International Journal of Health Sciences and Research
Volume 14; Issue: 2; February 2024
Website: www.ijhsr.org
Case Series *ISSN: 2249-9571*

Clinical Assessment of CytoSorb® as an Adjunct Therapy in Co-morbid Patients with Meningitis Sepsis - A Case Series

Dr. Harsh Sapra[1], Dr. Ila Bist[2]

[1]Senior Director & Head, Neuroanaesthesia & Neuro Critical Care, Medanta Medicity, Gurgaon
[2]Associate Consultant, Neuro Critical Care, Medanta Medicity, Gurgaon

Corresponding Author: Dr. Ila Bist

DOI: https://doi.org/10.52403/ijhsr.20240221

ABSTRACT

Objective: The aim of the case series is to provide evidence towards the effectiveness of CytoSorb® therapy in the treatment of meningitis sepsis.
Background: Meningitis sepsis affects 1.2 million people globally and results in about 0.2 million deaths each year. It is characterized by a heightened systemic inflammatory response leading to hydrocephalus, cerebral edema, infarction, and septic shock with multiorgan failure. Controlling the excessive release of cytokines and other inflammatory markers through hemoadsorption has been shown to be beneficial to patients.
Materials and Methods: In this case series, we administered CytoSorb® therapy as an adjunct rescue therapy along with antibiotics in six patients (35 to 67 years) with meningitis sepsis and other severe comorbidities.
Results: We found that CytoSorb® therapy led to hemodynamic stability, reduced mortality, and improvement in disease severity scores. Despite the diverse causes of meningitis sepsis and various comorbidities, all patients showed significant improvement in their clinical and biochemical parameters. Five of the six patients progressed towards a reduction in their treatment and an eventual recovery with no device-related adverse events.
Conclusion: Extracorporeal cytokine hemoadsorption using CytoSorb® appears to be a safe and effective therapy in the management of patients with meningitis sepsis with comorbidities.

Keywords: *meningitis sepsis, CytoSorb®, hemoadsorption, comorbidities, mortality, cytokine storm*

INTRODUCTION

Meningitis is defined as the inflammation of the meninges of brain and spinal cord, caused commonly due to viral or bacterial infections. This condition could be life threatening and is worsened by sepsis, thus resulting in organ failure, tissue damage and even death. Hydrocephalus, cerebral edema, infarction, and septic shock with multiorgan failure are clinical manifestations of meningitis sepsis owing to its severe inflammatory response [1, 2]. Despite advanced developments in pharmacological approaches as well as increased knowledge of basic pathophysiology and host-pathogen interactions in the last three decades, the global incidence of meningitis sepsis increased from 2.5 to 2.8 million and the mortality rate declined only by 21% [3-5]. Meningitis sepsis poses a major economic burden with 50% of survivors exhibiting serious neurological sequelae such as cognitive impairment, hearing loss, epilepsy and focal deficits [6]. Systemic and cerebral complications are causal factors for deaths in geriatric and paediatric patients respectively [7].

Meningitis, caused by a bacterial or viral infection that attacks the brain meninges, is characterized by hematopathological changes, fever and respiratory distress. Invasion of these bacteria/virus into the bloodstream via the nasopharynx mucosa, together with the body's anti-inflammatory defence mechanism triggers an immunological and inflammatory response causing multiple organ failure and sepsis-related complications. Hemodynamic instability, vasopressor requirement, raised cytokine levels, and severity scores (Sequential Organ Failure Assessment - SOFA, Acute Physiology and Chronic Health Evaluation II APACHE-II and Glasgow Coma Score - GCS) are indicators of the patient's condition in meningitis sepsis. These vital scores describe patient prognosis and morbidity, and also measure severity of the disease [8]. The overall scoring of SOFA lies between 0-24, where a score <7.5 indicates a higher survival chance, while a SOFA score >7.5 suggests an increase in the probability of patient's death [9]. APACHE-II scores are employed for the evaluation of patients to determine the degree and levels of therapeutic and diagnostic interventions. The overall scoring of APACHE-II lies between 0-17, and a score of < 15 is considered to be preferable for patient survival [9]. In addition, GCS describes the extent of unconsciousness in traumatic patients and it varies between 1-5 based on mild, moderate and severe disability, and death. GCS between 1-3 indicates an increased risk of patient death while GCS value of 4 or 5 is less severe and is associated with higher chances of survival [10]. Since bacterial meningitis can induce a dysregulated pro-inflammatory response in the body causing multiple organ failure, attenuating this overwhelming immune response may prove beneficial [11, 12]

CytoSorb® therapy, an extracorporeal blood purification technique, normalizes levels of inflammatory mediators (cytokine storm) thus reducing the inflammatory response and lowering the probability of multi-organ failure. As an effective technology for the removal of multiple cytokines, it has an excellent rate of adsorption for various inflammatory mediators viz. tumor necrosis factor-α (TNF-α), interleukin-8, 6, and 1b. It has been designed to ameliorate clinical outcomes associated with meningitis and septic conditions [13]. The device is effective in targeting wide range of toxins with molecular weight approximately 5-60 kDa. There are various studies which report the effectiveness and safety of CytoSorb® therapy. For instance, in a recent study, the use of CytoSorb® therapy in 135 septic cases did not exhibit any side effects [14]. Moreover, CytoSorb® therapy has shown tremendous potential in attenuating the inflammatory conditions in septic shock patients, thus ameliorating their survival. It has also been considered as an effective therapy in the management of hemophagocytic lymphohistiocytosis [14-18]. Additionally, several clinical studies have reported tremendous potential of CytoSorb® therapy in diverse segments including cardiac surgery, organ transplantation, liver failure and COVID-19 conditions [19-21]. A retrospective study conducted on 16 patients experiencing acute kidney injury and post-cardiopulmonary bypass systematic inflammatory response syndrome demonstrated significant reduction in IL-8 and IL-6 levels followed by enhanced hemodynamic stability in patients receiving Cytosorb® therapy [19].Another study investigated the protective effects of Cytosorb® therapy in organ dysfunction of brain-dead potential transplant donors and found that IL-6 (28%) removal was more pronounced with Cytosorb® therapy as compared to removal of TNF-α (8.5%) [20]. Recently, a multicenter, retrospective study was performed to evaluate the potential of Cytosorb® therapy combined with veno-venous extracorporeal membrane oxygenation in Covid-19 patients. The study reported that patients receiving combined therapy for 90 days had lower D-dimer levels with reduced mortality rate as compared to the non-survivors [21]. However, clinical data on the effectiveness of CytoSorb® in

sepsis associated with meningitis is limited. This current case series presents the use of CytoSorb® therapy as an adjunctive rescue therapy with antibiotics in patients suffering from sepsis associated meningitis.

CASE PRESENTATION

The present study is a case series designed to evaluate clinical efficacy of Cytosorb® as an adjunct therapy in six co-morbid adult patients. The patients selected were experiencing acute meningitis/acute meningoencephalitis with high serum levels of cytokines biomarkers. Cytosorb therapy was used on the day of surge of cytokine levels and markers of inflammation. It was generally applied for a minimum of 4 hours to a maximum of 8 hours.

Demographic and clinical characteristics of the patients are presented in **Table 1**. Changes in clinical parameters after CytoSorb® therapy are tabulated in **Table 2.**

Table 1. Patient's Demographic, Clinical Characteristics, Drugs Prescribed, and Outcome

Patient No.	Age (years)/ Sex	Medical History	Comorbidities	Treatment (pre-CytoSorb®)	Drugs (post-CytoSorb®)	Outcomes
1.	49/F	Diabetes Hypertension CKD on dialysis	Pyogenic meningitis with infective endocarditis	Meropenem Vancomycin Colistin	Minocycline Daptomycin Metrogyl	Survived
2.	35/M		Polytrauma Left parietal SDH, Pneumocephalus, Subarachnoid hemorrhage CSF leakage Right lung confusions	Meropenem, Voriconazole Colistin Linezolid	NA	Survived
3.	67/M	Diabetes Mellitus,	Cryptococcal meningitis with septic shock Communicating hydrocephalus	Amphotericin B, Meropenem, Polymyxin, Teicoplanin, hydrocortisone	Vancomycin Fluconazole Minocycline	Survived
4.	57/F	Diabetes Hypertension Rheumatic heart disease with balloon mitral valvotomy	Cardioembolic stroke CVA, Left middle cerebral artery infarct	Meropenem, Teicoplanin	Meropenem, Teicoplanin, Colistin, Anidulafungin	Survived
5.	52/M	Polytrauma with cerebral edema Diabetes Hypertension	Septic shock	Meropenem Vancomycin Colistin Ceftazidime	Voriconazole Intraventricular colistin	Survived
6.	59/ F	Hypertension Diabetes Myocardial infarction coronary artery disease post-PTCA COPD	Septic shock Traumatic subdural hematoma Acute intraventricular hemorrhage	Meropenem, Teicoplanin, Colistin, Ulinastatin, Ascorbic acid	Meropenem, Teicoplanin, Colistin, Tigecycline	Not Survived

CKD = Chronic kidney disease, NA= Not available, SDH= Subdural hematoma, CSF= Cerebrospinal fluid, CVA= Cerebrovascular accident, PTCA= Percutaneous transluminal coronary angioplasty, COPD= Chronic obstructive pulmonary disease

Table 2. Effect of CytoSorb® therapy on Various Clinical Parameters

		Clinical Parameters								
Patient No.		**PCT (ng/ml)**	**TLC (10^3/µl)**	**Platelets (10^3/µL)**	**CRP (mg/L)**	**Lactate (mmol/L)**	**Hemoglobin (g/dL)**	**Serum creatinine (mg/dL)**	**IL-6 (pg/mL)**	**IL-10 (pg/mL)**
1	Pre-CytoSorb®	38.63	15.98	315	72.6	4.3	7.6	5.3	176	16
	Post-CytoSorb®	7.24	11.42	284	40	2.1	6.8	3.5	53	10
2	Pre-CytoSorb®	39.23	7.99	238	256	0.83	8.8	1.8	388	20
	Post-CytoSorb®	20	8.36	245	134	1.3	8.6	2.0	316	16
3	Pre-CytoSorb®	96.59	7.22	80	396	4.11	9.1	0.56	600	20

	Post-CytoSorb®	1.28	7.81	50	115	2.14	8.8	0.6	420	12
4	Pre-CytoSorb®	170.75	16	340	399.3	1.43	12	5.23	20	200
	Post-CytoSorb®	11.25	11.9	258	56	1	10	3.17	340	20
5	Pre-CytoSorb®	150	34.4	400		2.9	9.0	0.43	42	100
	Post-CytoSorb®	16	11.73	236		1	8.8	0.40	15	12
6	Pre-CytoSorb®	64	79.48	112	210	4.04	7.4	1.3	1680	96
	Post-CytoSorb®	5	33.54	129	67	1.15	6.4	0.5	2280	64

Patient 1

A 49-year-old female patient with a medical history of diabetes mellitus, hypertension, and chronic kidney disease on maintenance hemodialysis was admitted to the hospital with pyogenic meningitis with infective endocarditis. Clinical examinations were conducted, and blood culture showed the presence of *Staphylococcus aureus* and *Enterococcus faecium*. Levels of procalcitonin (PCT) (38.63 ng/mL), C-reactive protein (CRP) (72 mg/L), serum lactate (4.1 mmol/L), interleukin - IL-6 (176 pg/mL), IL-10 (16 pg/mL) showed the presence of septic shock associated with meningitis, including multiple organ dysfunction syndrome (MODS). Antibiotic therapy with meropenem, vancomycin, and colistin was started.

CytoSorb® adsorber was commenced with hemodialysis (aPTT/ACT 26 seconds) for 4 hours in order to prevent further organ damage due to excessive inflammatory mediators. Reduction in PCT (7.24 ng/mL), CRP (40 mg/L), lactate (2.1 mmol/L), and IL-6 (53 pg/mL) levels were observed post-CytoSorb® therapy as presented in **Table 2**. X-ray findings showed no abnormalities after 14-days. Improvements in the SOFA score (7 to 5) and APACHE II score (from 17 to 12) were observed. Additionally, the patient had foul smelling loose motions despite the use of probiotics. Therefore, the antibiotics were switched to minocycline, daptomycin and metrogyl. The patient survived showing no adverse effects.

Patient 2

A 35-year-old male patient was admitted to the intensive care unit (ICU) of the hospital after falling from a significant height. He was diagnosed with polytrauma, left parietal subdural hematoma (SDH), pneumocephalus, subarachnoid hemorrhage, and cerebrospinal fluid (CSF) leakage. Clinical investigations indicated meningitis with a fever (38.2°C), and chest X-ray showing respiratory distress. SOFA, APACHE-II, and GCS scores were found to be 6, 14 and 6+T respectively. The arterial pH, bicarbonate, CRP and serum lactate levels of the patient were 7.42, 24.2 mmol/L, 256 mg/L and 0.83 mmol/L respectively. High PCT levels (39.23 ng/mL) and elevated IL-6 levels (388 pg/mL) indicated sepsis. Antibiotic therapy with meropenem, voriconazole, colistin and linezolid was started.

The patient arrived to the hospital with endotracheal tube and was already on ventilator support. CytoSorb® adsorber (1 device) was commenced with hemodialysis (aPTT 26.6 seconds) for 4 hours to alleviate the cytokine storm. His clinical parameters improved post-CytoSorb® therapy with reduced PCT (20 ng/mL), CRP (134 mg/L), and IL6 (316 pg/mL) levels **(Table 2)**. A significant improvement in SOFA and APACHE-II scores were observed i.e., 5 and 11 which reduced to 3 and 6 respectively, thereby ameliorating survival chances. X-rays finding showed resolved respiratory distress in the patient. The patient was hemodynamically stable with 37.6°C body temperature and 120/90 mm Hg blood pressure.

Patient 3

A 67-year-old male patient with a history of diabetes mellitus, cryptococcal meningitis and communicating hydrocephalus was admitted to our hospital due to altered sensorium with shock. General examinations were recorded. MRI and CT revealed a tiny infarction in the vermis-midbrain and external ventricular drain (EVD). The patient was intubated in the ICU due to his low GCS. He was initiated on inotropes, hydrocortisone and supportive treatment for deep vein thrombosis prophylaxis and antibiotic therapy (amphotericin-B, meropenem, polymyxin and teicoplanin). A blood transfusion was done to treat the low hemoglobin (Hb) levels. Cerebrospinal fluid (CSF) analysis showed high protein and lactate levels (5.7 mmol/L). CSF culture was positive for Cryptococcus confirming bacterial meningitis. VP shunt revealed bacterial growth on the tip. The patient developed septic shock with high PCT, CRP, lactate, and IL-6 levels as depicted by the Pre-CytoSorb values in **Table 2**.

Based on clinical investigations, hemodialysis was started together with CytoSorb® cartridge (2 devices) for 6 hours in view of the septic shock. Norepinephrine requirement was reduced from 20 mcg/kg/hr to 15 mcg/kg/hr after post-CytoSorb® therapy, which was reduced to zero after 14 days of follow-up. Improvement in clinical parameters from baseline were found; PCT (1.28 ng/mL), CRP (115 mg/L), serum lactate (2.14 mmol/L), PaO_2/FiO_2 (204 to 800), platelets (80 to $145x10^3$/microlitre), SOFA score (reduced from 7 to 2) and APACHE II score (reduced from 25 to 13) (**Table 2**). He was also managed by IV antibiotics, antifungals (vancomycin, fluconazole, minocycline), fluids, ventilator support and other supportive measures after pleural fluid tapping. He was transferred to ICU again due to his lethargic condition. EVD insertion was performed under aseptic conditions and a decrease in ventricular size was noted. He underwent conversion of right frontal EVD to right-sided ventriculoperitoneal shunt and was kept under observation. He was moved back to the wards after stability.

Patient 4

A 57-year-old female patient with a history of headache, sinusitis, high grade fever, neck rigidity and CSF indicative of meningitis was admitted to our hospital. She arrived to Medanta Medicity on Day 3 of illness with right-sided weakness, therefore an MRI of her brain was done. She was diagnosed with partially treated meningitis with left middle cerebral artery infarct. She additionally had a history of hypertension, diabetes mellitus and rheumatic heart disease with balloon mitral valvotomy (RHD-post BMV). She was intubated and on ventilator due to respiratory distress and poor GCS. Antibiotic therapy with meropenem, teicoplanin and colistin followed by anidulafungin was given in view of septic shock, multiple organ dysfunction and fungemia. Non-contrast CT of the brain showed multiply scattered hyper densities suggestive of hemorrhagic transformation.

She was initiated on CytoSorb® therapy for 8 hours in view of the septic shock with MODS as indicated by elevated PCT (>10 ng/mL) and CRP levels (>50 mg/L) [22]. Norepinephrine dose was reduced from 14.5 to 5 mcg/kg/hr post-therapy. Improvements in clinical parameters were noted after the 14-day follow-up: SOFA score (reduced from 10 to 4), APACHE II score (reduced from 22 to 14), PaO_2/FiO_2 (900). Reduction in PCT (11.25 ng/mL), CRP (56 mg/mL) and lactate (1 mmol/L) levels were observed as shown in **Table 2**. A transesophageal echocardiogram revealed a small mobile clot attached to the inferior vena cava-right atrium (IVC-RA) suspicious of rheumatic heart disease. In addition, the number of organ dysfunction in patient was found to be 3, therefore she was transferred to a hospital in stable condition for sustained low-efficiency dialysis (SLED) on alternate days, and simultaneously she was on injectable anticoagulants and antibiotics medications.

Patient 5

A 52-year-old male patient was a follow-up case of hypertension and diabetes mellitus. He was admitted with alleged history of road traffic accident few days back. He also had a history of extra-ventricular drainage (EVD) insertion, meningitis and septic shock along with polytrauma and cerebral edema. His GCS had deteriorated due to septic shock post EVD insertion in a local hospital. CSF analysis revealed low glucose levels (<50 mg/100mL) and high protein levels (>60 mg/dL) indicating bacterial meningitis. Antibiotic therapy with meropenem and vancomycin was given for 5 days due to bacterial growth in the CSF. Initial clinical examination showed elevated body temperature (39°C), endotoxin activity assay (EAA) level (0.8), PCT (150 ng/mL), serum lactate (2.9 mmol/L), IL-6 (42 pg/mL), IL-10 (100 pg/mL) andPaO_2/FiO_2 ratio (300). Based on severity scores (SOFA and APACHE-II) and clinical investigation, CytoSorb® adsorber was commenced with SLED (aPTT/ACT 31.1 seconds) for 8 hours. Vasopressor requirement (norepinephrine) was reduced from 1.3 mcg/kg/hr to 0.5 mcg/kg/hr post-CytoSorb® therapy. After 7- and 14-days follow-up period no vasopressor was required to stabilize the patient's condition. Reduction in serum lactate (1 mmol/L), IL-6 (15 pg/mL), and IL-10 (12 pg/mL) levels were observed as shown in **Table 2**. CRP levels could not be measured due to technical error. Improvements in other clinical parameters and disease severity scores were observed post CytoSorb® therapy: PaO_2/FiO_2 ratio (500), SOFA (reduced from 7 to 4) and APACHE-II (reduced from 26 to 21). The EVD was removed and patient was switched to colistin and ceftazidime fortum. After insertion of a fresh EVD, voriconazole and intraventricular colistin was started. However, the patient continued to have a fever and a low GCS despite proper antibiotic medication and care. The family was informed about the requirement for and complications of putting in a new EVD. The patient's condition was stable when his family discharged him from the hospital against medical advice.

Patient 6

A 59-year-old female patient was admitted to the hospital after a road accident. Clinical investigations were performed showing traumatic SDH and the patient was intubated and put on a ventilator. The patient with a history of hypertension, myocardial infarction, coronary artery disease post percutaneous transluminal coronary angioplasty (PTCA), type 2 diabetes mellitus, and respiratory distress, and was transferred to our hospital due to septic shock. Clinical investigations showed multiple bacterial growth in the blood indicating meningitis and high serum lactate levels (4.04 mmol/L), low platelet count, low GCS score (3+ET), high SOFA and APACHE (31) scores indicating sepsis. Antibiotic therapy (meropenem, teicoplanin and colistin) was initiated along with other treatments (Ulinastatin, ascorbic acid, micronutrients and vasopressors). The patient required inotropic support due to multiple organ failure. For the management of septic shock, CytoSorb® therapy (2 devices) was given. Initially, an improvement in the SOFA (9) and APACHE-II (23) scores were observed with a reduction in PCT (64 ng/mL), CRP (210 mg/L), and lactate (4.04 mmol/L) levels along with vasopressors requirement (**Table 2**). However, her condition deteriorated with worsening SOFA (18) and APACHE (32) scores showing high mortality chances after 7-day follow-up to CytoSorb® therapy. The worsening of SDH and respiratory acidosis was confirmed by bronchoscopy which revealed thick mucous plaques and significant ascites with right-sided pleural effusion. Bleeding was observed during drainage catheterization postponing the procedure. She suffered bradycardia followed by asystole and was declared dead.

DISCUSSION

Sepsis and meningitis cause substantial clinical and economic burden to healthcare

systems owing to their significant mortality and morbidity rates [23]. Effective and early empiric treatment can improve the survival rates in these patients. CytoSorb® therapy which alleviates the inflammatory mediators can be helpful in reducing the mortality rate as predicted in preclinical studies [24, 25]. CytoSorb® technique is promising in that it improves metabolic dysfunction and hemodynamic stability by removing pro-and anti-inflammatory cytokines and other pathogens in sepsis and septic shock [24-26]. A case report in a pediatric patient with severe septic shock associated with *Neisseria meningitides* showed stabilization in hemodynamics as well as improvement in metabolic disorders indicated by a reduction in lactate levels after symptomatic treatment along with CytoSorb® therapy. Reduction in PCT (52.73 to 1.02 ng/ml), CRP (136.8 to 14.7 mg/L), and interleukins (IL-6 and IL-10) were observed in a pediatric patient after therapy [27]. One other case report in a pediatric patient suffering from severe meningococcal meningitis accompanied by septic shock showed reductions in PCT, CRP, interleukins (IL-6 and IL-10) and vasopressor requirement post-CytoSorb® therapy along with antibiotics and other symptomatic treatments. Metabolic dysfunction and PaO_2/FiO_2 ratio were improved with resolved septic shock justifying the efficacy of cytokine adsorption (by CytoSorb® therapy) for the treatment of meningitis sepsis. Improvements in hemodynamic parameters and reduction in vasopressor requirement (up to $1/3^{rd}$ from the initial requirement) have been observed in this case series. In addition to hemodynamic stability, inflammatory mediators (IL-10, IL-6, cytokines) of patients were also found to be reduced (from 19 to 70%) after the use of CytoSorb® as an adjunct therapy.

In addition to inflammatory mediators and metabolic dysfunction, severity scores i.e., SOFA and APACHE are useful tools to help determine survival chances in meningitis sepsis. These vital scores describe patient prognosis and morbidity, and also measure severity of disease. SOFA scoring (0-24) is done on the basis of examination of six organ systems (neurological, renal, coagulation, hepatic, cardiovascular and respiratory) [8]. Moreover, APACHE score (0-74) measures disease severity based on patient's medical history, physiological measurements and age [28]. An increase in SOFA and APACHE scores might lead to higher mortality. A case series in three patients with meningococcal meningitis and two patients with pneumococcal meningitis reported a marked improvement in SOFA scores along with a reduction in inflammatory mediators and vasopressor requirement post-CytoSorb® therapy in all the patients except one [1]. A multi-centric prospective report has also shown improved survival rate by 8% in sepsis patients indicated by a reduction in SOFA (12.9 to 9.4) and APACHE-II (25.45 to 20.1) scores [29]. Improvement in SOFA and APACHE scores was observed in all patients in this case series except one (Patient 6) post-CytoSorb® therapy showing the improved survival chances of the patients. Even Patient 6 showed an improvement in APACHE and SOFA scores initially, but after follow-up, their condition deteriorated with subsequent worsening APACHE and SOFA scores.

Early predictions of sepsis development in meningitis patients through various biomarkers (EAA, interleukins, total leukocyte count and platelet count), hemodynamic instability, metabolic dysfunction (serum lactate levels) and mortality scoring (APACHE-II and SOFA), as well as early intervention based on clinical diagnosis, have been found to be successful in improving the survival rate. Initiation of CytoSorb® treatment within 24 hours has improved the survival rate of patients with meningitis sepsis as observed in various case series and reports [1]. The present case series has supported the early use of CytoSorb® to improve survival chances. The late diagnosis of meningitis and delayed initiation of CytoSorb® therapy (>24 hours) in addition to an already critical condition resulted in the death of patient 6 although even she showed a reduction in PCT, CRP, serum lactate and

IL-10 levels indicating improved metabolic and hemodynamic stability. However, due to her critical condition, no medical treatment could help her.

CytoSorb® therapy has been indicated for infective endocarditis, bacterial meningitis, multiple myeloma, aortic valve endocarditis, sepsis from enterotoxins, fungal/viral/bacterial sepsis, post-surgical patients with sepsis and kidney disease, immunocompromised patients and special populations (e.g. pediatric, geriatrics, chronic liver dysfunction and dialysis patients) [30]. In this case series, CytoSorb® therapy helped stabilize the clinical condition of patients with sepsis due to accident or trauma, tubercular meningitis, traumatic hematoma, cardioembolic stroke, cryptococcal meningitis with communicating hydrocephalus, and pyogenic meningitis with infective endocarditis. In addition to this, CytoSorb® has been shown to treat the patients ranging from pediatrics to geriatrics [31]. Similar observations have been reported in this case series showing an improvement in the clinical condition of patients aged 35 to 67 years by CytoSorb® therapy. Overall, four parameters can be considered as signs of successful CytoSorb® therapy in meningitis sepsis as observed in present case series: i. hemodynamic stability (indicated by decreased requirement for vasopressor agents), ii. improvement in metabolic dysfunction (indicated by reduction in lactate levels), iii. reduction in the levels of inflammatory markers and cytokines (PCT, CRP, IL-6, IL-10), and iv. reduction in severity scores (SOFA, APACHE-II and GCS).

However, there are certain limitations of this case series related to the design and nature of such studies. A small heterogenous patient pool makes comparisons difficult owing to their varied medical history and comorbidities. The lack of a control arm and the use of multiple and different treatment interventions (such as antibiotics, vasopressors, various medical procedures) apart from CytoSorb®, make it difficult to compare these patients and to attribute outcomes to CytoSorb® alone. These limitations should be considered in designing future studies or larger trials.

CONCLUSION

CytoSorb® therapy is a promising treatment option along with antibiotics in meningitis sepsis patients with high morbidities. This case series reports on the improvement in metabolic dysfunction and hemodynamic stability with no adverse effects post-CytoSorb® therapy. Furthermore, early initiation of CytoSorb® therapy is suggested to increase the survival chances in critically ill patients. Considering the positive clinical outcomes of this case series, larger studies with appropriate control arms are needed to objectively quantify the clinical efficacy of CytoSorb® therapy.

Declaration by Authors

Ethics approval: Not applicable

Acknowledgement: The authors acknowledge Knowledge Isotopes Pvt. Ltd.(http://www.knowledgeisotopes.com) for medical writing assistance.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

Informed consent: Not applicable as patients' identity has not been disclosed or compromised.

Availability of data and material: The data that support the findings of this study are available from the corresponding author, [IB], upon reasonable request.

Author's contribution

HS and IB were involved in the clinical care of the patient. They were involved in data collection and interpretation of the sequencing data. HS drafted the manuscript and it was critically revised by both authors. Both authors have seen the final draft and take full responsibility of the contents of the manuscript.

ORCID: HS: https://orcid.org/0000-0002-2500-7124

IB: 0009-0003-0624-7717

REFERENCES

1. Leonardis, F., et al., *Effect of hemoadsorption for cytokine removal in pneumococcal and meningococcal sepsis.* Case Reports in Critical Care, 2018. 2018.
2. Putz, K., K. Hayani, and F.A. Zar, *Meningitis.* Primary care: clinics in office practice, 2013. 40(3): p. 707-726.
3. Zunt, J.R., et al., *Global, regional, and national burden of meningitis, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016.* The Lancet Neurology, 2018. 17(12): p. 1061-1082.
4. Kastenbauer, S. and H.W. Pfister, *Pneumococcal meningitis in adults: Spectrum of complications and prognostic factors in a series of 87 cases.* Brain, 2003. 126(5): p. 1015-1025.
5. Muralidharan, R., F. Mateen, and A. Rabinstein, *Outcome of fulminant bacterial meningitis in adult patients.* European Journal of Neurology, 2014. 21(3): p. 447-453.
6. Pathan, N., S. Faust, and M. Levin, *Pathophysiology of meningococcal meningitis and septicaemia.* Archives of disease in childhood, 2003. 88(7): p. 601-607.
7. Hoogman, M., et al., *Cognitive outcome in adults after bacterial meningitis.* Journal of Neurology, Neurosurgery & Psychiatry, 2007. 78(10): p. 1092-1096.
8. Asmarawati, T.P., et al., *Predictive Value of Sequential Organ Failure Assessment, Quick Sequential Organ Failure Assessment, Acute Physiology and Chronic Health Evaluation II, and New Early Warning Signs Scores Estimate Mortality of COVID-19 Patients Requiring Intensive Care Unit.* Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine, 2022. 26(4): p. 464.
9. Ebrahimi, K., et al., *Determining and Comparing Predictive and Intensity Value of Severity Scores–"Sequential Organ Failure Assessment Score," "Acute Physiology and Chronic Health Evaluation 4," and "Poisoning Severity Score"–in Short-Term Clinical Outcome of Patients with Poisoning in an ICU.* Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine, 2018. 22(6): p. 415.
10. Chou, C., et al., *Comparison of the APACHE II, GCS and MRC scores in predicting outcomes in patients with tuberculous meningitis.* The International journal of tuberculosis and lung disease, 2010. 14(1): p. 86-92.
11. Brouwer, M.C., A.R. Tunkel, and D. van de Beek, *Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis.* Clinical microbiology reviews, 2010. 23(3): p. 467-492.
12. Barichello, T., et al., *Targets for adjunctive therapy in pneumococcal meningitis.* Journal of Neuroimmunology, 2015. 278: p. 262-270.
13. Ankawi, G., et al., *What have we learned about the use of cytosorb adsorption columns?* Blood purification, 2019. 48(3): p. 196-202.
14. Singh, Y., et al., *Hemoadsorption by extracorporeal cytokine adsorption therapy (CytoSorb®) in the management of septic shock: A retrospective observational study.* The International Journal of Artificial Organs, 2020. 43(6): p. 372-378.
15. Mehta, Y., et al., *Experience with hemoadsorption (CytoSorb®) in the management of septic shock patients.* World Journal of Critical Care Medicine, 2020. 9(1): p. 1.
16. Bonavia, A., et al., *Clinical utility of extracorporeal cytokine hemoadsorption therapy: a literature review.* Blood purification, 2018. 46(4): p. 337-349.
17. Friesecke, S., et al., *Extracorporeal cytokine elimination as rescue therapy in refractory septic shock: a prospective single-center study.* Journal of Artificial Organs, 2017. 20: p. 252-259.
18. Hinz, B., et al., *CytoSorb, a novel therapeutic approach for patients with septic shock: a case report*. 2015, SAGE Publications Sage UK: London, England.
19. Träger, K., et al., *Hemoadsorption treatment of patients with acute infective endocarditis during surgery with cardiopulmonary bypass-a case series*. 2017, SAGE Publications Sage UK: London, England.
20. Kellum, J.A., et al., *Feasibility study of cytokine removal by hemoadsorption in brain-dead humans.* Critical care medicine, 2008. 36(1): p. 268-272.
21. Song, T., et al., *CytoSorb therapy in COVID-19 (CTC) patients requiring extracorporeal membrane oxygenation: a multicenter,*

retrospective registry. Frontiers in Medicine, 2021. 8: p. 2688.
22. Povoa, P., et al., *C-reactive protein as an indicator of sepsis.* Intensive care medicine, 1998. 24: p. 1052-1056.
23. Salman, O., et al., *Systematic Review on the Acute Cost-of-illness of Sepsis and Meningitis in Neonates and Infants.* The Pediatric infectious disease journal, 2020. 39(1): p. 35-40.
24. Rugg, C., et al., *Hemoadsorption with CytoSorb in septic shock reduces catecholamine requirements and in-hospital mortality: a single-center retrospective 'genetic'matched analysis.* Biomedicines, 2020. 8(12): p. 539.
25. Peng, Z.-Y., M.J. Carter, and J.A. Kellum, *Effects of hemoadsorption on cytokine removal and short-term survival in septic rats.* Critical care medicine, 2008. 36(5): p. 1573.
26. Kogelmann, K., et al., *Hemoadsorption by CytoSorb in septic patients: a case series.* Critical Care, 2017. 21(1): p. 1-10.
27. Akcay, N., et al., *Immunoadsorption therapy for a meningococcemia patient with myocarditis, adrenal hemorrhage, and purpura fulminans: a case report.* Brazilian Journal of Anesthesiology, 2022. 72: p. 819-822.
28. Lee, M.A., et al., *Acute physiology and chronic health evaluation II score and sequential organ failure assessment score as predictors for severe trauma patients in the intensive care unit.* Korean Journal of Critical Care Medicine, 2017. 32(4): p. 340-346.
29. Paul, R., 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 Journal of Critical Care Medicine, 2021. 10(1): p. 22.
30. Träger, K., et al., *Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series.* The International Journal of Artificial Organs, 2016. 39(3): p. 141-146.
31. Brouwer, W.P., et al., *Hemoadsorption with CytoSorb shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study.* Critical Care, 2019. 23(1): p. 1-9.

How to cite this article: Harsh Sapra, Ila Bist. Clinical assessment of CytoSorb® as an adjunct therapy in co-morbid patients with meningitis sepsis - a case series. *Int J Health Sci Res.* 2024; 14(2):158-167. DOI: *10.52403/ijhsr.20240221*

******