Extracorporeal multimodal hemoperfusion with Efferon LPS to abrogate cell-free plasma DNA circulation in septic shock patients

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INTRODUCTION

Increased cell-free plasma DNA (cfpDNA) levels in critical illness are indicative of cell destruction and associate with endothelial damage, multiorgan failure, metabolomic alterations, proinflammatory signaling and mortality predicting in sepsis (1-4). Independently on causative or associative link of diminishing cfpDNA and/or course and outcome prediction, cfpDNA levels may represent a valuable biomarker indicative of successfulness of a care strategy in a particular patient.

OBJECTIVES

To determine if the multimodal hemoperfusion with Efferon LPS extracorporeal adsorber that binds LPS and proinflammatory mediators rapidly abrogates cfpDNA levels and associates with improvements of clinically significant variables in sepsis patients.

METHODS

Adult patients with septic shock (Sepsis-3) within first 12 hours since the start of vasopressors infusion were included in this **randomised** multicenter study. (NCT04827407). No differences in clinical and laboratory parameters found between HP and control groups at a baseline.

Patients undergoing **hemoperfusion** (**HP**, n=36) received two treatments, 24 hours apart. **Control group** (**CG**, n=20) underwent no HP and received conventional therapy only. HP was performed using Efferon LPS adsorbers containing mesoporous polymeric beads with the surface-immobilized LPS-selective ligand to remove both endogenous proinflammatory molecules and LPS [5-7]. Levels of C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6) were determined by ELISA at the baseline and 72 hours after inclusion in the study. Endotoxin levels were determined using the kinetic chromogenic LAL test. DNA concentration was determined by fluorimetry using SYBR green dye. STATA 16.0 (StataCorp, USA) and Excel 2019 with XLStat 2019 add-in (Addinsoft) were employed for statistical analysis.

RESULTS

Hemoperfusion yielded several clinical benefits:

(a) Increase of the cumulative hospital survival: sHR=2.2 (1.1-4.3, p=0.029, Grey test);
(b) Duration of septic shock in the survived patient cohorts: median time to blood pressure normalization was 57 (37; 80) hours in the ECH group versus 101 (58; 197) hours in the control (sHR = 2.20; 95% CI: 1.11-4.34; p = 0.029);
(c) Reversal of multiorgan failure expressed in decrease of SOFA scores values during 72 hrs (Table 1);
(d) Increase of PaO_2/FiO_2 index (Table 1);
(e) Decrease of proinflammatory biomarkers PCT, CRP, IL-6, and of bacterial LPS (Fig.1, A-D);
(f) Elimination of cfpDNA (Fig.2).

Table 1	time	0h	24h	72h
			Me (Q1; Q3)	
SOFA	Control	7.5 (6; 11)	9 (7; 11)	5 (4; 10)
	Hemoperfusion	7 (7; 9)	7 (5; 9)	3 (2; 6.5)
	P-value	0.83	**0.029**	0.17 **[0.007]**
Norepinephrine, mkg/kg/min	Control	0.6 (0.3; 0.9)	0.7 (0.3; 0.9)	0.5 (0.1; 0.7)
	Hemoperfusion	0.7 (0.4; 0.9)	0.5 (0.1; 0.8)	0.1 (0; 0.3)
	P-value	0.36	0.097	0.060 **[0.009]**
PaO_2/FiO_2	Control	239 (209;286)	250 (215;277)	235 (204; 290)
	Hemoperfusion	273 (233; 293)	285 (256; 313)	305 (289; 350)
	P-value	0.26	**0.012**	**<0.001 [<0.001]**

Figure 1. Levels of plasma biomarkers

** p < 0.05, ** p < 0.001, day 0 vs day 3 Wilcoxon test*

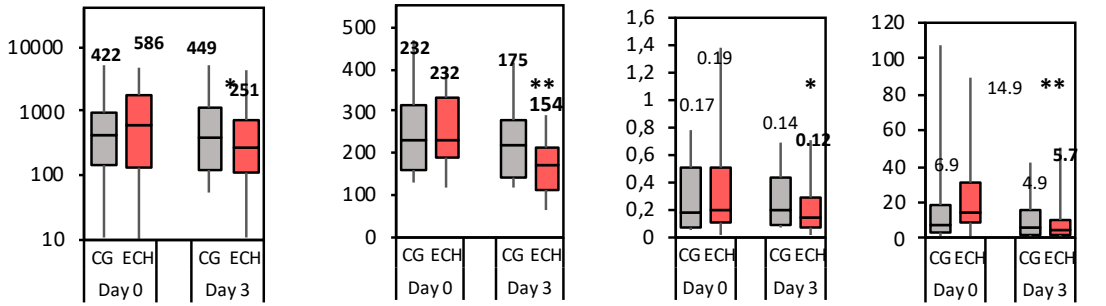
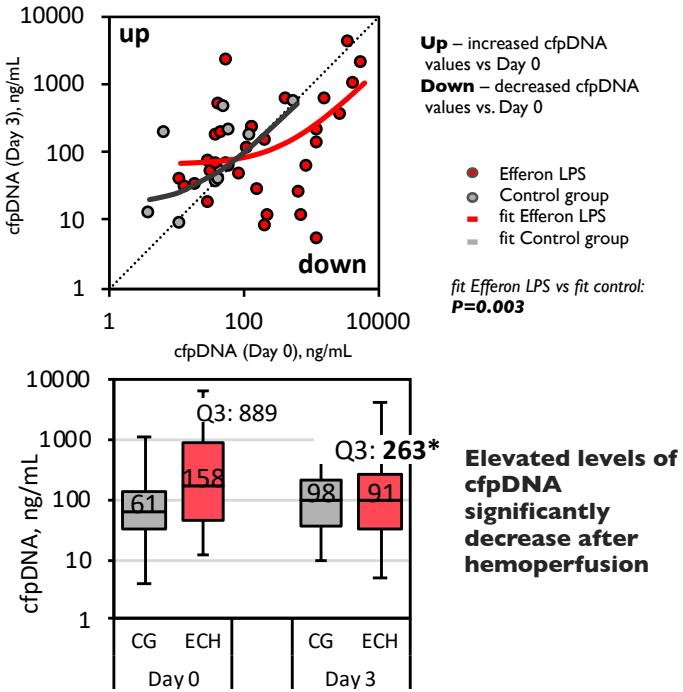


Figure 2. HP eliminates cell-free plasma DNA.



Elevated levels of cfpDNA significantly decrease after hemoperfusion

CONCLUSIONS

Treatment of septic shock patients with Efferon LPS resulted in significant clinical improvements associated with decrease of elevated cfpDNA levels.

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