Clinical Case Reports: Open Access

Yumed Text
OPEN ACCESS JOURNALS

Case Report | Vol 5 Iss 4
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.238

CytoSorb® in the Treatment of Severely-Ill Patient with Post-COVID-19 Complications: A Case Report

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Received: November 10, 2022; **Accepted:** November 28, 2022; **Published:** December 07, 2022

Abstract

Background: COVID-19 affects the respiratory tract leading to acute respiratory distress syndrome (ARDS) and serious pneumonia. Severe cases of COVID-19 are associated with hyperactive immune response characterized by the release of interleukins, interferons, chemokines, tumor-necrosis factors, and various other mediators. Use of CytoSorb®, an extracorporeal hemadsorption has been observed to alleviate the cytokine storm, hence ameliorate the pulmonary function and hemodynamic stability.

Case Summary: A 42-year-old man, a case of post-COVID-19 pneumonia was admitted in hospital with the complaints of headache, vomiting, and abdominal discomfort associated with generalized weakness. He had pre-existing comorbidities of diabetes, hypertension, and acute kidney injury. The blood parameters showed increased levels of inflammatory biomarkers which indicated the presence of cytokine storm and sepsis. The patient was given CytoSorb® therapy after 7 days of admission in ICU in two sessions of 18 and 20 hours using two separate devices at the interval of 6 hours. After the treatment, remarkable decreased in CRP values (39%), S. Creatinine (6.52%), S. Lactate (54%), leucocytes (44%) and PCT (33%) was observed. A reduction in IL-6 levels (from 5975 to 3171 pg/ml, 46.9%) and norepinephrine dose (from 8 to 0.2 mcg/kg/hr, 25%) was reported. The patient was discharged from hospital in 54 days in stable condition.

Conclusion: CytoSorb® therapy was effective in providing hemodynamic stability, improving organ dysfunction, and modulating the cytokine storm.

Keywords: ***Cytokine storm; Hemadsorption; Hemodynamic stability; Sepsis***

Citation: Paul R, Aleem MA, Gorla N, et al. CytoSorb® in the Treatment of Severely-Ill Patient with Post-COVID-19 Complications: A Case Report. Clin Case Rep Open Access. 2022;5(4):238.

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) also known as novel coronavirus 2019 (COVID-19) is a non-segmented, enveloped positive-sense RNA from the family beta-coronaviridae was first reported in Hubel, Wuhan, China [1]. There are 225 million confirmed cases and 4.64 million deaths globally according to a report by the World Health Organization (WHO). In India, the total number of confirmed cases was 3.3 million and 0.44 million deaths as of 16 September 202 [2]. COVID-19 is commonly associated with acute respiratory distress syndrome (ARDS) and severe pneumonia with a high mortality rate of 50%.[3,4] Further, 2% to 25% of severe COVID-19 cases have acute kidney injury (AKI) and are associated with a worse medical condition [5]. Approximately 20% patients infected with SARS-CoV-2 require admission to intensive care unit (ICU) with mortality rate of approximately 26% [6]. The severity of viral infection is associated with cytokine storm which in turn demonstrates the beginning of sepsis process involving higher serum levels of pro-inflammatory and anti-inflammatory cytokines [7,8]. The cytokines profile in COVID-19 is defined by the elevated level of interleukin (IL)-1, IL-2, IL-6, IL-7, monocyte chemoattractant protein 1 (MCP-1), granulocyte colony stimulating factor (GCSF), tumor necrosis factor-α (TNF-α), macrophage inflammatory protein 1-α, and interferon-γ inducible protein 10 [9,10]. Critical illness and mortality seems to be associated with this cytokine storm in patients suffering from COVID-19 [11].

CytoSorb® is an extracorporeal hemadsorption device that reduces the excess inflammatory cytokines in the blood of the critically ill patients with septic shock [12,13]. For COVID-19 patients; CytoSorb® has been introduced in the list of experimental treatments by the WHO [14]. It has been approved as Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) and Drugs Controller General of India (DCGI) for COVID-19 patients [15]. Using CytoSorb® therapy, more than 5,750 critically ill patients with COVID-19 infection have been treated in 30 countries [16]. Previous study conducted on patients with COVID-19 and associated AKI, ARDS, sepsis, and hyperinflammation were treated using CytoSorb® with continuous renal replacement therapy (CRRT) [5]. Here, we report a case of patient where CytoSorb® therapy was administered to a diabetic and hypertensive patient with post-COVID-19 pneumonia, lung fibrosis, rectal ulcer, critical illness neuropathy and AKI.

2. Case Presentation

On May 7, 2021, a 42-year-old Asian man with a history of hypertension and diabetes mellitus presented with complaints of headache, vomiting, and abdominal discomfort associated with generalized weakness. He was diagnosed with COVID-19 on May 1 and then admitted with post-COVID pneumonia with a severe cycle threshold (CT) score of 22/25, lung fibrosis, bedsore (grade-IV), rectal ulcer, acute kidney injury and critical illness neuropathy. On admission, his body temperature was 99°F, respiratory rate was 22 per minute, blood pressure was 120/90 mm Hg and pulse rate was 90 beats per minute. Based on clinical findings and evaluation, a treatment protocol was planned.

On May 16, the patient was incubated and shifted to the intensive care unit (ICU) on May 19. Till then, the patient was on antibiotics from the date of admission and changed to antifungal, one dose of Tocilizumab according to the culture report. The patient was on sustained low-efficiency dialysis (SLED) dialysis treatment. The tracheostomy was done and CytoSorb® device was started on May 26 (after 7 days of admission to ICU) in view of cytokine storm and continued for 18 hrs. After 6 hrs of interval, the second device was incorporated and ran for 20 hrs. The patient had seizures for which the antiepileptics drugs were administered.

The patient showed a mild improvement in APACHE II score decreasing from 28 to 24. Further, reduction in the total leucocytes count (TLC), procalcitonin (PCT) and platelet count by 20%, 33% and 10% respectively was observed. The change in norepinephrine (NE) dose from pre to post CytoSorb® therapy was 8 to 0.2 mcg/kg/hr (25%). The mean arterial pressure (MAP) showed an improvement of 16% from pre to post CytoSorb® therapy (67 to 78 mm Hg). There was a remarkable reduction in IL-6 levels from pre to post CytoSorb® therapy (5975 to 3171). Laboratory parameter pre and post CytoSorb® therapy are mentioned in TABLE 1. In addition, the PaO_2/FiO_2 ratio increased from 45% to 79% post CytoSorb® treatment.

TABLE 1. **Laboratory parameters of the patient before and after CytoSorb® therapy.**

Parameters	Pre-CytoSorb® therapy	Post-CytoSorb® therapy	Change in values: Pre use of second device	Change in values: Post use of second device
Urine output(ml/day)	190	180	204	190
Hemoglobin (g/dL)	10.02	10.02	10.04	10.11
Hematocrit (%)	34.8	30.01	21.07	16.65
CRP (mg/dL)	23.03	19.01	20.07	14.03
MAP (mm/Hg)	67	69	74	78
TLC (cells/ mm^3)	21.6	16.65	18.75	12.09
Platelets (cells/ mm^3)	4.22	3.78	4.48	4.22
S. Creatinine (mg/dL)	0.46	0.36	0.4	0.43
S. Lactate (mmol/L)	7.02	5.01	6.03	3.21
SGOT (U/L)	77	54	79	79
SGPT (U/L)	248	129	154	117
BUN (mg/dl)	45	51	68	54
Bilirubin (mg/dL)	0.5	0.7	0.5	0.7
Sodium (mmol/L)	154	147	141	134
Potassium (mmol/L)	5.5	4.4	4.9	3.9
Albumin (g/L)	3.17	3.01	2.74	3.09
Arterial pH	7.40	7.35	7.21	7.47
Bicarbonate	39	40	30	33
PaO2 (mmHg)	109	111	98	104
PaCO2 (mmHg)	59.7	57.02	51.04	49.01
PaO2/FiO2 (%)	45	55	60	79
D-dimer (ng/mL)	1149	940	441	435

CRP C-Reactive Protein; MAP: Mean arterial pressure, BUN: Blood urea nitrogen, SGOT: serum glutamic oxaloacetic transaminase, SGPT: serum glutamic pyruvic transaminase

Further, episodes of hematochezia were observed in the patient on June 3 for which one unit packet red blood cell (PRBC) was transfused. The patient was kept on pressure support with FiO_2 of 95% from June 19. The patient then required bilevel

positive airway pressure (BiPAP) with 10 litres of oxygen daytime and volume control at night. Further, he developed rectal bleeding on June 24 for which sigmoidoscopy was planned and Clexane was discontinued. Critical illness neuropathy was suspected as the patient developed weakness of right upper and lower limb for that physiotherapy was started and weakness improved. Further, vacuum dressing was given for bedsores, which healed them well. A large rectal ulcer with fistulous tract noted in distal rectum was observed which was followed by transfusion of PRBC. He continued to have rectal bleeding with clots which eventually decreased in four days. On June 28, rectal bleeding stopped, and he was shifted to tracheostomy ward with BiPAP support for both day and night time. Further, bedsore care, physiotherapy was taken care and antibiotics were changed according to the culture report. Rectal biopsy was obtained which showed ulceration with few cells showing features suspicious of cytomegalovirus infection for which Tab Gancyclovir was administered for 14 days. He was kept on a t-piece with oxygen decreasing the oxygen requirement and hence, weaning was continued. Tracheostomy decannulation was done as the patient was tolerating the t-piece well with a further reduced oxygen requirement and eventually started maintaining the oxygen saturation at room air. Besides, cefoperazone/sulbactam was administered for *Pseudomonas* infection in bedsore culture. On July 30, the patient was clinically improved and discharged in a hemodynamically stable condition from the hospital. He was further advised to continue vacuum dressing at home and to follow up in OPD.

3. Discussion

COVID-19 is the main cause of serious viral pneumonia which leads to ARDS. Previous reports have shown that 76.5% of the COVID-19 patients had cough and 88.9% had fever. Further, headache (17.7%) and fatigue (32.5%) were reported to be less common symptoms of COVID-19 [17,18]. We reported our clinical experience of a severely ill patient with post-COVID pneumonia, lung fibrosis, rectal ulcer, critical illness neuropathy and acute kidney injury with complaints of headache, vomiting, and abdominal discomfort; the patient recovered and survived after using CytoSorb® adjuvant therapy.

During the phase of COVID-19 or during recovery, the immune system weakens and becomes more susceptible to other infections in patients with pre-existing diseases [19]. The coronavirus binds to the alveolar epithelial cells and activates the adaptive and innate immune system releasing pro- and anti-inflammatory cytokines, leading to cytokine release syndrome. This is characterized by increased inflammatory cytokines and biomarkers like IL-2, IL-6, IL-7, macrophage inflammatory protein 1-α, TNF- α, GCSF, ferritin, pro-B-type natriuretic peptide (Pro-BNP), C-reactive protein (CRP) and D-dimer [20]. Specifically, COVID-19 leads to a drastic increase in IL-6 [21] which is the significant driver of ARDS and immune dysregulation [22]. Recently published study by Rieder et al. reported significant reduction in IL-6 levels post CytoSorb® therapy for COVID-19 patients [23]. Another study by Paul et. al showed significant decrease in APACHE II score (25.46 to 20.1; $p < 0.0001$), IL-6 level (52.3%), S.Creatinine (33.3%; $p = 0.0190$) and S.Lactate (39.4%; $p = 0.0120$) after the CytoSorb® treatment in the survivor group [24], demonstrating CytoSorb® might be an effective adjuvant therapy in sepsis and septic shock patients. Another study reported that patients treated with CytoSorb® therapy showed reduced levels of IL-6, CRP, PCT, S. Creatinine and TLC [25]. Other studies also report considerable reduced levels of IL-6 in several COVID-19 patients post CytoSorb® therapy [26,27]. In our patient, a similar pattern was observed where a reduction of 47%, 6.53% and 54% in the levels of IL-6, S.Creatinine and S.Lactate was reported after the CytoSorb® treatment.

According to a previous study, the oxygenation level (PaO_2/FiO_2) is an independent risk of mortality for the COVID-19 patients where it was observed that the PaO_2/FiO_2 was significantly higher in patients ($p<0.0001$) who survived [28]. In a recent study, reduction in levels of IL-6 by 40% and improvement in PaO_2/FiO_2 ratio was observed in 9 COVID patients hospitalized in ICU. Moreover, all the patients who were treated with hemoperfusion with CytoSorb® as adjuvant therapy survived except one [29]. A significant decrease from 612.85 pg/mL to 170.11 pg/mL in IL-6 level and a significant increase from 113 to 303.43 in PaO_2/FiO_2 ratio **(**$p<0.05$) were observed after post CytoSorb® therapy in critically ill COVID-19 patients with AKI as reported by Alharthy and co-workers [5]. Similar findings of decreased level of PCT, S.Lactate and CRP were reported postCytoSorb® therapy [22,30-32]. The present study is in correlation with the previous studies where decrease in CRP, PCT and TLC by 39%, 33% and 44%, respectively whereas an increase of 75% was observed in PaO_2/FiO_2 ratiopost CytoSorb® therapy (FIG. 1).

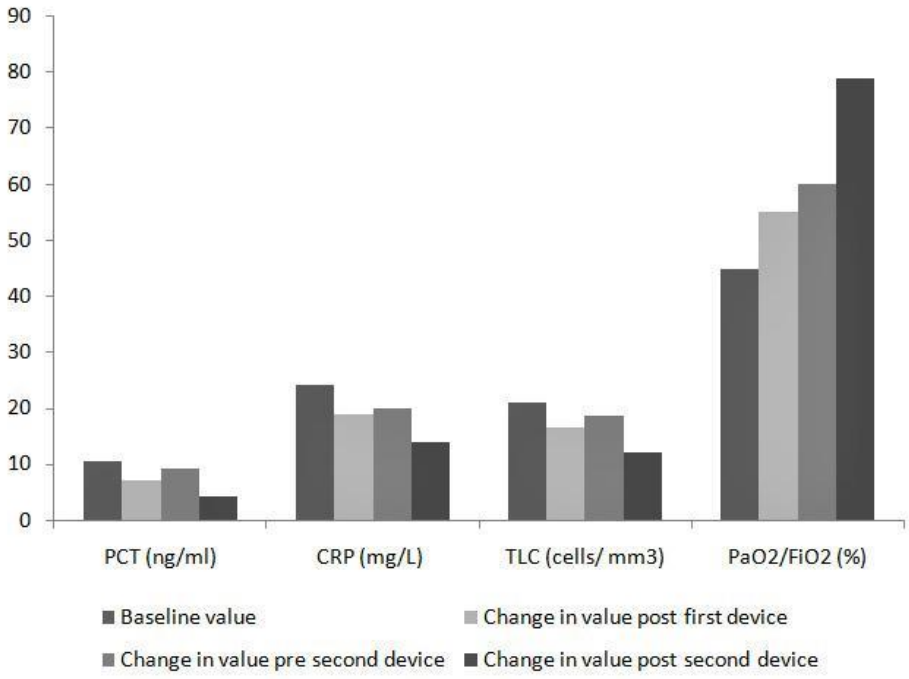

FIG. 1. **Change in Values of Biomarkers (From Pre and Post Use of First and Second CytoSorb® Device).**

We also used, Tocilizumab, a recombinant humanized IL-6 receptor blocker registered for treating cytokine release syndrome is administered in patients with COVID-19 with CytoSorb® therapy [33]. Previous study reported patients treated with CytoSorb® and Tocilizumab, showed significant reduction in IL-6 plasma levels, an improvement in both oxygenation (PaO2/FiO2 ratio) and inflammatory biomarkers (CRP, D-dimers, and ferritin). CytoSorb® therapy and Tocilizumab was noted as an effective and safe rescue therapy for COVID-19 patients with refractory acute respiratory failure associated with hyperinflammation and hypercytokinemia [34].

4. Conclusion

COVID-19 is a serious infection causing ARDS, pneumonia, and deaths worldwide. CytoSorb® as an adjuvant therapy played a very crucial role to regain control over the deteriorating condition of the patient. CytoSorb® is a potential safe and effective treatment for critically ill COVID and post-COVID patients.

5. Acknowledgement

The authors would like to acknowledge Mr. Saleemuddin Siraj and Mr. Sukrut Khadke for end-to-end coordination to conclude this case study under the leadership guidance of Mr. Pradeep Yanamala and Knowledge Isotopes Pvt. Ltd (www.knowledgeisotopes.com) for medical writing assistance.

6. Statement of Ethics

Study approval statement: NA
Consent to publish statement: NA

7. Conflict of Interest

The authors have no conflicts of interest to declare.

8. Funding

The author(s) received no specific funding for this work.

9. Author Contributions

The above authors have equally contributed towards ideation, data analysis and manuscript review.

10. Data Availability Statement

All data generated or analysed during this study are included in this published article. However, any further details can be made available by the corresponding author on reasonable request.

REFERENCES

1. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199-1207.
2. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Available at: https://covid19.who.int/, Accessed November 12, 2021.
3. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81.
4. Sinha P, Matthay MA, Calfee CS. Is a “cytokine storm” relevant to COVID-19? JAMA Intern Med. 2020;180(9):1152-4.
5. Alharthy A, Faqihi F, Memish ZA, 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 Organs. 2021;45(5):E101-E12.
6. Damiani M, Gandini L, Landi F, et al. Extracorporeal cytokine hemadsorption in severe COVID-19 respiratory failure. Respir Med. 2021;185:106477.

7. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
8. Schädler D, Pausch C, Heise D, et al. The effect of a novel extracorporeal cytokine hemoadsorption device on IL-6 elimination in septic patients: a randomized controlled trial. PloSOne. 2017;12(10):e0187015.
9. Petric D. The use of CytoSorb therapy in COVID-19 cytokine storm.
10. Pouladzadeh M, Safdarian M, Eshghi P, et al. A randomized clinical trial evaluating the immunomodulatory effect of convalescent plasma on COVID-19-related cytokine storm. Intern Emerg Med. 2021;16(8):2181-91.
11. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8.
12. Mehta Y, Mehta C, Kumar A, et al. Experience with hemoadsorption (CytoSorb®) in the management of septic shock patients. World J Crit Care Med. 2020;9(1):1.
13. Singh Y, Chhabra S, Lashkari K, et al. Hemoadsorption by extracorporeal cytokine adsorption therapy (CytoSorb®) in the management of septic shock: A retrospective observational study. Int J Artif Organs. 2020;43(6):372-8.
14. Deep A, Bansal M, Ricci Z. Acute kidney injury and special considerations during renal replacement therapy in children with coronavirus disease-19: perspective from the critical care nephrology section of the european society of paediatric and neonatal intensive care. Blood Purif. 2021;50(2):150-60.
15. Biocon Biologics gets DCGI approval for emergency use of CytoSorb to treat critical COVID-19 patients - Express Pharma. Available at: https://www.expresspharma.in/biocon-biologics-gets-dcgi-approval-for-emergency-use-of-cytosorb-to-treat-critical-covid-19-patients/, Accessed November 12, 2021.
16. https//cytosorb-therapy.com/en/covid-19/ [Last accessed on12th feb 2021].
17. Douedi S, Miskoff J. Novel coronavirus 2019 (COVID-19): a case report and review of treatments. Medicine. 2020;99(19):e20207.
18. Wang M, Luo L, Bu H, et al. One case of coronavirus disease 2019 (COVID-19) in a patient co-infected by HIV with a low CD4+ T-cell count. Int J Infect Dis. 2020;96:148-50.
19. Yazdanpanah F, Hamblin MR, Rezaei N. The immune system and COVID-19: Friend or foe? Life Sci. 2020;256:117900.
20. Alhazzani W, Evans L, Alshamsi F, et al. Surviving sepsis campaign guidelines on the management of adults with coronavirus disease 2019 (COVID-19) in the ICU: first update. Crit Care Med. 2021;49(3):e219-e34.
21. Pancani F, Pavani R, Quacquarelli A, et al. Successful use of CytoSorb in a Covid-19 patient with secondary septic shock due to a sacral decubitus infection. Int J Artif Organs. 2021;44(12):1034-8.
22. Hawchar F, Rao C, Akil A, et al. The potential role of extracorporeal cytokine removal in hemodynamic stabilization in hyperinflammatory shock. Biomedicines. 2021;9(7):768.
23. Rieder M, Wengenmayer T, Staudacher D, et al. Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation. Crit Care. 2020;24(1):1-2.
24. Paul R, Sathe P, Kumar S, et al. Multicentered prospective investigator initiated study to evaluate the clinical outcomes with extracorporeal cytokine adsorption device (CytoSorb®) in patients with sepsis and septic shock. World J Crit Care Med. 2021;10(1):22.
25. Mitzner SR, Gloger M, Henschel J, et al. Improvement of hemodynamic and inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: a case report. Blood Purif. 2013;35(4):314-5.

26. Berlot G, Tomasini A, Pognuz ER, et al. The combined use of tocilizumab and hemoadsorption in a patient with SARS-COV-2-19-associated pneumonia: a case report. Nephron. 2020;144(9):459-62.
27. Träger K, Fritzler D, Fischer G, et al. Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series. Int J Artif Organs. 2016;39(3):141-6.
28. Gu Y, Wang D, Chen C, et al. PaO2/FiO2 and IL-6 are risk factors of mortality for intensive care COVID-19 patients. Sci Rep. 2021;11(1):1-8.
29. Rizvi S, Danic M, Silver M, et al. Cytosorb filter: an adjunct for survival in the COVID-19 patient in cytokine storm? A case report. Heart Lung. 2021;50(1):44-50.
30. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. New Eng J Med. 2020;382(18):1708-20.
31. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Clinica Chim Acta. 2020;505:190-1.
32. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
33. Schleicher GK, Lowman W, Richards GA. Case study: a patient with asthma, Covid-19 pneumonia and cytokine release syndrome treated with corticosteroids and tocilizumab. Wits J Clin Med. 2020;2(Si1):47-52.
34. Ruiz-Rodríguez JC, Molnar Z, Deliargyris EN, et al. The use of cytosorb therapy in critically ill COVID-19 patients: Review of the rationale and current clinical experiences. Crit Care Res Pract. 2021;2021:7769516.