Journal of Advances in Medical and Pharmaceutical Sciences

Volume 26, Issue 11, Page 32-44, 2024; Article no.JAMPS.124048
ISSN: 2394-1111

An Observational Study on Clinical Benefits of CytoSorb in Patients with Severe Sepsis

Anand Nikumbhe [a*], Sudarshan Ballal [a], Rohan Augustine [a], Vishwanath Siddini [a] and Sunil Karanth [b]

[a] Department of Nephrology, Manipal Hospitals, Bangalore, Karnataka, India.
[b] Department of Critical Care Medicine, Manipal Hospitals, Bangalore, Karnataka, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/jamps/2024/v26i11723

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/124048

Original Research Article

Received: 05/08/2024
Accepted: 07/10/2024
Published: 15/10/2024

ABSTRACT

Background and Aim: Sepsis is a well-recognized healthcare issue worldwide. Despite research, the ability to positively influence outcome remains limited. Newer evidences have pointed that using adsorption of cytokines is beneficial during endotoxemia and sepsis. Therefore, this study was aimed to determine the clinical benefits of CytoSorb usage in patients with severe sepsis admitted in intensive care units (ICU).
Study Design: Prospective, observational, comparative study.
Material and Methods: Forty patients with sepsis admitted to ICU were included. The CytoSorb group included 20 patients who received CytoSorb therapy in addition to Standard-care (SOC) and 20 patients in SOC group who received SOC alone as per routine ICU protocols. Clinical and laboratory parameters were analyzed pre/post-treatment in both groups and compared.

**Corresponding author: E-mail: anikumbhe@gmail.com;*

Cite as: *Nikumbhe, Anand, Sudarshan Ballal, Rohan Augustine, Vishwanath Siddini, and Sunil Karanth. 2024. "An Observational Study on Clinical Benefits of CytoSorb in Patients With Severe Sepsis". Journal of Advances in Medical and Pharmaceutical Sciences 26 (11):32-44. https://doi.org/10.9734/jamps/2024/v26i11723.*

Results: CytoSorb and SOC groups were comparable at baseline. There was significant reduction in serum creatinine (2.59±2.0 vs. 2.89±1.2, mg/dl; *P*=0.042), serum lactate (3.26±1.1 vs. 3.27±0.9, mmol/lit; *P*<0.001), serum procalcitonin (2.75±2.4 vs. 3.39±3.5, ng/ml; *P*<0.001), serum CRP (90.2±57.4 vs. 175.6±100.9, mg/dl; *P*<0.001) and serum IL6 (1769.7±4444.1 vs. 256.8±392.4, pg/ml; *P*=0.03) levels in CytoSorb compared to SOC. There was significant improvement in mean arterial pressure (MAP) (65.75±1.8 vs. 62.75±2.8, mmHg; *P*<0.001) and reduction in norepinephrine dose (6.47±2.7 vs.10.65±3.6, mcg/min; *P*<0.001) in CytoSorb group reflecting better hemodynamic stability. The post-treatment increase in SOFA score was lesser in CytoSorb group (11.85±2.9) than SOC group (12.3±2.3), but was not significant (*P*=0.135).
Conclusion: CytoSorb therapy along with SOC was associated with significant improvements in hemodynamic stability, MAP and Norepinephrine requirements than SOC alone in severe sepsis.

Keywords: Cytosorb; cytokine reduction; SOFA score; hemodynamic stability; sepsis.

1. INTRODUCTION

Sepsis remains a significant cause of mortality and morbidity worldwide, despite advancements in antimicrobial medication, resuscitative methods, and ventilator care. The condition is characterized by a dysregulated immune response to an infection, leading to organ dysfunction and failure, with septic shock being a severe form of the disease associated with a high case fatality rate [1,2].

Septic shock can cause severe hypotension, and is characterized by high amounts of cytokines generated during the accelerated immune phase. These cytokines play a significant role in causing vascular collapse and exacerbating inflammation, which can lead to tissue damage through ischemia, reperfusion, and organ hypoperfusion [3].

In recent decades, extracorporeal blood purification methods have been developed to modulate the immune response and cytokines in patients with sepsis [4]. These include hemofiltration with large volume, high cut-off membranes, adsorption alone, and combined plasma filtration with adsorption [4,5,6,7]. Although the evidence for their usage is currently evolving, studies examining their usefulness, safety, and innovative possibilities continue to grow [4,5,6]. Adsorption treatment is currently one of the most rapidly growing fields, with adsorption cartridges with additional functionalities being developed [4,7].

The use of hemoadsorption to reduce cytokines is a new method for purifying blood that was created to decrease the large amounts of pro and anti-inflammatory substances produced during the initial phases of sepsis [8]. Evidence is pointing that adding an extracorporeal cytokine adsorber to the treatment plan leads to effective removal of dangerous cytokines and might be useful for patients with severe sepsis [9,10].

The CytoSorb (manufactured by CytoSorbents Corporation, Monmouth Junction, NJ, USA) whole blood adsorber is a medical device developed for use in Clinical settings where cytokine levels are elevated. Its distinct attributes, such as the highly porous biocompatible polymer, have the ability to attach to various hydrophobic substances with molecular weights up to around 60 kDa, which is where most cytokines are located. This device eliminates cytokines from the bloodstream in order to mitigate the excessive immune response associated with sepsis and helps to achieve better clinical outcomes [11,12].

Cytokine reduction by hemoadsorption is a novel blood purification therapy that is designed to reduce the high quantities of pro-inflammatory and anti-inflammatory mediators generated in the early stages of sepsis [7]. Hemoadsorption by CytoSorb may be beneficial in septic shock patients by attenuating cytokine storm, improving hemodynamic stability, and reducing vasopressor requirements [10].

This study was aimed to evaluate the clinical benefits of CytoSorb usage in patients with severe sepsis. The primary objective was to investigate whether treatment with CytoSorb and standard of care (SOC) was associated with improvements in hemodynamic stability, mean arterial pressure (MAP), and norepinephrine requirements compared to SOC alone. The secondary objectives included evaluating the safety of CytoSorb treatment, examining the reduction in inflammatory biomarkers such as Interleukin-6 (IL6) and C- reactive proteins (CRP), and markers of sepsis, such as procalcitonin and serum lactate.

2. MATERIALS AND METHODS

This was a prospective, observational study among patients with severe sepsis or septic shock, conducted at Multidisciplinary ICU and Department of Nephrology, Tertiary care hospital in Bangalore, India from February 2020 to November 2021.

This study was conducted in compliance with xxx Ethics Committee (EC) requirements as per applicable regulations. All study documents were reviewed and approved by Institutional Ethics Committees (IEC) on 27th February 2020 prior to initiation of the study.

2.1 Study Participants

Total forty (N=40) patients of sepsis with multiorgan dysfunction were part of the study. Patients received CytoSorb therapy along with standard of care (CytoSorb group) or standard of care alone (SOC group) as per routine ICU protocols and were accordingly divided into CytoSorb and SOC group with 20 patients in each group.

2.2 Cytosorb Score

CytoSorb score was calculated for each patient using a five-point scoring system Patients with CytoSorb score 8-13 were considered to be part of the study (Supplementary file) [10,11,12].

2.3 Inclusion and Exclusion Criteria

The study included male or non-pregnant female patients above 18 years of age with confirmed diagnosis of sepsis or septic shock with CytoSorb Score between 8 to 13.

Patients with terminal illness (e.g., malignancy, chronic kidney diseases (CKD), chronic liver diseases (CLD)) or immunosuppressed state like HIV infection or on immunosuppressant therapy were excluded from the study.

2.4 Study protocol

All patients admitted to multidisciplinary intensive care unit with sepsis and multiorgan dysfunction were considered for the study according to the inclusion and exclusion criteria. After initial stabilization, patients with CytoSorb Score between 8 to 13 who received CytoSorb therapy along with standard of care as per routine ICU protocols comprised the CytoSorb group while patient who received only standard of care comprised the SOC group. Duration of CytoSorb therapy was 24 hours for CRRT (Continuous Renal Replacement Therapy) and 6-8 hours for SLED (Slow Low Efficiency Dialysis) depending on mode of dialysis. Serum cytokine-IL6 measured before initiation and 24 hours after completion of CytoSorb therapy were evaluated.

After the first session of CytoSorb treatment, the following parameters were reassessed:

- Mean Arterial pressure (MAP).
- Inotropic requirements.
- Renal parameters.
- SOFA score.
- Serum lactate levels.
- Serum interleukin 6 (IL-6) levels.

Other laboratory parameters that were measured before and after treatment with CytoSorb:

- Hemoglobin.
- Leucocyte counts.
- Platelets.
- Serum Electrolytes.
- Liver function tests.
- Procalcitonin levels, CRP levels

2.5 Statistical Analysis

Data were entered into a Microsoft Excel datasheet and was analyzed using SPSS 22 version software. Data was expressed in descriptive statistics. The Chi-square test or Fischer's exact test (for 2x2 tables only) was used as a test of significance for qualitative data. An independent t-test was used as a test of significance between two quantitative variables. *P*-value of <0.05 was considered as statistically significant.

3. RESULTS

Total 40 patients with sepsis were included in the study. As per ICU protocols, 20 patients who received CytoSorb treatment along with the SOC were considered in CytoSorb group and 20 patients who received only SOC were considered in SOC group.

3.1 Demographics and Comorbidities

The mean age for CytoSorb and SOC groups was 45.05±17.03 years and 51.90±9.99 years respectively. No statistically significant difference

was noted between two groups with respect to age (*P*=0.131) or gender (*P*=0.176). Distribution of subjects according to comorbidities diabetes mellitus (n=10 in CytoSorb, n=10 in SOC), hypertension (n=13 in CytoSorb and n=12 in SOC) and cardiovascular disease (n=5 in CytoSorb, n=4 in SOC) between groups also found no statistical difference (*P*=1.0).

3.2 Type of Renal Replacement Therapy

Total 29 patients (72.5%) received CRRT while 11 patients (27.5%) received SLED. Number of patients receiving CRRT was 15 in CytoSorb group (75%) and 14 in SOC group (70%) while 05 patients in CytoSorb group (25%) and 06 patients in SOC group (30%) received SLED. No statistically significant difference was noted.

3.3 Cause of Sepsis

The etiology/cause of infection in sepsis patients were comparable between both the groups (Table 1).

3.4 Baseline Clinical and Laboratory Parameters

Baseline clinical and laboratory parameters like serum creatinine, LFTs and PAO2/FIO2 ratio were comparable between CytoSorb and SOC groups. However, SOFA score, serum lactate and procalcitonin were more severe in CytoSorb group than SOC group (Table 2).

3.5 Comparison of Various Parameters pre and Post Treatment Between CytoSorb and SOC Group

3.5.1 Blood Parameters

No statistically significant difference was observed in hemoglobin, platelets, white blood cell count, bilirubin, SGOT, SGPT, albumin before and after treatment in both the groups. A comparison of pre/post- treatment mean values between both the groups showed a significant reduction in serum creatinine (*P*=0.04), lactate (*P*<0.001), procalcitonin (*P*<0.001), CRP (*P*<0.001) and IL6 (*P*=0.03) levels (Table 3).

Table 1. Etiology/cause of Sepsis

Cause of Sepsis	SOC plus CytoSorb	SOC
COVID-19	8 (40%)	9 (45%)
Pneumonia	1 (5%)	2 (10%)
Urosepsis	4 (20%)	2 (10%)
Post COVID-19 Mucor	1 (5%)	1 (5%)
Cholangitis	-	2 (10%)
Cellulitis	1 (5%)	-
Viral Pneumonia	1 (5%)	1 (5%)
Dengue Fever	2 (10%)	1 (5%)
Post COVID-19 Sepsis	1 (5%)	1 (5%)
Scrub Typhus	-	1 (5%)
Leptospirosis	1 (5%)	-

SOC- Standard of Care

Table 2. Baseline clinical and laboratory parameters in the two groups

Parameters	SOC plus CytoSorb	SOC	*P*- value
Creatinine (mg/dl)	2.68	3.46	0.3
Lactate (mmol)	2.57	3.75	<**0.001**
Bilirubin (mg/dl)	2.03	2.48	0.6
Procalcitonin (ng/ml)	2.36	5.45	**0.007**
CRP (mg/dl)	108.45	172.7	**0.01**
IL6 (pg/ml)	6125.15	91.7	**0.03**
MAP (mmhg)	66.2	63.4	**<0.001**
PaO2/FiO2	220	229	0.5
Norepinephrine Dose (mcg/min)	7.2	8	0.1
SOFA Score	10.95	11.65	**0.01**

SOC- Standard of Care

Table 3. Comparison of pre and post treatment of key blood parameters between groups

Groups	SOC plus CytoSorb (Mean±SD)			SOC (Mean±SD)			P-value
Parameter	**Pre**	**Post-treatment**	**Difference**	**Pre**	**Post-treatment**	**Difference**	
Creatinine (mg/dl)	3.46 ± 3.16	2.59 ± 2.09	-0.87 ± 1.82	2.68 ± 1.50	2.89 ± 1.20	0.21 ± 1.44	0.042
Lactate (mmol)	3.75 ± 0.64	3.26 ± 1.07	-0.49 ± 1.10	2.57 ± 0.54	3.27 ± 0.97	0.70 ± 1.06	<0.001
Procalcitonin (ng/ml)	5.45 ± 4.58	2.75 ± 2.41	-2.7 ± 3.92	2.36 ± 1.51	3.39 ± 3.55	1.03 ± 2.37	<0.001
CRP (mg/dl)	172.7 ± 82.77	90.25 ± 57.49	-82.4 ± 73.81	108.45 ± 81.28	175.6 ± 100.97	67.15 ± 101.85	<0.001
IL6 (pg/ml)	6125.15 ± 11959.18	1769.75 ± 4444.09	-4355.4 ± 9100.4	91.7 ± 68.507	256.85 ± 392.404	165.15 ± 374.5	0.032

SOC- Standard of Care

3.5.2 Mean Arterial pressure (MAP)

A comparison between mean values of MAP pre (CytoSorb: 63.40±2.32 mmHg; SOC: 66.20±1.90 mmHg) and post- treatment (CytoSorb: 65.75±1.83 mmHg; SOC: 62.75±2.88 mmHg) between both the groups showed a significant (*P*<0.001). improvement in MAP in the CytoSorb group (Fig. 1).

3.5.3 Norepinephrine dose

Comparison of mean norepinephrine dose pre (CytoSorb: 8.00±1.835 mcg/min; SOC: 7.20±1.908 mcg/min) and post-treatment (CytoSorb: 6.47±2.750 mcg/min; SOC: 10.65±3.674 mcg/min) between both the groups showed a significant (*P*<0.001) decrease in requirement of norepinephrine dose in the CytoSorb group (Fig. 2).

3.5.4 PaO2/FiO2

A comparison between PaO2/FiO2 ratio pre and post- treatment between both the groups presented in Table 4 and it showed no significant difference between both the groups.

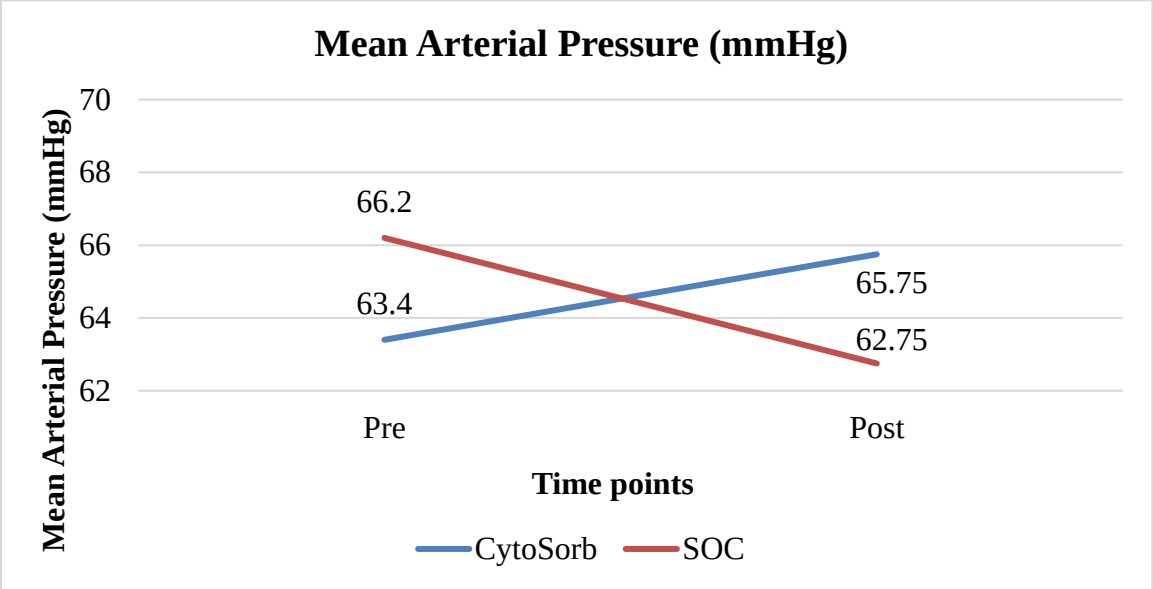

Fig. 1. Comparison of pre and post mean values of Mean Arterial Pressure between groups

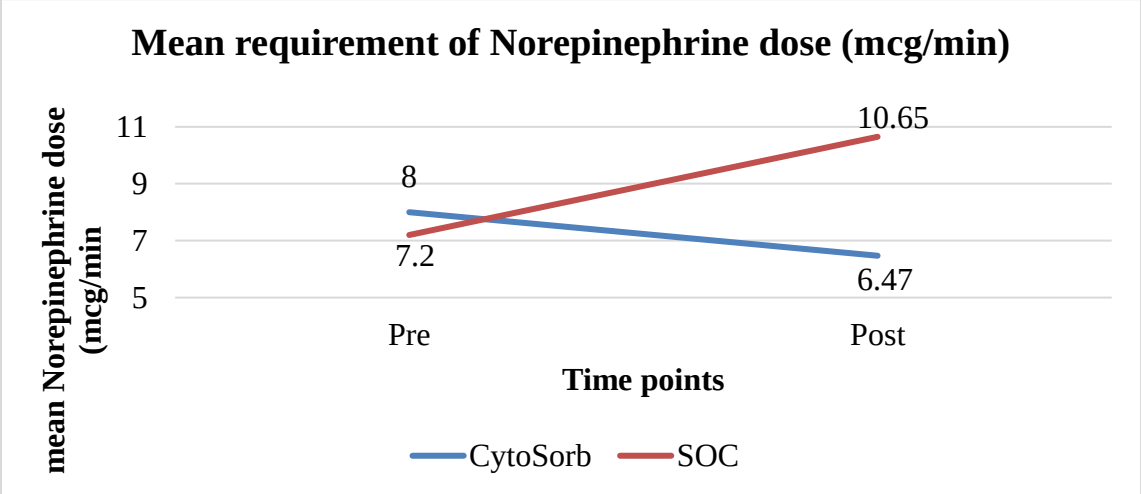

Fig. 2. Comparison of pre and post mean requirement of norepinephrine dose between groups

3.5.5 CNS Parameters

A comparison between Glasgow Coma Scale (GCS) values pre and post- treatment between both the groups presented in Table 5 and it showed no significant difference between both the groups.

3.5.6 SOFA Score

A comparison between SOFA scores pre and post- treatment between both the groups presented in Table 6. The SOFA score at baseline was significantly higher in the CytoSorb group than in the SOC group (*P*=0.016). There was no statistically significant difference found between both the groups with respect to SOFA score post- treatment. (*P*=0.135). However, increase in the SOFA score was relatively lesser in the Cytosorb group than the control group. Though it did not reach statistical significance.

3.6 Mortality

The distribution of subjects according to mortality between groups did not show any statistical (*P*=1.00) significance (Fig. 3).

Table 4. Comparison of pre and post-treatment PaO2/FiO2 ratio between groups

Parameter	Groups	Mean	SD	*P*-Value
PaO2/FiO2 - Pre (mmHg)	SOC plus CytoSorb	229.00	39.32	0.554
	SOC	220.00	54.58	
PaO2/FiO2 - Post (mmHg)	SOC plus CytoSorb	215.50	37.48	0.252
	SOC	197.50	58.02	

SOC- Standard of Care

Table 5. Comparison of pre and post-treatment Glasgow Coma Scale (GCS) values between groups

Parameter	Groups	Mean	SD	*P*-Value
GCS – Pre	SOC plus CytoSorb	10.90	0.78	0.791
	SOC	10.80	1.47	
GCS - Post	SOC plus CytoSorb	10.60	1.35	0.767
	SOC	10.45	1.79	

SOC- Standard of Care, GCS- Glasgow Coma Scale

Table 6. Comparison of pre and post mean SOFA scores between groups

Parameter	Groups	Mean	SD	*P*-Value
SOFA Score - Pre	SOC plus CytoSorb	11.65	0.87	0.016
	SOC	10.95	0.88	
SOFA Score - Post	SOC plus CytoSorb	11.85	2.92	0.597
	SOC	12.30	2.38	
Pre - Post	SOC plus CytoSorb	-0.20	2.62	0.135
	SOC	-1.35	2.11	

SOC- Standard of Care

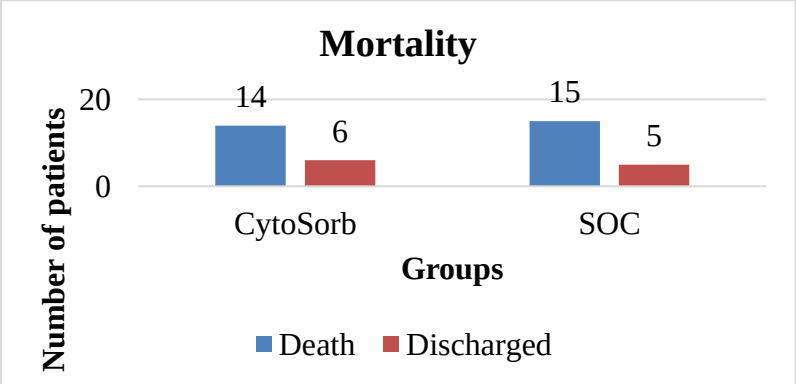

Fig. 3. Distribution of patients according to mortality in the two groups

This study was aimed at determining the clinical benefits of Cytosorb therapy in addition to standard of care in patients with severe sepsis. The primary endpoint was to assess the decrease in inotropic requirement. The secondary endpoints were a decrease in the SOFA score, Lactate clearance and ICU mortality.

4. DISCUSSION

4.1 Demographics

Regarding age distribution, the average age of patients in the CytoSorb group was 45 years, and in the SOC group, it was 52 years. The age distribution of the population was comparable to the findings of the study by Schädler et al,[13] where the mean age was 66 ± 10 years [13].

4.2 Comorbidities

The comorbidities commonly encountered were diabetes mellitus, hypertension, and cardiovascular disease. However, compared to Friesecke et al, [14] our study showed a higher prevalence of diabetes mellitus, hypertension, and ischemic heart disease.

4.3 Type of Renal Replacement Therapy (RRT)

Among the 20 patients treated with CytoSorb, 75% received CRRT and 25% received SLED while in the SOC group, 70% received CRRT and 30% received SLED. Similar studies, such as those conducted by Schädler et al, [13] and Kogelmann et al, [15] CRRT was the mode of renal replacement therapy used in patients [13,15].

4.4 Cause of Sepsis

The most common source of infection in the study was Lower respiratory tract infection. Respiratory tract infections accounted for 50% in CytoSorb and 60% in the SOC group, respectively. Our observation was similar to Friesecke et al, [14] where lower respiratory tract infection (55%) was the most common focus of infection, followed by intra-abdominal sepsis (30%) [14].

4.5 Hematological Parameters

Our study did not demonstrate any adverse hematological effects due to CytoSorb therapy over and above standard of care alone. In the study by SchädlerSchädler et al,[13] a significant drop in platelet counts in patients treated with CytoSorb was observed [13]. Study by Singh et al, [16] found a significant decrease in WBC counts from pre-CytoSorb to post-CytoSorb treatment [16].

4.6 Renal Functions

After treatment, the CytoSorb group showed a statistically significant reduction in serum creatinine levels compared to the SOC group ($p=0.042$). In a similar study conducted by Schädler et al, post-treatment there was no significant difference in serum creatinine in both the groups [13].

4.7 Liver Functions

We did not find any statistically significant difference in total bilirubin levels between the CytoSorb and SOC groups.

Schädler et al, reported baseline total bilirubin levels of 10.0 [5.5-19.1] and 9.7 [6.0-17.9] mg/dl in the CytoSorb and control groups, respectively [13]. After treatment, the CytoSorb group had significantly lower serum albumin levels than the control group, while no significant difference was found in total bilirubin levels between the two groups [13].

4.8 Serum Lactate

The SOC group had significantly lower serum lactate levels at baseline ($p<0.001$) than the CytoSorb group. After treatment, serum lactate levels decreased significantly to 3.26 ± 1.07 mmol/lit in the CytoSorb group, while in the SOC group, it increased to 3.2 ± 0.9 mmol/lit. There was a significant reduction in serum lactate levels in the CytoSorb group compared to the SOC group ($P<0.001$). Another study by Kogelmann et al, [15] found that median serum lactate levels decreased by 26.4% after treatment with CytoSorb, while our study showed a 13% reduction in serum lactate levels in the CytoSorb group [15].

4.9 Serum Procalcitonin

At baseline, the SOC group was found to have significantly lower procalcitonin levels than the CytoSorb group ($P= 0.007$). However, after treatment, the CytoSorb group had significantly lower procalcitonin levels compared to the SOC

group, with levels of 2.7 ± 2.4 ng/mL and 3.3 ± 3.5 ng/mL, respectively (*P*< 0.001). Another study conducted in India by Singh et al, [16] also reported a significant reduction in serum procalcitonin levels following CytoSorb therapy, with a decrease from 36.06 ± 33.86 ng/mL to 12.58 ± 12.98 ng/mL post-treatment [16].

4.10 CRP Levels

Post-treatment, the CytoSorb group had a significantly lower mean serum CRP level of 90.2 ± 57.4 mg/dl compared to the SOC group's mean of 175 ± 100.9 mg/dl (*P*<0.001). A study by Mehta et al, [12] also examined serum CRP levels before and after CytoSorb treatment. Their results showed a reduction in mean serum CRP levels from 165.68 ± 169.26 at baseline to 120.33 ± 63.72 after treatment, representing a 27.4% reduction. However, this reduction was not statistically significant [12].

4.11 Serum IL6 Levels

The baseline serum IL6 levels were significantly higher in the CytoSorb group than in the SOC group (p=0.03). Our study found a statistically significant decrease in serum IL6 levels in the CytoSorb group compared to the SOC group (p=0.03). In a study conducted by Schädler et al [13], the baseline serum IL6 levels were 552 [162 ± 874] pg/ml in the CytoSorb group and 590 [125 ± 2147] pg/ml in the control group. However, their study found no significant reduction in serum IL6 levels post-treatment in both groups [13]. In a recent study by Mehta et al, [12] in India, baseline serum IL6 levels were 1962.04 ± 229.09 pg/ml before treatment, and there was an 87% reduction in IL6 levels after CytoSorb therapy [254.09 ± 223.62, (*P*<0.0001)] [12]. Another study investigated the effects of CytoSorb hemoperfusion on plasma levels of various cytokines using the repeated human experimental endotoxemia model [17]. The study reported significant reduction of 71% in plasma levels of IL6 (*P*=0.003) compared to SOC group during the first LPS challenge [17].

4.12 Mean Arterial Pressure (MAP)

After treatment, the CytoSorb group had a MAP of 65.75 ± 1.8 mmHg, while the SOC group had a MAP of 62.75 ± 2.8 mmHg. Our study found that the improvement in post-treatment MAP in the CytoSorb group was statistically significant compared to the SOC group (*P*<0.001). Mehta et al, [12] also conducted a study and reported a baseline MAP of 62.82 ± 9.73 mmHg and a post-CytoSorb treatment MAP of 68.23 ± 7.50 mmHg, which represented an 8.6% improvement, but this change was not statistically significant (*P*=0.18) [12].

4.13 Vasopressor Requirement

The initial dose of norepinephrine was somewhat similar in both the CytoSorb and SOC groups, with CytoSorb group at 8.0±1.8 mcg/min and SOC group at 7.2±1.9 mcg/min. After treatment, CytoSorb group had a norepinephrine dose of 6.4±2.7 mcg/min, whereas SOC group had a dose of 10.6±3.6 mcg/min. This represented a significant reduction in norepinephrine dose in the CytoSorb group compared to the SOC group (*P*< 0.001). Mehta et al, [12] study had similar results, with a decrease in norepinephrine dose from 17.68±15.45 mcg/min before CytoSorb to 14.04±10.46 mcg/min after CytoSorb treatment, but this decrease was not statistically (*P*=0.3) significant [12].

4.14 Ventilation Parameters

The initial PaO2/FiO2 ratio was not significantly different between the CytoSorb and SOC groups. After treatment, the PaO2/FiO2 ratio was 215.5 ± 37.4 mmHg in the CytoSorb group and 197.5 ± 58.0 mmHg in the SOC group, and there was no significant difference between the groups in our study. In Hawchar et al, [5] study, the baseline PaO2/FiO2 ratio was 173.2 ± 64.2 mmHg in the CytoSorb group and 249.5 ± 127.6 mmHg in the control group. After 24 hours of treatment, the PaO2/FiO2 ratio was 293.9 ± 207.1 mmHg in the CytoSorb group and 227.5 ± 100.4 mmHg in the SOC group. However, the improvement in the CytoSorb group was not statistically significant [5].

4.15 CNS Parameters

The comparison of CNS parameters of study patients was done using the Glasgow Coma Scale (GCS). After treatment, the GCS score of the CytoSorb and SOC groups was 10.6 ± 1.3 and 10.4 ± 1.7, respectively. No significant difference between the pre- and post-treatment GCS scores was found in both groups. Similarly, in Mehta et al, study no significant difference was noted in GCS scores between pre- and post-treatment [12].

4.16 SOFA Score

The baseline SOFA score of the patients in the cytosorb group was 11.65 ± 0.8 and in the SOC

group was 10.95 ± 0.8. SOFA score at baseline was markedly higher in the cytosorb group than the SOC group (*P*=0.016). The post-treatment SOFA score of patients in the cytosorb group was 11.85 ± 2.9 and in the SOC group was 12.3 ± 2.3 and this was not statistically significant. (*P*=0.135). However, increase in the SOFA score was relatively lesser in the cytosorb group than the SOC group. Though it did not reach statistical significance. Similarly, Hawchar et al, [5] found no significant difference in the SOFA score between the CytoSorb and the control group at baseline or after treatment [5].

4.17 Mortality

In this study, patients who received CytoSorb treatment had mortality rate of 70%, while SOC group had mortality rate of 75%. Although, the mortality rate was 5% lower in CytoSorb group, this difference was not significant. Similarly, Hawchar et al, [5] showed a mortality rate of 50% for both the CytoSorb and control groups [5].

Given the complexity of these syndromes, the assessment of CytoSorb® treatment efficacy should focus on hemodynamic stability, inflammatory biomarkers, and improvement in organ function rather than solely on mortality rates. This approach allows for a more comprehensive understanding of patient responses during critical illness. Similar strong agreement has been documented in a consensus statement, which highlights that 90.91% of experts agree that the evaluation of CytoSorb® therapy efficacy should focus on endpoints such as hemodynamic stabilization, inflammatory biomarkers, and improvement in organ function, rather than solely on mortality [18].

5. CONCLUSION

Our study indicates that using a combination of CytoSorb and SOC for sepsis patients with septic shock resulted in significant improvements in hemodynamic stability, mean arterial pressure, and Norepinephrine requirements compared to SOC alone. Additionally, the CytoSorb group showed significant reductions in inflammatory biomarkers like IL6 and CRP, as well as sepsis markers such as procalcitonin and serum lactate.

6. LIMITATIONS

The sample size was small. Data like cardiac output, cardiac index and systemic vascular resistance required invasive hemodynamic monitoring and was not available. The CytoSorb score has been retrospectively evaluated where cores of 8-13 were considered ideal for recommending CytoSorb® therapy. It is important to note that this score has not been prospectively validated. The follow up period was limited i.e. till hospital discharge, so the long-term benefits could not be validated.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

DECLARATION ON DATA AVAILABILITY

The data that support the finding of this study is available from the corresponding author on reasonable request. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient”.

ETHICAL APPROVAL

“All authors hereby declare that study have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.”

Ethics approval: Approved by Ethics Committees (IEC) on 27th February 2020

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Angus DC, van der Poll T. Severe sepsis and septic shock. N Engl J Med. 2013 Aug 29;369(9):840-51.
   DOI: 10.1056/NEJMra1208623.
   Erratum in: N Engl J Med. 2013; 369: 2069. PMID: 23984731.
2. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al.

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-10.
DOI: 10.1001/jama.2016.0287
PMID: 26903338; PMCID: PMC4968574.

3. MacKenzie IM. The haemodynamics of human septic shock. Anaesthesia. 2001; 56: 130-44.
DOI: 10.1046/j.1365-2044.2001.01866.x.
PMID: 11167473.
4. Honore PM, Hoste E, Molnár Z, Jacobs R, Joannes-Boyau O, Malbrain MLNG, et al. Cytokine removal in human septic shock: Where are we and where are we going? Ann Intensive Care. 2019;9(1):56.
DOI: 10.1186/s13613-019-0530-y
PMID: 31089920; PMCID: PMC6517449.
5. Hawchar F, László I, Öveges N, Trásy D, Ondrik Z, Molnar Z. Extracorporeal cytokine adsorption in septic shock: A proof of concept randomized, controlled pilot study. J Crit Care. 2019;49:172-178.
DOI: 10.1016/j.jcrc.2018.11.003
Epub 2018 Nov 10. PMID: 30448517.
6. László I, Trásy D, Molnár Z, Fazakas J. Sepsis: From Pathophysiology to Individualized Patient Care. J Immunol Res. 2015;2015:510436.
DOI: 10.1155/2015/510436.
Epub 2015 Jul 15. PMID: 26258150; PMCID: PMC4518174.
7. Govil D, Kumar GP. Extracorporeal Therapy in Sepsis. Indian J Crit Care Med. 2020; 24: S117-S121.
DOI: 10.5005/jp-journals-10071-23382
PMID: 32704217; PMCID: PMC7347068.
8. Monard C, Rimmelé T, Ronco C. Extracorporeal Blood Purification Therapies for Sepsis. Blood Purif. 2019; 47: 1-14.
DOI: 10.1159/000499520
9. Kellum JA, Song M, Venkataraman R. Hemoadsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor-kappaB DNA binding, and improves short-term survival in lethal endotoxemia. Crit Care Med. 2004;32:801-805.
DOI:10.1097/01.ccm.0000114997.39857.69.
PMID: 15090965.
10. Basu R, Pathak S, Goyal J, Chaudhry R, Goel RB, Barwal A. Use of a novel hemoadsorption device for cytokine removal as adjuvant therapy in a patient with septic shock with multi-organ dysfunction: A case study. Indian J Crit Care Med. 2014;18:822-8244.
11. Bonavia A, Groff A, Karamchandani K, Singbartl K. Clinical Utility of Extracorporeal Cytokine Hemoadsorption Therapy: A Literature Review. Blood Purif. 2018;46:337-349.
DOI: 10.1159/000492379.
Epub 2018 Sep 3. PMID: 30176653.
12. Mehta Y, Mehta C, Kumar A, George JV, Gupta A, Nanda S, et al. Experience with hemoadsorption (CytoSorb®) in the management of septic shock patients. World J Crit Care Med. 2020;9(1):1-12.
DOI: 10.5492/wjccm.v9.i1.1.
PMID: 32104647; PMCID: PMC7031623.
13. Schädler D, Pausch C, Heise D, Meier-Hellmann A, Brederlau J, Weiler N, et al. The effect of a novel extracorporeal cytokine hemoadsorption device on IL-6 elimination in septic patients: A randomized controlled trial. PLoS One. 2017;12(10):e0187015.
DOI: 10.1371/journal.pone.0187015.
PMID: 29084247; PMCID: PMC5662220.
14. Friesecke S, Stecher SS, Gross S, Felix SB, Nierhaus A. Extracorporeal cytokine elimination as rescue therapy in refractory septic shock: a prospective single-center study. J Artif Organs. 2017 Sep;20(3):252-259.
DOI: 10.1007/s10047-017-0967-4
Epub 2017 Jun 6. PMID: 28589286.
15. Kogelmann K, Jarczak D, Scheller M, Drüner M. Hemoadsorption by CytoSorb in septic patients: a case series. Crit Care. 2017; 21: 74.
DOI: 10.1186/s13054-017-1662-9
PMID: 28343448; PMCID: PMC5366999.
16. Singh YP, Chhabra SC, Lashkari K, Taneja A, Garg A, Chandra A, 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):372-378.
DOI: 10.1177/0391398819891739.
Epub 2019 Dec 23. PMID: 31868078.
17. Jansen A, Waalders NJB, van Lier DPT, Kox M, Pickkers P. CytoSorb hemoperfusion markedly attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo. Crit Care. 2023 Mar 21;27(1):117.
DOI: 10.1186/s13054-023-04391-z.
PMID: 36945034; PMCID: PMC10029173.

18. Mehta Y, Ansari AS, Mandal AK, Chatterjee D, Sharma GS, Sathe P, Umraniya PV, Paul R, Gupta S, Singh V, Singh YP. Systematic review with expert consensus on use of extracorporeal hemoadsorption in septic shock: An Indian perspective. World J Crit Care Med. 2024;13(1):89026.
DOI: 10.5492/wjccm.v13.i1.89026.
PMID: 38633478; PMCID: PMC11019629.

APPENDIX- SUPPLEMENTARY FILE

Supplementary file

CytoSorb® score checklist:

Clinical variables	Severity score		
	1	2	3
Hemodynamic parameter			
MAP	> 70 mmHg with or without vasopressor support	> 65 mmHg high dose single vasopressor (0.3 µg/mL)	> 65 mmHg high dose of multiple vasopressors
Septic shock	< 24 h	24-48 h	> 48 h
Renal parameter			
Acute oliguria	< 0.5 mL/kg/h for 6 h	< 0.5 mL/kg/h for 12 h or longer	< 0.3 mL/kg/h for 24 h or anuria for 12 h
S. Creatinine	Increase to >1.5-fold	Increase to >2-fold	> 4 mg/dL or greater
RRT	Not on RRT	On RRT < 24 h	On RRT > 24 h
Respiratory parameter			

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/124048