

# Blood purification treatment and cytokine removal using Cytosorb® device in critically ill patients with COVID-19 infection



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## Background

Acute kidney injury (AKI) is a complication of SARS-CoV-2 disease, associated with worse clinical outcomes. Renal replacement therapy (RRT) in combination with sequential extracorporeal blood purification therapies (EBPT) might support renal function, attenuate systemic inflammation, and prevent or mitigate multiple organ dysfunctions.

## Methods

We retrospectively analyzed 20 patients admitted in ICU for ARDS and who developed moderate-to-severe AKI requiring RRT. Cytokine hemadsorption with Cytosorb® was performed in association with CRRT. The main indication for this treatment was the worsening of hemodynamic and respiratory conditions and suspicion of cytokine storm. The protocol consisted in the use of 3-4 cartridges in total; among these, the first 2 were changed after 12 hours of treatment to maximize cytokine removal, while the others after 24 hours. We examined comorbidities, clinical and laboratory characteristics and the impact of treatment in terms of mortality rate and changes in data before and after treatment.

## Results

Nineteen patients (95%) had an AKI at any time during their ICU stay. Of these, 5 patients (25%) had AKI stage II and 14 patients (70%) had AKI stage III. All patients included in this subgroup were mechanical ventilated and required vasopressor's use. Mean prescribed CRRT dose was  $31.2 \pm 11.7$  ml/kg/h. The median time to starting RRT after ICU admission was 7 days (IQR 3.5-15 days) and the median duration was 7 days (IQR 2.5-12.5 days). Mean SOFA score at the time of RRT start was extremely high ( $14.5 \pm 2.8$ ). Mortality rate was important (18 patients, 90%) in our cohort. Comparing clinical and laboratory data before and after treatment, a significant improvement of inflammatory markers was reported, with the reduction of C-reactive protein (CRP, 143 [62.1- 328.5] vs 83.5 [66.7-153.5] mg/L); however, no significant changes in IL-6, WBC and PCT values were observed. A slight increase of PaO<sub>2</sub>/FiO<sub>2</sub> were described, although not statistically significant (PaO<sub>2</sub>/FiO<sub>2</sub> ratio 144 [82.7-174.2] vs 183 [132-355.5] mmHg).

## Conclusion

Our experience supports the need of an adequate timing for the use of Cytosorb® in critically ill patients with Covid-19. Although a discrete efficacy in improving inflammatory cascade, the late use of EBPT, when organ dysfunction was already ongoing, didn't impact survival.

Main outcomes after EBPT		ICU ADMISSION	PRE-TREATMENT	POST-TREATMENT	p-value
N° patients who completed treatment Nr (%)	12 (60%)				
Difference hospital admission/admission UTI (Days Median, IQR)	3 (0.5 – 8)				
Difference ICU admission / First RRT Treatment (Days Median, IQR)	7 (3.5-15)				
Death (Nr; %)	18 (90%)				
Length of ICU Stay (Days Median, IQR)	12 (6.5-21)				
Length of Stay from First Treatment (Days Median, IQR)	5 (1-10)				
		CRP (mg/L)	143 (62.1-328.5)	83.5 (66.7-153.5)	0.025
		MAP (mmHg)	87.8 ± 8.3	81.9 ± 15.8	0.265
		PaO <sub>2</sub> /FiO <sub>2</sub> ratio (mmHg)	136 (89-232.2)	144 (82.7-174.2)	0.068
		Lactate (mmol/L)	1.35 (1-2.1)	1.9 (1.2-4.1)	0.135
		WBC (10 <sup>3</sup> /mcg)	11.1 ± 4.4	11.5 ± 8.1	0.613
		IL6 (pg/ml)	90.1 (28.7-317.5)	178 (43-2866.5)	0.791
		PCT (ng/ml)	0.13 (0-0.6)	1.1 (0.59-5.04)	0.420
		D-dimers (mcg/L)	3376.5 (708.5-9080)	5110 (2278-10550)	0.508

Figure 1: Outcomes after EBPT, laboratory and clinical parameters before and after treatment