Octreotide and Continuous Hemofiltration *versus* Continuous Hemofiltration Alone in Severe Acute Pancreatitis Complicated with Acute Respiratory Distress Syndrome

Lei Huang[1], Hongxia Zhu[2] and Jianxiang Gu[3]

ABSTRACT

The objective of this study was to compare effects of octreotide and continuous hemofiltration *versus* continuous hemofiltration alone in the treatment of severe acute pancreatitis (SAP) complicated with acute respiratory distress syndrome (ARDS). It was an experimental study carried out from April 2016 to April 2018. A total of 86 cases of SAP complicated with ARDS were randomly divided into group A and group B, with 43 cases in each group. Group A was given continuous hemofiltration alone, and group B was given continuous hemofiltration combined with octreotide. The research findings showed that serum tumor necrosis factor (TNF-α), interleukin-1 (IL-1), IL-6, IL-8, diamine oxidase (DAO), endotoxin, D-lactic acid levels and acute physiology and chronic health evaluation (APACHE II) and systemic inflammatory response syndrome (SIRS) scores of group B were lower than those of group A (all $p<0.001$) after treatment. There was no significant difference in mortality between two groups after 90 days of discharge ($p=0.306$). Compared with continuous hemofiltration alone, treatment with continuous hemofiltration plus octreotide is higher in efficiency, but did not translate into improved mortality.

Key Words: *Severe acute pancreatitis, Acute respiratory distress syndrome, Continuous hemofiltration, Octreotide.*

Severe acute pancreatitis (SAP) is a clinically common digestive system disease caused by trypsin self-digesting the pancreas, often leading to systemic inflammatory response syndrome and multiple organ failure.[1] Acute respiratory distress syndrome (ARDS) is a clinical syndrome characterised by refractory hypoxemia.[2] ARDS is also one of the common complications of SAP. It is caused by systemic inflammatory reaction, excessive synthesis of inflammatory mediators and damage to the lung tissue, which can lead to shortness of breath, respiratory distress and other symptoms.

At present, the clinical treatment of SAP complicated with ARDS is mechanical ventilation treatment, but this method easily causes respiratory lung injury due to the long-term use of the ventilator. The treatment effect is not satisfactory. Persistent hemofiltration is a continuous alternative to the blood purification by the kidneys. It can slowly and permanently remove excess water and solutes through a biological membrane of a certain pore size. Previous studies have shown that continuous hemofiltration may reduce local and systemic complications and mortality in patients with SAP.[3] Octreotide is a synthetic octapeptide cyclic compound as well as a protective hormone with the function similar to that of natural endogenous somatostatin.[4] There are few reports on the clinical efficacy of continuous hemofiltration alone or that combined with octreotide in the treatment of SAP complicated with ARDS.[5]

The objective of this study was to compare the effects of octreotide and continuous hemofiltration *versus* continuous hemofiltration alone in the treatment of SAP complicated with ARDS.

This study was conducted at the Intensive Care Unit, Lianshui County People's Hospital, Huai'an, China, from April 2016 to April 2018, after approval from the Hospital Ethical and Research Committee. A total of 86 patients of SAP complicated with ARDS were selected as subjects. Inclusion criteria were patients confirmed SAP complicated with ARDS; visit time <48h, aged 18-70 years. Exclusion criteria were special populations such as pregnant and lactating women, those with malignant tumors, drug allergies; patients with chronic respiratory failure, blood, immune system and other serious diseases. The patients were randomised into group A and group B, with 43 cases in each group. Group A was given continuous hemofiltration alone: a single-needle

[1] *Intensive Care Unit, Lianshui County People's Hospital, Huai'an, 223400, China*
[2] *Department of Gastroenterology, Lianshui County People's Hospital, Huai'an, 223400, China*
[3] *Department of Gastroenterology, Huai'an Second People's Hospital and The Affiliated Huaian Hospital of Xuzhou Medical University, 223400, China*

Correspondence: Jianxiang Gu, Department of Gastroenterology, Huai'an Second People's Hospital and The Affiliated Huaian Hospital of Xuzhou Medical University, 223400, China
E-mail: fqeadiz@163.com

Received: October 11, 2018; Revised: January 02, 2019; Accepted: January 10, 2019

double-lumen catheter was placed in the right femoral vein or internal jugular vein cannula in the patient, and continuous hemofiltration was performed using a German Braun Diapact CRRT hemofiltration machine. The replacement solution was formulated with Port. The final ion concentration was Na^+ = 143 mmoL/L, Cl^{-1} = 16 mmoL/L, HCO_{3-} = 334.9 mmoL/L, Ca^{2+} = 2.07 mmoL/L, Mg^{2+} = 1.56 mmoL/L, and K^+ = 3.6 mmoL/L. All patients underwent continuous hemofiltration within 12 hours after admission to the ICU. Each treatment was continued at the bedside for a duration of 20-24 hours. The blood flow during the treatment was set at 180-200 mL/minute. The replacement solution was infused by pre-dilution method; the flow rate was 2-4 L/h; meanwhile, 250 mL of 5% sodium bicarbonate was infused at a uniform speed. The patient was treated with unfractionated heparin for anticoagulation. The first dose was 20 mg/h, and the additional dose was 3-8 mg/h. Patients in group B were given a small amount of 0.6 mg octreotide dissolved in 50 mL normal saline on the basis of treatment in group A, and the flow rate was 2 mL/h.

Before and after treatment, 5 mL of elbow venous blood was collected from both groups. Serum levels of tumor necrosis factor (TNF-α), interleukin-1 (IL-1), IL-6, IL-8 were determined by double antibody sandwich enzyme-linked immunosorbent assay (ELISA). Activity of serum diamine oxidase (DAO) was detected by spectrophotometry. Plasma endotoxin levels were measured using an automatic biochemical analyser, and plasma D-Lactic acid levels were detected by enzyme-linked UV spectrophotometry.

Acute physiology and chronic health evaluation (APACHE II) and systemic inflammatory response syndrome (SIRS) scores were compared between the two groups before and after treatment. The total score of APACHE II is 71 points. The higher the score, the more serious the condition is. The SIRS scoring system has a total of 32 points. The higher the score, the more serious the condition is. ICU mortality and mortality in 90 days after discharge were observed in both groups.

Data was analysed in SPSS version 25. Measurement data showed in mean ±SD, examined by independent sample t-test. Frequencies and percentages were calculated for categorical variables, and Chi-square test was applied to compare the categorical variables. P-value of less than or equal to 0.05, was considered statistically significant.

Among 86 patients, 49 (56.98%) were males and 37 (43.02%) were females; aged 28-69 years, mean age 64.51 ±2.17 years; visit time 3-45 hours, mean visit time 21.36 ±2.82 hours; respiratory rate 21-30 times/minute, mean respiratory rate 26.24 ±1.73 times/minute.

There were no significant differences in serum TNF-α, IL-1, IL-6, IL-8, DAO, endotoxin, D-lactic acid, APACHE II and SIRS scores between two groups before treatment (p=0.857, 0.947, 0.970, 0.908, 0.875, 0.877, 0.914, 0.962 and 0.936, respectively); Serum TNF-α, IL-1, IL-6, IL-8, DAO, endotoxin and D-lactic acid, APACHE II and SIRS scores in group B were lower than those in group A after treatment (all p<0.001, Table I).

There were no deaths at ICU in both groups. On the 90th day after discharge, three patients (6.98%) died in group A and one patient (2.33%) died in group B, all of whom died of multiple organ failure. There was no significant difference in mortality between the two groups after 90 days of discharge (p=0.306).

This study found that patients with SAP complicated with ARDS had higher levels of serum inflammatory mediators TNF-α, IL-1, IL-6 and IL-8 before treatment. This is basically consistent with previous research reports.[5] After further analysis, it was found that continuous hemofiltration combined with octreotide

Table I: Comparison of related indicators between two groups.

Indices	Time	Group A (n=43)	Group B (n=43)	p-value
TNF-α (ng/L)	Before treatment	471.24 ±32.75	472.56±34.81	0.857
	After treatment	276.53 ±28.17	209.72 ±21.04	<0.001
IL-1 (pg/L)	Before treatment	77.32 ±6.52	77.41 ±5.93	0.947
	After treatment	51.66 ±3.49	40.16 ±2.25	<0.001
IL-6 (ng/L)	Before treatment	52.33 ±3.27	52.36 ±3.41	0.970
	After treatment	38.86 ±2.95	30.04 ±1.83	<0.001
IL-8 (ng/L)	Before treatment	427.43 ±22.61	428.01 ±23.55	0.908
	After treatment	185.67 ±16.94	103.33 ±11.78	<0.001
DAO (U/mL)	Before treatment	7.62 ±1.53	7.67 ±1.41	0.875
	After treatment	4.75 ±1.08	3.21 ±0.75	<0.001
Endotoxin (EU/mL)	Before treatment	4.23 ±0.87	4.26 ±0.92	0.877
	After treatment	2.87 ±0.36	2.01 ±0.25	<0.001
D-lactic acid (mg/L)	Before treatment	10.58 ±1.24	10.61 ±1.33	0.914
	After treatment	6.39 ±0.57	5.24 ±0.46	<0.001
APACHE II scores	Before treatment	26.32 ±5.61	26.38 ±6.04	0.962
	After treatment	16.85 ±3.29	11.07 ±2.76	<0.001
SIRS scores	Before treatment	2.78 ±0.63	2.79 ±0.52	0.936
	After treatment	1.83 ±0.46	1.25 ±0.31	<0.001

treatment can reduce the levels of serum inflammatory factors TNF-α, IL-1, IL-6 and IL-8 and clear inflammatory mediators in the body more effectively than continuous hemofiltration alone. Octreotide can prevent neutrophil activation and inhibit the expansion of inflammatory mediators by inhibiting the production and release of cytokines such as TNF-α, IL-1, IL-6, and IL-8. Continuous hemofiltration can also remove various cytokines and inflammatory mediators in the body by adsorption/filtration through diffusion or convection. Octreotide and continuous hemofiltration can play a synergistic role, so the combined effect of the two to remove the inflammatory mediator is better than the effect of continuous hemofiltration alone.

Serum DAO, D-lactic acid and endotoxin levels can be used to assess intestinal barrier function.[6] This study found that continuous hemofiltration combined with octreotide treatment can more effectively improve intestinal mucosal permeability, reduce endotoxemia and intestinal mucosal barrier function damage compared with continuous hemofiltration treatment alone. It indicated that continuous hemofiltration combined with octreotide has a better protective effect on intestinal barrier function in SAP patients complicated with ARDS.

This study found that continuous hemofiltration combined with octreotide treatment can be more effective in reducing APACHE II and SIRS scores, and thus more beneficial to the improvement of clinical symptoms and prognosis; but it did not reduce the rate of death. Considering that, it may be related to the small sample size and short clinical observation time. Thus it is necessary to further include more SAP patients complicated with ARDS and extend the clinical observation time for research.

REFERENCES

1. Tao Y, Tang C, Feng W, Bao Y, Yu H. Early nasogastric feeding *versus* parenteral nutrition in severe acute pancreatitis: A retrospective study. *Pak J Med Sci* 2016; **32**:1517-21.
2. Rashid MM, Murtaza B, Gondal ZI, Mehmood A, Shah SS, Abbasi MH, *et al*. Injection sclerotherapy for haemorrhoids causing adult respiratory distress syndrome. *J Coll Physicians Surg Pak* 2006; **16**:373-5.
3. Guo J, Huang W, Yang XN, Jin T, ALtaf K, Javed MA, *et al*. Short-term continuous high-volume hemofiltration on clinical outcomes of severe acute pancreatitis. *Pancreas* 2014; **43**: 250-4.
4. Jain A, Gardner S, Chitturi S, Aggarwal V. Octreotide as a bridge to definitive surgery in a patient with cirrhosis and a large spontaneous abdominal wall haematoma. *Intern Med J* 2018; **48**:1273-4.
5. Cui HX, Xu JY, Li MQ. Efficacy of continuous renal replacement therapy in the treatment of severe acute pancreatitis associated acute respiratory distress syndrome. *Eur Rev Med Pharmacol Sci* 2014; **18**:2523-6.
6. Xiao-Bo Y, Qiang L, Xiong Q, Zheng R, Jian Z, Jian-Hua Z, *et al*. Efficacy of early postoperative enteral nutrition in supporting patients after esophagectomy. *Minerva Chir* 2014; **69**:37-46.