LITERATURE-SERVICE 10 | 20

Dear ladies and gentlemen, dear ADVOS users and interested parties,
we are pleased to present you another issue of our ADVOS Literature Service. We regularly select one or more papers from international journals which might be of interest to you in connection with our ADVOS procedure. This month we have selected the following:

EXTRACORPOREAL MULTIORGAN SUPPORT INCLUDING CO_2-REMOVAL WITH THE ADVANCED ORGAN SUPPORT (ADVOS) SYSTEM FOR COVID-19: A CASE REPORT.

Huber et al.

Key message

The ADVOS treatment was able to remove up to 86 ml/min CO_2 using a specially designed bicarbonate free concentrate at blood flows between 200-300 ml/min using regional citrate anticoagulation. The case report of Huber et al. showed that the ADVOS therapy (Advanced Organ Support) could be a good treatment option in COVID-19 patients suffering from multi organ failure (MOF) because it is less invasive (e.g. conventional dialysis catheters, 10-times lower blood flow than ECMO, absence of gas phase).

Background

The new coronavirus (SARS-CoV-2) can cause respiratory, intestinal, hepatic and neuronal diseases leading to acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), and death in severe cases. Most COVID-19 patients have moderate symptoms and recover quickly, but some need intensive care. The mortality rate of COVID-19 patients who require mechanical ventilation is high.

Here the authors report the case of an 80-year-old man suffering from COVID-19 and progressive ARDS and MOF with oliguria, septic shock, hepatic dysfunction and mixed acidosis with a SOFA score of 13. The potential use of the ADVOS multi device for renal and hepatic support, CO_2 elimination and the control of the acid-base balance at low blood flows was discussed.

Case Report

The 80-year-old COVID-19 patient was admitted to the ICU due to ARDS and respiratory acidosis. He did not respond to standard medical treatment consisting of mechanical ventilation and prone positioning. This developed into MOF with renal, circulatory and hepatic involvement (Figure 1). 24 hours after admission, the patient developed atrial fibrillation. Prof. Dr. Huber and his team started the ADVOS treatment based on the indication for hepatic failure, mixed acidosis and renal replacement therapy. There was interdisciplinary consensus not to initiate ECMO due to old-age, prolonged ventilation, and MOF (respiratory, renal, circulatory hepatic failure and thrombocytopenia) with a SOFA-score >10.

Eight 24-hour ADVOS sessions with regional citrate anticoagulation were performed (clotting occurred only in 1 of the 8 sessions). Optimization of the arterial pCO_2 and the pH was attempted by adapting the device settings to the actual need of the patient (e.g. dialysate pH ≥8.5, blood flow ≥200 ml/min and alkaline concentrate with reduced bicarbonate). In addition, continuous ultrafiltration was performed with the ADVOS device to reduce pulmonary edema.

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During the first 24 hours acidosis was corrected (pH 7.30 vs. 7.19 at baseline). Additionally, $PaCO_2$ and HCO_3^- levels improved. When a dialysate without bicarbonate was used, more CO_2 was eliminated. The mean estimated CO_2 elimination rate was 48±23 mL/min with peaks of 86 mL/min. Moreover, the ADVOS therapy significantly improved the respiratory parameters and vasopressor requirements compared to baseline (PaO_2/FiO_2 116 vs. 62 mmHg; noradrenalin minimum 0.04 vs. 0.35 µg/kg/h at beginning of the extracorporeal treatment).

On top of this, the course of hemodynamic parameters analyzed by transpulmonary thermodilution suggested effectiveness of ultrafiltration, despite an atrial fibrillation-related increase in global end-diastolic volume index (GEDVI).

To note, even short interruptions of the ADVOS treatment for periodic exchange of the ADVOS device repeatedly resulted in reversible deteriorations, in particular of $PaCO_2$ and pH.

In spite of optimum medical treatment, the patient suffered from hemoptysis, superinfections with *Klebsiella oxytoca* and *Aspergillus fumigatus*. Death occurred after a sudden cardiac arrest, together with a non-resuscitation order. Coagulation and inflammation parameters suggest that a combined septic event together with COVID-19 associated hyperinflammation ultimately lead to coagulopathy, shock and associated fulminant organ failure.

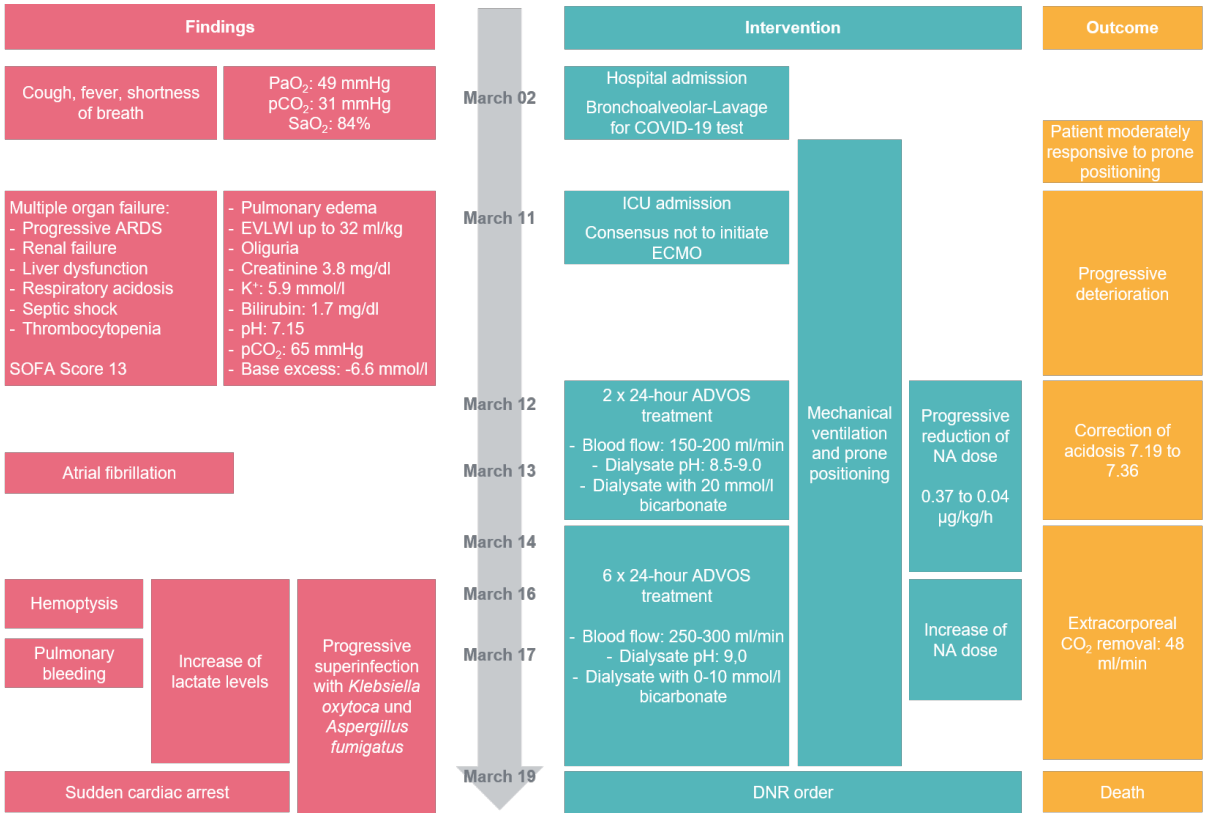

Figure 1. Timeline of findings and interventions for the COVID-19 patient with multiple organ failure. ARDS: acute respiratory distress syndrome; EVLWI: extravascular lung water index; K^+: potassium concentration; ICU: intensive care unit; PaO_2: arterial pO_2; $PaCO_2$: arterial pCO_2; SOFA: sequential organ failure assessment; ECMO: extracorporeal membrane oxygenation.

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The authors conclude:

This case provides evidence on the feasibility of the ADVOS system for CO_2 removal and acidosis correction in patients with ARDS and COVID-19. Acidosis can impair coagulation, reduces hemoglobin-oxygen-affinity, promotes pulmonary vasoconstriction and is associated with systemic hyperinflammation in the critically ill. Accordingly, the restoration of acid-base homeostasis is also important in COVID-19 patients. Combined and less invasive approaches such as the ADVOS therapy might be a good treatment option in predominantly older patients with MOF and with contra-indications to ECMO.

We think that

COVID-19 is characterized by symptoms of viral pneumonia including fever, fatigue, dry cough, and lymphopenia. A serious problem of the SARS-CoV-2 infection is an acute respiratory distress syndrome (ARDS), which appears more often in older adults, patients with immune disorders and co-morbidities. Many of the older patients who become critically ill have concomitant conditions such as cardiovascular disease, liver disease, or kidney disease.

So far, the treatment options in critically ill patients are insufficient and unsatisfactory. There are several types of extracorporeal organ support including renal replacement therapy (RRT), Extracorporeal CO_2 Removal (ECCO2R) or extracorporeal liver support. These procedures target single detoxification organs and fail to address multiple organ failure as a systemic disease.
In addition, in cases where artificial ventilation is not sufficient to preserve blood oxygenation levels, extracorporeal membrane oxygenation (ECMO) might be used. ECMO provides extended cardiac and respiratory support to people whose heart and lungs are not able to give a sufficient amount of gas exchange or perfusion to preserve life. O_2 is added and CO_2 is removed. In the case presented, the patient might not have been suitable at all, as several ECMO registers and the EOLIA study indicate lower efficacy in patients of old age and multi organ failure (SOFA score >10 and prolonged mechanical ventilation (> 7 days)).

The role of extracorporeal organ support therapies in the treatment of COVID-19 patients is to reduce the toxic burden in the body and to support the lung function by removing CO_2. As pointed out by Huber et al. in this case report, “combined and less invasive approaches such as ADVOS might be a treatment option in predominantly old-age-COVID-19 patients with MOF and with contra-indications to ECMO.”

The ADVOS therapy is the first blood purification treatment for combined liver, lung, and kidney support and direct blood pH correction integrated in one device. All this, with low invasiveness and blood flows is common to conventional hemodialysis. Recent data reveal that the ADVOS treatment improves expected survival in MOF by up to 30%. No serious side-effects have occurred so far in more than 600 patients (over 3,500 treatments). Especially for extracorporeal CO_2 removal only limited other options exist. In case of severe lung failure (severe COVID-19 infection), the ADVOS treatment is available side by side with mechanical ventilation and is thought to shorten/prevent the need for intubation, reducing the length of stay in the ICU and lowering side effects of ventilation. Studies are currently being planned to test these features.

In conclusion, as shown in this case report, preliminary data show great potential for the ADVOS therapy in patients developing lung failure during the COVID-19 outbreak. The ADVOS treatment with its broad application spectrum can have a positive impact on the future situation and provide promising multi organ support in a population dying from severe multi organ failure triggered by viral infections and further aggravated by patient’s previous comorbidities.

If you have further questions or suggestions - please contact us at marketing@advitos.com.

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