Effect of Plasma NE, ET-1levels and Lung Function on Continuous Blood Purification Treatment for Ards

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Abstract: Objective: To discuss the effect of plasma neutrophil elastase (NE), endothelin -1 (ET-1) levels and lung function on continuous blood purification (CBP) treatment for acute respiratory distress syndrome (ARDS). Methods: 73 ARDS patients were selected and randomly divided into observational group (n = 39) and control group (n = 34), patients on control group received conventional treatment, and observational group added CBP treatment. The plasma NE, ET-1 levels were detected before treatment (T0), 1d post-treatment (T1), 2d (T2), 3d (T3) respectively, and the alveolar oxygenation function, airway function were compared between the two group. Results: Compared with the control group, the plasma NE levels at T2, T3 and plasma ET-1 levels at T1, T2, T3of observational group and were significantly reduce (P <0.05). Compared with T0, the PaO2 at T3 of both groups were significantly rise, and PaCO2, PaO2 / FiO2 were significantly reduce (P <0.05), and PaO2, PaCO2, PaO2 / FiO2 of observational group were significantly lower than that of control group (P <0.05); Compared with T0, the FEV1, FEV1 / FVC of both groups were significantly reduce (P <0.05), and observational group were significantly lhigher than that of control group (P <0.05). Conclusion: CBP can improve alveolar oxygenation function, airway function, and its mechanism involving the elimination of plasma fraction NE ARDS patients, ET-1, anti-inflammatory. This electronic document is a “live” template. The various components of your paper [title, text, heads, etc.] are already defined on the style sheet, as illustrated by the portions given in this document.

Keywords: Acute respiratory distress syndrome; Continuous blood purification; Neutrophil elastase; Endothelin-1

1. Introduction

Acute respiratory distress syndrome (ARDS) is one of the common clinical critical emergencies. It is mainly caused by severe trauma, infection, shock, sepsis, major surgery and other inflammatory mediators released by the body, resulting in increased endothelial permeability of pulmonary capillaries, increased extrapulmonary pulmonary water accumulation, serious imbalance of ventilation/blood flow ratio, and systemic. oxygen metabolism disorder [1]. Continuous blood purification (CBP) has been widely used in the treatment of ARDS because it can remove some inflammatory mediators [2]. In theory, CBP can reduce systemic inflammatory response, reduce the permeability of pulmonary capillary endothelial cells, reduce pulmonary edema, and thus improve pulmonary function. Therefore, this study was to observe the changes of plasma NE and ET-1 levels in ARDS patients before and after CBP treatment, and to observe the improvement of alveolar oxygenation and airway function before and after CBP treatment, so as to explore the improvement of lung function in ARDS patients after CBP treatment.

2. Materials and Methods

2.1. General information

Seventy-three patients with ARDS admitted to our hospital from January 2017 to June 2018 were selected [3], all of them met the diagnostic criteria defined in Berlin in 2012, excluding those with hypertension, diabetes and cardiac dysfunction, and those who died within 72 hours after treatment. The subjects were divided into observation group and control group according to random number table method, including 39 patients in observation group, 25 males and 14 females, aged 29-59 years, with an average age of (39.84 ± 7.37) years, APACHE II score of 16-20 points, with an average score of (17.66 ± 1.03); primary diseases: 13 cases of multiple injuries, 9 cases of pulmonary infection, 8 cases of sepsis, 5 cases of severe pancreatitis, 3 cases of abdominal infection, and central nervous system. Nervous system infection occurred in 1 case. There were 34 patients in the control group, 23 males and 11 females, aged 28-57 years, with an average age of (38.59 ± 7.40); APACHE II score of 15-20 points, with an average score of (17.36 ±1.25); primary diseases: multiple injuries in 10 cases, pulmonary infection in 9 cases, sepsis in 7 cases, severe pancreatitis in 5 cases, abdominal infection in 2 cases, and Central nervous system infection in 1 case.

There was no significant difference between the two groups in terms of gender, age, APACHE II grade distribution of primary diseases and other general data ($P > 0.05$), which was comparable.

2.2. Method

All patients were given routine treatment by establishing artificial airway after entering ICU and using ventilator to control/assist breathing. The patients in the observation group were treated with CBP on the basis of the above treatment. The left femoral vein catheter was used to establish vascular access. Bedside continuous venous hemofiltration (CVVH) was performed with the bedside hemofiltration system (BM25, Bater Company, USA). PlasmfluxP2S produced by Fesenius Company, Germany was used. The plasma separator and AV600s blood filter were equipped with 150 ml/min blood volume, 1.52-2 h replacement time and 1500-2000 ml/d fresh frozen plasma volume. The pre-dilution method was used to input the replacement solution of bicarbonate. The replacement amount was (45.0 ± 11.5) L, the dehydration amount was (1500 ± 1100) ml/time, and the dehydration rate was (3.5 ± 2.5) ml/(kg·h). The blood routes were anticoagulated with heparin, those with bleeding tendency were anticoagulated with low molecular weight heparin, those with severe bleeding tendency or active bleeding were treated with heparin-free method, and the blood routes and filters were washed intermittently with sodium chloride solution.

2.3. Observation indicators

Venous blood 5 ml was collected before treatment (T_0), 1 day (T_1), 2 days (T_2) and 3 days (T_3) and placed in an EDTA-K2 anticoagulant tube. The plasma was centrifuged within 30 minutes (3000r/min) for 15 minutes. The plasma was stored at -40℃. The plasma neutrophil elastase (NE) and endothelin-1 (ET-1) levels were detected by double antibody sandwich ABC-ELISA. Arterial blood was collected at T0 and T3 respectively. The partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) were measured, and the oxygenation index (PaO_2/FiO_2) was calculated. The forced expiratory volume (FEV_1), the percentage of forced expiratory volume occupied by forced vital capacity (FEV_1/FVC) and the maximum expiratory flow (MMEF) were measured in both groups.

2.4. Statistical data processing

All the data were analyzed by SPSS17.0 statistical software. The measurement data were expressed in the form of $\bar{x} \pm s$. The measurement data between groups were compared by t test and the counting data were tested by x^2. The difference was statistically significant with $P < 0.05$.

3. Results

3.1. Comparison of plasma NE and ET-1 levels between two groups before and after treatment

At T0, there was no significant difference in plasma NE and ET-1 levels between the two groups ($P > 0.05$), and the levels of plasma NE and ET-1 decreased significantly after treatment ($P < 0.05$); compared with the control group, the plasma NE levels in the observation group at T_2 and T_3 decreased significantly, while the plasma ET-1 levels at T_1, T_2 and T_3 decreased significantly ($P < 0.05$), which showed that CBP treatment could significantly reduce the plasma NE and ET-1 levels. See Table 1.

Table 1. Comparison of plasma NE and ET-1 levels between two groups before and after treatment ($\bar{x} \pm s$)

Group	Number of cases		T_0	T_1	T_2	T_3
Observation group	39	NE (ng/mL)	74.28±27.621	55.73±34.621	50.29±27.7012	46.33±25.4512
		ET-1(ng/L)	128.53±20.841	98.69±18.6812	79.63±15.5012	61.85±13.2012
Control group	34	NE (ng/mL)	73.76±27.091	67.48±32.571	63.84±29.551	58.57±26.671
		ET-1(ng/L)	127.49±21.461	116.22±20.691	108.85±16.931	85.63±12.551

Note: Compared with T0, $^1P < 0.05$; compared with control group, $^2P < 0.05$.

3.2. Comparison of alveolar oxygenation function between two groups before and after treatment

At T_0, there was no significant difference in PaO_2, $PaCO_2$ and PaO_2/FiO_2 between the two groups ($P > 0.05$). At T_3, PaO_2 and PaO_2/FiO_2 in the two groups were significantly higher than that in T_0, while $PaCO_2$ and PaO2/FiO_2 in the observation group were significantly higher than those in the control group, while $PaCO_2$ and PaO2/FiO_2 in the observation group were significantly lower than those in the control group ($P < 0.05$), suggesting that CBP treatment may be available. Effectively improve alveolar oxygenation function in patients with ARDS. See Table 2.

Table 2. Comparison of PaO_2, $PaCO_2$ and PaO_2/FiO_2 before and after treatment in two groups ($\bar{x} \pm s$)

Group	Number of Cases	PaO_2(mmHg)		$PaCO_2$(mmHg)		PaO_2/FiO_2	
		T_0	T_3	T_0	T_3	T_0	T_3
Observation	39	62.63±3.52	90.60±3.111	54.69±3.51	36.28±2.861	274.64±20.67	369.87±23.411

group							
Control group	44	63.44±3.48	81.57±3.321	55.22±3.47	46.55±3.341	283.00±19.92	322.58±22.251
		0.986	11.937	0.647	14.154	1.753	8.810
		0.094	0.001	0.180	0.001	0.063	0.001

Note: Compared with T_0, $^1P < 0.05$.

3.3. Comparison of airway function between two groups before and after treatment

At T_0, there was no significant difference in FEV_1, FEV_1/FVC and MMEF between the two groups ($P > 0.05$). At T_3, FEV_1, FEV_1/FVC and MMEF in the two groups were significantly lower than those in the T_0 group ($P < 0.05$), but FEV_1, FEV_1/FVC and MMEF in the observation group were significantly higher than those in the control group ($P < 0.05$), suggesting that CBP treatment can effectively improve the airway function of ARDS patients. See Table 3.

Table 3. Comparison of FEV1, FEV1/FVC and MMEF before and after treatment in two groups ($\bar{x} \pm s$)

Group	Number of cases	Fev_1 (L)		Fev_1/Fvc (%)		Mmef (ml/s)	
		T_0	T_3	T_0	T_3	T_0	T_3
Observation group	39	3.14±0.28	2.96±0.241	87.40±6.03	80.27±5.291	3.18±0.25	2.76±0.241
Control group	44	3.07±0.25	2.31±0.201	87.13±5.46	71.38±4.561	3.17±0.28	2.53±0.211
t value		1.120	12.462	0.199	7.633	0.161	4.327
p value		0.089	0.001	0.629	0.001	0.746	0.001

Note: Compared with T_0, $^1P < 0.05$.

4. Discussion

ARDS is a systemic inflammatory response syndrome with respiratory distress and intractable hypoxemia as its main clinical characteristics. At present, it is believed that the pathogenesis of ARDS is the injury of vascular endothelial cells caused by excessive inflammation of the body caused by various causes, which leads to the increase of pulmonary capillary endothelial permeability, the accumulation of extrapulmonary pulmonary water, the serious imbalance of ventilation/blood flow ratio, and the systemic oxygen metabolism. Disorders, intractable hypoxemia, disease progression can cause multiple organ dysfunction, even failure, especially lung dysfunction is common [4].

There are many kinds of inflammatory cells rich in neutrophil Elastase (NE) in extravascular lung water of ARDS patients [5]. In addition, alveolar epithelial cells and alveolar macrophages can also produce endothelin-1 (ET-1) and other cytokines, which can aggravate vascular endothelial cell injury and inflammation, increase pulmonary capillary endothelial permeability, thus aggravating ARDS. NE is one of the members of serine protease superfamily. It is synthesized and secreted by neutrophils, monocytes, T lymphocytes and mast cells, and has a strong pro-inflammatory effect. The high level of NE can affect the barrier function of airway mucosa and lung tissue compliance by destroying the balance between NE and endogenous protease inhibitors or degrading connective tissue proteins, extracellular matrix, fibronectin, alveolar surfactant, etc. [6-8]. ET-1 is the strongest vasoconstrictor known to be produced mainly by endothelial cells, alveolar epithelial cells, alveolar macrophages and fibroblasts. Excessive release of ET-1 can cause abnormal pulmonary capillary systolic and diastolic function, increase pulmonary vascular permeability, and promote the release of TNF-α, IL-beta, IL-β and other inflammatory mediators, aggravating the inflammatory reaction process and vascular endothelial cell damage [9-10]. NE and ET-1 have strong pro-inflammatory effects and play a key role in systemic inflammation. High levels of NE and ET-1 can increase pulmonary capillary endothelial permeability, lead to the accumulation of extrapulmonary pulmonary water, and promote the progression of ARDS. CBP is often used in ARDS treatment because of its advantages of maintaining acid-base balance, clearing part of inflammatory mediators and enhancing organ function. It can reduce inflammatory reaction and vascular endothelial injury by convection of replacement fluid. At the same time, it can clear excess fluid in vivo through ultrafiltration, and reduce extrapulmonary lung water, thereby improving lung ventilation function and sustaining. Stabilize acid-base balance, stabilize vital signs, and achieve the goal of treatment [11]. NE and ET-1 are both large and medium molecular substances. In theory, CBP can be used for convective clearance. The results showed that the plasma NE and ET-1 levels in the observation group were significantly lower than those in the control group after treatment. It was confirmed that CBP could effectively eliminate some NE and ET-1 in the plasma of ARDS patients by convection, thus alleviating systemic inflammation. In addition, the results of this study show that CBP quality can significantly improve alveolar oxygenation and airway function in ARDS patients, indicating that CBP treatment can effectively remove part of NE and ET-1 in plasma, affect the inflammatory reaction network in patients, thus inhibiting the inflammatory reaction process in patients, reducing pulmonary capillary permeability, reducing

pulmonary edema, and improving alveolar oxygenation and airway function.

In conclusion, CBP can clear some NE and ET-1 in plasma of ARDS patients, alleviate inflammation, improve alveolar oxygenation and airway function. However, this study only preliminarily discussed some inflammatory mediators, alveolar oxygenation and airway function in patients with ARDS caused by CBP. There are still some shortcomings, such as fewer cases included and shorter observation time, which may have some impact on the results of the study. Therefore, further cumulative cases and prolonged observation time are needed to further study.

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