

CLINICAL IMPROVEMENT IN HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS WITH DAILY ADSORPTIVE HEMOPERFUSION



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Objectives:

A 39 year-old male with HIV (virus-free on HAART; CD4 > 200) presented with fever, dyspnea and lymphadenopathy. After a prolonged hospitalization with an extensive malignancy and infectious workup (including biopsies of bone marrow, lymph nodes, and liver), a diagnosis of hemophagocytic lymphohistiocytosis (HLH) was made (ferritin 9,623ng/mL, IL-2Rα 82,265pg/mL [reference range 3,592-9,734pg/ml]), pancytopenia, persistent fever, hepatosplenomegaly [1-3]. Despite immunomodulatory treatment (high dose dexamethasone, rituximab, tocilizumab, and IVIG), anti-tuberculosis, and antimicrobial therapy, he continued to deteriorate (hypotension, hyponatremia, encephalopathy, AKI and transfusion- and multiple pressor- dependency).

He was started on daily 6-hour combined hemodialysis/hemoperfusion (Fresenius polysulfone F180NR®/ CytoSorb® cartridge, HD/HP) for 7 days [4]. IRB approval was obtained for compassionate use of CytoSorb®, which is only available outside the USA for treatment of hypercytokinemia.

Hemodynamics began to stabilize during the first treatment, followed by marked and steady improvement in liver function and mental status (following commands and communicating non-verbally with staff/family), paralleled by a reduction in pressor (Fig1), oxygen (considered for extubation), and blood product requirements. 4 days after the last HD/HP, however, he started to deteriorate, and subsequently died. Autopsy revealed disseminated aspergillosis (brain, kidney, lung, and liver), a complication previously associated with high dose steroid, rituximab, and tocilizumab administration [5-9], but not CytoSorb®.

Methods:

On Day 1 of HD/HP, plasma samples were collected at 0 min, 15 min, 180 min, 360 min, and 15 min post-treatment from the ports before and after CytoSorb®, and before and after dialyzer. On Days 2 to 7 of HD/HP, samples were collected at the beginning and 15 min after the end of the treatment, and 2 hours post-treatment on Day 7. Samples were frozen at -70°C and were analyzed in duplicates with Human Cytokine/Chemokine, Adipocyte and Soluble Cytokine Receptor Magnetic Bead Panels (EMD Millipore, USA) on a Luminex100® System.

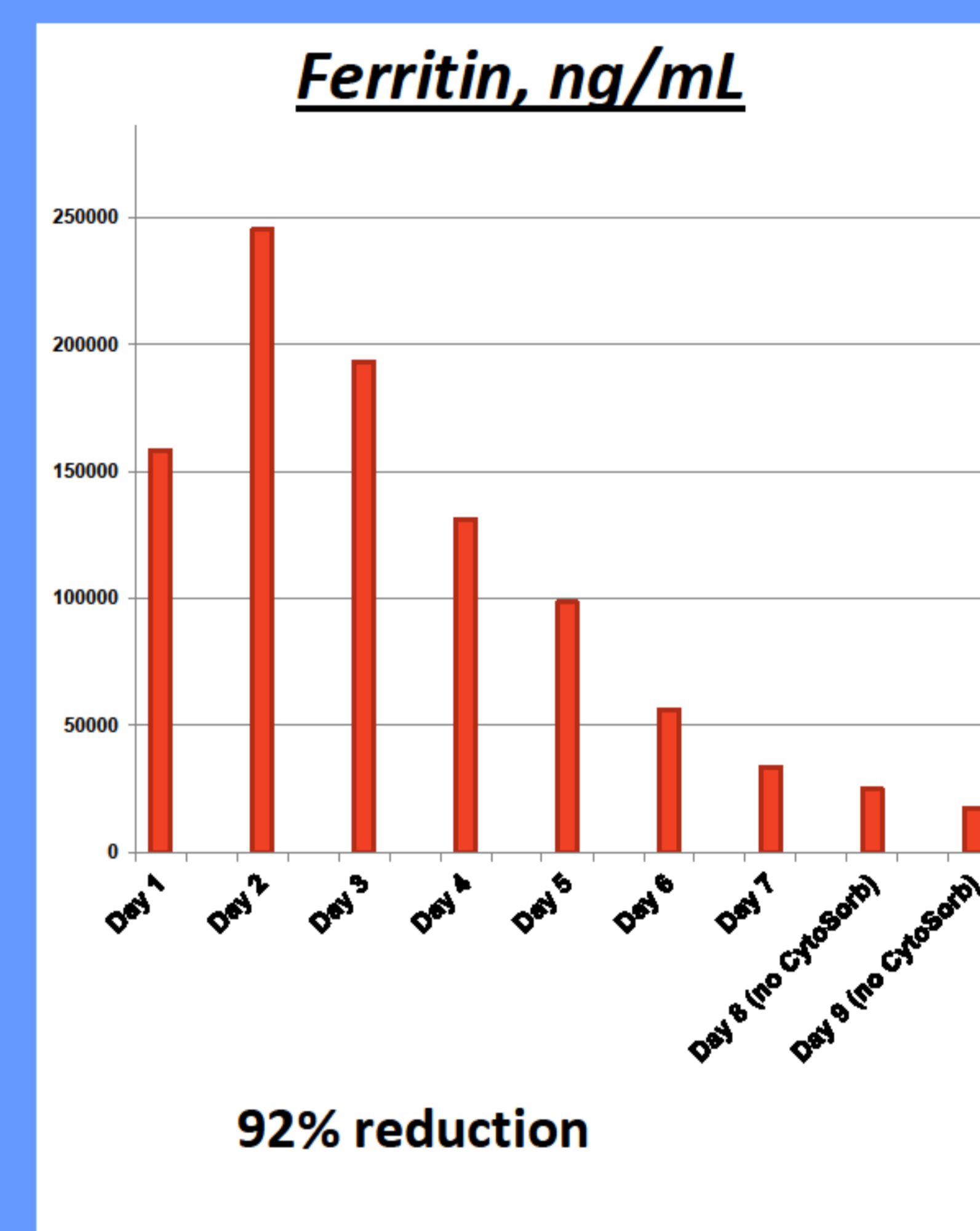
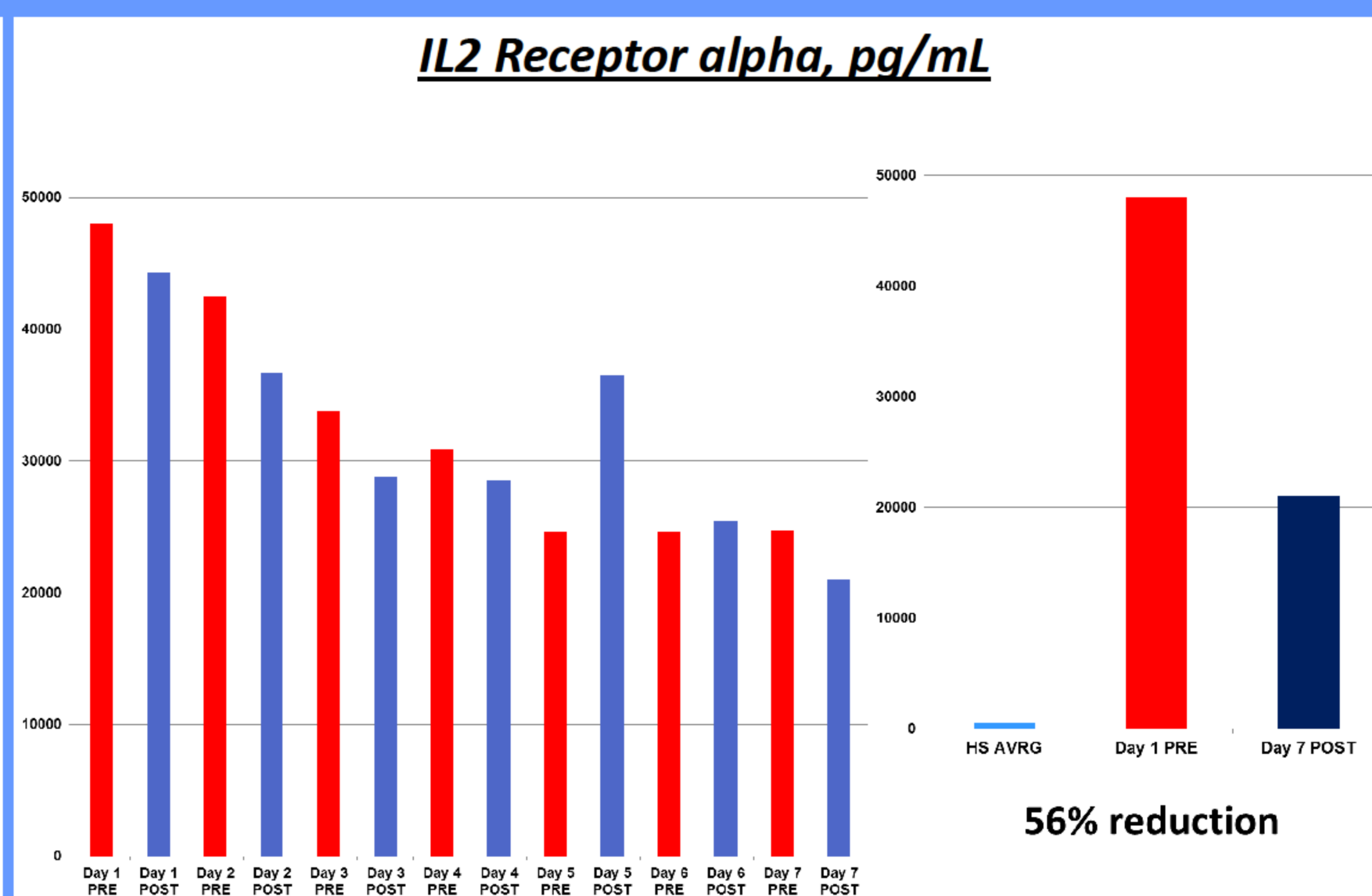
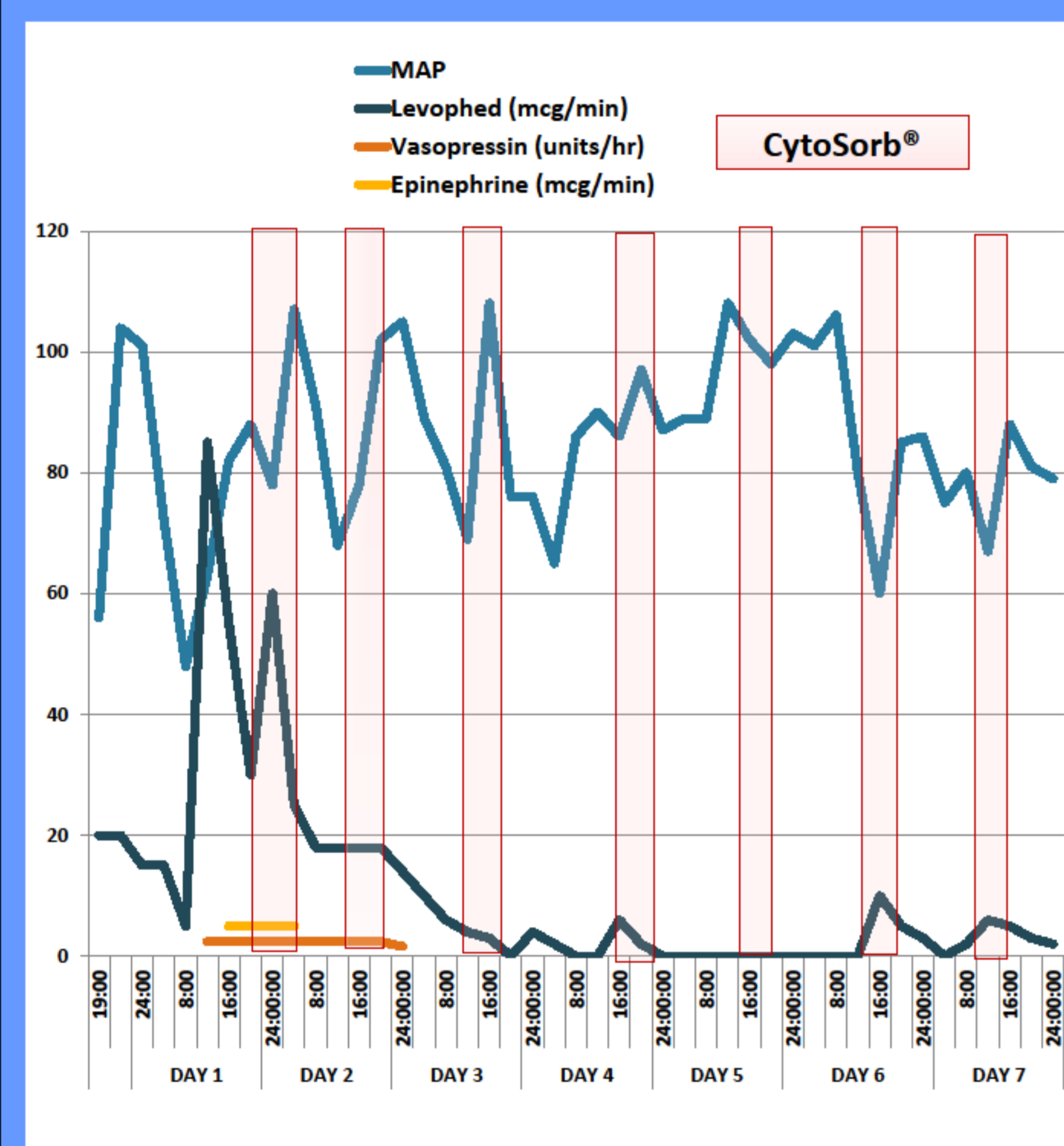


Fig 1. Reduced pressor requirements

Fig 2. Reduction in IL-2Rα. (HS AVRG – healthy subjects, average, N=11)

Fig 3. Reduced ferritin concentrations

Results:

Comparison of plasma concentrations before and after CytoSorb® during Day 1 confirmed significant clearance of cytokines by the cartridge (Table1). Analysis also revealed sequential reductions in IL-2Rα, (Fig2) IFN-γ, TNFα, IL-6, IL-8, IL-10, eotaxin, other cytokines and ferritin (Fig3), as well as a rise in adiponectin during the 7 day course.

Molecule	CytoSorb	Dialyzer
IL-8	29.38	7.94
IP-10	19.94	1.50
Eotaxin	27.00	-0.35

Table 1. Average % reduction of cytokines plasma concentration by CytoSorb and dialyzer

Conclusions:

Marked clinical improvement was associated with cytokines clearance by CytoSorb® (measured by concentration differences before and after cartridge) and not other immunosuppressive agents. HLH carries a mortality >50%, due to cytokine release [10-16]. Adsorptive HP offers a promising new treatment.

References:

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