Effects of hemodialysis combined with hemoperfusion on severe acute pancreatitis

Zhehne Li[1], Guixi Wang[2], Guodong Zhen[1], Yuliang Zhang[2], Jiaqiang Liu[2], Shanmei Liu[2]

[1]Department of Emergency, Yishui Center Hospital of Linyi City, Linyi, China
[2]Department of Hemodialysis, Yishui Center Hospital of Linyi City, Linyi, China

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ABSTRACT

Background/Aims: Severe acute pancreatitis (SAP) is characterized by persistent organ failure. This research aimed to evaluate the effect of hemodialysis combined with hemoperfusion on SAP.

Materials and Methods: Thirty-seven patients who were treated with hemoperfusion combined with hemodialysis were included in group O, and 31 patients treated with conventional therapy and hemoperfusion were included as control (group C). Leukocyte count, neutrophil percentage, amylase (AMY), blood urine nitrogen (BUN), creatinine (Cr), and total bilirubin (TBIL) were noted. The time when symptoms disappeared as well as complications after treatment was recorded.

Results: Leukocyte count, neutrophil percentage, AMY, BUN, Cr, and TBIL in two groups were remarkably decreased after treatment. However, these indexes were significantly lower in group O than those in group C after treatment, especially the neutrophil percentage, AMY, BUN, Cr, and TBIL. The time when the symptoms disappeared was 3.01±1.02 days in group O, which was shorter than 5.56±1.88 days in group C. There were 4 patients with acute renal failure and 2 patients had multiple organ failure in group C after treatment. But only 1 patient developed acute renal failure in group O. The difference in complications between two groups was significant ($p<0.024$).

Conclusion: The combination of hemodialysis and hemoperfusion could have a better effect on SAP in removing toxic metabolites and inflammation mediators. It not only shortens the time of symptoms disappearing but also decreases the incidence of complications and the mortality.

Keywords: Hemodialysis, hemoperfusion, severe acute pancreatitis, amylase, acute renal failure

INTRODUCTION

Severe acute pancreatitis (SAP) is characterized by persistent organ failure, which is set in motion by the activation of cytokine cascades resulting in systemic inflammatory response syndrome (1-3). Clinical symptoms of SAP include nausea, emesis, fever, stomach ache, and even shock. Moreover, SAP has a high incidence and fatality rate due to the development of pancreatic and extra-pancreatic necrosis, subsequent infection, and multisystem organ failure (4,5). According to many studies, SAP is a devastating disease with mortality ranging from 10% to as high as 85% (5-8). There are also many complications impeding the recovery from SAP. More than 80% of deaths associated with SAP are attributed to the complications caused by bacterial infection in pancreatic necrosis (9). Decreasing the inflammatory response and the incidence of complications is important in the treatment of SAP. However, the treatment of SAP is complicated owing to limited knowledge about the pathogenesis and multicausality of this disease, uncertainties in outcome prediction, and few effective treatment modalities. Nowadays, there are many new approaches for treating SAP (10). In this study, we evaluated the treatment effect of hemodialysis combined with hemoperfusion on SAP.

MATERIALS AND METHODS

Patients

Sixty-eight patients with SAP admitted to our hospital between December 2013 and December 2016 were retrospectively investigated. All patients were with a median age of 32.4±8.8 and a weight of 62.8±12 kg. The inclusion criteria were the following: 1) acute severe pancreatitis: characteristic abnormal pain, serum amylase and/or lipase ≥3 times of upper limit of normal range; 2) severity index of Balthazar's CT score (with contrast) ≥grade D, APACHE

ORCID IDs of the authors: Z.L. 0000-0003-1869-244X; G.W. 0000-0002-6032-1899; G.Z. 0000-0002-3169-918X; Y.Z. 0000-0002-0381-5681; J.L. 0000-0002-8890-6629; S.L. 0000-0002-0352-6337.

Address for Correspondence: **Yuliang Zhang** E-mail: **yuliangzhang112@sohu.com**
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II (acute physiology and chronic health evaluation II) ≥8, C-reactive protein ≥150 mg/L; 3) the age of men and women ≥18 years; 4) no other serious diseases; and 5) acceptance of informed consent (11,12). The exclusion criteria were the following: 1) hypersensitivity to fish, egg, or soy proteins; 2) blood triglycerides >3 mmol/L; 3) severe hepatic impairment; 4) serious disturbances to blood clotting; 5) acute shock; 6) general contraindications in infusion therapy; 7) patients with unstable clinical conditions must not take nutrition by intravenous infusion; and 8) other acute or chronic inflammatory diseases.

There were 37 patients who accepted hemoperfusion combined with hemodialysis (observational group, group O), and 31 patients who were only treated with conventional therapy and hemoperfusion were included as control (group C).

Patient management

All patients accepted the conventional therapy including fasting, gastrointestinal decompression, and intravenous infusion. Some side effects were also treated. Pethidine was used to relieve the grabbing pain in the abdomen, and antibiotics were used in the treatment of SAP to prevent pancreatic necrosis and infection (13). When using antibiotics, we should pay attention to whether patients were sensitive to bacterial translocation. Quinolones and imipenem combined with metronidazole and second- or third-generation cephalosporins were also used. Somatostatin helped to relieve the pain in the abdomen by inhibiting the secretion of pancreatic juice and the production of related enzyme (14). For the first time, 100 μg somatostatin or octreotide intravenous injection was applied. Then, 250 μg/h somatostatin and 25-50 μg octreotide were applied for 3 to 7 days. Intravenous injections of proton pump inhibitors and histamine-2 receptor antagonists were used to decrease gastric acid and to prevent stress ulcer (15). Patients complicated with respiratory failure should be assisted breathing with respirators. Patients with heart failure and circulatory disturbance were also treated (16).

On the basis of conventional therapy, patients in group C were applied hemoperfusion by hemoperfusion cartridge (HA330), and patients in group O were managed not only with hemoperfusion but also with hemodialysis by blood dialyzer (Fresenius 4008 Hemodialysis System). The machines were washed with 5% glucose injection, and the preflush of these machines was performed with heparin-saline. The flow speed of preflush was approximately 100 mL/min, and blood flow speed was 180-200 mL/min. The combination therapy continued for 2 h.

Clinical observations

During the treatment, patients' heart rate, body temperature, and respiratory rate were in real-time supervision. Leukocyte count, neutrophil percentage, amylase (AMY), blood urine nitrogen (BUN), creatinine (Cr), and total bilirubin (TBIL) were measured. In addition, the time when symptoms disappeared and the complications after treatment was recorded.

Statistical analysis

Statistical analysis was performed with the SPSS version 21.0 (IBM Corp.; Armonk, NY, USA) GCS score, consciousness recovery time, and indexes levels were shown as mean±standard deviation and analyzed by t-test. The complications of SAP after treatment were analyzed by Chi-squared test. There was a statistically significant difference at $p<0.05$.

RESULTS

Basic information of patients

There were 37 patients in group O and 31 patients in group C. The median ages in group O and group C were 32.5±8.2 and 32.3±9.4, respectively. The weight of patients was 62.0±12.40 kg and 63.60±11.5 kg, respectively. The statistical analysis result showed that there was no difference in age, gender, and weight between the two groups ($p>0.05$) (Table 1).

Table 1. Basic information of patients

Terms		Group O	Group C	p
Number		37	31	
Age		32.5±8.2	32.3±9.4	0.795
Gender	male	28	26	0.406
	female	9	5	
Weight (kg)		62.0±12.40	63.60±11.5	0.354
Leukocyte ($\times 10^9$/L)		17.1±2.9	16.9±3.2	0.731
Neutrophil percentage		0.83±0.07	0.84±0.05	0.676
AMY (U/L)		1005±146	996±139	0.096
BUN (mmol/L)		29.7±3.2	31.5±2.9	0.230
Cr (μmol/L)		277±40	265±43	0.089
TBIL (mmol/L)		69±14	65±17	0.152

T-test method was used for the comparison between two groups in age, gender, and weight; there is no difference between two groups in these terms

AMY: amylase; BUN: blood urine nitrogen; Cr: creatinine; TBIL: total bilirubin

Table 2. The biochemical indexes of patients before and after treatment; the "before" and "after" represent the indexes values before and after treatment with hemodialysis and hemoperfusion, respectively. "p-value" means the statistical results between two groups after treatment

	Group O		Group C		
Term	Before	After	Before	After	p
Leukocyte ($\times10^9$/L)	17.1±2.9	11.5±1.6[a]	16.9±3.2	12.4±1.9[a]	0.023
Neutrophil percentage	0.83±0.07	0.49±0.08[a]	0.84±0.05	0.62±0.05[a]	1.21×10^{-6}
AMY (U/L)	1005±146	105±35[a]	996±139	158±38[a]	3.01×10^{-12}
BUN (mmol/L)	29.7±3.2	7.5±2.1[a]	31.5±2.9	10.2±2.4[a]	7.35×10^{-7}
Cr (μmol/L)	277±40	61±20[a]	265±43	155±49[a]	1.60×10^{-19}
TBIL (mmol/L)	69±14	21±19[a]	65±17	42±11[a]	8.12×10^{-5}
APACHE II	23±11	12±4[a]	22±12	15±5[a]	0.001

a: there is a difference between the index values before and after treatment in the group; the statistical analysis of these biochemical indexes was performed with t-test; p: analysis value of the comparison between the indexes of two groups after treatment

p<0.05 indicates a statistical significant difference

AMY: amylase; BUN: blood urine nitrogen; Cr: creatinine; TBIL: total bilirubin; APACHE II: acute physiology and chronic health evaluation II

Biochemical indexes before and after treatment

During the management of hemodialysis and hemoperfusion, heart rate, body temperature, and respiratory rate were observed in real time to ensure safety. There was no significant difference in these vital signs after treatment compared with those before treatment, which demonstrated that hemodialysis and hemoperfusion did not have much influence on these vital signs.

Otherwise, some biochemical indexes were also detected to evaluate the treatment effect. Compared with leukocyte count, neutrophil percentage, AMY, BUN, Cr, and TBIL before treatment, these indexes were remarkably decreased after treatment (P<0.05). However, after treatment, they were significantly lower in group O than those in group C (P<0.05), especially neutrophil percentage ($p=1.21\times10^{-6}$), AMY ($p=3.01\times10^{-12}$), BUN ($p=7.35\times10^{-7}$), Cr ($p=1.60\times10^{-19}$), and TBIL ($p=8.12\times10^{-5}$), with significant difference (p<0.001). The clinical score of APACHE II improved, and APACHE II score after treatment was significantly lower in group O than that in group C (p=0.001) (Table 2). Patients in group O recovered better.

Symptoms and complications after treatment

After treatment, the symptoms (pain, fever, and emesis) of all patients disappeared. The time of symptoms disappearing in group O was 3.01±1.02 days, which was much shorter than 5.56±1.88 days in group C ($p=4.31\times10^{-21}$). Otherwise, there were 4 patients complicated with acute renal failure and 2 patients with multiple organ failure in group C after treatment. Only 1 patient developed acute renal failure in group O. There were significant differences in complications between two groups (p<0.024) (Table 3). Furthermore, there were no deaths after treatment.

Table 3. The symptoms and complications in patients after treatment

Terms		Group O	Group C	p
Symptom disappear (day)		3.01±1.02	5.56±1.88	4.31×10^{-21}
Complications	Acute renal failure	1	4	0.024
	Multiple organ failure	0	2	
Mortality		0	0	

The statistical analysis of complications was performed with Chi-squared test. p<0.05 indicates a statistically significant difference

DISCUSSION

SAP has a high fatality rate due to multiple organ failure. The death of patients is related to inflammations induced by many factors (17). There is a cascade reaction in which the mononuclear macrophage, neutrophil, digestive enzymes, metabolites, and other inflammatory mediators were involved and lead to multiple organ failures (18). Blood purification therapy could effectively remove the inflammatory mediators (19). Hemodialysis could clear cholerythrin, BUN, and Cr and regulate the acid-base balance. In addition, hemoperfusion could adsorb inflammation mediators such as tumor necrosis factor-α, IL-1, IL-6, IL-8, and prothrombin activation factor to reduce

the inflammation reaction, and it could play an adsorption role in ALT and AMY (20-22). Therefore, the combination of hemodialysis and hemoperfusion might take full advantages of them benefiting the reduction of inflammation response and a decrease in the incidence of complications. Our research results also proved this.

In this study, leukocyte count, neutrophil percentage, AMY, BUN, Cr, and TBIL decreased after treatment both in group O and group C ($p<0.05$). This demonstrated that hemodialysis and hemoperfusion could play a cleaning function in the treatment of SAP. However, the decrease of these indexes in group O was much more than those in group C, with a statistically significant difference ($p<0.001$). This demonstrated that the improvement of patients in group O was much better. Thus, the combination of hemodialysis and hemoperfusion could lead to a better treatment effect.

In addition, the incidence of complications also supported this. In this study, the incidence of complications in group O was much lower than that in group C ($p=0.024$). The clinical symptoms in group O disappeared within 3.01±1.02 days. As a contrast, the symptoms in control group disappeared within 5.56±1.88 days, which is much higher than that in group O ($p=4.31\times10^{-21}$).

In conclusion, the combination of hemodialysis and hemoperfusion could have a better effect on removing toxic metabolites and inflammation mediators in the treatment of SAP. It not only shortens the time of symptoms disappearing but also decreases the incidence of complications and the mortality. The combination of hemodialysis and hemoperfusion provides a new method for the treatment of SAP. It should be well used in the clinical therapy of SAP. In addition, more studies are necessary to thoroughly understand the pathogenesis and multicausality of SAP to improve the current treatment methods.

Ethics Committee Approval: This study obtained the ethics committee approval from the Linyi Central Hospital.25

Informed Consent: All patients were well informed the content of this study and signed the informed consent.

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