that occurs in interstitial lung disease (ILD) having chronic and progressive in nature, post-ARDS fibrosis typically is not progressive but nonetheless can be severe and limiting. The recovery period for post-ARDS fibrosis is approximately one year and the residual deficits persist, but generally do not progress. According to the data available, the Foundation states that at this time, there is no known cure for pulmonary fibrosis regardless of its cause.[4]

At the same time, the treatment of patients with ARDS is a challenge for health care professionals. There are experimental and clinical studies proving that mechanical ventilation, which is necessary for life support in patients with acute respiratory distress syndrome, can cause lung fibrosis, which may significantly contribute to morbidity and mortality[7]. Therefore, scientists and practitioners are looking for ways to address these conflicting challenges. Together with studies on the processes of fibrotic tissues formation at the cellular level and the methods of the process' regulation, techniques based on the physical and physiological features of the lungs during the disease period are introduced. They do not solve the problem of all patients with ARDS, but give a chance for recovery and protect against the formation of fibrosis in the lungs to some of them, and thus reduce the mortality rate of ARDS. For example, the US has developed and implemented a specific patient positioning technique that is used in ICU for those connected to mechanical ventilators. (5Guidance For: Prone Positioning in Adult Critical Care). It is confirmed that such a position, used instead of supine one, makes it possible to reduce the number and severity of ARDS complications.

In order to find useful and economically effective methods of treating patients with COVID-19, as well as to prevent known complications, the working group of doctors, including Tsvyr Olena, Chikurova Alla and Tsvyr Dmitro, developed a complex method of effective treatment of the patients infected with SARS-CoV-2. The proposed method of treatment showed consistently positive results for the selected group of patients, characterized by fast (12-20 hours) elimination of symptoms and complete recovery within the next two weeks.

The treatment complex included medications:
- intramuscular injections of recombinant human interferon α-2b (Laferobion 3 0000 0000 or Laferon) - twice daily for patients with fever and once daily for others;
- broad-spectrum antibiotic (Azithromycin 500mg),
- if required, hormonal therapy (Dexamethasone), drugs to reduce fever, anticoagulants were added according to the patient's condition

and **long-term** irradiation of patients with a **low-intensity UHF-VHF therapy device BIOL**, namely, the first 24-72 hours the device was used continuously during the day and night with short breaks; in the following days the time of exposure was reduced to 12 hours a day.[6]

Note: Dexamethasone may be useful for the short-term in severe, intubated, COVID-19 patients, but could be outright dangerous during recovery since the virus will not only persist, but the body will be prevented from generating protective antibodies.
Instead, a pulse of intravenous dexamethasone may be followed by administration of nebulized triamcinolone to concentrate in the lungs only.

Main outcomes: after the first day of treatment, there was an evident positive dynamics, manifested in the decrease of temperature and a reduction of airway spasms. The course of treatment was 7-10 days. All patients were discharged from the hospital.
Briefly about the device: The device of low-intensity UHF-VHF therapy BIOL is intended for modulation of the patient's immune system, prevention of fibrosis, treatment and prevention of diseases of a viral nature, shortening the postoperative rehabilitation period and relieving pain.

Manufacturer of the device: Limited Liability Company "**BIOPROMIN**" (Kharkiv, Ukraine – State Reg. No 32947837)

The company production facilities are certified according to EN ISO 13485: 2016 by the authorized national certification body, SE "Ukrainian Medical Center of Certification" of the Ministry of Health of Ukraine (certificate №041 dated 29.12.2018), and by the authorized certification body in Europe TUV NORD (certificate No.AC090 MD / 1944 / 4983/2020 dated 02-04-2020).

The device BIOL has been certified in Ukraine since 2010 and complies with the requirements of the current Medical Device Technical Regulation approved by CMU Resolution No. 753 (Confirmation Certificate No. U.A.TR.039.065, updated 02/20/2020).
European certification was in 2012 (CE certificate No.5-628-500-0911 from 2012-06-20).
The device BIOL is included into the State Register of Medical Equipment and Medical Devices of Ukraine: Certificate №8900 / 2009, order № 1163, date of order: 15.09.2014 (Link)

Indications for use according to the IFU:
The device is intended for modulation of the patient's immune system, treatment and prevention of diseases of a viral nature, shortening the postoperative rehabilitation period and relieving pain, preventing fibrosis, treatment of pathologies of the prostate gland. It is recommended for use in complex therapy of diseases under the supervision of a medical care professional.
Individual use of the device is recommended as prescribed by a physician, who determines the duration and number of sessions, as well as controls the course of treatment using clinical analysis data and patient diagnosis results.

Recommendations for use of the BIOL device for hospitalized and infected patients with the SARS-CoV-2 virus.
After analyzing existing data and available information regarding patients infected with the SARS-CoV-2 virus, it was determined that the most harm done to the patients was severe inflammation, which was caused by the corona virus. This hyperinflammation caused by COVID-19, known as the "cytokine storm", requires the use of corticosteroids to prevent deterioration to a very severe form of acute respiratory distress syndrome (Acute Respiratory Distress Syndrome (ARDS)), and also requires the use of drugs that reduce high blood coagulation indicators. Improving the effectiveness of treatment is also achieved by intravenous administration of large doses of ascorbic acid (high-dose intravenous ascorbic acid). Thus, the combined use of drugs and the BIOL device can achieve a sharp reduction in the need for artificial lung ventilation. Additionally, the use of the BIOL device favourably affects the expansion of the blood vessels of patients, increasing the flow of oxygen to the cells, which improves the effectiveness of the drugs. The use of drugs in conjunction with the BIOL device should be performed before the intensive care unit ICU. The use of drugs based on the active substance bovhyaluronidase azoximer in combination with the BIOL device should prevent the occurrence of fibrous tissues, or significantly reduce their amount.

TO CONTROL INFLAMMATION & EXCESS CLOTTING
In all COVID-19 hospitalized patients, the therapeutic focus must be placed on early intervention utilizing powerful, evidence-based therapies to counteract:
—The overwhelming and damaging inflammatory response
—The systemic and severe hyper-coagulable state causing organ damage
By initiating the protocol within 6 hours of presentation in the emergency room, the need for mechanical ventilators and ICU beds will decrease dramatically.

Recommended monitoring when using the BIOL device:
A predictor of the severe course of the disease (for patients infected with SARS-CoV-2 coronavirus) is an increased value of the **suPAR** protein (soluble urokinase Plasminogen Activator Receptor) **≥ 6 ng / ml**.
Thus, when using the BIOL device, we recommend monitoring the amount of suPAR protein in the blood of patients. A decrease in suPAR9 levels to normal values gives a positive prognosis of patient survival.
In the course of treatment, it is necessary to monitor such indicators: **LDH, hs-CRP, Lymphocyte, D-dimer.**
If the following indicators meet the following requirements (**LDH<365 U/l**, **hs-CRP<41.2 md/l**, **Lymphocyte>14.7%**)[17], then the prognosis for patients will be positive.

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