Case Report

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

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Abstract

CytoSorb® (CytoSorbents Corporation, USA) is a novel sorbent hemoadsorption device for cytokine removal. The aim of this study was to examine the clinical use of CytoSorb® in the management of patient with septic shock. We used this device as an adjuvant to stabilize a young patient with multi-organ failure and severe sepsis with septic shock. A 36-year-old female patient was hospitalized with the complaints of malaise, general body ache, and breathing difficulty and had a medical history of diabetes mellitus type II, hypertension, obstructive sleep apnea, hypothyroidism and morbid obesity. She was diagnosed to have septic shock with multi-organ dysfunction (MODS) and a low perfusion state. CytoSorb® hemoadsorption column was used as an attempt at blood purification. Acute physiology and chronic health evaluation score, MODS score, and sequential organ failure assessment score were measured before and after the device application. CytoSorb application as an adjuvant therapy could be considered in septic shock.

Keywords: CytoSorb, hemoadsorption, septic shock, systemic inflammatory response syndrome

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Introduction

The mortality rates of patients with septic shock still hovers at around 60% and is more frequent in the Intensive Care Units.[1] Extracorporeal blood purification therapies are being explored in patients with sepsis to improve outcomes. Hemoadsorption using CytoSorb® (CytoSorbents Corporation, USA) is a recent technology that has shown rapid *in vitro* and *in vivo* elimination of many key cytokines including interleukin-6 (IL-1), IL-6, tumor necrosis factor (TNF) and IL-10 that cannot be filtered using current blood purification techniques.[2-5] CytoSorb® columns are comprised of porous, absorbent polymer beads slightly larger than a grain of salt that are highly compatible with blood and use size selectivity 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.[6]

Mitzner *et al*. reported that CytoSorb® was efficacious and well-tolerated in a patient with chronic kidney failure and septic shock.[7] We report the use of CytoSorb® to stabilize a female patient having septic shock with a low perfusion state and multi-organ dysfunction (MODS).

Case Report

A 36-year-old female patient was admitted to our hospital with the complaints of general body ache for last 3 days, malaise and breathing difficulty for the last 2 days before admission. The patient had a history of diabetes mellitus type II, obstructive sleep apnea, hypertension, hypothyroidism and morbid obesity. On examination, she had tachycardia (120 bpm),

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tachypnea (36/min) and leukocytosis (white blood cell count > 52,000). She was suspected to have a urinary tract infection (pus cell count - 12–15 cells). She was started on antibiotics (meropenem, 500 mg thrice a day) after sending relevant cultures and prescribed vasopressors [Table 1], adequate fluid resuscitation and also required mechanical ventilation. She continued to deteriorate with decreasing urine output. She was intubated in 4 h of admission and became anuric in 6 h. Her sequential organ failure assessment (SOFA) score was 15, MODS score was 10 and acute physiology and chronic health evaluation (APACHE II) score was 30 after 24 h of the admission.

The patient was diagnosed as having septic shock (urosepsis) with a low perfusion state and MODS (acute respiratory distress syndrome, acute kidney injury, arterial hypotension). A hemoadsorption column (CytoSorb®) was added after 16 h of admission along with continuous renal replacement therapy for 24 h. The flow rate was maintained at 250 ml/min. The patient was anticoagulated with heparin to be maintained at an activated partial thromboplastin time of 30–40 s. After 12 h the patient improved hemodynamically while the patient was on inotropic support, intravenous hydrocortisone and other supportive measures along with CytoSorb. Noradrenalin could be stopped after this time period, and other vasopressors were gradually weaned out [Table 1]. Corticosteroids (intravenous hydrocortisone), 100 mg thrice daily were given till the patient was on inotropic support. The patient stabilized after 3 days during which CytoSorb was also applied daily. At this time, the urine output increased with improvement in ventilator parameters. Her SOFA score at this time was 4, MODS score was 5 and APACHE II score was 7. The laboratory parameters before and after CytoSorb® therapy were within normal range and are depicted in Table 2.

Table 1: Vasopressor schedule before and after CytoSorb® therapy

Vassopressor	Dose before CytoSorb® therapy	Dose after CytoSorb® therapy		
		Day 1	Day 2	Day 3
Epinephrine (μg/kg/min)	0.6	0.6	Nil	Nil
Norepinephrine (μg/kg/min)	0.1	1.0	0.2	0.02
Dopamine (μg/kg/min)	20	20	5	Nil
Vasopressin (IU/min)	0.06	0.06	0.02	Nil

Table 2: Laboratory parameters before and after treatment with CytoSorb®

Parameter	Before treatment	After treatment
Hemoglobin (g/dL)	9.9	8.1
Hematocrit (%)	31.9	25.7
Leucocytes (mm^3)	52.1	9.6
Platelets (mm^3)	359	100
aPTT (s)	29.3	32.3
INR	1.24	1.2
Lactate (mmol/L)	4.4	0.7
Creatinine (mg/dL)	2.33	1.58
Urea (mg/dL)	19.1	21.2
Sodium (mmol/L)	128.5	139.9
Potassium (mmol/L)	4.5	3.9
Calcium (mmol/L)	1.00	1.11
Total protein (g/dL)	8.4	5.5
FBS/RBS (mg/dL)	96	145
SGPT (U/L)	849	420.1
SGOT (U/L)	769.6	269.1

aPTT: Activated partial thromboplastin time; INR: International normalized ratio; FBS/RBS: Fasting blood sugar/Random blood sugar; SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic oxaloacetic transaminase

Discussion

We report one of the first cases treated with standard treatment along with CytoSorb® as an adjuvant therapy in a patient with septic shock and multi-organ failure. The therapy was well-tolerated, and the patient stabilized after 3 days of treatment.

Patients with septic shock require aggressive management and frequent mechanical ventilation, vasopressor therapy and renal replacement therapy.[1] Hemoadsorption may be beneficial in these patients based on clinical plausibility and experimental evidence. However, there is a paucity of high-quality evidence at present. In animal models with septic shock, hemoadsorption with CytoSorb® was associated with reduced inflammation and significantly improved overall survival.[8] An *in vitro* study conducted by Peng *et al*., showed that hemoadsorption using a cartridge containing CytoSorb® beads reduces anti-inflammatory cytokines (TNF, IL-1β, IL-6, and IL-10) and significantly improves mean arterial pressure ($P < 0.05$) and overall survival ($P < 0.01$) in rats with cecal ligation and puncture-induced sepsis.[5] Rimmelé *et al*. performed hemoadsorption *ex vivo* on blood samples taken from 21 patients with septic shock and 12 healthy volunteers. They observed an upregulation of IL-8 and modulation of cell-mediated immunity with hemoadsorption, which could ameliorate an organ injury.[9,10]

The CytoSorb® technology uses beads that are composed of biocompatible polystyrene divinylbenzene copolymer. These beads capture and adsorb cytokines and other middle molecular weight molecules. The first randomized controlled clinical trial conducted with CytoSorb® in septic patients with acute lung injury observed a significant reduction in cytokines and was well-tolerated.[3] In our patient, we did not observe any adverse event and the hemogram and clinical chemistry

parameters before and after CytoSorb® treatment were within normal limits [Table 2].

CytoSorb® is effective in reducing postoperative systemic inflammatory response syndrome.[11] In a case study by Hetz *et al*., a 60-year-old female who had forearm fracture developed surgical wound infection that progressed to necrotizing fasciitis and septic shock after surgical wound care. After 4 days of the treatment with CytoSorb® therapy, a significant reduction of IL-6 and an overall improvement in the condition of the patient were observed.[12] Similarly, various other case studies on humans have also reported that CytoSorb® therapy could reduce several inflammatory mediators in the patient with hypodynamic or pneumogenic septic shock.[13,7]

In the present study, a successful outcome in a case of septic shock and multiorgan failure where CytoSorb was used as an adjuvant therapy is reported. She had a high predicted mortality with an APACHE II score of 30. She was managed with standard of care treatment along with the use of adjuvant therapy wherein she received three consecutive treatments with CytoSorb® hemadsorption column. CytoSorb® therapy in septic shock patients with multi-organ failure might be an option as rescue therapy. However, further studies with prospective randomized control design would be necessary to establish the benefit of this therapy as an adjuvant in septic shock.

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