

APPLICATION OF METHYLENE BLUE IN THE TREATMENT OF COVID-19

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In 2009, in the intensive care unit of the Central City Clinical Hospital of Almaty, due to the ineffectiveness of the methods of treatment of patients with atypical pneumonia that existed at that time, we developed our own method of treatment, which consisted of intravenous administration of methylene blue (MB) solution at a dose of 2 mg / kg of body weight followed by irradiation of the blood or body of patients with ultraviolet light.

Four patients with severe lung injury and who were on mechanical ventilation were treated. After the treatment, all 4 patients were discharged with recovery. These data have not been published.

The basis for the development of this method of treatment at that time was the technology of inactivation of viruses in donor blood components (plasma, platelets) "Macopharma", which is based on the use of methylene blue solution.

Methylene blue belongs to the group of phenothiazine base dyes. Dyes of this class are able to penetrate into the structure of viral nucleic acids and firmly bind to DNA / RNA guanosine residues. This stops the replication of the virus and its spread throughout the body.

Methylene blue has been used successfully in medicine for many decades, mainly as a local antiseptic, acting on bacteria, viruses and fungi. It is also used parenterally (intravenously) as an antidote for many acute poisoning, heparin overdose, as an antimalarial drug, for sepsis, etc. The drug in the used dose has practically no side and toxic effects.

To date, it has been proven that MS effectively acts on CoV-2 during inactivation of donor plasma in vitro (<https://www.researchsquare.com/article/rs-17718/v1>).

Also, when reviewing the literature, there are recent publications on the theoretical substantiation of the use of MB as an antiviral drug, observation of cancer patients who had contact with infected CoV-2 who received MS infusions and subsequently none of them contracted coronavirus infection.

In May 2020. With the onset of a sharp surge in morbidity, due to the lack of drugs for etiological treatment, MB began to be used in the "off-label" mode for patients with signs of CVI who agreed to use it. The treatment was carried out on an outpatient basis.

The criteria for prescribing MB were clinical signs of intoxication, intoxication in combination with signs of pneumonia and respiratory failure. The duration of the disease was no more than 10 days (from 4 to 10). All patients underwent infusion of MB solution at the rate of 2 mg / kg of body weight once a day, for three days in a row, in physiological sodium chloride solution or 5% glucose solution.

All observed patients showed regression of all symptoms by 2-4 days after the start of treatment. None of them were subsequently admitted to hospitals.

According to approximate data, about 3,000 people of different ages have undergone treatment. Directly observed treatment was carried out in 76 patients. Of these, the virus was identified in 27 people. CT examination - 14 of them with signs of specific lesions of the lungs, CT1-2.

Clinically interesting cases.

A 30-year-old patient (resuscitator) with a mild course of the disease. CVI was confirmed by PCR. After 16 days from the onset of the disease PCR positive, IgM 1.7; IgG 6.5. An infusion of MS was carried out for 2 days, after which the tests were repeated - PCR negative, IgM 0.9, IgG7.3.



Spouses 55 and 58 years old, have been ill for more than 3 weeks, PCR positive on the 7th day of the disease, CT picture is specific, CT2 in both. Symptoms of intoxication, low-grade fever, and cough persist. On the 26th day, the control PCR was positive in both, IgM 3.7 / 3.5, IgG 6.5 / 7. An infusion of MB was carried out for 1 day, then for 2 days, the drug was taken orally at 100 mg 3 times a day. After that, the tests were repeated - PCR was negative in both, IgM decreased by about 2 times, IgG remained at the same level.

Patient 46 years old (doctor), had had CVI in May 2020. In mild form, PCR has been confirmed. Re-ill at the beginning of October 2020. - symptoms of general intoxication, hyperthermia, cough. PCR positive, on CT - specific changes, CT2. Treatment with remdesivir was started together with MB. The dynamics of the state is positive, there is no temperature after the first MB infusion. PCR negative 4 days after the start of MB treatment.

There are also observations on the use of methylene blue in a clinic in patients with COVID-19 upon admission to the ICU and in need of oxygen therapy. When used during the first week from the onset of the disease, in addition to improving well-being and reducing dependence on oxygen, positive dynamics were noted in the analyzes - an increase in the level of lymphocytes, a decrease in CRP and ferritin.

When using methylene blue in patients on mechanical ventilation with severe lung damage (CT3-4) and with a disease duration of more than 2 weeks, no clinical or laboratory effect was observed.

Conclusion.

A solution of methylene blue (MB) has a proven efficacy against the SARS-CoV-2 virus in vitro and is used to inactivate blood components.

When used in patients with proven or suspected coronavirus infection at the initial stage of the disease, MB has shown clinical and laboratory efficacy as an etiotropic drug.

When used in patients with already severe lung damage, the effectiveness of MB was not noted.

Taking into account the absence of side effects, MB can be recommended for etiotropic therapy for COVID-19 in the early stages of the disease in the off-label mode.