Invest Clin 64(1): 41 - 52, 2023 https://doi.org/10.54817/IC.v64n1a04

Effects of somatostatin in combination with early hemoperfusion on inflammatory, hemorheological and oxidative parameters during the treatment of acute pancreatitis.

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Keywords: somatostatin; hemoperfusion; acute pancreatitis; inflammatory response; stress response.

Abstract. We aimed to evaluate the effects of somatostatin combined with early hemoperfusion on inflammatory and stress responses during acute pancreatitis (AP) treatment. A total of 159 AP patients treated from September 2016 to January 2020 were randomly divided into three groups A-C (n=53). In addition to routine treatment, groups A-C were additionally given somatostatin, early hemoperfusion, and somatostatin combined with early hemoperfusion, respectively. Their inflammatory factors, stress response, intestinal mucosal barrier, hemorheological indices, recovery time, length of stay, clinical efficacy, and adverse reactions were compared. The levels of serum interleukin-10 (IL-10), catalase and glutathione peroxidase rose in the three groups after ten days of treatment, compared with values before treatment, being the highest rise in group C. The levels of IL-18, tumor necrosis factor-α, soluble intercellular adhesion molecule-1, procalcitonin, high mobility group protein B1, lipid hydrogen peroxide, advanced oxidation protein products, epinephrine, cortisol, D-lactic acid, diamine oxidase, and endotoxin decreased after ten days of treatment compared with those before treatment, which were lowest in group C ($P<0.05$). After ten days of treatment, the levels of hemorheological indices were significantly lower than those before treatment ($P<0.05$). Compared with groups A and B, group C had a shorter recovery time of urine amylase, bowel sound and passing gas, remission time of abdominal pain, length of stay, and a higher total response rate ($P<0.05$). During AP treatment, somatostatin combined with early hemoperfusion effectively relieved inflammatory and stress responses, protected the intestinal mucosal barrier function and improved the hemorheology, thereby promoting the recovery and benefiting the prognosis of patients.

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Efectos de la somatostatina en combinación con hemoperfusión precoz sobre parámetros inflamatorios, hemorreológicos y oxidativos durante el tratamiento de la pancreatitis aguda.

Invest Clin 2023; 64 (1): 41 – 52

Palabras clave: somatostatina; hemoperfusión; pancreatitis aguda; respuesta inflamatoria; respuesta al estrés.

Resumen. Nuestro objetivo fue evaluar los efectos de la somatostatina combinada con hemoperfusión temprana sobre las respuestas inflamatorias y de estrés durante el tratamiento de la pancreatitis aguda (PA). Un total de 159 pacientes con PA tratados entre septiembre de 2016 y enero de 2020 se dividieron aleatoriamente en tres grupos A-C (n=53). Con base en el tratamiento de rutina, los grupos A-C recibieron además somatostatina, hemoperfusión temprana y somatostatina combinada con hemoperfusión temprana, respectivamente. Se compararon sus factores inflamatorios, respuesta al estrés, barrera de la mucosa intestinal, índices hemorreológicos, tiempo de recuperación, tiempo de estancia, eficacia clínica y reacciones adversas. Los niveles séricos de interleucina-10 (IL-10), catalasa y glutatión peroxidasa aumentaron en los tres grupos después de 10 días de tratamiento, comparados con los valores antes del tratamiento, siendo más elevados en el grupo C. Los niveles de IL-18, factor de necrosis tumoral α, molécula de adhesión intercelular 1 soluble, procalcitonina, proteína B1 del grupo de alta movilidad, peróxido de hidrógeno lipídico, los productos proteicos de oxidación avanzada, epinefrina, cortisol, ácido D-láctico, diaminooxidasa y endotoxina disminuyeron después de 10 días de tratamiento en comparación con los previos al tratamiento, que fueron más bajos en el grupo C (P<0,05). Después de 10 días de tratamiento, los índices hemorreológicos fueron significativamente menores que los previos al tratamiento (P<0,05). En comparación con los grupos A y B, el grupo C tuvo un tiempo de recuperación más corto de amilasa en orina, sonido y escape intestinal, tiempo de remisión del dolor abdominal y tiempo de estancia, y una tasa de respuesta total más alta (P<0,05). Durante el tratamiento de la AP, la somatostatina combinada con hemoperfusión precoz alivia eficazmente las respuestas inflamatorias y de estrés, protege la función de la barrera de la mucosa intestinal y mejora la hemorología, favoreciendo la recuperación y beneficiando el pronóstico de los pacientes.

Received: 27-06-2022 Accepted: 30-09-2022

INTRODUCTION

Acute pancreatitis (AP) is a common acute abdominal disease typified by the acute episode of severe persistent upper abdominal pain. Due to multiple etiological factors, pancreatic enzymes in the pancreas are activated, causing local inflammatory responses in pancreatic tissues, such as autodigestion, edema, bleeding, and necrosis. With the progression of AP, systemic inflammatory response syndrome occurs in severe cases, accompanied by organ dysfunction and even death [1]. Recently, the imbalance

between inflammatory and oxidative stress responses is considered a crucial cause for the onset and exacerbation of AP. Therefore, balancing the inflammatory response and eliminating oxygen-free radicals are the key to AP treatment [2]. Somatostatin can inhibit the secretion and biological activity of pancreatic enzymes and exert therapeutic effects by suppressing autodigestion. Blood purification treatment can protect organ function by restoring the blood's internal environment to normal [3]. Currently, somatostatin is often combined with early hemoperfusion in the clinical treatment of AP patients. However, the effects on inflammatory and stress responses remain largely unknown. In this study, the clinical efficacy of somatostatin combined with early hemoperfusion on AP patients was assessed, and the changes in their inflammatory and stress responses were analyzed, aiming to investigate the possible mechanism of action and to provide a scientific basis for clinical treatment.

MATERIALS AND METHODS

Baseline clinical data

This study has been approved by the ethics committee of our hospital and a written informed consent has been obtained from all patients. A total of 159 AP patients treated in our hospital from September 2016 to January 2020 were selected and divided into groups A, B, and C (n=53) using a random number table. In group A, the patients were 34-76 years old, with an average of 51.26 ± 8.93 years. There were 32 males and 21 females. The body mass index (BMI) was 22.15 ± 1.48 kg/m^2 on average, and the duration from onset to admission was 3-71 h, averaging 24.62 ± 5.39 h. Regarding the severity of the disease, there were 28 mild, 21 moderate-severe, and four severe cases. As to the pathogenesis, there were 15 cases of biliary pancreatitis, 22 cases of alcoholic pancreatitis, and 16 cases of overeating-induced pancreatitis. About complications, hyperlipidemia occurred in 11 cases, diabetes mellitus in 14 cases, and hypertension in 28 cases. In group B, the patients were 33-74 years old, with an average of 50.94 ± 8.87 years. There were 29 males and 24 females. BMI was 21.89 ± 1.45 kg/m^2 on average, and the duration from onset to admission was 2-72 h, averaging 24.73 ± 5.41 h. In terms of the severity of the disease, there were 29 mild, 19 moderate-severe, and five severe cases. Regarding the pathogenesis, there were 14 cases of biliary pancreatitis, 21 cases of alcoholic pancreatitis and 18 cases of overeating-induced pancreatitis. As to complications, hyperlipidemia occurred in 13 cases, diabetes mellitus in 11 cases and hypertension in 29 cases. In group C, the patients were 34-75 years old, with an average of 51.32 ± 9.04 years. There were 31 males and 22 females. BMI was 22.07 ± 1.46 kg/m^2 on average, and the duration from onset to admission was 2-71 h, with an average of 24.58 ± 5.37 h. In terms of the severity of the disease, there were 31 mild, 17 moderate-severe, and 5 severe cases. As to the pathogenesis, there were 17 cases of biliary pancreatitis, 19 cases of alcoholic pancreatitis, and 17 cases of overeating-induced pancreatitis. Concerning complications, hyperlipidemia occurred in 14 cases, diabetes mellitus in 12 cases and hypertension in 27 cases. The three groups had comparable baseline clinical data (P>0.05) (Table 1).

Inclusion and exclusion criteria

Inclusion criteria: 1) Patients who met the diagnostic criteria in the Expert Consensus on TCM Diagnosis and Treatment of Acute Pancreatitis (2017) developed by the Society of Digestive Diseases, China Association of Traditional Chinese Medicine [4]; 2) those admitted within 72 h after onset; 3) those treated for the first time; 4) those without contraindications to hemoperfusion or history of drug allergy; 5) those admitted for over 14 d; 6) those with complete clinical data; 7) those who and whose families voluntarily signed the informed consent.

Table 1
Baseline clinical data.

	Group A (n=53)	Group B (n=53)	Group C (n=53)	Statistical value	*P*
Age (year)	51.26±8.93	50.94±8.87	51.32±9.04	F=0.282	0.892
BMI (kg/m^2)	22.15±1.48	21.89±1.45	22.07±1.46	F=0.762	0.324
Duration from onset to admission (h)	24.62±5.39	24.73±5.41	24.58±5.37	F=0.823	0.192
Severity				$\chi2$=0.723	0.948
Mild	28	29	31		
Moderate-severe	21	19	17		
Severe	4	5	5		
Pathogenesis				$\chi2$=0.649	0.958
Biliary pancreatitis	15	14	17		
Alcoholic pancreatitis	22	21	19		
Overeating-induced pancreatitis	16	18	17		
Complication				$\chi2$=0.818	0.936
Hyperlipidemia	11	13	14		
Diabetes mellitus	14	11	12		
Hypertension	28	29	27		

BMI: Body mass index.

Exclusion criteria: 1) Patients complicated with dysfunction of vital organs such as the heart, liver, or kidney, acute/chronic infectious diseases, or endocrine diseases that may affect the stress state; 2) those with a history of acute/chronic pancreatitis; 3) those with diabetes mellitus, hypertension, tumors or trauma; 4) those with mental disorders or language dysfunction; 5) those who were transferred to another hospital or quit halfway, received other therapeutic regimens or had poor compliance; 6) pregnant or lactating women.

Treatment methods

All patients were deprived of water and food immediately after admission, and conventional therapies were performed, such as gastrointestinal decompression, the supplement of blood volume, anti-infection, as well as correction of water-electrolyte and acid-base disorders. For group A, somatostatin (NMPN H20066708, Yangtze River Pharmaceutical Group, China) was applied based on conventional therapy: 6 mg of somatostatin was diluted in 500 mL of normal saline and continuously intravenously pump-infused (4 mL/L) (Sigma-Aldrich Labware, USA). For group B, early hemoperfusion was performed based on conventional therapy: The vascular access was constructed using a femoral vein single-needle double-cavity catheter and connected to a hemodialysis machine (Philips, USA). The blood was anticoagulated with low-molecular-weight heparin (Sigma-Aldrich, USA) at an initial dose of 5000 U, with 250 U additionally supplemented hourly. Hemoperfusion was conducted using a HA330 resin hemoperfusion cartridge (Zhuhai Livzon Diagnostics Inc., China) at a flow rate of 150-200 mL/min for 2 h, 3-5 times daily as needed. For group C, somatostatin in combination with early hemoperfusion was employed based on conventional

therapy, and the dosage and method were the same as those for the other two groups.

Observation indices

Before and after 10 d of treatment, 5 mL of peripheral cubital venous blood was drawn and centrifuged, and the serum was collected.

Inflammatory factors interleukin-10 (IL-10), IL-18, tumor necrosis factor-α (TNF-α), soluble intercellular adhesion molecule-1 (sICAM-1), procalcitonin (PCT) and high mobility group protein B1 (HMGB1) in the serum were detected by enzyme-linked immunosorbent assay (ELISA), according to the instructions of corresponding kits (Abcam, USA).

Stress response indices: Oxidative indices (lipid hydrogen peroxide (LHP) and advanced oxidation protein products (AOPPs)) and antioxidative indices (catalase (CAT) and glutathione peroxidase (GSH-Px)) were determined using immunofluorescence assay kits (Thermo Fisher Scientific, USA). Additionally, stress hormones epinephrine (E) and cortisol (COR) were determined by radioimmunoassay kits (North Bioengineering Institute, Beijing, China).

Intestinal mucosal barrier indices D-lactic acid (D-LAC), diamine oxidase (DAO), and endotoxin (ET) in the serum were detected by ELISA kits (Abcam, USA).

Hemorheological indices: before treatment and after 10 d of treatment, the platelet adhesion rate, plasma-specific viscosity, whole blood-specific viscosity (high). and thrombus length were observed.

Urine amylase was detected by an ELISA kit (Abcam, USA), and its recovery time was recorded. The recovery time of bowel sound and exhaust, remission time of abdominal pain, together with the length of stay were also recorded.

After treatment for 10 d, clinical efficacy and adverse reactions were observed. Evaluation criteria for clinical efficacy: Cured: The laboratory test indices returned to normal, and the clinical symptoms disappeared. Markedly effective: The laboratory test indices were improved significantly, and the clinical symptoms were significantly relieved. Effective: The laboratory test indices and clinical symptoms were improved. Ineffective: The laboratory test indices had no improvement or even worsened, and the clinical symptoms were not changed or even exacerbated. Total response rate = (cured + markedly effective + effective cases)/total cases × 100%.

Statistical analysis

All data were statistically analyzed by the SPSS 20.0 software (IBM Inc., USA). The quantitative data were expressed as means ± standard deviations ($\bar{x} \pm s$). Multigroup comparisons were performed by one-way analysis of variance, and those at different time points were conducted with repeated measures analysis of variance. In the case of statistical significance, intergroup comparisons at the same time point were carried out by the independent t test, and the paired t test was used for intragroup comparisons at various time points. The numerical data were represented as percentage (%) and subjected to the χ^2 test. $P<0.05$ was considered statistically significant.

RESULTS

Levels of inflammatory factors

Before treatment, the levels of inflammatory factors IL-10, IL-18, TNF-α, sICAM-1, PCT and HMGB1 had no statistically significant differences among the three groups ($P>0.05$). At 10 d after treatment, the level of serum IL-10 rose in the three groups compared with that of before treatment, higher in group C than that in groups A and B. In contrast the levels of other indices declined in the three groups, lower in group C than those in groups A and B, showing statistically significant differences ($P<0.05$) (Table 2).

Table 2
Levels of inflammatory factors.

Index	Group A (n=53)	Group B (n=53)	Group C (n=53)	F	P
IL-10 ($\bar{x}$ ± s, ng/L)					
Before treatment	9.87±1.02	10.11±1.06	9.98±1.03	1.018	0.236
10 days after treatment	15.18±1.46*	14.97±1.52*	20.36±2.19*ab	14.325	0.0001
IL-18 ($\bar{x}$ ± s, ng/L)					
Before treatment	463.27±45.81	459.13±46.07	461.49±45.87	0.564	0.637
10 days after treatment	170.32±18.49*	167.91±17.85*	138.46±14.52*ab	10.318	0.0001
TNF-α ($\bar{x}$ ± s, ng/L)					
Before treatment	185.41±20.36	182.53±20.78	179.85±19.96	0.847	0.259
10 days after treatment	93.62±11.28*	94.15±10.86*	72.03±6.78*ab	9.653	0.0001
sICAM-1 ($\bar{x}$ ± s, ng/mL)					
Before treatment	24.95±2.61	25.13±2.68	24.87±2.59	0.501	0.612
10 days after treatment	13.27±1.45*	12.96±1.37*	5.13±0.64*ab	34.698	0.0001
PCT ($\bar{x}$ ± s, ng/mL)					
Before treatment	6.48±0.73	6.52±0.69	6.47±0.71	0.359	0.704
10 days after treatment	3.79±0.42*	3.85±0.40*	1.68±0.23*ab	28.076	0.0001
HMGB1 ($\bar{x}$ ± s, ng/mL)					
Before treatment	15.24±1.67	15.18±1.63	14.97±1.58	0.755	0.391
10 days after treatment	10.18±1.13*	9.97±1.08*	5.26±0.61*ab	28.634	0.0001

Compared with before treatment, *P<0.05; compared with group A, aP<0.05; compared with group B, bP<0.05. HMGB1: High mobility group protein B1; IL: interleukin; PCT: procalcitonin; sICAM-1: soluble intercellular adhesion molecule-1; TNF-α: tumor necrosis factor-α.

Levels of stress response indices

No statistically significant differences were found in the levels of stress response indices LHP, AOPPs, CAT, GSH-Px, E, and COR among the three groups before treatment (P>0.05). At 10 d after treatment, the levels of serum CAT and GSH-Px rose in the three groups compared with those before treatment, higher in group C than those in groups A and B, whereas the levels of LHP, AOPPs, E, and COR declined in the three groups, lower in group C than those in groups A and B, displaying statistically significant differences (P<0.05) (Table 3).

Levels of intestinal mucosal barrier indices

Before treatment, there were no statistically significant differences in the levels of intestinal mucosal barrier indices D-lac, DAO and ET among the three groups (P>0.05). At 10 d after treatment, the levels of these indices declined in the three groups compared with those before treatment, and the differences were statistically significant (P<0.05). At 10 d after treatment, group C had significantly lower levels of serum D-lac, DAO and ET than the other two groups (P<0.05) (Table 4).

Table 3
Levels of stress response indices.

Index	Group A (n=53)	Group B (n=53)	Group C (n=53)	F	P
LHP ($\bar{x}$ ± s, μmol/L)					
Before treatment	23.78±2.59	24.05±2.63	23.91±2.60	0.523	0.495
10 days after treatment	14.26±1.47*	13.98±1.42*	7.52±0.83*[ab]	26.491	0.0001
AOPPs ($\bar{x}$ ± s, μmol/L)					
Before treatment	8.41±0.92	8.37±0.89	8.45±0.93	0.472	0.651
10 days after treatment	5.39±0.56*	5.44±0.57*	2.96±0.31*[ab]	27.628	0.0001
CAT ($\bar{x}$ ± s, U/L)					
Before treatment	17.04±2.12	16.88±2.09	16.96±2.11	0.381	0.696
10 days after treatment	25.63±2.87*	24.75±2.83*	33.18±3.76*[ab]	10.612	0.0001
GSH-Px ($\bar{x}$ ± s, g/L)					
Before treatment	27.16±2.95	26.97±2.89	27.14±2.93	0.435	0.758
10 days after treatment	36.52±3.78*	35.68±3.71*	49.36±5.07*[ab]	13.786	0.0001
E ($\bar{x}$ ± s, ng/mL)					
Before treatment	0.72±0.11	0.69±0.10	0.70±0.09	1.369	0.147
10 days after treatment	0.45±0.06*	0.43±0.05*	0.18±0.02*[ab]	24.757	0.0001
COR ($\bar{x}$ ± s, ng/mL)					
Before treatment	251.16±27.38	249.57±26.81	250.43±27.19	0.602	0.763
10 days after treatment	142.09±15.26*	138.64±14.92*	87.58±9.61*[ab]	20.941	0.0001

Compared with before treatment, *P<0.05; compared with group A, [a]P<0.05; compared with group B, [b]P<0.05. AOPPs: Advanced oxidation protein products; CAT: catalase; COR: cortisol; E: epinephrine; GSH-Px: glutathione peroxidase; LHP: lipid hydrogen peroxide.

Table 4
Levels of intestinal mucosal barrier indices.

Index	Group A (n=53)	Group B (n=53)	Group C (n=53)	F	P
D-lac ($\bar{x}$ ± s, mg/L)					
Before treatment	3.96±0.58	4.12±0.63	4.07±0.62	1.265	0.173
10 days after treatment	1.97±0.29*	2.05±0.31*	1.15±0.18*[ab]	14.356	0.0001
DAO ($\bar{x}$ ± s, IU/mL)					
Before treatment	16.42±1.75	15.96±1.72	16.28±1.73	0.956	0.147
10 days after treatment	9.38±0.96*	9.24±0.93*	5.04±0.51*[ab]	28.927	0.0001
ET ($\bar{x}$ ± s, EU/mL)					
Before treatment	10.13±1.24	9.98±1.07	10.02±1.16	0.548	0.506
10 days after treatment	6.87±0.65*	6.75±0.62*	3.29±0.38*[ab]	36.439	0.0001

Compared with before treatment, *P<0.05; compared with group A, [a]P<0.05; compared with group B, [b]P<0.05. DAO: Diamine oxidase; D-LAC: D-lactic acid; ET: endotoxin.

Levels of hemorheology indices

Before treatment, there were no statistically significant differences in the platelet adhesion rate, plasma-specific viscosity, whole blood-specific viscosity (high), and thrombus length among the three groups (P>0.05). At 10 d after treatment, the hemorheology indices significantly declined in the three groups compared with those before treatment (P<0.05). They declined successively in group A, B and C, and the differences were statistically significant between any two groups (P<0.05) (Table 5).

Recovery time and hospital stay length

In group C, the recovery time of urine amylase, bowel sound and exhaust, remission time of abdominal pain, and length of stay were all significantly shorter than those of groups A and B (P<0.05). However, there were no significant differences between groups A and B (Table 6).

Clinical treatment outcomes and adverse reactions

The total clinical response rate was significantly higher in group C than that in

Table 5
Levels of hemorheology indices.

Index	Group A (n=53)	Group B (n=53)	Group C (n=53)	F	P
Platelet adhesion rate ($\bar{x}$ ± s, %)					
Before treatment	79.58±13.42	80.37±14.15	79.94±13.86	0.285	0.649
10 days after treatment	52.91±8.27*	43.21±6.86*[a]	31.28±5.73*[ab]	7.592	0.0001
Plasma specific viscosity ($\bar{x}$ ± s, %)					
Before treatment	2.24±0.25	2.19±0.23	2.21±0.24	1.063	0.186
10 days after treatment	1.89±0.18*	1.54±0.16*[a]	1.17±0.12*[ab]	15.478	0.0001
Whole blood specific viscosity (high) ($\bar{x}$ ± s, mPa·s)					
Before treatment	6.52±0.73	6.49±0.71	6.50±0.72	0.314	0.821
10 days after treatment	5.14±0.62*	4.08±0.53*[a]	3.21±0.34*[ab]	16.871	0.0001
Thrombus length ($\bar{x}$ ± s, mm)					
Before treatment	56.87±17.24	55.97±17.16	56.48±17.22	0.249	0.788
10 days after treatment	43.29±11.56*	31.28±8.45*[a]	20.31±4.69*[ab]	9.510	0.0001

Compared with before treatment, *P<0.05; compared with group A, [a]P<0.05; compared with group B, [b]P<0.05.

Table 6
Recovery time and hospital stay length.

Item	Group A (n=53)	Group B (n=53)	Group C (n=53)	F	P
Recovery time of urine amylase ($\bar{x}$ ± s, d)	7.49±0.89	7.26±0.85	5.73±0.64[ab]	10.688	0.0001
Recovery time of bowel sound ($\bar{x}$ ± s, d)	5.76±0.73	5.83±0.79	2.45±0.31[ab]	23.975	0.0001
Recovery time of exhaust ($\bar{x}$ ± s, d)	6.04±0.81	6.07±0.82	2.69±0.42[ab]	18.709	0.0001
Remission time of abdominal pain ($\bar{x}$ ± s, d)	3.58±0.45	3.65±0.46	1.87±0.29[ab]	21.427	0.0001
Hospital stay length (± s, d)	18.61±2.29	18.78±2.34	15.24±1.76[ab]	6.834	0.0001

Compared with group A, [a]P<0.05; compared with group B, [b]P<0.05.

groups A and B, and the difference was statistically significant (P<0.05). No statistically significant difference was found in the incidence rate of adverse reactions among the three groups (P>0.05) (Table 7).

DISCUSSION

In recent years, the theories of pancreatic autodigestion, pancreatic microcirculation disorder, the excessive response of inflammatory mediators and intestinal bacterial translocation have been recognized as the pathogeneses of AP [5]. Therefore, patients with AP are often treated by relieving the pancreatic autodigestion and inflammatory response, and improving the pancreatic microcirculation and intestinal flora balance. As a peptide hormone containing 14 amino acids, somatostatin has been confirmed to possess a potent inhibitory effect on the secretion of gastric acid and pepsin. It can also inhibit pancreatic autodigestion *via* various ways, the most direct of which is to inhibit pancreatic secretion by reducing the content of pancreatic enzyme, thereby weakening its digestive function. Moreover, the Oddi's sphincter preventing the discharge of pancreatic juice out of the body, is also relaxed, thus promoting the discharge of pancreatic juice [6]. Toxic substances in human blood, including endogenous and exogenous poisons and their metabolites, are adsorbed by hemoperfusion through a large number of active adsorbents in a circulation perfusion device placed outside the body, so that the toxic substances are effectively discharged out of the body, and not ingested by organs, thus purifying the blood [7].

Massive secretion of pancreatic enzymes leads to autodigestion of the pancreas and its surrounding tissues and organs, during which a large number of inflammatory mediators are quickly released in local lesions and penetrate the bloodstream, thereby inducing a strong systemic inflammatory response [8]. Then the inflammatory response worsens the damage to the pancreas and its surrounding tissues. TNF-α released by monocyte-macrophages upon the stimulation of various factors is considered the primary mediator inducing the inflammatory response. During pancreatic injury, TNF-α promotes the release of a variety of inflammatory mediators through activating multiple cells, thus leading to chain reactions [9]. The pro-inflammatory cytokine IL-18 produced by the activation of monocytes and macrophages can bind to the receptor to induce the expressions of various ILs and

Table 7
Clinical treatment outcomes and adverse reactions.

Item	Group A (n=53)	Group B (n=53)	Group C (n=53)	χ^2	*P*
Total response rate (%)	67.92	60.38	90.57[ab]	15.799	0.015
Cured (case)	6	5	11		
Markedly effective (case)	12	10	19		
Effective (case)	18	17	18		
Ineffective (case)	17	21	5		
Incidence rate of adverse reactions (%)	7.55	9.43	5.66	0.541	0.763
Acute respiratory distress syndrome (case)	2	3	2		
Upper gastrointestinal bleeding (case)	1	0	1		
Shock (case)	1	2	0		

Compared with group A, [a]P<0.05; compared with group B, [b]P<0.05.

chemokines, ultimately inducing the inflammatory cascade [10] As an anti-inflammatory, cytokine IL-10 is able to inhibit the proliferation and differentiation of immune cells, thereby hindering the progress of inflammatory respons [11] The inflammatory factor sICAM-1 with the function of immunoglobulin can act on leukocytes to promote their adhesion, aggregation and penetration through endothelial cells, so that they can reach the site of inflammation, thereby enhancing the inflammatory response [12] When trauma or infection becomes worse, large amounts of PCT will be released into the blood, and its level is positively correlated with the severity of disease [13]. The late inflammatory mediator HMGB1 can enhance the inflammatory response through various pathways, ultimately amplifying the inflammation [14]. In this study, somatostatin and early hemoperfusion could effectively suppress the secretion and release of pro-inflammatory factors in patients with AP, and promote the release of anti-inflammatory factors, thereby inhibiting the inflammatory response. Moreover, somatostatin combined with early hemoperfusion had a more significant effect, indicating that there is a synergistic effect between somatostatin and hemoperfusion, which effectively lowers the severity of AP in patients, consistent with the results of multiple previous reports [15].

Stress response is involved in the occurrence and development of AP. Pancreatic autodigestion-induced damage of the pancreas and its surrounding tissues and systemic inflammatory response can trigger the body's stress state. During this process, the body's oxidation/antioxidation imbalance and massive release of oxygen free radicals directly cause vascular endothelial injury and vascular hyperconstriction, thus leading to ischemia and even irreversible necrosis of tissues and organs. In addition, the secretion of various stress hormones will be enhanced due to the up-regulated activity of the hypothalamus-pituitary-adrenal axis [16]. Therefore, the content of oxidative factors LHP and AOPPs, antioxidant factors CAT and GSH-Px, and stress hormones E and COR can objectively reflect the stress state and the severity of the disease in patients. In this study, the results revealed that somatostatin and hemoperfusion could balance the oxidation/antioxidation state and regulate the neuro-endocrine function in patients with AP through up-regulating antioxidant factors and down-regulating oxidative factors and stress hormones, so that the patient's systemic stress was alleviated. Besides, the synergistic effect of somatostatin and hemoperfusion was more significant. When the intestinal mucosa epithelium and its barrier function are damaged, the intestinal bacterial ferment D-lac and the highly-active endonuclease DAO can enter the blood circulation. At the early stage of intestinal barrier dysfunction, ET can translocate, leading to intestinal endotoxemia and the release of inflammatory factors, and worsening the systemic inflammatory response in patients. In this study, somatostatin and hemoperfusion could reduce the levels of serum D-lac, DAO and ET in patients, indicating that both treatment methods have a protective effect on the intestinal mucosal barrier function in patients with AP. Additionally, the combination of them has a better protection effect.

The results are consistent with previous literature reports [17], i.e. somatostatin can reduce the endotoxin level through activating the liver reticuloendothelial system and enhancing its phagocytosis, thereby improving the endotoxemia symptoms. In addition, such an effect is related to the ability of hemoperfusion to scavenge endogenous and exogenous poisons and their metabolites [18]. In this study, it was found that somatostatin and hemoperfusion could improve the hemorheological indices of patients with AP to different degrees. It is speculated that the reason is closely related to the ability of somatostatin to effectively weaken the release of platelet-activating factors and reduce vascular permeability, and the ability of hemoperfusion to purify the blood. Besides, in the

group C, the recovery time of urine amylase, bowel sound and exhaust, remission time of abdominal pain and length of stay were all shorter than those in groups A and B, and the total clinical response rate was higher than that in groups A and B. It can be seen that somatostatin combined with hemoperfusion is more conducive to the recovery of patients and can improve clinical efficacy.

In conclusion, somatostatin combined with early hemoperfusion can effectively reduce the inflammatory and stress responses, protect the intestinal mucosal barrier function, and improve the hemorheology in the treatment of AP, thereby promoting recovery and benefitting the prognosis of patients. Such therapy has essential practical application value in clinical practice, which is worthy of popularization in the future.

ACKNOWLEDGEMENTS

We thank all coauthors for their significant contributions.

Conflict of interest

None to declare

Funding/Support

This study was not financially supported.

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Authors' contributions

HZ and JH designed this study and significantly revised this paper; BY, YF, DZ and YL performed this study, analyzed clinical data and drafted this paper. All authors have approved the submission and publication of this paper.

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