CORRELATION BETWEEN SERUM PAF, G-CSF, AND SE-SLT LEVELS AND SEVERITY OF ACUTE PANCREATITIS

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ABSTRACT

Objective: *To analyze the correlation between the changes of serum platelet activating factor (PAF), granulocyte colony stimulating factor (G-CSF), and soluble E-selectin (SE-SLT) in patients with acute pancreatitis (AP).*

Methods: *Seventy-two cases of AP patients in our hospital from August 2019 to July 2020 were selected and divided into a mild acute pancreatitis group (MAP group) with 36 cases and a severe acute pancreatitis group (SAP group) with 36 cases; 72 healthy people were selected as the normal control group. The Ranson score, CTSI, Balthazar CT grade, and levels of serum PAF, G-CSF, and SE-SLT were compared and analyzed between the MAP group and the SAP group, as well as the control group. Spearman correlation was also used to analyze the correlation between serum PAF, G-CSF, SE-SLT, and severity of disease.*

Results: *Compared with the normal control group, the levels of PAF, G-CSF, and SE-SLT in the MAP group and the SAP group were significantly higher (P<0.05), and the levels of PAF, G-CSF, and SE-SLT in the SAP group were significantly higher than those in the MAP group (P<0.05). The levels of serum PAF, G-CSF, and SE-SLT in the SAP group were significantly higher than those in non-death group (P<0.05). Compared with the normal control group, the Ranson score and cts of the MAP group and the SAP group were significantly increased (P<0.05), and the SAP group was significantly higher than the MAP group, and the difference was statistically significant (P<0.05); the serum PAF, G-CSF, and SE-SLT in the MAP group and the SAP group were significantly positively correlated with Ranson score and CTSI (P<0.05).*

Conclusion: *The serum levels of PAF, G-CSF, and SE-SLT are higher in patients with acute pancreatitis, and they are related to the severity of the disease and the prognosis. It is of great importance to evaluate the severity of acute pancreatitis and use that information as a guide to clinical diagnosis, treatment, and prognosis.*

Keywords: *Acute pancreatitis, PAF, G-CSF, SE-SLT, severity, correlation.*

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Introduction

The main clinical features of acute pancreatitis (AP) are acute, severe upper-abdominal pain; vomiting; nausea; and elevated pancreatin. Different locations of pancreatic lesions can cause pain in different parts of the abdomen. Pancreatic head lesions cause pain mainly in the right upper abdomen that radiates to the right shoulder. If the lesion is in the tail of the pancreas, the reverse is true[(1)]. The severity of AP varies, and mild cases (about 80% of patients) can be cured without an operation by using the routine clinical treatment of symptomatic internal medicine. In severe cases, the disease progresses rapidly, and the mortality rate is high; these include non-reversible and self-limited pancreatic inflammation and must be treated by surgery, as is the case for about 20% of AP patients[(2)].

At present, the pathogenesis of AP is not clear. Previous studies have found that most cases in China are caused by biliary tract diseases, while scholars elsewhere believe that alcoholism is the main cause besides biliary tract diseases. In recent years, some scholars have found that the early stage of AP is marked by systemic inflammatory response, and the pathogenesis is closely related to inflammatory factors. Platelet activating factor (PAF), as a marker of platelet activation, is involved in the pathological process of pancreatic microcirculation disorder, which can promote the aggregation of platelets in the pancreatic vessels and cause pancreatic circulation disorder. Granulocyte colony stimulating factor (G-CSF) is a glycoprotein growth factor that can regulate the proliferation, differentiation, and activation of hematopoietic cells in vivo. It has been used effectively for the treatment of granulocytopenia and other symptoms in clinical practice.

The level of soluble E-selectin (SE-SLT) can reflect the activation status of vascular endothelial cells in vivo, which is of great significance for the development of AP and the occurrence of organ failure. However, there have been few reports on the expression of serum PAF, G-CSF, and SE-SLT in patients with acute pancreatitis and their clinical significance. Therefore, this study aimed to explore the correlation between changes in serum PAF, G-CSF, and SE-SLT and the severity of the disease.

Materials and methods

General information

This study was conducted with the approval of the hospital ethics committee. Seventy-two patients with AP who came to our hospital from August 2016 to September 2017 were selected as the research subjects. According to the clinical diagnosis and classification criteria of mild and severe pancreatitis in the guidelines formulated by the Pancreatology Group of the Digestive Diseases Society of Chinese Medical Association, patients were divided into a mild acute pancreatitis group (MAP group) with 36 cases and a severe acute pancreatitis group (SAP group) with 36 cases[3].

The inclusion criteria were:

• Characteristic abdominal pain of acute pancreatitis[4];

• Serum amylase and/or lipase ≥3 times the upper limit of normal value; characteristic CT findings of acute pancreatitis (diffuse pancreatic volume enlargement or only lesion site enlargement, lesion site density is lower than normal pancreatic tissue). The CT grade of the MAP group was below D, and that of SAP group was above D.

The exclusion criteria were:

• Diseases of the vascular, blood, and immune systems;

• Recent use of hormone drugs;

• Tumors, autoimmune disease, drug use, and traumatic AP;

• Severe heart, liver, and renal insufficiency;

• Systemic diseases such as diabetes and chronic inflammation;

• Pregnancy and lactation.

In addition, 72 healthy subjects without any organic lesions or infection were selected as the normal control group. Patients and their family members agreed to participate in this study, and informed consent was obtained. There was no statistical significance in gender, age, and other general data among the three groups (P>0.05), which showed comparability (see Table 1).

Group	n	Gender (M/F)	Age (year)	BiliaryAP	Hyperlipidemic AP
MAP	36	21/15	56.87±12.42	22 (61.11)	14 (38.89)
SAP	36	19/17	57.86±12.12	17 (47.22)	19 (52.78)
Control g	72	42/30	56.78±13.01	-	-
χ^2/F		0.340	0.092	1.399	0.0708
P		0.844	0.911	0.237	0.9652

Table 1: Comparison and analysis of three groups of general data ($\bar{x}\pm s$).

Serological sample collection

After admission, all patients underwent feeding, gastrointestinal decompression, fluid supplementation, inhibition of pancreatic secretion, inhibition of trypsin activity, and treatment and nursing according to medical advice. According to the principle of aseptic operation, 5 mL of fasting venous blood was collected from the MAP group and the SAP group after admission. These blood samples were kept at room temperature for 2 hours and centrifuged at 3000 r/min for 10 minutes; then the upper serum was collected and stored at -20 °C for measurement. In the normal control group, venous blood was extracted during physical examination and treated and stored in the same way.

Observation indexes

Enzyme-linked immunosorbent assay (ELISA), purchased from Shanghai Hengyuan Biochemical Reagents Co., Ltd., was used to determine the

changes in serum levels of PAF, G-CSF, and SE-SLT.

The Ranson score, CTSI, and Balthazar CT score of the MAP group, SAP group, and normal control group were recorded. Specific criteria for determining the Ranson score are shown in Table 2; the highest possible total score is 11 points. The higher the score, the higher the severity of the patient's disease and the higher the mortality. The Ranson score is derived from metrics at admission and 48 hours after admission. Balthazar CT classification is divided into five grades: A, B, C, D, and E. Each grade is classified according to the CTSI scoring standard; the CT severity index (CTSI) is equal to the severity grade of acute pancreatitis plus the degree of pancreatic necrosis.

Indicators	score
Indicators at admission	
Age >55year	1 point
Blood glucose >11.1mmol/L	1 point
AST >250U/L	1 point
LDH >350U/L	1 point
WBC >13× 10^9/L	1 point
Indicators at admission after 48h	
Ca^+ <2mmol/L	1 point
PaO_2 <60mmHg	1 point
Base deficit >4mmol/L	1 point
Blood BUN >1mool/L	1 point
HCT >10%	1 point
Fluid loss >6L	1 point
Total	

Table 2: Ranson score.

Project	score
Severity grading	
Grade A: Normal pancreas	0 point
Grade B: localized exudative enlargement of the pancreas	1 point
Grade C: abnormal pancreatic parenchyma with mild peri-pancreatic inflammatory changes	2 points
Grade D: Monopancreatic effusion with cellulitis, usually in the anterior renal space	3 points
Grade E: multiple areas of peripancreatic effusion, or inflammation in the pancreas, peripancreatic accumulation of gas	4 points
Degree of pancreatic necrosis (% pancreatic necrosis)	
0%	0 point
<30%	2 points
30%-50%	4 points
>50%	6 points

Table 3: Balthazar-CTSI score.
Note: There are 3 grades of severity: Grade I, 0-3 points; Grade II, 4-6 points; Grade III, 7-10 points. Anything above Grade I is considered severe.

Statistical analysis

The statistical software SPSS 20.0 was used for data statistics, and the measurement data was expressed as standard deviation ($\bar{x}\pm s$). The t-test was used for comparison between the two groups, and one-way analysis of variance was used for comparison between multiple groups.

Spearman correlation analysis was used for the correlation between changes in serum PAF, G-CSF, and SE-SLT levels and the severity of the disease. The comparison between the data was statistically significant if P<0.05.

Results

Comparison of serum levels of PAF, G-CSF, and SE-SLT among the three groups

Compared with the normal control group, serum PAF, G-CSF, and SE-SLT levels in the MAP group and the SAP group were significantly increased (P<0.05); the levels of serum PAF, G-CSF, and SE-SLT in the SAP group were significantly higher than those in the MAP group, and the difference was statistically significant (P<0.05), as shown in Table 4.

Group	n	PAF (pg/ml)	G-CSF (μg/ml)	sE-SLT (ng/ml)	Hyperlipidemic AP
Control group	72	40.69±17.12	46.33±1.40	12.69±2.51	14 (38.89)
MAP group	36	71.34±12.56*	172.36±17.58*	69.66±6.88*	19 (52.78)
SAP group	36	112.87±26.85*#	214.63±28.32*#	85.74±15.49*#	-
F		21.158	24.418	148.701	0.0708
P		<0.001	<0.001	<0.001	0.9652

Table 4: Comparative analysis of serum levels of PAF, G-CSF, and SE-SLT in the three groups ($\bar{x}\pm s$).
*Note: *means compared with normal control group, P<0.05 and #means compared with MAP group, P<0.05.*

Comparison of PAF, G-CSF, and SE-SLT levels in SAP patients with different outcomes

The levels of serum PAF, G-CSF, and SE-SLT in SAP patients with disease and death were significantly higher than those in the non-disease and non-death group, and the difference was statistically significant (P<0.05), as shown in Table 5.

Comparison of Ranson scores and CTSI among the three groups

Ranson score and CTSI were significantly higher in the MAP and SAP groups compared with normal controls (P<0.05). The SAP group was significantly higher than the MAP group, and the difference was statistically significant (P<0.05), as shown in Table 6.

Group	n	PAF (pg/ml)	G-CSF (μg/ml)	sE-SLT (ng/ml)
Non-disease group	9	85.26±10.48	192.37±23.11	83.23±12.02
Death group	27	110.26±27.48	210.45±26.03	75.48±11.60
t		2.644	2.875	2.165
P		0.012	0.007	0.038

Table 5: Comparison of PAF, G-CSF, and SE-SLT levels in SAP patients with different ($\bar{x}\pm s$).

Group	n	Ranson score (point)	CTSI (point)
Control group	72	1.00±0.001	0.001±0.001
MAP group	36	20.19±2.23*	21.01±2.21*
SAP group	36	24.89±3.51*#	25.32±3.34*#
F		1031.266	1024.833
P		<0.001	<0.001

Table 6: Ranson score and CTSI comparative analysis of the three groups ($\bar{x}\pm s$).
*Note: *means compared with normal control group, P<0.05 and #means compared with MAP group, P<0.05.*

Spearman correlation analysis

Spearman correlation analysis showed that serum PAF, G-CSF, and SE-SLT levels in the MAP group and SAP group were significantly positively correlated with Ranson score and CTSI (P<0.05), as shown in Table 7.

Evaluation parameter	PAF		G-CSF		sE-SLT	
	r	*P*	*r*	*P*	*r*	*P*
Ranson score	0.269	0.017	0.635	0.023	0.723	0.013
CTSI	0.482	0.001	0.586	0.031	0.589	0.045

Table 7: Correlation analysis of serum PAF, G-CSF, and SE-SLT levels with Ranson score and CTSI in AP patients ($\bar{x}\pm s$).

Discussion

AP is a common acute abdominal disease in general surgery. When patients develop the disease, a large amount of trypsin in the body is activated in the pancreas, which causes the digestion and edema of the pancreatic tissue itself, which leads to ischemia and necrosis. MAP patients have mild symptoms, self-limited, good prognosis, and low mortality, while SAP patients have a more serious clinical course, often accompanied by organ dysfunction or necrosis, abscess or false abscess, and other local complications, with a high mortality and high risk factor[5]. Therefore, it is of great clinical value to accurately judge the early condition of AP, grasp the developmental direction of the disease as far as possible, and develop a complete and reasonable treatment plan. At present, biomarker assessment, multi-organ parameter assessment, and diagnostic imaging are common assessment categories. In terms of biomarkers, how to use more sensitive indicators for early detection of AP, accurately identify and judge the severity of the disease, and improve the prognosis have always been the goals of clinical research. Serum PAF is a bioactive, endogenous phospholipid and the strongest platelet inducer known at present[6].

It can promote platelet adhesion, lead to the formation of pancreatic microvascular circulation thrombosis, cause pancreatic circulation disorder, and stimulate the production of other cytokines and inflammatory transmitters[7]. Severe AP can lead to multiple organ dysfunction, and PAF is a key cytokine involved. Some studies have shown that PAF is a key mediator involved in systemic inflammatory response syndrome, and its microcirculation disturbance is one of the main causes of ASP[8]. G-CSF is a bone marrow hematopoietic proliferation factor, which can stimulate the proliferation and differentiation of granulocytes and enhance the function of mature granulocytes, and plays an important role in the non-specific immune process[9]. Clinically, G-CSF is mainly used to prevent and treat bone marrow hematopoietic dysfunction and myelodysplastic syndrome, prevent the potential infection complications caused by leucopenia, and accelerate recovery from neutropenia caused by infection[10]. Relevant data have shown that serum G-CSF level in AP patients can rise rapidly with the severity of the disease and decrease to normal levels after inflammation and infection control[11].

As a member of the cell selectin family, SE-SLT is a cell adhesion molecule, which mainly mediates the initial adhesion between polymorphonuclear leukocytes and endothelial cells[12]. SE-SLT is only actively expressed in activated vascular endothelial cells, and its content will increase rapidly when endothelial cells perceive the stimulation from inflammatory factors. Relevant data show that SE-SLT can be used as an indicator to judge the severity and prognosis of systemic inflammatory response syndrome[13].

The results of this study showed that the levels of serum PAF, G-CSF, and SE-SLT in the MAP group and the SAP group were significantly higher than those in the control group (P<0.05), and the SAP

group was significantly higher than the MAP group (P<0.05); the levels of serum PAF, G-CSF, and SE-SLT in the disease-death group were significantly higher than those in the non-death group (P<0.05), suggesting that serum PAF, G-CSF, and SE-SLT are involved in the occurrence and development of AP and can predict the condition of AP patients to a certain extent. Spearman correlation analysis showed that serum PAF, G-CSF, and SE-SLT levels in the MAP group and the SAP group were significantly positively correlated with Ranson score and CTSI (P<0.05). The Ranson score is the earliest scoring system used to predict the severity of acute pancreatitis, and the higher the total score, the more severe the disease is[14]. Balthazar CT grading can assess the condition of AP patients and predict their prognosis accurately. The combination of the two items can best reflect the overall situation and local lesions of AP patients, and monitor the severity of the disease[15]. These results suggest that serum PAF, G-CSF, and SE-SLT can play a positive guiding role in clinical treatment and prognosis evaluation of patients with AP.

In conclusion, changes in serum levels of PAF, G-CSF, and SE-SLT in AP patients have important effects on pancreatic function and are significantly correlated with the severity of the disease. Detection of these factors is conducive to timely evaluation and monitoring of pancreatic function and prognosis recovery in AP patients. However, due to the limited samples in this study, the results will be deviated to a certain extent, which makes further analysis and research necessary.

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