RESEARCH ARTICLE

Continuous blood purification ameliorates clinical signs and corrects the plasma phospholipid levels of patients with multiple organ dysfunction syndromes

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Background: Multiple organ dysfunction syndromes (MODS) is reported as a leading cause of mortality in intensive care units. Recently, continuous blood purification (CBP) has been mostly applied for MODS treatment. Thus, the purpose of this study was to investigate the effects of CBP on plasma phospholipid level in patients with MODS.

Methods: A total of 126 patients with MODS and 120 healthy people were collected. The serum cytokine levels, blood biochemical parameters, and blood gas indexes were detected, and the correlation among phospholipid compounds with serum cytokine levels, blood biochemical parameters, and blood gas indexes was analyzed.

Results: Before CBP, levels of body temperature, RR, HR, CVP, IL-6, IL-10, TNF- α , BUN, SCr, PaCO₂, SM747, and LPC540 were obviously higher, and pH, HCO₃⁻, PaO₂, SaO₂, PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 were lower in the MODS group than those in the control group. During CBP, the MODS group had gradually declined RR, CVP, levels of IL-6, IL-10 and TNF- α , BUN, SCr, PaCO₂, SM747, and LPC540 and increased HCO₃⁻, PaO₂ and SaO₂, PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747. Besides, levels of PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 had an obvious negative correlation with levels of TNF- α , IL-10, IL-6, BUN, SCr, and PaCO₂, and a significant positive correlation with levels of HCO₃⁻, PaO₂, and SaO₂.

Conclusion: CBP could effectively ameliorate clinical signs of patients with MODS and correct the plasma phospholipid levels.

KEYWORDS

CBP, Multiple organ dysfunction syndromes, Plasma phospholipid levels, Serum cytokines

1 | INTRODUCTION

The multiple organ dysfunction syndromes (MODS) is defined as a disease entity with a high mortality rate and featured by a sequential failure of some organ systems through a trigger event, most generally sepsis.¹ MODS and sepsis are primary reasons of mortality and morbidity in the intensive care unit (ICU).² And about 30% patients with acute kidney injury admitted to the ICU mostly correlate with

MODS.³ Moreover, it is reported that endothelial activation leading toward vascular barrier breakdown has a significant impact on the pathophysiology of MODS in sepsis.⁴ In fact, with the reference of previous study, mostly, MODS is defined as the last step in a series of events correlated with unchecked inflammatory responses and vascular homeostasis losing.⁵ And because of conflicting diagnoses and small sample size of the organ failure, the outcomes and epidemiology of MODS are incompletely featured in the pediatric group.⁶ One of the characteristics of MODS is the inadequately high heart rate with prognostic relevance.⁷ Moreover, the release of inflammatory mediators,

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including tumor necrosis factor- α (TNF)- α and interleukin (IL)-6, was involved in MODS.⁸ It is known that blood biochemical indexes and gas indexes can also be served as indicators of MODS.⁹ In spite of the early and proper antibiotic therapies still that are the foundation of effective treatment for the septic shock, accumulating research data have proved that those therapies lead to the antibiotic dose optimization in serious ill patients, especially those with MODS.¹⁰ Advancements have been received in gaining a better understanding in pathophysiology of MODS and burn sepsis, in protection and treatment of burn shock and also in the revising definition of sepsis and MODS.¹¹ Previously, MODS is a high-risk disease with a fatality rate of 70%, and to advance its treatment, currently, many scholars have investigated the physiological and pathological differences in MODS.¹² Continuous blood purification (CBP) has been mostly applied for the treatment of patients with MODS including the acute respiratory distress syndrome.¹³

In the previous study, it was found that CBP could remove humoral mediators which included cytokines from the blood and it was used to treat multiple organ failure (MOF).¹⁴ CBP has been generally performed for the renal replacement treatment in patients with serious syndrome, as CBP could nonselectively eliminate stabilize hemodynamics and inflammatory mediators, it has also been well-known in the past years in treatment of sepsis, congestive heart failure, multi-organ dysfunction, and other diseases.¹⁵ CBP was gradually taking the place of intermittent hemodialysis as a renal replacement therapy for patients who were in severe conditions.¹⁴ As CBP has exerted great impacts on advancing organs function and removing inflammatory mediators, CBP had been used for nonrenal diseases in the past 10 years, but few data have been guided in children with MODS and sepsis, particularly in China.¹⁶ Besides, phospholipids are major structural components of cellular membranes, participated in a various processes including cellular proliferation and death programs.¹⁷ Phospholipids showed asymmetrical distribution between outer and inner leaflets in plasma membrane.¹⁸ Fatty acids are preferentially incorporated in the sn-2 (middle) position of phospholipids, which are related to the risk of heart failure.¹⁹ However, few studies have clarified the correlation among CBP, plasma phospholipid levels, and MODS. Therefore, the aim of this study was to demonstrate the effects of CBP on plasma phospholipid levels in patients with MODS.

2 | MATERIALS AND METHODS

2.1 | Ethical statement

The study conducted by us was approved by Ethics Committee of Shandong Provincial Qianfoshan Hospital, and all patients or their guardians were informed and signed informed consent.

2.2 | Study subjects

A total of 126 patients with MODS (58 males and 68 females) treated in Shandong Provincial Qianfoshan Hospital from January 2013 to January 2016 with mean age of 50.10 ± 11.10 years (age ranges from 30 to 74 years) were enrolled in our study. All cases were in line with

the revised MODS standard proposed by American College of Chest Physicians/Critical Care Medicine Society: (1) systemic inflammatory response syndrome met the following criteria for both points and above: (i) body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; (ii) heart rate (HR) >90 times per min; (iii) breathing >20 times per min or partial pressure of carbon dioxide <32 mm Hg; (iv) leukocyte count $<4000/\text{mm}^3$ or $>12\,000/\text{mm}^3$ or immature leukocyte $>10\%$. (2) organ dysfunction met the following criteria for both points and above: (i) renal function defect (oliguria, the amount of serum creatinine increased within 24 hours $>80\text{ }\mu\text{mol/L}$); (ii) metabolic disorder (lactic acid content $>2\text{ }\mu\text{mol/L}$ or buffer excess $>5\text{ mEq/L}$); (iii) neurologic impairment (Glasgow coma scale²⁰ <15); (iv) hematopoietic dysfunction (platelet $<75\,000/\text{mm}^3$ or decreased degree within 24 hours $>50\%$); (v) diffuse dysfunction of blood coagulation (effects of nonadverse drug >1.5 [the international standardization ratio], or the titer of fibrin degradation product $>10\text{ }\mu\text{g/mL}$, or D-two dimer $>0.5\text{ }\mu\text{g/mL}$); (vi) abnormal liver function (serum bilirubin $>20\text{ }\mu\text{mol/L}$); (3) there were serious trauma, infection, delayed resuscitation, shock, massive tissue necrosis, and other factors. All the patients were treated by the CBP, mechanical ventilation, infusion support, and the use of vasoactive agents. Besides, according to the conditions of the disease, multiple CBP was required. Exclusion criteria were as follows: (1) patients with MODS complicated with immunity, diseases of endocrine system or acquired immune deficiency syndrome (AIDS) and other basic diseases; (2) CBP was terminated due to a variety of causes or accidents, including the waiver of treatment; (3) insufficient blood collection; (4) died during CBP. Meanwhile, 120 healthy persons (66 males and 54 females) receiving healthy physical examination in Shandong Provincial Qianfoshan Hospital during the same period were selected and view as the control group with a mean age of 52.60 ± 8.70 years (age ranges from 33 to 77 years). There was no statistical significance in comparisons of the age and gender between the MODS and control groups ($P > .05$).

2.3 | CBP

Double lumen catheter with a length of 24 cm and a size of 14 F was used for jugular vein catheterization to establish the vascular access and to conduct continuous veno-venous hemofiltration (CVVH) treatment. German Fresenius AV600S polysulfone membrane filter was used with blood flow at 250-300 mL/min and displacement fluid rate at 4000 mL/h. In addition, replacement fluid was supplied via replacing the front. Before filter, small molecule heparin was performed for systemic anticoagulation with 2000-4000 units of first dose, maintenance dose at 200-400 U/h, and clotting time for 150-200 seconds. When the patients had coagulopathy and active bleeding, they were treated by heparin-free CVVH and rinsed by saline every half an hour. Moreover, all patients treated with the CVVH mode had the same displacement fluid rate and frequency replacement of filter. The duration of each CBP was 20 h. The conditions were observed and the common complications such as hemodynamic instability and bleeding were timely treated. If necessary, the patients will be adopted compound vasoconstriction drugs and infusion support timely.

2.4 | Sample collection, treatment, and monitoring

The levels of body temperature, respiratory rate (RR), HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and central venous pressure (CVP) in the MODS and control groups during the CBP were monitored. Two venous blood samples in patients from the MODS group were collected before CBP (0 h), at 6 h, 12 h, and 24 h, at the same time, two blood samples were also collected from the control group. One of the two samples was centrifuged at 2000 g/min for 10 minutes (room temperature) with the serum collected for testing serum cytokine levels including IL-6, IL-10, and TNF- α , blood biochemical indexes including blood urea nitrogen (BUN) and serum creatinine (Scr). The other sample was added with heparin anticoagulation and centrifuged at 8000 g/min for 5 minutes with plasma collected for detecting phospholipid levels and the blood gas indexes immediately including pH, HCO₃⁻, partial pressure of oxygen in artery (PaO₂), partial pressure of carbon dioxide in artery (PaCO₂), and arterial oxygen saturation (SaO₂).

2.5 | Detection of serum cytokine levels, blood biochemical indexes, and blood gas indexes

The levels of IL-6, IL-10, and TNF- α were examined by enzyme-linked immunosorbent assay (ELISA), and the reagent kit was purchased by Beijing ZSGB Biological Technology Co Ltd. (Beijing, China). Additionally, the operations were simply described as follows: samples of IL-6, IL-10, and TNF- α were captured from IL-6, IL-10, and TNF- α monoclonal antibodies in the enzyme-labeled plate. After rinsing, the samples were added with biotin-labeled anti-human IL-6, IL-10, and TNF- α , the secondary antibody, to form sandwich immune complex. After that, the samples were added with horseradish peroxidase-labeled biotin with avidin specific binding secondary antibody. Besides, the samples were colored by substrate of horseradish peroxidase. The optical density (OD value at 450 nm was tested.

The concentrations of IL-6, IL-10, and TNF- α in the samples were counted via standard curve. Blood biochemical indexes were detected by OLYMPUS AU2700 automatic blood biochemical analyzer and blood gas analysis by GEM Premier3000 blood gas analyzer.

2.6 | Plasma phospholipid detection

The high-performance liquid chromatography/mass spectrometry was applied to detect plasma phospholipid. Time-of-flight mass spectrometer Agilent 1100 LC-TOF/MS was purchased from Agilent Technologies (Palo Alto, CA, USA), and chromatographic column Nucleosil, 100-5 OH, 250 mm $\times$ 3.0 mm was purchased from Macherey-Nagel (Germany). Chromatographic conditions were as follows: mobile phase: A phase, n-hexane; B phase, isopropanol/water/formic acid/ammonia (volume ratio was 86: 13: 0.9: 0.1), current speed was 0.2 mL/min with 35°C column temperature, isocratic elution for 0 ~ 60 minutes, 30% A and 70% B. Injection volume was 20 μ L with ESI⁻ of mass spectrometry, 341.3 kPa of atomizing gas pressure, 9.0 L/min drying gas flow rate, 350°C temperature of drying gas, and 400 ~ 1000 m/z of range

in scanning-mass spectrometry. Phospholipid standard was purchased from Avanti Polar Lipids, Inc., (Alabaster, AL, USA), including phosphatidylethanolamine (PE) (C18: 0/C20: 4), phosphatidylinositol (PI) (C18: 0/C20: 4), phosphatidylcholine (PC) (C18: 0/18: 0), phosphatidylserine (PS) (C18: 0/C18: 1), phosphatidylglycerol (PG) (C16: 0/C18: 1), sphingomyelin (SM) (dC18: 1/C18: 0), and lysophosphatidylcholine (LPC) (16: 0).

2.7 | Statistical analysis

The SPSS 21.0 statistical software was utilized for statistical analysis. The measurement data were represented as mean $\pm$ standard deviation and tested by normality test. The *t* test was used for measurement data and the chi-squared was used for enumeration data comparison. The Pearson was applied for correlation analysis. A value of *P* < .05 was considered to be statistically different.

3 | RESULTS

3.1 | Better general conditions of the patients with MODS during the CBP

As the levels of body temperature, RR, HR, and CVP could be regarded as the indicators of MODS, the differences in these levels between normal and MODS groups were detected. The levels of body temperature, RR, HR, and CVP in the MODS group before CBP were obviously higher than those in the control group (all *P* < .05), and the levels of RR, HR, and CVP in the MODS group during CBP also apparently higher than those in the control group (all *P* < .05). The levels of SBP, DBP, and MAP in the MODS group during CBP had no significantly difference (all *P* > .05), levels of body temperature and HR reduced with 6 h from beginning (both *P* < .05), and then kept steady until the end of treatment. Besides, levels of RR and CVP decreased gradually with the duration of CBP (both *P* < .05) (Table 1). Therefore, the results indicated that CBP ameliorated the general conditions of MODS.

3.2 | Lower levels of IL-6, IL-10, and TNF- α in the MODS group during the CBP

ELISA was used to measure the levels of IL-6, IL-10, and TNF- α in the control and MODS groups before and during the CBP. Levels of IL-6, IL-10, and TNF- α in the MODS group were significantly higher than those of the control group before and during the CBP (all *P* < .05). Moreover, in the progression of CBP, patients in the MODS group had gradual declined levels of IL-6, IL-10, and TNF- α with the duration of CBP (all *P* < .05) (Table 2). Thus, the findings implied that CBP decreased the inflammatory responses in patients with MODS.

3.3 | Decreased levels of BUN, Scr, and PaCO₂ and increased levels of HCO₃⁻, PaO₂, and SaO₂ in the MODS group during the CBP

Blood biochemical indexes and blood gas indexes were measured to judge the effects of CBP in patients with MODS. Before the

TABLE 1 The difference in body temperature, RR, HR, CVR of the patients with MODS during the CBP treatment

Items	Control	MODS			
		Before treatment	Treatment for 6 h	Treatment for 12 h	Treatment for 20 h
Body temperature	36.60 ± 0.40	38.60 ± 0.30	37.30 ± 0.40	37.20 ± 0.40	37.10 ± 0.30
RR (min ⁻¹)	16.00 ± 1.00	42.70 ± 5.80*	34.20 ± 4.20***	28.00 ± 2.90****	22.20 ± 1.20****
HR (min ⁻¹)	76.00 ± 4.00	133.50 ± 13.90*	121.70 ± 14.50***	118.60 ± 12.30***	117.89 ± 24.00***
SBP (mm Hg)	125.00 ± 5.20	122.80 ± 11.30	124.00 ± 11.00	125.00 ± 11.70	125.60 ± 11.00
DBP (mm Hg)	68.00 ± 7.30	70.00 ± 9.80	70.00 ± 4.70	69.00 ± 7.70	68.00 ± 8.20
MAP (mm Hg)	81.30 ± 7.20	83.80 ± 13.70	83.33 ± 13.80	82.30 ± 11.60	81.30 ± 12.90
CVP (cm H ₂ O)	6.20 ± 0.60	26.00 ± 2.00*	21.00 ± 1.00***	16.00 ± 0.80****	11.10 ± 0.70****

CBP: continuous blood purification; RR, respiratory rate; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; CVP, central venous pressure; MODS, multiple organ dysfunction syndromes.

**P* < .05, compared with the control group.

***P* < .05, compared with before treatment.

****P* < .05, compared with treatment for 6 h.

*****P* < .05, compared with treatment for 12 h.

TABLE 2 The levels of IL-6, IL-10, and TNF-α in patient with MODS during the CBP treatment

Items	Control	MODS			
		Before treatment	Treatment for 6 h	Treatment for 12 h	Treatment for 20 h
TNF-α (ng/L)	82.26 ± 6.07	49.37 ± 5.78*	21.26 ± 2.37***	34.21 ± 2.82****	61.62 ± 3.45****
IL-10 (ug/L)	75.00 ± 11.3	247.45 ± 15.19*	208.77 ± 14.53***	172.42 ± 8.24****	134.19 ± 14.82****
IL-6 (pg/mL)	63.39 ± 6.66	282.63 ± 14.75*	209.66 ± 15.51***	167.29 ± 4.96****	117.50 ± 5.04****

IL, interleukin; TNF-α, tumor necrosis factor α; MODS, multiple organ dysfunction syndromes; CBP: continuous blood purification.

**P* < .05, compared with the control group.

***P* < .05, compared with before treatment.

****P* < .05, compared with treatment for 6 h.

*****P* < .05, compared with treatment for 12 h.

CBP, BUN, SCr, and PaCO₂ in the MODS group were significantly higher than those of the control group (all *P* < .05), and pH, HCO₃⁻, PaO₂, and SaO₂ were apparently lower than those of the control group (all *P* < .05). All the blood biochemical indexes and blood gas indexes in the MODS group were improved compared with before treatment in the progression of the CBP. However, with the duration of the CBP, levels of BUN, SCr, and PaCO₂ gradually reduced, and levels of HCO₃⁻, PaO₂, and SaO₂ gradually increased. The level of pH increased within 6 h of the CBP and then kept steady until the end of treatment (Table 3). Therefore, the results of our study showed that CBP alleviated clinical signs in patients with MODS.

3.4 | Elevated levels of PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747, and reduced levels of SM747 and LPC540 during the CBP

The high-performance liquid chromatography/mass spectrometry was applied to detect plasma phospholipid. The levels of SM747 and LPC540 in the MODS group were obviously higher than those of the control group before the CBP (all *P* < .05), but other phospholipid compounds including PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 apparently lower than those of the control group

(all *P* < .05). And PS810 level in the MODS group had no obvious difference with the duration of the CBP (*p* > .05). Moreover, in the MODS group, levels of PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 gradually increased, but levels of SM747 and LPC540 gradually decreased with the duration of the CBP (Table 4). Thus, the result demonstrated that CBP played positive roles in the patients with MODS.

3.5 | Correlation among phospholipid compounds with serum cytokine levels, blood biochemical parameters, and blood gas indexes

Correlation of phospholipid compounds with serum cytokine levels, blood biochemical parameters, and blood gas indexes was analyzed. The result showed that levels of PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 had an obvious negative correlation with levels of TNF-α, IL-10, IL-6, BUN, SCr, and PaCO₂ (all *P* < .05), a significant positive correlation with levels of HCO₃⁻, PaO₂, and SaO₂ (all *P* < .05). Furthermore, levels of SM747 and LPC540 had an apparent positive correlation with levels of TNF-α, IL-10, IL-6, BUN, SCr, and PaCO₂ (all *P* < .05), an obvious negative correlation with levels of HCO₃⁻, PaO₂, and SaO₂ (all *P* < .05). Meanwhile, except that SM747 and LPC54 were

TABLE 3 The difference of blood biochemical indexes and blood gas indexes in patient with MODS during the CBP treatment

Items	Control	MODS			
		Before treatment	Treatment for 6 h	Treatment for 12 h	Treatment for 20 h
BUN (mmol/L)	5.30 ± 1.10	44.61 ± 7.91*	34.14 ± 5.16**	23.18 ± 2.94****	11.705 ± 1.69****
SCr (μmol/L)	53.00 ± 7.30	555.80 ± 12.06*	395.25 ± 85.65**	269.30 ± 41.45****	214.65 ± 15.04****
pH	7.40 ± 0.11	7.11 ± 0.01*	7.26 ± 0.14	7.31 ± 0.14	7.39 ± 0.80
HCO ₃ ⁻ (mmol/L)	31.90 ± 1.20	4.05 ± 0.95*	13.00 ± 0.78**	22.15 ± 1.04****	31.85 ± 1.64****
PaO ₂ (mm Hg)	89.60 ± 8.5	44.40 ± 5.68*	56.85 ± 6.07**	68.02 ± 5.47****	79.89 ± 1.87****
PaCO ₂ (mm Hg)	35.60 ± 1.50	75.95 ± 7.15*	65.85 ± 5.25**	55.14 ± 3.17****	44.50 ± 3.85****
SaO ₂ (%)	99.70 ± 1.90	47.81 ± 8.16*	58.15 ± 6.70**	69.01 ± 1.14****	79.81 ± 1.49****

MODS, multiple organ dysfunction syndromes; CBP: continuous blood purification; BUN, blood urea nitrogen; Scr, serum creatinine; PaO₂, partial pressure of oxygen in artery; PaCO₂, partial pressure of carbon dioxide in artery; SaO₂, arterial oxygen saturation.

*P < .05, compared with the control group.

**P < .05, compared with before treatment.

***P < .05, compared with treatment for 6 h.

****P < .05, compared with treatment for 12 h.

TABLE 4 The difference in phospholipid compounds in patient with MODS during the CBP treatment

phospholipid compounds (m/z)	Control	MODS			
		Before treatment	Treatment for 6 h	Treatment for 12 h	Treatment for 20 h
PE750 (μg/mL)	79.10 ± 11.17	24.99 ± 2.75*	38.21 ± 2.886**	50.88 ± 1.24****	63.56 ± 3.74****
PI885 (μg/mL)	60.96 ± 5.21	9.04 ± 5.23*	21.96 ± 2.67**	35.34 ± 2.41****	48.09 ± 3.9****
PC792 (μg/mL)	402.40 ± 27.40	291.00 ± 23.00*	313.90 ± 17.60**	335.90 ± 28.90****	415.80 ± 30.50****
PC826 (μg/mL)	191.80 ± 18.20	146.80 ± 9.80*	159.80 ± 7.20**	173.30 ± 19.70****	229.90 ± 20.50****
PC830 (μg/mL)	286.90 ± 21.50	225.60 ± 12.30*	240.10 ± 12.30**	256.40 ± 11.30****	269.60 ± 10.50****
PC854 (μg/mL)	148.70 ± 10.00	110.90 ± 8.30*	117.10 ± 5.60**	125.10 ± 5.10****	131.10 ± 5.40****
PC802 (μg/mL)	634.70 ± 32.50	525.10 ± 26.60*	541.10 ± 25.20**	567.20 ± 25.40****	592.10 ± 25.60****
PG747 (μg/mL)	299.70 ± 11.80	0.9 0 ± 0.10*	1.00 ± 0.10**	1.10 ± 0.10****	1.20 ± 0.10****
PS810 (μg/mL)	0.73 ± 0.12	2.4 0 ± 0.20	2.50 ± 0.20	2.40 ± 0.10	2.50 ± 0.10
SM747 (μg/mL)	41.24 ± 10.30	260.90 ± 18.30*	247.10 ± 15.60**	233.10 ± 15.10****	220.10 ± 15.40****
LPC540 (μg/mL)	31.03 ± 4.68	42.10 ± 2.60*	38.10 ± 2.20**	35.20 ± 2.40****	32.10 ± 2.00****

MODS, multiple organ dysfunction syndromes; CBP: continuous blood purification.

*P < .05, compared with the control group.

**P < .05, compared with before treatment.

***P < .05, compared with treatment for 6 h.

****P < .05, compared with treatment for 12 h.

related to the pH, the other phospholipid compounds had no correlation with the pH (all $P > .05$) (Table 5). Thus, the findings showed that phospholipid compounds were associated with serum cytokine levels, blood biochemical parameters, and blood gas indexes.

4 | DISCUSSION

MODS is defined as the primary reason of death in the surgical and the trauma patients, and it is now accepted as a series of physiologic derangements, instead of all-or-nothing phenomena.²¹ And it remains popular and the major cause of mortality in the surgical ICU.²² The therapy to treat this severe disease was through sepsis

effectively by adsorbing endotoxin or inflammatory cytokines.²³ Recently, it was reported that CBP could ameliorate prognosis of patients with MODS, but the accurate effects are still unclear.²⁴ Therefore, this study was to investigate that the effects of CBP on plasma phospholipid levels in patients with MODS.

First of all, the levels of body temperature, RR, HR, CVP in the MODS group before CBP were obviously higher than those in the control group. MODS can be featured by over one organ system failing, particularly during the critical illness; also, MOD, particular in the kidneys and livers, might obviously influence pharmacokinetics of various drugs which are presently administered in seriously ill patients.²⁵ HR is one of the relative prognostic indexes both in the common population and the patients with the cardiovascular

TABLE 5 Correlation of phospholipid compounds with serum cytokine levels, blood biochemical parameters, and blood gas indexes

Items r phospholipid compounds (m/z)	TNF- α	IL-6	IL-10	BUN	SCr	pH	HCO ₃	PaO ₂	PaCO ₂	SaO ₂
PE750	-0.884*	-0.881*	-0.886*	-0.894*	-0.876*	-0.053	0.884*	0.881*	-0.890*	0.889*
PI885	-0.875*	-0.851*	-0.853*	-0.853*	-0.868*	-0.083	0.867*	0.872*	-0.872*	0.870*
PC792	-0.818*	-0.814*	-0.810*	-0.820*	-0.828*	-0.031	0.812*	0.829*	-0.830*	0.831*
PC826	-0.762*	-0.754*	-0.743*	-0.759*	-0.766*	0.042	0.742*	0.754*	-0.765*	0.777*
PC830	-0.820*	-0.841*	-0.850*	-0.847*	-0.826*	0.089	0.846*	0.844*	-0.837*	0.834*
PC854	-0.722*	-0.754*	-0.770*	-0.748*	-0.714*	0.049	0.758*	0.733*	-0.747*	0.748*
PC802	-0.768*	-0.782*	-0.774*	-0.786*	-0.765*	0.053	0.752*	0.764*	-0.771*	0.793*
PG747	-0.433*	-0.421*	-0.432*	-0.426*	-0.458*	0.098	0.422*	0.444*	-0.463*	0.434*
PS810	-0.062	-0.041	-0.051	-0.045	-0.057	-0.081	0.050	0.051	-0.062	0.061
SM747	0.541*	0.536*	0.549*	0.545*	0.531*	0.147*	-0.537*	-0.537*	0.558*	-0.566*
LPC540	0.663*	0.682*	0.692*	0.692*	0.672*	-0.057*	-0.681*	-0.683*	0.700*	-0.699*

IL, interleukin; TNF- α , tumor necrosis factor α ; BUN, blood urea nitrogen; SCr, serum creatinine; PaO₂, partial pressure of oxygen in artery; PaCO₂, partial pressure of carbon dioxide in artery; SaO₂, arterial oxygen saturation.

* $P < .05$.

disease, but in crucially ill MODS.²⁶ Previous study suggested that both HR variability and RR variability increased during the sedation interruption, and patients with low and medium MODS had a greater rise in HR variability during the sedation interruption.²⁷ Despite a large number of physiological states could affect isolated values, a relative higher CVP has been correlated with worse results in many situations, including the septic shock, mostly due to not only the fluid overload but the related important influence in the heart dysfunction on the values.²⁸ Besides, levels of IL-6, IL-10, and TNF- α in the MODS group were significantly higher than those of the control group before and during the CBP. It was reported that a pronounced upregulation in levels of IL-6, TNF- α , and inducible nitric oxide synthase showed in the MODS group,²⁸ which was in line with our study. Additionally, TNF- α , IL-6 and IL-10 and myeloperoxidase activities were obviously increased, and important histopathological differences in the organs were found through lipopolysaccharide challenge.²⁹ Furthermore, absence of endogenous IL-10 promoted organ dysfunction and mortality related to zymosan-induced MODS.³⁰

Secondly, before the CBP, BUN, SCr, and PaCO₂ in the MODS group were significantly higher than those of the control group, and pH, HCO₃, PaO₂, and SaO₂ were apparently lower than those of the control group. Mean levels of BUN, SCr in the intermittent hemodialysis group were obviously higher than those in the continuous renal replacement therapy group,³¹ which consists with the result of this study. The respiratory dysfunction increased in the arterial PaCO₂ and reduced in the arterial PaO₂.³² Furthermore, the levels of pH, PaO₂, and HCO₃ were higher and PaCO₂ was lower apparently than those before the continuous renal replacement therapy in 30 patients with acute respiratory distress syndrome in patients with MODS.³³

Last, we also found that levels of SM747 and LPC540 in the MODS group were obviously higher than those of the control group before the CBP, but other phospholipid compounds including PE750, PI885, PC792, PC826, PC830, PC854, PC802, and PG747 apparently lower than those of the control group. Phospholipid metabolism is a leading sphingolipid in the membranes of mammalian cells, and lipid class is exactly abundant the endocytic recycling compartment, in plasma membrane, and the trans Golgi network.³⁴ And further detection of plasma phospholipid levels could be a risk factor for the coronary artery disease.³⁵ LPC is defined as a bioactive proinflammatory lipid produced via the pathological activities.³⁶ PI is a vital element in all kinds of plants and animals, no toxicity report was showed while purified PI is orally administrated to the animals.³⁷ An apparent (29%) reduced in the labeling of PC was tested in kidney of ether-treated hamsters.³⁸ Furthermore, mass spectrometry measurement of >300 phospholipids in the lung tissues from Abca3 mice indicated a surprised reduction of PG levels as well as selective reductions in PC species including short acyl chains.³⁹ In addition, through analyzing, there were correlations among phospholipid compounds with serum cytokine levels, blood biochemical parameters, and blood gas indexes. It was reported that CBP was efficient in the treatment of pediatric septic shock via advancing oxygenation, adjusting the metabolic acidosis, stabilizing blood pressure, gaining tissue perfusion, and excreting medium molecule substances.⁴⁰ CBP and thymosin alpha1 could promote cellular immunity in patients with serious sepsis, improving the recovery of organ function and better prognosis.⁴¹ As reflected in our study, CBP could effectively alleviate clinical signs of patients with MODS and correct the plasma phospholipid levels.

Collectively, our study indicated that CBP could effectively alleviate clinical signs of patients with MODS and correct the plasma

phospholipid levels, suggesting that CBP could be a new underlying target for the treatment of MODS.

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