



## A RETROSPECTIVE ANALYSIS OF EFFICACY OF HEMOADSORPTION (CYTOSORB®) IN REFRACTORY SEPTIC SHOCK PATIENTS AS AN ADJUVANT

### Nephrology

<b>Dr. Mandarapu Surendra*</b>	Consultant Nephrologist, Department of Nephrology, Ramesh Hospitals, Guntur, Andhra Pradesh, Pin code 522 004 *Corresponding Author
<b>Dr. Bharath Cherukuri</b>	Critical Care Physician, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Sai Kumar</b>	Consultant Nephrologist, Department of Nephrology, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Nagasri Haritha</b>	Consultant Cardiologist, Department of Cardiology, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Lakshmi Kantham</b>	Consultant Gynaecologist and Obstetrician, Department of Gynaecology and Obstetrics, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Silpa</b>	Critical Care Physician, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Bhavya</b>	Critical Care Physician, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Srikanth</b>	Critical Care Physician, Ramesh Hospitals, Guntur, Andhra Pradesh, India.
<b>Dr. Jyothi</b>	Critical Care Physician, Ramesh Hospitals, Guntur, Andhra Pradesh, India.

### ABSTRACT

Dysregulated response of cytokines can result in hyper-inflammatory conditions called cytokine storm, commonly seen in sepsis and septic shock. The current study assessed hemoadsorption device - CytoSorb® for its efficiency as an adjuvant in treating patients suffering from septic shock. Total 8 patients enrolled were subjected to hemoadsorption therapy along with the standard treatment. The results of the study revealed significant improvement in clinical and haemodynamic parameters before and after initiation of CytoSorb® therapy. Out of 8 patients, 6 showed a positive outcome while 2 did not survive. The results of this study show that the use of hemoadsorption therapy can be considered in critically ill ICU patients as a safe and effective adjuvant therapy along with the standard treatment for a better outcome in patients.

### KEYWORDS

Sepsis, Septic Shock, Cytokines, Hemoadsorption

### INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction resulting due to a dysregulated host response to infection. Septic shock is one of the most severe condition representing a highly fatal state in critically ill patients that leads to a considerable morbidity and mortality [1]. Despite improved understanding of the underlying pathophysiology and significant advancement in antibiotic therapy, resuscitative strategies, ventilator management, the septic shock incidence persists to increase and is likely to be related to high mortality rate—30 to 50% or more [2, 3].

Septic shock may lead to multiple organ dysfunction syndrome (MODS) that requires early and aggressive treatment for favorable patient outcome [4]. To confront this circumstance, cytokine hemoadsorption is considered as an effective and safe option in managing sepsis in critically ill patients [5]. Extracorporeal cytokine hemoadsorption therapy is an emerging technology used for treating dysregulated inflammatory condition like sepsis, although the clinical evidence supporting its outcoming advantages is scarce. In this technique, toxins and other mediators are bound to the extracorporeal circuit and removed from the blood compartment [6]. Columns consist of porous, absorbent polymer beads that are slightly larger than a grain of salt and highly compatible with blood which selectively uses size to target molecules between 10,000 and 50,000 Da. During blood purification, smaller toxic molecules enter the pores and channels in each bead and adhere to the internal surface of the beads through hydrophobic interactions with the neutral lipophilic surface of the polymer, while larger essential blood proteins are passed back to the patient through the filter [7]. In order to assess the efficacy of hemoadsorption using CytoSorb® as an adjuvant therapy, the present study was conducted in patients suffering from septic shock.

### MATERIALS AND METHODS

This retrospective analysis was conducted for a period of 9 months i.e. 1<sup>st</sup> October 2017 to 31<sup>st</sup> June 2018. A total number of 8 patients who

were admitted to the ICU with diagnosis of sepsis were enrolled into the study. Written consent was obtained from the patient attender prior to the initiation of treatment. This therapy was considered in those septic shock patients who are unresponsive to maximal inotropic support (Dopamine  $\geq 15$ mcg/kg/min, Nor-adrenaline  $\geq 0.25$  mcg/kg/min)

for a period of at least 6 hours. Hemoadsorption column CytoSorb® (CytoSorbents Corporation, USA) was used in extracorporeal circuit for the for a period of 24 hours in 6 patients and two patients deteriorated and expired on CytoSorb® therapy. Variables like Total leucocyte count, mean arterial pressure, lactate, vasopressors requirement was recorded and tabulated in Microsoft excel.

### STATISTICAL ANALYSIS

Variables like Total leucocyte count, mean arterial pressure, lactate, vasopressors requirement was recorded and tabulated in Microsoft excel. Data of patients who survived for the therapy ( six patients) were statistically analyzed in Epi Info Software using paired t-test before and after the hemoadsorption therapy to understand the efficacy.

### RESULTS

In the present study, 8 patients diagnosed with septic shock and multi-organ failure were treated with standard treatment along with CytoSorb® as an adjuvant therapy (Table 1). During the treatment period, hemoadsorption therapy was well-tolerated, and the patients were stabilized after 24 hours of treatment.

**Table 1: Patient Demographics**

Sl.No.	Age	Sex	Diagnosis at admission	Outcome
1	25	Female	PRIMI with 28 weeks of gestation (IUD), Solitary left kidney with Acute pyelonephritis, Sepsis-MODS-AKI, ARDS	Survived

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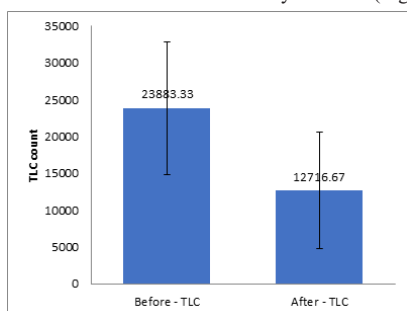
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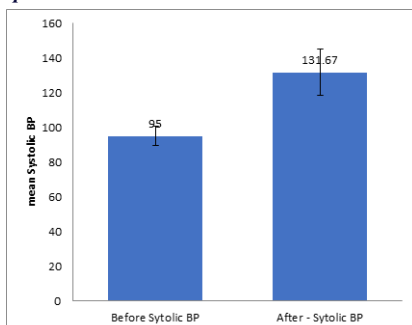
2	39	Male	Sepsis with MODS, Acute hepatitis, Acute kidney injury, Thrombocytopenia	Survived
3	20	Female	PRIMI with term gestation, Amniotic fluid embolism syndrome with sepsis with severe ARDS	Survived
4	26	Male	Sepsis with MODS with Septic shock, Acute liver failure and Acute kidney injury Post cardiac arrest status, ARDS	Survived
5	31	Male	Dengue shock syndrome, MODS, Septic Shock, Acute kidney injury	Expired
6	20	Male	Urosepsis MODS Septic shock Acute kidney injury	Expired
7	38	Male	Left leg necrotizing fascitis, septic shock with MODS, Acute kidney injury	Survived
8	19	Female	Fulminant hepatic failure, MODS, Septic shock	Survived

IUD- Intra uterine death, MODS- Multiple organ dysfunction syndrome, AKI- Acute kidney injury, ARDS- Acute respiratory distress syndrome.

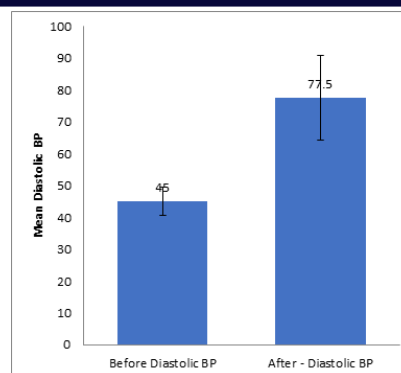
The comparison of variables such as total leukocytes count (TLC), mean arterial pressure (MNP), lactate, vasopressors requirement before and after the hemoadsorption therapy showed significant results. Out of 8 patients, 6 patients survived and completely recovered. The remaining 2 patients (Patient No 5 & 6) did not respond to the treatment and were unable to survive. The mean TLC before and after initiation of CytoSorb® was  $23883.33 \pm 9018.962$  and  $12716.67 \pm 7911.616$  respectively and mean difference was found to be statistically highly significant before and after the initiation of CytoSorb® ( $p=0.001$ ). The mean systolic blood pressure before and after initiation of CytoSorb® was  $95.00 \pm 5.477$  and  $131.67 \pm 13.292$  respectively and statistically highly significant ( $p$  value= $0.001$ ). The mean diastolic blood pressure before and after initiation of CytoSorb® was  $45.00 \pm 4.472$  and  $77.50 \pm 13.323$  respectively and found to be statistically highly significant ( $p$  value= $0.002$ ). The mean MAP before and after initiation of CytoSorb® was  $61.50 \pm 1.643$  and  $95.67 \pm 12.193$  respectively. The results of the paired t test showed that the mean difference between the MAP before and after the initiation of CytoSorb® was found to be significant highly statistically ( $p=0.001$ ). The mean vasopressor requirement before and after initiation of CytoSorb® was 0.69 and 0.3 respectively. There was highly statistical significance ( $p=0.0006$ ) found between before and after the initiation of CytoSorb®. The mean lactate before and after initiation of CytoSorb® was  $5.17 \pm 4.446$  and  $2.0 \pm 0.632$ , respectively. The mean difference between lactate was not found statistically significant ( $p=0.138$ ) before and after the initiation of CytoSorb®. (Figure 1-5).



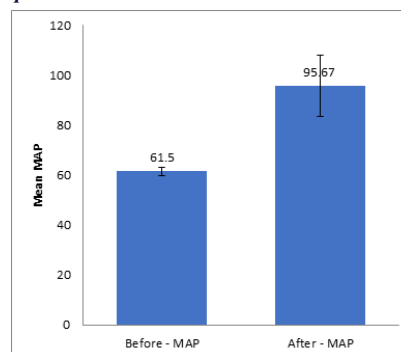
**Figure 1: Mean Total Leucocyte Count before and after hemoadsorption**



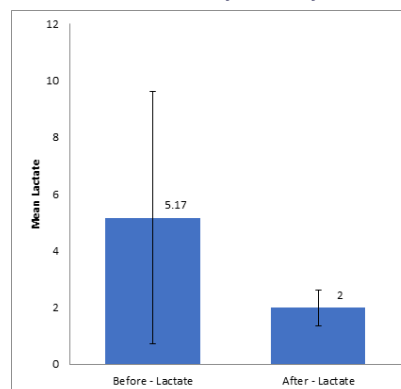
**Figure 2: Mean Systolic Blood Pressure before and after hemoadsorption**



**Figure 3: Mean Diastolic Blood Pressure before and after hemoadsorption**



**Figure 4: Mean Arterial Pressure before and after hemoadsorption**



**Figure 5: Mean Lactate before and after hemoadsorption**

## DISCUSSION

Patients in septic shock require aggressive management and frequent mechanical ventilation, vasopressor therapy and renal replacement therapy [8]. Based on clinical plausibility and experimental evidence, hemoadsorption may be beneficial in these patients. Hemoadsorption has an advantage in reducing a range of the pro-inflammatory cytokines effectively rather than targeting an individual cytokine. The Cytosorb® has been used in ICU settings for treating sepsis. Several studies have shown its safety and efficacy in reducing the systemic inflammatory response. The experimental studies prove that hemoadsorption with CytoSorb® reduced inflammation and considerably enhanced overall survival [9]. In a case study conducted by Hetz *et al.*, a 60-year-old female had developed surgical wound infection due to forearm fracture that advanced to necrotizing fasciitis and septic shock after surgical wound care. After 4 days of treatment with CytoSorb® a significant reduction of IL-6 was observed along with an overall improvement in the condition of the patient [10]. Similarly, various other case studies on patients with septic shock had reported reduction of several inflammatory mediators when treated using CytoSorb® therapy [11,12].

To date largest case series is published by Kogelman *et al* [13]. In this retrospective analysis they reported outcome of twenty-six critically ill patients and concluded that CytoSorb® therapy was associated with lower mortality rates when compared to standard therapy. Our case

study showed a similar outcome. Our study results showed significant reduction in vasopressor therapy and is in line with Kogelman et al study. In addition, our study showed significant reduction in TLC. Serum lactate levels decreased after CytoSorb® therapy but statistically significant was not achieved, in contrast to the Kogelman et al., study which showed significant reduction of lactate levels [13]. This contrast finding could be due to very small sample size in our series.

CytoSorb® therapy might be an option as rescue therapy in septic shock patients with multi-organ failure. However, to establish the benefit from this therapy as an adjuvant in septic shock, further studies with prospective randomized control design would be necessary. However, our case study has important limitations — small sample size and no control arm.

## CONCLUSION

This study reported an effectively positive outcome with cytokine hemoabsorbent treatment as an adjuvant along with standard treatment in a high-risk mortality cases of septic shock with organ damage. Cytokine hemoabsorption therapy can be considered as a rescue therapy in patients with severe sepsis or septic shock along with the standard treatment for the better outcomes. However, further multicenter prospective studies are required with large sample size in order to establish the benefit of CytoSorb® in the treatment of septic shock.

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