

Efficacy of plasma exchange in septic shock: a case report

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Abstract

The mortality rate for severe sepsis and septic shock remains high. Additionally, this life-threatening state poses serious difficulties for the treatment of patients. Unfortunately, the mechanism of sepsis is complex and not well understood. In this paper, we present the case of a 2.5-year-old female with septic shock treated with plasma exchange (PE) as a nonstandard therapy. We analysed the medical history of disease, including patient data, physical examination, laboratory tests and treatment. Unexpectedly, we achieved clinical improvement after the first PE. During PE, the dose of catecholamine was reduced. In addition, the level of C-reactive protein seemed to be a better predictor of the efficacy of PE in septic shock compared to procalcitonin. We conclude that PE may improve the survival rate for patients with septic shock. These data could be useful in the search and introduction of new or alternative methods of treatment for critically ill children.

Key words: septic shock, treatment, therapeutic plasma exchange; septic shock, children

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Sepsis and septic shock frequently lead to multiorgan failure, and as a result, the mortality rate ranges from 20 to 60% [1–3]. The mechanism of sepsis is complex and are not well understood. It is known that bacterial sepsis and septic shock result from the overproduction of inflammatory mediators as a consequence of immune recognition of bacteria or bacterial products [4]. Many factors are involved in the pathophysiology of sepsis, making it highly difficult to treat. The experimental use of a monoclonal anti-TNF antibody (afelimomab) demonstrated a beneficial effect on survival in sepsis [5]. However, it is highly unlikely that any single modulatory regimen targeting a single mediator will be successful in reducing mortality in severe sepsis or septic shock [1]. One non-selective method targeting multiple pathways is plasma exchange (PE), which can remove numerous harmful or toxic mediators from the circulation [6].

The aim of this article is to present the efficacy of treatment with PE in a small child with septic shock.

CASE REPORT

A 2.5-year-old girl of Caucasian ethnicity was admitted to the Paediatric Intensive Care Unit (PICU) due to systemic inflammatory response syndrome with multiorgan dysfunction secondary to pneumonia. She presented with no significant past medical history. The laboratory findings revealed anaemia, thrombocytopenia, renal and hepatic failure, coagulopathy and elevated C-reactive protein (CRP) and procalcitonin (PCT) concentrations (Table 1). Treatment with intravenous administration of broad-spectrum antibiotic therapy (vancomycin, meropenem), diuretics, erythrocyte concentrate and fresh-frozen plasma was initiated. Despite this therapy, respiratory and cardiovascular insufficiency with uncompensated hypotension occurred within

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the next few hours. Intensive treatment, including mechanical ventilation, continuous infusion of catecholamines and pharmacological therapy, was started. Typical clinical signs for septic shock, such as severe bleeding from the oral mucosa and central catheters, were observed. Due to the unresponsiveness of the patient to conventional intensive therapy and the presence of a life-threatening condition, PE was performed as a rescue therapy, with a plasma volume exchange of 50 mL kg⁻¹ using fresh-frozen plasma. The Prisma device (Gambro, Sweden) and membrane plasma separation method (MPS) were used. Each PE session was conducted using a double-lumen central catheter and continued for 2 to 3 hours; hemodiafiltration was also required.

After the first PE, the bleeding stopped. Because of the improvement in the general condition of the patient and the laboratory test results (e.g., the reduction in CRP, aspartate aminotransferase (AST) and fibrinogen levels), daily PE was continued for the next 3 days. After four sessions of PE, a significant improvement was observed in terms of laboratory findings and a reduction in the catecholamine dosage (Table 1, Fig. 1).

After 4 days, hypotension and an elevated white blood cell count were observed, resulting in the need for an increased dose of vasopressors. Despite intensive treatment, we observed deterioration in the general status of the patient and laboratory test results. As a result, subsequent PE sessions were performed (within the next 3 days), allowing for a reduced norepinephrine dosage. A decrease in the white blood cell count was observed once again, though the general condition of the patient improved. Spontaneous diuresis started at the end of 4th week of the disease course. The final diagnosis was determined to be septic shock associated with pneumonia caused by *Streptococcus pneumoniae*. The patient was discharged from the ICU after 1 month of intensive treatment and from the hospital 2 months later. Despite the return of diuresis, the patient was diagnosed with end stage renal disease and treatment with peritoneal dialysis was necessary for the next year. After dialysis, renal function improved significantly, reaching second stage renal disease.

DISCUSSION

Indications for the use of PE are primarily neurologic, immunologic or haematologic diseases. During PE it is possible to remove large molecular weight substances from the plasma, such as autoantibodies, immunoglobulins, leukocytes, platelets, abnormal red cells and circulating immune complexes, as well as protein-bound substances, toxins and cytokines. However, current guidelines for PE do not cover severe sepsis and septic shock [6]. There are several reports to suggest that PE may be a relevant adjuvant to conventional treatment and may reduce mortality in individuals with severe sepsis and septic shock [1, 4, 7, 8].

Table 1. Clinical and laboratory data

Day of hospitalization	No of PE	HGB (g dL ⁻¹)	WBC (GL ⁻¹)	PLT (GL ⁻¹)	Fibrinogen (mg dL ⁻¹)	INR	d-dimer (µg L ⁻¹)	CRP (mg dL ⁻¹)	PCT (ng mL ⁻¹)	AST (U L ⁻¹)	Creatinine (mg dL ⁻¹)	BP (mm Hg)	NE dose (µg kg ⁻¹ min ⁻¹)	DX dose (µg kg ⁻¹ min ⁻¹)	DBT dose (µg kg ⁻¹ min ⁻¹)
1	I	8.7	5.9	36	1380	1.44	8558	46		2853	2.55	60/20	1	-	-
2	II	8.2	11.68	74	294	1.26	4026	12.54	≥ 10	649	0.76	105/85	1-0.3	1.3	-
3	II	11.7	19	75	349	0.80	553	7.13	≥ 10	580	0.56	100/40	0.15	1.3	-
4	IV	12.4	20.7	86	271	0.88	333	4.19	≥ 10	403	0.4	115/73	0.05	1.3	-
5		14.4	29.96	92	287	1.05	358	3.42	≥ 10	293	0.47	135/95	0.05-0	1.3	-
9	V	9.9	38	225	382	1.02	3780	4.8	≥ 2	108	0.67	100/55	0.26	-	5.4
10	VI	10.5	39	275	307	1.10	1782				0.72	120/60	0.5		5.4
11	VII	10.3	24	256	211	1.16		2.42	≥ 0.5		0.73	125/75	0.32		5.4
12		13.8	19	227	310	1.04	763	2.76		58	0.74	125/70	0.2		3.5
32		13.8	20.98	148	480	1.10		3.49		23	1.49	123/70			

PE — plasma exchange; HGB — haemoglobin level. CRP — C-reactive protein. PCT — procalcitonin. Fibr. — fibrinogen; NE — norepinephrine; DX — dopexamine; DBT — dobutamine

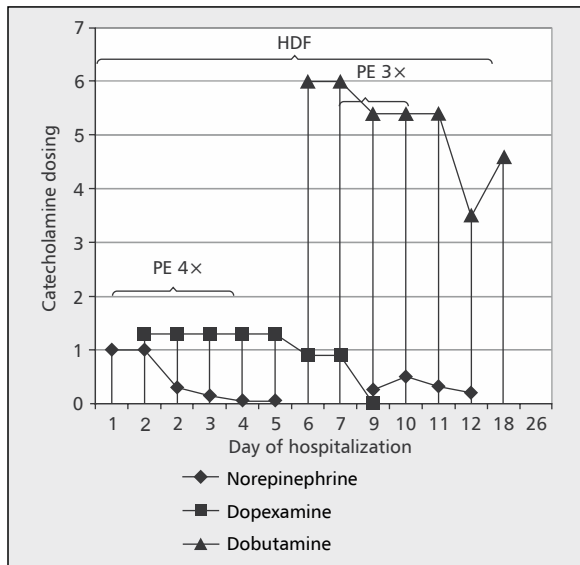


Figure 1. Catecholamine dosing in relation to PE. All doses given in µg kg⁻¹ min⁻¹

In the present case, a dramatic reduction in bleeding and the achievement of haemodynamic stability was observed after the first PE. For this reason, PE may be deemed a life-saving treatment. In addition, PE resulted in an improvement in laboratory tests, including the coagulation profile, a reduction in the CRP level and AST activity.

A reduction in the catecholamine dose was observed after the first PE session with a further dose reduction following the next PE sessions. The greatest reduction in dosing was observed when comparing norepinephrine with dobutamine and dopexamine (Fig. 1). Similar outcomes were obtained in a study of 11 paediatric patients [7]. Improvements in the coagulation profile and organ function were achieved in our patients after 4 to 5 separations, which is consistent with the principle of PE. To remove 90% of harmful substances, four to five exchanges are necessary with the plasma volume exchange ranging from 30 to 40 mL kg b.w.⁻¹ [9]. Therefore, a single PE may be insufficient. Four PEs were performed initially; however, due to the reappearance of septic shock requiring increased catecholamines, PE was performed an additional 3 times. Afterward, haemodynamic stability and a reduction in the norepinephrine dose were again successfully achieved (Table 1, Fig. 1). PE was terminated, and we observed no side effects of this therapy.

Interestingly, the PCT level was reduced only after the 4th PE, while a decrease in the CRP concentration was observed after the first separation (Fig. 2). Both PCT and CRP are biomarkers of a bacterial infection. The issue of whether one is a better or more sensitive biomarker in sepsis remains under discussion [10]. In our study, the level of CRP decreased early during treatment when compared to PCT. The half-life of PCT is 25–30 h, peaking after bacterial toxin stimuli at 6–8 h [11], while the CRP

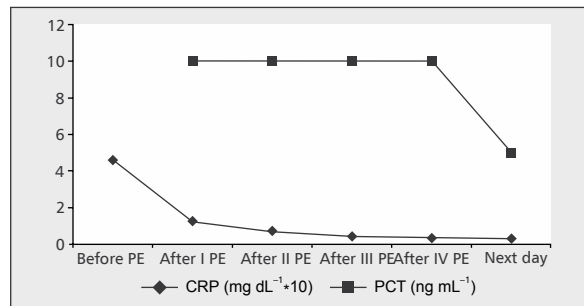


Figure 2. C-reactive protein (CRP) and procalcitonin (PCT) levels during PE sessions (normal ranges: CRP < 0.5 mg dL⁻¹; PCT < 0.5 ng mL⁻¹).

half-life is approximately 19 h, peaking approximately 48 h [12]. Therefore, the reduction in CRP level we observed shortly after beginning PE may predict the effectiveness of this therapy and suggest a clinical improvement. It should be noted that in this study, PCT measurement was determined using a semi-quantitative method and real changes in the concentration of this inflammatory marker were difficult to assess. However, the CRP level seems to be a better predictor of the efficacy of PE in septic shock than PCT.

The beneficial effect of PE in the treatment of septic shock in our patient was evident. Some authors argue that these results were due to the removal of circulating endotoxins and cytokines, such as tumour necrosis factor-α and interleukin-1β [13]. However, multiple unsuccessful attempts to block the inflammatory response have been made. Moreover, the anti-inflammatory response to sepsis induces immunoparalysis and may be deleterious to the patient. The goal of treatment in severe sepsis should be the restoration of homeostasis rather than the selective inhibition of pro- or anti-inflammatory mediators [4]. It should be noted that in a subsequent patient, a 17-year-old boy with septic shock following multiple traumas but without coagulopathy, we also observed clinical and laboratory improvement (unpublished data). After five PE sessions, a reduction in catecholamine dosing and in CRP and PCT levels was achieved. However, the effect of PE in this case was not as profound compared to our first case and it is difficult to state definitively that the improvement we observed was mainly due to PE. However, we believe that PE was helpful in the second case. Using fresh-frozen plasma as the replacement fluid, PE replenishes many deficiencies, in not only coagulation factors and inhibitors, such as protein C, S and antithrombin but also the immunoglobulins IgM and IgA. This may improve the humoral and cellular inflammatory response and demonstrates the broad applicability of PE in sepsis.

CONCLUSION

In conclusion, our data support previous findings that early intervention using PE may improve the efficacy of

treatment in septic shock with severe coagulopathy. PE may reduce the dose of catecholamines required in patients. These data may aid in the search for new or alternative methods of treatment for critically ill children.

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