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Considerations regarding the use of CytoSorb as adjuvant therapy in patients with Covid-19/ novel Coronavirus (Sars-CoV-2) infections

The purpose of this document is to illustrate the rationale and the possibilities of using CytoSorb therapy as an adjuvant therapy in the treatment of some complications in patients with severe COVID-19 infection, in order to respond to the requests received regarding the possible application of this therapy in the above mentioned patients.

General aspects

- The virus infects the respiratory epithelium of the lower airways, causing widespread damage via cytopathic effects, resulting in severe inflammation and pneumonitis. [1]
- In more than 20% of COVID-19 patients, an exacerbated inflammatory response, expressed through a "cytokine storm", can lead to a "capillary leak syndrome", determining a state of respiratory insufficiency, which may rapidly evolve into ARDS (Acute Respiratory Distress Syndrome) and other complications, with the consequent need for hospitalization in ICU. [1, 2] In particular, among the patients treated in ICU, the incidence of ARDS is 61%, while the other complications may be: shock (30%), acute heart damage (22%) and acute renal failure (8.3%). [2]
- As a sepsis-like syndrome and multi organ dysfunction might frequently occur due to the virus itself or to a superimposed bacterial infection, so that extracorporeal organ support therapies should be considered, such as dialytic therapies and hemoperfusion. [3] Among these, there is also a CytoSorb therapy, designed to remove cytokines and other circulating mediators from the blood.
- In addition, the clinical picture could be aggravated by the iatrogenic effects of the therapeutical systems used, ECMO in particular, capable of inducing and maintaining an excessive inflammatory response through various mechanisms [4, 10-11].

Criteria / Clinical features for the use of CytoSorb therapy in patients with 2019 nCoV:

CytoSorb could be used as adjunctive therapy, not as a primary therapy

Based on current clinical data CytoSorb therapy has shown its ability to rapidly stabilize hemodynamic with profound vasopressor reduction. Moreover, the therapy has even been associated with a substantial reduction of mortality in patients with refractory septic shock, on the basis of different clinical cases, retrospective and prospective studies. Additionally, first publications about to the successful use of CytoSorb therapy in viral infections such as influenza are available. [4-9]

In patients with 2019 nCoV, CytoSorb Therapy should be considered in case of:

- Profound vasoplegia with elevated levels of lactate and high need for vasopressors (e.g. NE > 0.3 µg/kg/min) not responding to standard therapy, with combined indication for /running (continuous)

renal replacement therapy (C)RRT. In this case, CytoSorb therapy should started within the first 6 to maximum 24 hrs after start of standard therapy.

- Very severe respiratory distress syndrome, such as indication for prone positioning to ensure adequate oxygenation under mechanical ventilation with combined indication for /running (continuous) renal replacement therapy (C)RRT. [10].
- Indication for use of ECMO/ECLS therapy. [4, 10-11]

General Indications for CytoSorb therapy

The guidelines for the use of the CytoSorb Therapy are available on the request of the clinicians, who remain the only responsible for prescribing the treatment. In addition, the support service is constantly available to discuss all the technical and usage problems.

For these types of patients, it is generally advisable to replace the first sorbent after 12 hours. Subsequently, the duration of treatment and the replacement of the sorbent should be decided on the basis of the clinical course (e.g. degree of hemodynamic instability, lung dysfunction), and the type of treatment used. The maximum treatment time per sorbent is 24 hours.

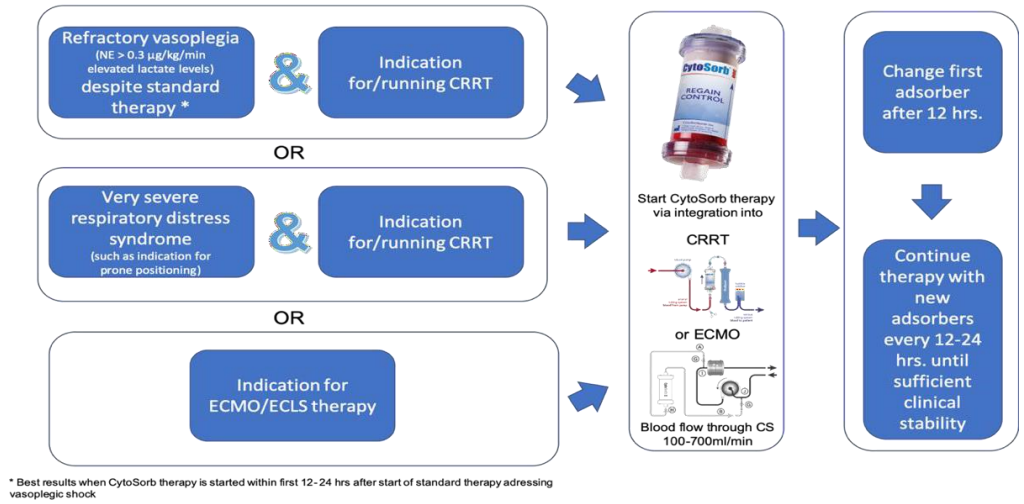
Anticoagulation should be effective from the start of treatment with no special adaptations of any anticoagulant protocol are necessary. The specifications and operational requirements of the manufacturer of the system on which CytoSorb is used should be respected.

The usual contraindications for extracorporeal blood circuits should be applied and the instructions contained in the CytoSorb IFU followed.

Remarks:

A further remark on the use of CytoSorb concerns data on the impact of this sorbent therapy on antibiotics and antiviral drugs. While studies on the adsorption of various types of antibiotics are available, data on plasma levels of antiviral drugs are still scarce to date. The results of animal studies indicate a low sorbent removal of Ganciclovir and anecdotal reports on CytoSorb therapy in patients with influenza treated with Oseltamivir (Tamiflu) did not state any abnormalities indicating relevant removal by CytoSorb.

In principle, however, it is always advisable to choose a dosage for antiviral and / or antibiotic therapy at the upper limit of the recommended range and to perform therapeutic drug monitoring.



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