Paediatric patient with dengue fever and associated multi-organ dysfunction syndrome (MODS) receiving hemoadsorption using Cytosorb® A case report on clinical experience

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ABSTRACT — OBJECTIVE: *Dengue is an arboviral disease, spreads by female aedes mosquito, which has hepatotoxic effects on multiple organ systems. Cytokine extracorporeal hemoadsorption (Cytosorb®) is considered to be a successful adjunctive therapy for adult patients to reduce bilirubin and toxic metabolites.*

PATIENTS AND METHODS: *Here we present a case of a 10-year-old, Indian male patient who was admitted to our hospital with dengue haemorrhagic fever and associated Systemic inflammatory response syndrome (SIRS), acute fulminant hepatic failure with encephalopathy and oliguria. Post hepatoprotective strategies, over a 36 hour period an increase was observed in hepatic parameters with Serum glutamic oxaloacetic transaminase (SGOT)- 11,391(IU/L), Serum glutamic pyruvic transaminase (SGPT)- 4,572 (IU/L), platelets-17,000 (/µL) and total bilirubin of 7.2 mg/dl: 5.1 mg/dL and 2.1 mg/dL of direct and indirect, respectively. In view of the Multi Organ Dysfunction Syndrome (MODS) adjunctive therapy with Cytosorb® was initiated.*

RESULTS: *After an 18 hour procedure, his liver function tests (LFTs) improved with SGOT-8,003 (IU/L), SGPT-3,573 (IU/L); total bilirubin-4.8 mg/dl and platelet count remarkably increased to 108000 (/µL). LFTs decreased and normalized values were attained over 5 days. The patient was extubated on day 9 of admission and was later discharged in an active, afebrile and hemodynamically stable condition.*

CONCLUSIONS: *Cytosorb® along with standard care, can be a safe and advantageous extracorporeal therapy option to treat paediatric dengue patients with MODS.*

KEYWORDS
DHF, MODS, Acute fulminant liver failure, Hemoadsorption, Cytosorb®.

INTRODUCTION

Sepsis is described as a life-threatening organ dysfunction caused by a dysregulated host response to infection[1]. Dengue is an arboviral disease with significant impact on the disease burden in tropical countries. It spreads from the bite of a Female Aedes mosquito. The virus seems to have some hepatotoxic effects which involve mild elevations in serum bilirubin, elevated transaminases and derangements in

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serum albumin with a profound effect on multiple organ systems[2]. Hepatomegaly is present in both dengue fever (DF) and dengue hemorrhagic fever (DHF) but predominantly in DF[2]. The extent of hepatomegaly in dengue patients varies from 4-52%[3]; in various settings, clinical jaundice has been detected in the range of 1.7%-17%[4] and hyperbilirubinemia has been found to be as high as 48%[5]. Although asymptomatic in most cases, clinical manifestations such as jaundice, and acute liver failure (ALF) may complicate the clinical image. Certainly, dengue has been implicated as an important cause of ALF in endemic countries. Additionally, dengue has a wide spectrum of other manifestations. Here we present a case of a 10-year-old Indian male patient who was with DHF and subsequently Multi Organ Dysfunction Syndrome (MODS), treated with standard of care and adjuvant extracorporeal cytokine elimination therapy using Cytosorb®.

CASE REPORT

A 10-year old, 26 kg, Indian male child presented to Rainbow Hospital (Vijayawada, India) was admitted with a history of intermittent high grade fever associated with chills, cough, vomiting, facial puffiness and painful abdomen.

On examination, the patient was found to be febrile, lethargic, tachypnoeic and maintaining saturation 99% at room air with Pulse Rate (PR)-116/min, Blood Pressure (BP)-116/80 mmHg and Respiratory Rate (RR) 36/min. Dengue serology was NS1 and IgG reactive. Ultrasonography (USG) of the patient's abdomen showed moderate ascites with bilateral pleural effusion. Complete blood count and biochemical parameters were performed. Blood culture with isolated *E. coli* and urine culture was positive for Candida. Patient fulfilled Systemic Inflammatory Response Syndrome (SIRS) criteria and was thus admitted to paediatric intense care unit (ICU).

In ICU the patient was started on mechanical ventilation, IV fluids and IV antibiotics. In view of the persistent thrombocytopenia (platelets 17,000 /μL) the patient received multiple single and random donor platelet (SDP and RDP) transfusions. The patient had associated coagulopathy, activated partial thromboplastin time (aPTT)-56.3 and internationalised normalised ratio (INR) 2.1, and was given fresh frozen plasma (FFP) transfusions with Vitamin-K injection. In view of encephalopathy and shock the patient was intubated and ventilated.

Antibiotic and antifungal therapies with Meropenem, Vancomycin and Fluconazole were initiated. Multiple episodes of severe hypotension and bradycardia were treated with adrenaline, noradrenaline, dopamine and increased dose of inotropic agents.

For acute fulminant hepatic failure, the patient Liver Function Tests (LFTs) were closely monitored. In spite of hepatoprotective strategies (N-Acetyl Cysteine infusion (NAC)), over a 36 hour period, a drastic increase was observed in the parameters monitored for SIRS (transaminases and bilirubin) with serum glutamic oxaloacetic transaminase (SGOT)-11,391(I-U/L), serum glutamic pyruvic transaminase (SGPT)-4,572 (IU/L), total bilirubin 7.2mg/dL; direct, 5.1mg/dL and indirect 2.1mg/dL respectively.

On the 3rd day the decision to commence hemoadsorption with a cytokine adsorber (Cytosorb®) was taken. Blood flow was maintained at 40 ml/min without anticoagulant. The adsorber was placed in a post dialyzer position. Due to the paucity of recommendations in the literature and the fact that a flow of only 60 ml/min – 1/5 of the recommended flow for hemoadsorption of 200 ml/min - could be maintained throughout the Hemodiafiltration (HDF) process, the procedure was maintained for 18 hours. Considering the lack of evidence in the paediatric population, a single Cytosorb® adsorber was used.

This case study was conducted in accordance with International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) and principles of Ethics.

RESULTS

After an 18 hour adsorber time, patient LFTs were improved SGOT-8,003(IU/L), SGPT-3,573 (IU/L); total bilirubin-4.8 mg/dL with direct bilirubin-2.4 (Table 1). Liver function tests also started decreasing and normalized over 5 days. Similarly, significant improvements in the platelet counts were also achieved (Table 2).

DISCUSSION

Dengue viral infections are known for presenting a diverse clinical spectrum, ranging from asymptomatic illness to detrimental dengue shock syndrome

Table I. Parameters monitored for SIRS pre-Cytosorb® and 18 hours post-Cytosorb®.

	Pre-Cytosorb®	18 hours Post-Cytosorb®
Bilirubin (mg/dL)	7.2	4.8
Direct (mg/dL)	5.1	2.4
Indirect (mg/dL)	2.1	2.4
SGOT (U/L)	11,391	8,003
SGPT (U/L)	4,572	3,573

SGOT: serum glutamic oxaloacetic transaminase;
SGPT: serum glutamic pyruvic transaminase.

Table II. Pre-Cytosorb® and 5 days post-Cytosorb® relevant laboratory investigations with maximum values.

Laboratory parameters	Pre-Cytosorb® [max]	5 Days Post-Cytosorb® [max]
Hb (g/dL)	14.9	12
WBC (x 10^3/µL)	8	4.5
Platelets (/µL)	17,000	1,00800
CRP (mg/L)	5	0.7
Na+ (mEq/L)	130	126
K+ (mEq/L)	4.8	3.2
Serum Creatinine (mg/dL)	0.5	0.5
aPTT (sec)	56.3	---

Hb: Haemoglobin; WBC: White Blood Cell; CRP: C-Reactive Protein; Na+ : Sodium; K+: Potassium; aPTT : Activated Partial Thromboplastin Time

(DSS)[6]. The degree of liver dysfunction in children with dengue infection varies from mild injury with elevation of transaminase activity, hepatomegaly, to jaundice and fulminant hepatic failure[7].

Hemoadsorption using Cytosorb® has proven to be a safe and efficacious extracorporeal treatment modality in adults for treating complications of liver failure such as hepatic encephalopathy, hemodynamic instability and progressive hyperbilirubinemia[8]. Recently, Khan et al[8] reported on the successful clinical application of extracorporeal Cytosorb® hemoadsorption in a case of dengue fever with MODS treated with standard care along with extracorporeal assist device (Cytosorb®)[9]. However, there is a scarcity of reports on extracorporeal therapy concerning the paediatric population.

The pathophysiology involving a cytokine storm leading to endothelial cell leakage is well established with DF, DHF and DSS. Cytosorb® therapy modulates the immune response through eliminating excessive cytokine levels[10]. Hemoadsorption using Cytosorb® is intended as adjunctive treatment for patients with increased cytokine levels in the setting of SIRS, and septic shock. Additionally, it reduces various other endogenous and exogenous compounds from the blood such as myoglobin and bilirubin[11].

In the present case report, despite the standard treatment for thrombocytopenia, hyperbilirubinemia and transaminitis, 18 hours of hemoadsorption using Cytosorb® was deemed to be successful.

As far as the treatment outcome of hemoadsorption using Cytosorb® in paediatric patients is concerned, to the best of our knowledge, this case is the first report on the application of Cytosorb® hemoadsorption in a paediatric patient with dengue fever and MODS, treated successfully along with standard of care. However, since literature regarding hemoadsorption in the paediatric population is limited, larger prospective studies are required to evaluate the exact advantage and possible adverse effects.

CONCLUSIONS

Cytosorb® along with standard care, can be a safe and advantageous extracorporeal therapy option to treat paediatric dengue patients with MODS. CytoSorb can be considered as an option for rescue therapy in patients undergoing sepsis and septic shock.

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Conflicts of interest:
The authors declare no conflict of interest

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