The International Journal of Artificial Organs / Vol. 32 / no. 1, 2009 / pp. 31-38

Artificial Kidney and Dialysis

Effects of coupled plasma filtration adsorption on immune function of patients with multiple organ dysfunction syndrome

H.-J. MAO, S. YU, X.-B. YU, B. ZHANG, L. ZHANG, X.-R. XU, X.-Y. WANG, C.-Y. XING

Department of Nephrology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province People's Hospital, Nanjing, Jiangsu Province - PR China

ABSTRACT: Objective: *To investigate the effects of coupled plasma filtration adsorption (CPFA) on the immune function of patients with multiple organ dysfunction syndrome (MODS).*
Methods: *This study was a prospective, pilot, before-and-after self-crossover, clinical trial. Seven patients diagnosed with MODS and severe infection were randomly allocated to both 10 hours of CPFA and 10 hours of high-volume hemofiltration (HVHF) with a 12-hour interval and in random order. Serum concentrations of 7 cytokines including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), interleukin-10 (IL-10), interleukin-1 receptor antagonist (IL-1Ra), and soluble tumor necrosis factor receptors 1 and 2 (sTNFR1 and sTNFR2) were measured during each treatment. The HLA-DR expression by the blood monocytes and the TNF-α production by the patients' blood (both spontaneous and lipopolysaccharide stimulated) were tested before and after the treatment. TNF-α production of normal human monocytes (THP-1 cells) incubated in vitro with the patient plasma was also measured. Results: During CPFA, the fall in serum TNF-α and rise in serum IL-1Ra coincided with the rise in ratios of sTNFR2/TNF-α and IL-1Ra/IL-1β ($p<0.05$), which were different from those seen within HVHF ($p<0.05$). HLA-DR expression increased after CPFA (84.32% ± 4.63% vs. 73.65% ± 11.52%, $p=0.037$), but there was no change after HVHF ($p>0.05$). Spontaneous and lipopolysaccharide-induced TNF-α production increased over time with CPFA ($p=0.038$, $p=0.034$, respectively), but did not change with HVHF ($p>0.05$). Patient plasma suppressed the production of TNF-α by cultured normal monocytes. This effect decreased over time with CPFA ($p=0.041$), but there was no effect with HVHF ($p>0.05$).*
Conclusions: *CPFA was superior to HVHF in increasing the ratios of antiinflammatory to proinflammatory mediators, improving antigen presentation ability, and restoring leukocyte responsiveness. These findings suggest a potential role for CPFA in the treatment of MODS. (Int J Artif Organs 2009; 32: 31-8)*

KEY WORDS: Adsorption, Coupled plasma filtration adsorption, Cytokines, High-volume hemofiltration, Multiple organ dysfunction syndrome

INTRODUCTION

Sepsis is a kind of inflammatory cascade response caused by the local and systemic releasing of microbial components, leading to the production of inflammatory cytokines. Excessive production of inflammatory cytokines appears to cause the diffused damage and multiple organ dysfunctions. Many studies have found that the level of the inflammatory state was closely related to the prognosis of patients with sepsis; therefore, attenuating these inflammatory states has become one of the target goals of sepsis treatment. Although many studies have confirmed that continuous renal replacement therapy (CRRT) can eliminate inflammatory cytokines, its influence on their level in blood is small (1).

Peripheral blood mononuclear cells (PBMCS) play an

0391-3988/031-08 $25.00/0

important role in the occurrence and development of systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS). In sepsis, the immune effector cells can not carry out their monitor functions, further worsening the inflammation condition and causing damage to the organism (2). Coupled plasma filtration adsorption (CPFA) was proposed by Tetta et al (3) in 1998. This technique, which applied filtration and adsorption in traditional CRRT technology to increase the clearance of the relevant molecules in sepsis.

The purpose of our study was to compare CPFA with high-volume hemofiltration (HVHF) and to observe the impact of CPFA on serum cytokine levels and its influence on the antigen-presenting function and secretory function of monocytes.

SUBJECTS AND METHODS

Subject enrolment criteria and exclusion criteria

Patients were selected who were 18-80 years old; fulfilled the SIRS clinical diagnostic criteria promoted by the ACCP/SCCM in 1991 (5) and the MODS diagnostic criteria promoted by the Academic Meeting of Critical Care Medicine in China in 1995; with or without acute renal failure; and an Acute Physiology and Chronic Health Evaluation (APACHE) II score ≥8. Excluded from the study were those with absolute contraindications for renal replacement therapy.

Four men and 3 women were selected, and all signed the informed consent letter before treatment. Their average age was 55.29 ± 16.89 years. Their average APACHE II score was 22.43 ± 6.99, and the number of organ failures was 3.57 ± 1.13 before treatment. The 7 patients' general clinical characteristics are shown in Table I.

Therapeutic program

This was a prospective, pilot, before-and-after, self-crossover clinical study. Each patient underwent both CPFA and HVHF for 10 hours besides routine therapy. CPFA and HVHF were scheduled randomly at intervals of 12 hours.

A double-lumen catheter was inserted into the internal jugular vein or the femoral vein to establish vascular access, and blood flow ranged from 150 to 200 ml/min. Ultrafiltration depended on the clinical condition of the water balance. Low-molecular-weight heparin dose was adjusted, basing on clinical bleeding and clotting in the pipeline.

CPFA was carried out using the ACH-10 CRRT machine (Asahi Kasei Corporation, Japan). The filtration of plasma, obtained with a plasma separator (PF2000N, 0.35 m^2; Gambro, Sweden), was at a rate of 30 ml/min. The plasma then entered into a resin cartridge (HA-330I; Zhuhai Lizhu Group, Biological Material Co, Ltd., China). The outlet of the plasma separator was connected with a hemodialyzer (F6, polysulfone, 1.3 m^2; Fresenius, Germany). The flow rate of dialysis fluid was 2 l/hour. The adsorber was changed every 5 hours (Fig. 1).

HVHF was carried out using the Dipact CRRT machine (Braun, Germany), and the hemofiltrator was an AV600 filter (polysulfone, 1.4 m^2; Fresenius, Germany). The flow rate of exchange fluid was 6 l/hour, and thus the total amount was 60 L per treatment (Fig. 2).

TABLE I - GENERAL CLINICAL DATA OF THE 7 PATIENTS BEFORE BLOOD PURIFICATION TREATMENT

Patient	Sex	Age	Based diseases	Number of failed organs	Etiology	APACHE II score
1	M	57	Diabetic nephropathy, acute cerebral infarction, pulmonary infection, chronic renal failure acute exacerbation	3	*Pseudomonas aeruginosa*	31
2	F	58	Rheumatic heart disease after mitral valve and aortic valve replacement, acute myocardial infarction, acute renal failure, pulmonary infection, DIC	5	UN	29
3	M	63	Suppurative cholangitis, septic shock, acute renal failure	5	*Escherichia coli*	28
4	M	24	Sepsis, acute pneumonia, acute renal failure, ARDS	4	Highly pathogenic avian influenza virus	18
5	F	74	Acute pneumonia, ARDS, dermatomyositis	2	Cytomegalovirus and *Candida krusei*	20
6	F	43	Severe acute pancreatitis, acute renal failure, ARDS	3	UN	12
7	M	68	Acute intestinal obstruction, acute renal failure	3	UN	19

ARDS = acute respiratory distress syndrome; DIC = disseminated intravascular coagulation; UN = pathogen unknown.

Detection of cytokines

Samples were taken at 0, 5, and 10 hours during CPFA and HVHF. The serum cytokine levels of TNF-α, IL-1β, IL-6, IL-10, IL-1Ra, sTNFR1, and sTNFR2 were measured by enzyme-linked immunosorbent assay (ELISA), strictly according to the manufacturer's instructions. Human tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, and IL-10 ELISA kits were obtained from Jingmei Biotech Company (Jingmei Biotech, Shanghai, China), and human interleukin-1 receptor antagonist (IL-1Ra), and soluble tumor necrosis factor receptors 1 and 2 (sTNFR1, and sTNFR2) ELISA kits were obtained from America Biosource Company (America Biosource, San Diego, CA, USA).

Detection of expression of HLA-DR in patient monocytes

Heparin anticoagulated blood samples were collected at 0 and 10 hours of CPFA and HVHF to measure the expression of HLA-DR in monocytes. Monoclonal antibody included HLA-DR-FITC, CD45-PerCP, and contrast of the same type (BD Biosciences, San Diego, CA, USA). Flow cytometry was with a FACS Calibur (Becton Dickinson, San Jose, CA, USA). CellQuest software was used for analysis.

Measuring secretion of TNF-α in patient whole blood

The ability of patients' whole blood to produce TNF-α, spontaneously or stimulated by lipopolysaccharide (LPS; *Escherichia coli* O55:B5; Sigma, St. Louis, MO, USA), was measured. Anticoagulated blood samples of 5 mL were collected at 0 and 10 hours of CPFA and HVHF. The samples were mixed with 0.5 mL of RPMI 1640 (Gibco, USA), then incubated with or without 10-ng LPS at 37°C in 5% CO_2 for 3 hours. The supernatant liquid was collected to measure the level of TNF-α.

Detection of impact of patient plasma on TNF-α secretion by normal monocytes

THP-1 cells, belonging to human monocytic leukemia cell lines, were purchased from Peking Union Cell Bank. The cells were synchronized for 12 hours and then cultured in RPMI 1640 culture solution containing 50% patient plasma, for 12 hours. The supernatant liquid was collected to detect the level of TNF-α. Patient plasma was collected at 0, 5, and 10 hours of CPFA and HVHF. THP-1 cells cultured with RPMI 1640 containing 50% of normal plasma or with RPMI 1640 only, were used as positive and negative control, respectively.

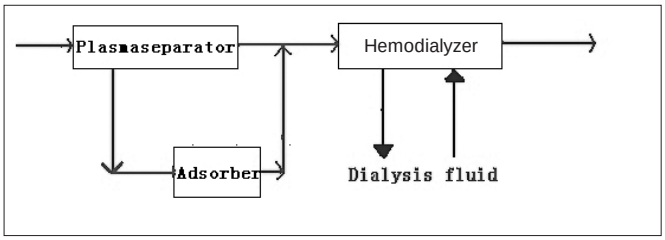

Fig. 1 - *Flow chart of coupled plasma filtration adsorption.*

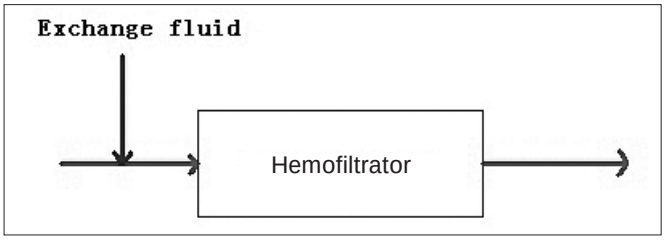

Fig. 2 - *Flow chart of high-volume hemofiltration.*

Data analysis

All data are presented as means ± standard deviation and analyzed by SPSS 13.0 statistical software. All cytokine data were analyzed by repeated measures ANOVA. Statistical evaluation was performed by Student's *t*-test for paired data. Statistical significance was considered to be a p value of <0.05.

RESULTS

Clinical effects of the therapies

One CPFA and 1 HVHF session were completed for each patient. Three patients followed the sequence of CPFA then HVHF, and 4 patients followed the reverse order. According to the formula of Wong and William (6), the average predictive mortality of the patients was 0.54. In

the end, of the 7 patients, 5 survived. Of 6 patients who had renal failure before treatment, 4 restored their kidney functions. Mean arterial pressure (MAP) increased and dopamine requirement decreased during CPFA, which was the same as during HVHF ($p>0.05$). APACHE II score decreased from 25.25 ± 7.18 to 19.00 ± 6.83 with CPFA ($p<0.05$), and it also decreased with HVHF, but this latter trend was not statistically significant ($p>0.05$). CPFA improved kidney function and oxygenation index, maintained electrolyte balance and acid-base balance effectively, as did HVHF ($p>0.05$). C-reactive protein (CRP) (mg/L) decreased significantly during CPFA ($p<0.05$) but only had a decreasing trend with HVHF ($p>0.05$). CPFA and HVHF both showed significant differences in change of CRP (Tab. II).

Serum cytokine level

During CPFA, the serum level of TNF-α decreased and the level of IL-1Ra increased gradually over time. The level of the other cytokines did not change. The ratios of sTNFR2/TNF-α and IL-1Ra/IL-1β increased gradually and reached statistical significance at 10 hours compared with 0 hours.

During HVHF, the level of serum IL-1β decreased and IL-1Ra increased obviously at 5 hours, but returned to baseline at 10 hours. The ratio of IL-1Ra/IL-1β increased markedly at 5 hours but dropped to baseline at 10 hours. The concentrations of the other cytokines and the ratios of sTNFR1/TNF-α and sTNFR2/TNF-α did not apparently change at the various times ($p>0.05$).

The serum levels of the 7 kinds of cytokines did not differ between the CPFA and HVHF groups at 0 hours. But the impact of these 2 therapies on the level of TNF-α, IL-1Ra, and the ratios of sTNFR2/TNF-α and IL-1Ra/IL-1β was significantly different ($p<0.05$) (Tab. III).

Expression of HLA-DR in patient monocytes

The expression of HLA-DR in normal monocytes was 95.6% ± 2.4%, but in patient monocytes it was 75.21% ± 12.49% before treatment, significantly lower than normal ($p<0.05$). The expression ratio increased after CPFA (10 hours) but not after HVHF (Tab. IV).

Secretion of TNF-α in patient blood

The secretion levels of TNF-α in the patients' blood were 291.95 ± 26.21 pg/mL and 217.83 ± 73.67 pg/mL before CPFA, and 402.80 ± 74.48 pg/mL and 303.35 ± 28.39 pg/mL after CPFA, when LPS or no LPS, respectively, was added the patients' anticoagulated blood. Under the above 2 conditions, differences between before and after CPFA had statistical significance ($p=0.038$ and $p=0.034$). In contrast, the secretion level of TNF-α, with or without LPS, had no obvious differences between before and after HVHF ($p>0.05$). CPFA and HVHF had significantly different effects on the autocrine or activated secretion of TNF-α from the patients' blood ($p=0.025$ and $p=0.031$).

Secretion of TNF-α by THP-1 cells

THP-1 cell production of TNF-α was inhibited by the plasma drawn from the arterial and venous blood lines at the beginning of CPFA (0 hours). The inhibitory action of ar-

TABLE II - PHYSIOLOGICAL AND LABORATORY VARIABLES DURING CPFA AND HVHF

	Therapy time	APACHE II	MAP (mm Hg)	Heart rate (/min)	Temp (°C)	BUN (mmol/L)	Cr (μmol/L)	WCC (10^9/L)
CPFA	T0	25.25 ± 7.18	99.00 ± 18.02	110.75 ± 32.28	38.2 ± 0.36	20.25 ± 11.52	365.75 ± 87.01	11.14 ± 4.46
	T10	19.00 ± 6.83*	120.75 ± 20.02*	86.75 ± 12.84	36.32 ± 1.01*	11.82 ± 7.39*	184.00 ± 102.36*	13.78 ± 3.72
HVHF	T0	27.00 ± 5.29	92.33 ± 18.33	84.00 ± 16.52	38.07 ± 0.73	15.99 ± 8.55	372.82 ± 201.38	10.71 ± 7.85
	T10	22.33 ± 5.13	115.33 ± 18.50*	92.33 ± 8.73	36.80 ± 0.69	11.22 ± 4.57*	206.45 ± 67.44*	10.83 ± 8.38
		Hb	BPC (10^9/L)	PH	PaO_2/FiO_2	$PaCO_2$ (mm Hg)	HCO_3 (mmol/L)	CRP (mg/L)
CPFA	T0	96.60 ± 24.13	69.20 ± 33.51	7.44 ± 0.07	171.71 ± 94.65	24.42 ± 3.31	19.44 ± 3.73	124.92 ± 43.88
	T10	97.80 ± 15.63	87.80 ± 47.07	7.41 ± 0.07	297.26 ± 204.46*	31.4 ± 6.35	21.68 ± 1.93	94.66 ± 35.43*
HVHF	T0	108.33 ± 18.86	68.33 ± 51.82	7.41 ± 0.08	185.05 ± 99.67	31.72 ± 5.05	20.85 ± 3.53	143.50 ± 30.98
	T10	112.00 ± 23.15	66.33 ± 46.48	7.42 ± 0.07	265.45 ± 173.77*	34.25 ± 4.24	22.58 ± 2.47	129.56 ± 46.82†

BPC = blood platelet cells; BUN = blood urea nitrogen; CPFA = coupled plasma filtration adsorption; Cr = blood creatinine; CRP = C-reactive protein; Hb = hemoglobin; HCO_3 = bicarbonate radical; HVHF = high-volume hemofiltration; MAP = mean arterial pressure; $PaCO_2$ = arterial blood partial pressure of carbon; PaO_2/FiO_2 = oxygenation index; PH = arterial blood PH; T0 = at 0 hours; T10 = after 10 hours; Temp = body temperature; WCC = white cell count

*$p<0.05$, T0 vs.T10.

†$p<0.05$, CPFA vs. HVHF.

TABLE III - SERUM CYTOKINES LEVEL OR THEIR RATIO DURING CPFA AND HVHF

		0 hours	5 hours	10 hours	p Value (vs. T0)
TNF-α pg/mL	CPFA	344.52 ± 123.30	276.41 ± 128.11	198.62 ± 100.65*	0.023
	HVHF	355.41 ± 97.38	324.99 ± 129.01	379.69 ± 111.23†	
IL-1Ra pg/mL	CPFA	648.38 ± 265.91	864.51 ± 167.62	859.95 ± 195.09*	0.031
	HVHF	780.46 ± 194.31	834.30 ± 203.14*	547.42 ± 185.57§	0.030
IL-6 pg/mL	CPFA	166.42 ± 78.29	194.65 ± 102.34	184.90 ± 89.35	
	HVHF	177.87 ± 98.33	165.31 ± 87.19	156.78 ± 103.42	
IL-10 (pg/mL)	CPFA	367.44 ± 101.23	441.49 ± 135.12	493.23 ± 128.29	
	HVHF	465.87 ± 87.80	485.55 ± 98.23	461.93 ± 105.36	
IL-1β (pg/mL)	CPFA	20.26 ± 8.38	23.73 ± 7.42	27.10 ± 11.19	
	HVHF	29.44 ± 12.52	18.77 ± 6.79*	28.25 ± 9.39	0.041
sTNFR1 (ng/mL)	CPFA	26.58 ± 7.89	26.38 ± 8.52	28.19 ± 8.34	
	HVHF	30.35 ± 8.68	32.51 ± 9.53	31.07 ± 10.21	
sTNFR2 (ng/mL)	CPFA	62.78 ± 12.32	92.71 ± 9.34	83.30 ± 7.98	
	HVHF	83.68 ± 11.23	79.61 ± 7.09	84.74 ± 11.34	
IL-1Ra/IL-1β	CPFA	41.81 ± 7.48	51.58 ± 13.23	82.89 ± 16.57*	0.027
	HVHF	23.63 ± 9.45	57.45 ± 14.12*	24.22 ± 10.22‖	0.018
sTNFR1/TNF-α (ng/pg)	CPFA	0.082 ± 0.032	0.109 ± 0.023	0.143 ± 0.011	
	HVHF	0.090 ± 0.027	0.112 ± 0.034	0.101 ± 0.028	
sTNFR2/TNF-α (ng/pg)	CPFA	0.220 ± 0.062	0.302 ± 0.098	0.480 ± 0.101*	0.031
	HVHF	0.241 ± 0.056	0.248 ± 0.038	0.232 ± 0.041¶	

CPFA = coupled plasma filtration adsorption; HVHF = high-volume hemofiltration.
T10 (T5) vs. T0, *p<0.05. CPFA vs. HVHF; †p=0.024, §p=0.032; ‖p=0.016; ¶p=0.038.

TABLE IV - INFLUENCE ON EXPRESSION OF HLA-DR IN MONOCYTES

	Positive rate of HLA-DR %	
	T0	T10
CPFA	73.65 ± 11.52	84.32 ± 4.63*
HVHF	81.85 ± 17.27	79.76 ± 15.72†

CPFA = coupled plasma filtration adsorption; HVHF = high-volume hemofiltration; T0 = at 0 hours; T10 = after 10 hours.
*The expression of HLA-DR in monocytes increased clearly after CPFA (p=0.037).
†CPFA and HVHF showed significant differences in their influence on the expression of HLA-DR in monocytes (p=0.015).

terial plasma on THP-1 was clearly stronger than that of venous plasma. The quantity of secreted TNF-α inhibited by arterial plasma was significantly lower than that inhibited by venous plasma. This phenomenon was also observed in HVHF (Fig. 3). The inhibitory action was gradually weakened with CPFA, but not HVHF (Fig. 4).

DISCUSSION

Inflammatory cytokines have been one of the targets for the treatment of sepsis. With the failure of monoclonal antibodies or the other antiinflammatory factor treatments, the expectation has grown that we will be able to remove the inflammatory factors. The focus of this has shifted to continuous blood purification (CBP). TNF-α is one of the common inflammatory factors which exists in the tripolymer form of biological activity. Because its molecular weight is 54 kDa, only its inactive monomer (17 kDa) can be examined in the filtrate of CBP. IL-10 (35-40 kDa) and sTNFR1 and sTNFR2 (the extracellular domain of the TNF receptor, 30-33 kDa) also can not cross the hemofiltration membrane. Convective removal is limited even if the inflammatory cytokines of small molecular weight can be removed through convection. The clearance of the inflammatory molecules is mainly through absorption during hemofiltration (7). Previous HVHF studies using an AN69 membrane have shown a removal effect on IL-8 and IL-10, which was secondary to adsorption rather than convection (8). In our HVHF study using polysulfone membranes, we did not observe any change in serum cytokine levels. There may be differences in ad-

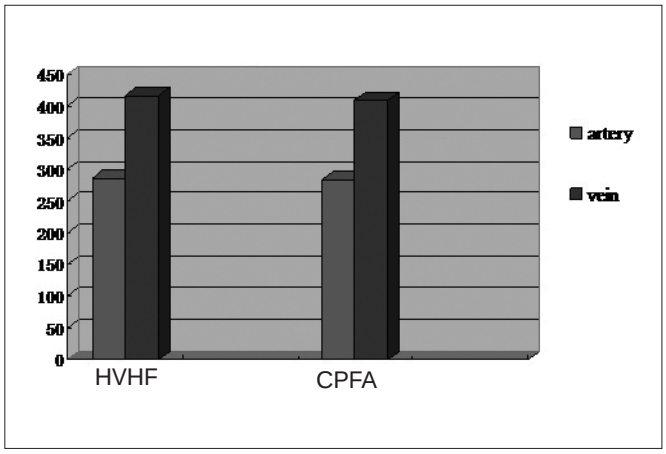

Fig. 3 - *In coupled plasma filtration adsorption (CPFA), the TNF-α secretion level (pg/mL) of THP-1 cells inhibited by arterial plasma was significantly lower than that by venous plasma at 0 hours of treatment (p=0.04). In high-volume hemofiltration (HVHF), a similar result was seen. (p=0.03).*

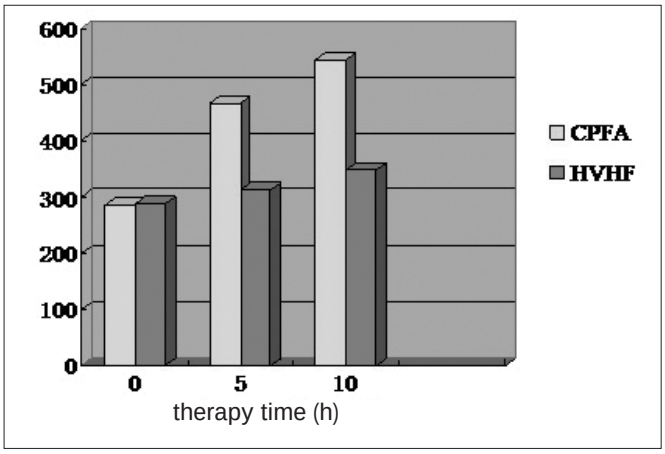

Fig. 4 - *The level of THP-1 secretion of TNF-α inhibited by plasma which was collected at 10 hours of coupled plasma filtration adsorption (CPFA), increased remarkably compared with that at 0 hours of treatment (p=0.04); but at 10 hours of high-volume hemofiltration (HVHF), no significant difference was seen compared with 0 hours (p=0.67).*

sorption between AN69 and polysulfone membranes.

Because of the rapid saturation of the absorption ability of the hemofiltration membrane, to increase the clearance of cytokines, one must either replace hemofilters frequently or introduce adsorbents. The introduction of adsorption devices in CPFA can greatly strengthen the adsorption removal of soluble inflammatory mediators in theory. We observed that the serum level of TNF-α dropped progressively with CPFA. TNF-α is the most important inflammatory cytokine in SIRS and MODS, which begins the inflammatory cascade response and participates in the tissue or cell damage. Therefore, the effective elimination of TNF-α during CPFA is beneficial to the treatment of MODS and sepsis. Whether the HA330 resin adsorber used in this study can adsorb α2-MG, the carrier of the cytokines in the plasma, like other adsorbers such as Amberchrome CG300md (9), is unknown.

In the mid-1990s, Bone proposed that the inflammatory response can cause the production of inflammatory medium and antiinflammatory cytokines synchronously, so the outcome of inflammatory response would depend on the balance of these 2 kinds of medium (3). It is more important to pay attention to the balance of inflammatory and antiinflammatory media than simply to the level of inflammatory medium. In this regard, we found that with CPFA, not only the level of IL-1Ra increased gradually, but also the ratios of sTNFR2/TNF-α and IL-1Ra/ IL-1β increased. This result can not be explained entirely by the adsorption-based elimination during CPFA. It seems more likely that the elimination of certain inflammatory factors can affect the production of some other cytokines (including antiinflammatory factors) through a feedback or mutual restriction mechanism in the complicated cytokine network, thus reaching the new balance in plasma of inflammatory medium. So from this point of view, the effect of CPFA on the treatment of MODS was not merely limited to increasing the clearance of some inflammatory mediums, but extended to an impact on the cytokine network.

HLA-DR expressed in monocytes is the critical effector molecule with regard to the antigen-presenting process, which is one of the important functions of the mononuclear cells. Low level expression of HLA-DR reflects the suppressed condition of the immune function of monocytes, which can be closely related to severity and prognosis, as shown in the acute pancreatitis (10). In our study, the expression of HLA-DR before treatment was clearly lower than normal, which provided evidence that patients with MODS and severe infection are in a state of immune dysfunction. After CPFA, the level of HLA-DR increased significantly, which revealed that CPFA had improved the antigen-presenting function of monocytes and adjusted the immune function well.

It has been reported that the production of inflammatory cytokines is inhibited in sepsis patients, and that the recovery of the production has a positive correlation with survival rate (11). This study used the level of TNF-α se-

creted by the patients' blood, spontaneously or after LPS stimulation, to evaluate the reactivity of the patients' leukocytes. We observed that the spontaneous secretion and LPS-stimulated secretion of TNF-α both gradually increased with CPFA $p<0.05$, which indicated that CPFA could help to resume the reactivity of immune cells. In the experiment observing the influence of patient plasma on secretion of TNF-α by THP-1 cells, we found that patient plasma could inhibit this secretion and that this effect was weakened gradually after CPFA. From this result, we concluded that CPFA removed some soluble suppressant molecules existing in the patients' plasma. This purification action would improve immune responsiveness and perhaps have a beneficial effect on clinical prognosis. Meanwhile we observed that CPFA could improve hemodynamics, which was similar to the results of other researchers (12). Thus we can infer that the immune mechanism is perhaps involved in the function of abnormal blood vessels.

In conclusion, in this study we found that CPFA can adjust the balance of the inflammatory response, improve the reactivity and antigen presentation ability of leukocytes, which is substantial and supplementary to the theory that continuous blood purification is able to rebuild immune homeostasis (13). This suggests that CPFA has broader application prospects in the treatment of MODS.

ACKNOWLEDGEMENTS

Financial support
This study received a subsidy from the New Technology Imported Project (200506) of Jiangsu Province People's Hospital, China.

Conflict of interest statement
This manuscript has been seen and approved by all authors, and no author has any proprietary interest.

The poster titled "Effects of coupled plasma filtration adsorption on the immune function of patients with MODS and severe infection" has been presented at Renal Week 2008, for the American Society of Nephrology in Philadelphia, PA, USA.

Address for correspondence:
Xiao-Yun Wang
Department of Nephrology
The First Affiliated Hospital of Nanjing Medical University
Guangzhou Road 300
Nanjing, Jiangsu Province
210029 China
e-mail: huijuanmao@126.com

REFERENCES

1. Hack CE, Aarden LA, Thijs LG. Role of cytokines in sepsis. Adv Immunol 1997; 66: 101-95.
2. Wakabayashi Y, Kamijou Y, Soma K, Ohwada T. Removal of circulating cytokines by continuous haemofiltration in patients with systemic inflammatory response syndrome or multiple organ dysfunction syndrome. Br J Surg 1996; 83: 393-4.
3. Bone RC. Immunologic dissonance: a continuing evolution in our understanding of the systemic inflammatory response syndrome (SIRS) and the multiple organ dysfunction syndrome (MODS). Ann Intern Med 1996; 125: 680-7.
4. Tetta C, Cavaillon JM, Camussi G, et al. Continuous plasma filtration coupled with sorbents. Kidney Int Suppl 1998; 66: S186-9.
5. Bone RC, Sibbald WJ, Sprung CL. The ACCP-SCCM consensus conference on sepsis and organ failure. Chest 1992; 101: 1481-3.
6. Wong DT, William A. Predicting outcome in critical care: the current status of the APACHE prognostic scoring system. Can J Anaesth 1991; 38: 374-83.
7. De Vriese AS, Colardyn FA, Philippé JJ, et al. Cytokine removal during continuous hemofiltration in septic patients. J Am Soc Nephrol 1999; 10: 846-53.

8. Cole L, Bellomo R, Journois D, et al. High-volume haemofiltration in human septic shock. Intensive Care Med 2001; 27: 978-86.
9. Tetta C, Cavaillon JM, Schulze M, et al. Removal of cytokines and activated complement components in an experimental model of continuous plasma filtration coupled with sorbent adsorption. Nephrol Dial Transplant 1998; 13: 1458-64.
10. Yu WK, Li WQ, Li N, et al. Mononuclear histocompatibility leukocyte antigen-DR expression in the early phase of acute pancreatitis. Pancreatology 2004; 4: 233-43.
11. Weighardt H, Heidecke CD, Emmanuilidis K, et al. Sepsis after major visceral surgery is associated with sustained and interferon-gamma resistant defects of monocyte cytokine production. Surgery 2000; 127: 309-15.
12. Ronco C, Brendolan A, Lonnemann G, et al. A pilot study of coupled plasma filtration with adsorption in septic shock. Crit Care Med 2002; 30: 1250-5.
13. Li LS, Liu ZH. Continuous blood purification: is one kind of technology assisting the reconstruction of the immunity steady condition? Chin J Nephrol Dial Transplant 2003; 12: 1-2.