

CytoSorb® therapy for the treatment of post covid-19 patient associated complications of pneumonia and sepsis: A case report

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Abstract

Cytokine storm during the COVID-19 results in multiple organ failure, sepsis and septic shock. CytoSorb® therapy, could help overcome the cytokine storm syndrome by flushing out the all the toxins from the circulatory system and thereby reducing the time of recovery period and post recovery recurrent infections in COVID-19 patients. Here, we present a case of a 59-year-old man with post COVID-19 sequelae admitted in emergency department with elevated inflammatory biomarkers indicating sepsis and cytokine storm. The patient was initially supported with mechanical ventilation and later was given CytoSorb® therapy in two sessions of 16 hrs each using two separate devices at the interval of 4 hrs. By the end of the treatment, there was remarkable improvement in CRP values (67.6%), serum creatinine (increased by 6.4%), serum lactate (70%) and PCT (71%). A decrease in IL-6 levels (81.3%) and reduction in norepinephrine (NE) dose by 87% was reported. The patient was discharged from ICU in 10 days and from hospital in 15 days.

CytoSorb® therapy provides hemodynamic stability and improves organ dysfunction. It helps in reducing number of days of hospital stay, use of vasopressors and ventilation support.

Keywords

COVID-19; Post COVID-19 complications; Dyspnea; CytoSorb® therapy; Cytokine storm.

Introduction

Worldwide, over 180 million individuals have been infected with COVID- 19 and 165 million have been estimated to be recovered. However, post-infection recovery times and long-term complications such as neurological, respiratory, physical and mental health are now becoming more apparent [1-4]. “Cytokine storm” that results in endothelial inflammation, microvascular thrombosis, and multiple organ failure is often associated in critically ill patients with COVID-19 [5,6]. The threat of COVID-19 and post COVID-19 complications is more commonly reported in patients with some pre-existing disorders such as diabetes, hypertension, cardiovascular, renal, or hepatic impairment [7-9].

Approximately, 17% of patients with COVID-19 pneumonia require invasive mechanical ventilation. In India, approximately 10 to 20% patients require intensive care unit (ICU) admission and 3 to 10% patients require intubation and mechanical ventilation [10]. At this time, any alternative approach is needed which not only reduces the load of intubation and respiratory support but also improves the clinical outcomes thereby cutting the cost of invasive procedures and long hospitalization stay.

CytoSorb® (CytoSorbents Europe GmbH Müggelseedamm 131, 12587 Berlin, Germany), an extracorporeal hemadsorption device and a well-established treatment for overcoming cytokine storm in critically ill patients with septic shock could be an alternative therapy to reduce the invasive use of mechanical ventilation and intubation and combating cytokine storm to treat post COVID-19 complications [11,12]. The device has been widely used in ARDS, sepsis and multi system failure across many countries including China [13-18]. Recently, this therapy was approved by the FDA (United States) and DCGI (India) for its use in COVID-19 [19]. Here, we present a case of a post-COVID patient with multiple comorbidities treated with CytoSorb® therapy.

Case Presentation

A 59-year-old man reinfected with COVID-19 was admitted to the hospital with the symptoms of pneumonia, lung fibrosis (CTPA- negative) and sepsis. He had recovered from COVID-19, a month earlier. He had complaints of fever, chest discomfort, sweating and shortness of breath (SOB-IV) for the last one day. He was a known case of chronic sinusitis, diabetes mellitus and hypertension. His demographic details, clinical conditions were recorded in CRF at the time of admission.

His sputum culture report showed the presence of bacterial infections; *Klebsiella pneumonia* and Biofire assay of sputum showed *Pseudomonas* and *Actinobacterbaumeni*. The cytometric bead array (CBA) report depicted high level of interleukin 6 (IL-6; 1256 pg/ml). The elevated IL-6, low oxygen level; PaO₂ 71.6 kPa, tachypnea (>24 breaths/min) indicated the presence of sepsis. Other laboratory findings; CRP: 9.32 mg/L, S. lactate 5.6 mmol/L and serum creatinine 2.16 µmol/L were indicative of the sepsis and cytokine storm. He was immediately shifted to ICU and initially supported with bi-level positive airway pressure (BIPAP) mechanical ventilator, a noninvasive mechanical ventilation procedure and subsequently put on invasive ventilation due to increasing respiratory distress after a day. Due to worsening clinical condition, CytoSorb® therapy was commenced post three days of admission to the ICU. He was treated with two CytoSorb® devices at an interval of 4 hrs; each device was administered for 16 hrs. The patient was kept on *sustained low efficiency dialysis* (SLED) dialysis at a flow rate of 140 ml/min. Along with the CytoSorb® therapy and dialysis, the patient was prescribed antibiotics Meropenem 1 gm BD, Levofloxin 750 mg OD, Polymixin, antifungals, anticoagulants, diuretics and other supportive therapies.

After the use of first device, there was a sharp decline in CRP values (65.02%) from baseline. By the end of the treatment, (after the use of second device) it reduced to 67.6%. A decrease in IL-6 levels (from 1256 to 234 pg/ml, 81.3%) after the use of second CytoSorb® device was reported. Other parameters including serum lactate, serum creatinine, SGOT, SGPT continued to improve till end of the therapy. Changes in all the parameters and biomarkers of sepsis after the use of first and second device are represented in (Table 1 and Figure 1) respectively. Post application of second device, norepinephrine (NE) dose reduced

by 87% (from 15 ml to 2 ml).

He was discharged from ICU after 10 days; mechanical ventilation was weaned off on fourth day of therapy. He was discharged from hospital in a stable condition.

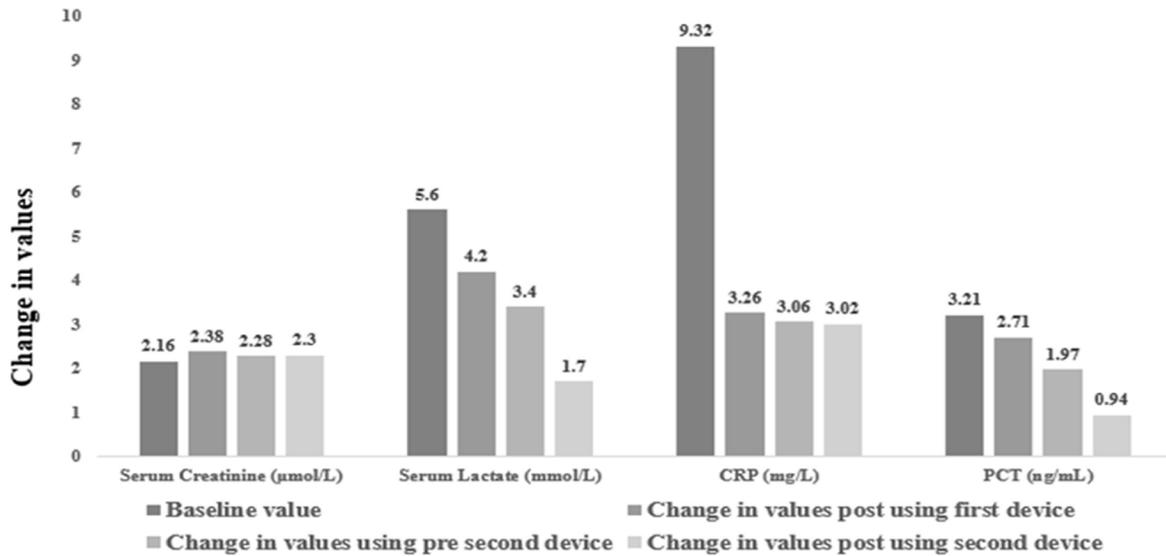


Figure 1: Change in values of biomarkers of sepsis (From baseline to pre and post use of first and second CytoSorb® device).

Table 1: Change in clinical parameters from baseline (day of hospital admission) pre and post use of first and second CytoSorb® device).

Laboratory Findings	Pre CytoSorb® (Baseline)	Change in values: Post use of first device	Change in values: Pre use of second device	Change in values: Post use of second device	Percentage change post use of first device	Percentage change pre use of second device	Percentage change post use of second device
Hemoglobin (g/dL)	13.5	13.4	11.7	11.4	-0.74	-13.33	-15.56
Hematocrit	39.7	35.5	34.3	34	-10.58	-13.60	-14.36
Leucocytes (10 ³)	20.64	14.22	23.06	13.64	-31.10	11.72	-33.91
Platelet Count (10 ³ /microliter)	2.15	2.33	2.81	3.29	8.37	30.70	53.02
BUN (mmol/L)	158	114	158	122	-27.85	0.00	-22.78
Bilirubin (µmol/L)	1.2	1.1	0.9	1.7	-8.33	-25.00	41.67
SGOT (units per litre)	69	79	82	54	14.49	18.84	-21.74
SGPT (units per litre)	76	76	74	70	0.00	-2.63	-7.89
PaO2 (kPa)	71.6	78.2	80.3	81.02	9.22	12.15	13.16
PaCO2 (kPa)	25.6	39.2	46.2	42.9	53.13	80.47	67.58
FiO2	60	70	80	90	16.67	33.33	50.00
Body Temperature (Degrees Fahrenheit)	103	101	100	98	-1.94	-2.91	-4.85
Heart Rate (beats/min)	114	112	104	104	-1.75	-8.77	-8.77
Respiratory Rate (breaths/min)	24	22	22	21	-8.33	-8.33	-12.50
Mean Arterial Pressure (mm Hg)	65	70	74	80	7.69	13.85	23.08
PEEP	8	8	6	6	0.00	-25.00	-25.00

Discussion

A recent systematic review reported that COVID infection is associated with more than 50 other medical complications that last weeks to months after initial recovery, also called Long-COVID or COVID long-haulers [20]. Hence, COVID-19 and post COVID-19 treatment is a long and multimodal approach that requires prolonged treatment with antiviral, steroidal drugs and other adjunctive therapies. Extracorporeal cytokine hemoadsorption is the latest technology in the treatment of dysregulated inflammatory states such as sepsis [21,22].

The patient in this case presentation was a case of post sequelae COVID-19 patient who was readmitted to hospital with the complaint of SOB/ dyspnea and other comorbidities. It is reported that dyspnea is more common in COVID-19 patients with ≥ 2 comorbidities than in those with one comorbidity (55.4% vs 34.1%). Presence of dyspnea is an important risk factor for long hospitalization stay and severity and may be associated with mortality of COVID-19 or recurrence of COVID-19 symptoms [23]. This patient was readmitted post one month of COVID-19 diagnosis. His lab investigations at the time of admission; elevated IL-6, CRP, serum lactate, serum creatinine and respiratory dysfunctions indicated the presence of sepsis that might not have been completely cleared when he was undergoing COVID-19 treatment or during his recovery phase. It is reported that during COVID -19 phase and in recovery period, the immune system gets weaker and more susceptible to other infections which is more pronounced in patients with pre-existing ailments [24]. A study by Klock et al; in critically ill ICU admitted COVID-19 patients concluded that recurrence of symptoms in post recovery period is caused by either due to persistence of the primary COVID-19 infection or super infection with another virus or even bacteria due to the compromised immune system [25]. This patient was also found positive with other bacterial infections and had multiple comorbidities indicating the high risk of recurrent infections.

CytoSorb® device plays a pivotal role for control of ongoing inflammatory response. The mechanism involves the nonspecific removal of the peaks of the circulating cytokines both in the pro- and in the anti-inflammatory side assuming that those cytokines with the highest concentration will be removed in higher amount. It helps to avoid the comeback of severe derangement of the immune system and to regain an improved level of the immunological response of the host [26]. The present case report was a case of the patient who was immune compromised and required the management not only with standard treatment of vasopressors, antibiotics and respiratory support but a filtration system which could purify the overall circulatory system. Hence, he was treated with CytoSorb® therapy. This unique therapy can absorb bacterial exotoxins, myoglobin, free hemoglobin, bilirubin, activated complement and hosts of other inflammatory agents which can lead to fatal systemic inflammatory response syndrome (SIRS) [12].

We treated this patient with two CytoSorb® devices; the results were remarkable even after the single application; a reduction in the vasopressor dose (47%), cytokine levels (50%), leucocytes (31%) and in diagnostic markers such as PCT (39%), CRP (67%), serum creatinine (5.5%) and S. lactate (39%) were observed. Our results are similar to a study by Mitzner and coworkers' who reported that the use of CytoSorb® in a patient with septic shock and acute kidney failure decreased the levels of IL-6, CRP, serum creatinine, PCT, and leucocytes during the treatment and in the following days. CytoSorb® hemoadsorber treatment appeared to be safe and was well tolerated by the patient [27]. Rizvi et al reported a case of

51-year-old man who developed ARDS after infection with COVID-19. He received the cytokine filter therapy (CytoSorb®) and CRRT for 12 days. A total of 8 CytoSorb® devices were used and filter was changed after every 12 hours. The patient showed an improvement after treatment and CytoSorb® therapy helped to prevent his imminent death [28].

Generally, patients with septic shock and sepsis are prescribed vasopressors or inotropes in order to maintain hemodynamic parameters [29]. This patient was also a known case of hypertension and diabetes. His blood pressure values were normal at the time of discharge from ICU (129/84). This indicates that CytoSorb® therapy helped to wean him from vasopressor support hence improved his hemodynamic stability. Oxygen levels (PO_2) improved by 9% and 13% post the use of first and second device, respectively. Mechanical intubation was started prior to CytoSorb® therapy and was extubated at the time of discharge from ICU. The patient was discharged from the hospital in a stable condition on 14 June 2021.

Conclusion

The therapy can be added with standard care of treatment for the patients admitted in ICU and undergoing any kind of treatment due to septic shock or caused due to post COVID-19 complications. The device itself has no adverse events. It provides hemodynamic stability and improves organ dysfunction. It helps to reduce the use of vasopressors, ventilation support and longer hospitalization.

Declarations

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References

1. Pai MYB, Park ASH, Chen BFL, Toma JT, Pai HJ. Health Complications in Patients Recovering from COVID-19: A Narrative Review of Post-COVID Syndrome. *J Adv Med Biomed.* 2021; 115-29.
2. Fraser E. Long term respiratory complications of covid-19. *British Medical Journal Publishing Group;* 2020. 370.
3. Al-Ramadan A, Rabab'h O, Shah J, Gharaibeh A. Acute and post-acute neurological complications of COVID-19. *Neurol Int.* 2021; 13: 102-19.
4. Shanbehzadeh S, Tavahomi M, Zanjari N, Ebrahimi-Takamjani I, Amiri-Arimi S. Physical and mental health complications post-COVID-19: Scoping review. *J Psychosom Res.* 2021; 110525.
5. Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C. Cytokine storm in COVID-19: the current evidence and treatment strategies. *Front Immunol.* 2020; 11: 1708.

6. Faix JD. Biomarkers of sepsis. *Crit Rev Clin Lab Sci.* 2013; 50: 23-36.
7. Leung C. Clinical features of deaths in the novel coronavirus epidemic in China. *Rev Med Virol.* 2020; 30: e2103.
8. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L ,et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* 2020; 97: 829-38.
9. Yang J, Feng Y, Yuan M, Yuan S, Fu H, Wu B ,et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *DIABETIC MED.* 2006; 23: 623-8.
10. Mehta Y, Chaudhry D, Abraham O, Chacko J, Divatia J, Jagiasi B ,et al. Critical care for COVID-19 affected patients: Position statement of the Indian society of critical care medicine. *Indian J Crit Care Med.* 2020; 24: 222.
11. Shum HP, Yan WW, Chan DTM. Extracorporeal blood purification for sepsis. *Hong Kong Med J* 2016.
12. Rimmelé T, Kellum JA. Clinical review: blood purification for sepsis. *Crit Care.* 2011; 15: 1-10.
13. Chastain DB, Stitt TM, Ly PT, Henao-Martínez AF, Franco-Paredes C, Osae SP, editors. Countermeasures to Coronavirus Disease 2019: Are Immunomodulators Rational Treatment Options—A Critical Review of the Evidence. *Open forum infectious diseases*; 2020: Oxford University Press US.
14. Friesecke S, Stecher S-S, Gross S, Felix SB, Nierhaus A. Extracorporeal cytokine elimination as rescue therapy in refractory septic shock: a prospective single-center study. *J Artif Organ.* 2017; 20: 252-9.
15. Calabrò MG, Febres D, Recca G, Lembo R, Fominskiy E, Scandroglio AM ,et al. Blood purification with CytoSorb in critically ill patients: single-center preliminary experience. *Artif Organ.* 2019; 43: 189-94.
16. Kogelmann K, Scheller M, Drüner M, Jarczak D. Use of hemoadsorption in sepsis-associated ECMO-dependent severe ARDS: A case series. *J Intensive Care Soc.* 2020; 21: 183-90.
17. Alharthy A, Faqih F, Memish ZA, Balhamar A, Nasim N, Shahzad A ,et al. Continuous renal replacement therapy with the addition of CytoSorb® cartridge in critically ill patients with COVID-19 plus acute kidney injury: a case-series. *Artif Organ.* 2021; 45(5): 101-12.
18. Rampino T, Gregorini M, Perotti L, Ferrari F, Pattonieri EF, Grignano MA ,et al. Hemoperfusion with CytoSorb as Adjuvant Therapy in Critically Ill Patients with SARS-CoV2 Pneumonia. *Blood Purif.* 2020; 1-6.
19. Biocon Biologics gets DCGI approval for emergency use of CytoSorb to treat critical COVID-19 patients. Available on URL: <https://www.expresspharma.in/latest-updates/biocon-biologics-gets-dcgi-approval-for-emergency-use-of-cytosorb-to-treat-critical-covid-19-patients/>. Last accessed on 31 May 2021.
20. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A ,et al. More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis. Available at SSRN 3769978. 2021.
21. Polat G, Ugan RA, Cadirci E, Halici Z. Sepsis and septic shock: current treatment strategies and new approaches. *Eurasian J Med.* 2017; 49(1): 53.
22. Bonavia A, Groff A, Karamchandani K, Singbartl K. Clinical utility of extracorporeal cytokine hemoadsorption therapy: a literature review. *Blood Purif* 2018;46(4):337-49.
23. Gao Yd, Ding M, Dong X, Zhang Jj, Kursat Azkur A, Azkur D ,et al. Risk factors for severe and critically ill COVID-19 patients: A review. *Allergy.* 2021; 76(2): 428-55.
24. SeyedAlinaghi S, Afsahi AM, MohsseniPour M, Behnezhad F, Salehi MA, Barzegary A ,et al. Late Complications of COVID-19; a Systematic Review of Current Evidence. *Arch Acad Emerg Med.* 2021; 9(1).
25. Klok F, Kruip M, Van der Meer N, Arbous M, Gommers D, Kant K ,et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020; 191: 145-7.
26. Ronco C, Reis T, De Rosa S. Coronavirus epidemic and extracorporeal therapies in intensive care: si vis pacem para bellum.

Blood Purif. 2020; 49(3): 255-8.

27. Mitzner SR, Gloger M, Henschel J, Koball S. Improvement of hemodynamic and inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: a case report. *Blood Purif* 2013;35(4):314-5.

28. Rizvi S, Danic M, Silver M, LaBond V. Cytosorb filter: An adjunct for survival in the COVID-19 patient in cytokine storm? a case report. *Heart-Lung*. 2021; 50(1): 44-50.

29. Pollard S, S. B. Edwin and C. Alaniz. Vasopressor and inotropic management of patients with septic shock. *Pharmacy Ther*. 2015; 40(7): 438.

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