CHANGES AND CLINICAL SIGNIFICANCE OF OBESTATIN, PAF, M30 AND M65 LEVELS IN PATIENTS WITH SEVERE PANCREATITIS

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ABSTRACT

Objective: *To analyze the clinical significance of Obestatin, platelet activating factor (PAF), M30 and M65 levels in patients with severe acute pancreatitis.*

Methods: *From January 2017 to February 2018 in our hospital patients with digestive internal medicine clinic of SP 82 cases, including 41 patients with MAP for MAP groups, 41 patients with SAP for SAP group, and 41 healthy adults in the physical examination center of our hospital during the same period were the control group. Comparing the changes of the three groups of Obestatin, interleukin 1 (IL-1β), tumor necrosis factor alpha (TNF-α), PAF, M30, M65, and interleukin - 17 (IL-17).*

Results: *Obestatin, IL-1β and TNF-α levels in MAP group and SAP group were significantly higher than those in the control group, and Obestatin, IL-1β and TNF-α levels in MAP group were significantly lower than those in SAP group, with statistically significant differences (P<0.05). PAF levels of patients in the MAP group and the SAP group were significantly higher than those in the control group, and PAF levels of patients in the SAP group were significantly higher than those in the MAP group, with statistically significant differences (P<0.05). The serum M30 and M65 levels of patients in the MAP group and SAP group were significantly higher than those in the control group, and the M30/M65 ratio was significantly lower than that in the control group. Obestatin, PAF, M30 and M65 have good specificity and sensitivity in the diagnosis of patients with acute pancreatitis. Obestatin is positively correlated with PFA, M30 and M65 levels in patients with ASP (P<0.05).*

Conclusion: *The levels of Obestatin, PAF, M30 and M65 in SAP patients have important diagnostic value in determining the severity of SAP patients, which is conducive to the selection of early treatment measures, effective control of inflammatory response, prevention and treatment of complications, and reduction of mortality.*

Keywords: *Severe acute pancreatitis, obestatin, PAF, M30, M65, clinical significance.*

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Introduction

Acute pancreatitis(AP) is clinically common acute abdominal disease, mainly for acute upper abdominal pain, fever, nausea, vomiting, etc., mainly divided into mild acute pancreatitis and severe acute pancreatitis[1]. Mild acute pancreatitis (MAP) is self-limiting, prognosis is good. Under the action of inflammatory reaction medium, 21% ~ 28% of patients develop severe acute pancreatitis (SAP)[2], with onset nasty, fast development, have different degree of pathological changes, poor prognosis and difficult to cure, easy cause sepsis, multiple organ failure and fatality rate of 40%[3]. Obestatin is believed to promote the survival of islet B cells and inhibit the development of pancreatitis[4]. Platelet Activation Factor (PAF) is an endogenous inflammatory mediator, which is an important diagnostic criterion for SAP[5]. M30 can recognize keratin 18 after activation and cleavage[6]. M65 can detect the death of islet cells[7]. Therefore, this study will investigate the changes and clinical significance of Obestatin, PAF, M30 and M65 levels in patients with severe acute pancreatitis.

Data and methods

Research objects

A total of 82 SP patients admitted to the department of gastroenterology of our hospital from January 2017 to February 2018 were selected, including 41 MAP patients in the MAP group and 41 SAP patients in the SAP group.

Inclusion criteria:

• All met the diagnostic criteria formulated by the Chinese medical association;

• All were admitted to hospital within 24 h after onset;

• AP was diagnosed by CT examination.

• Informed consent was signed with the consent of patients and their families;

• Approved by the hospital ethics committee.

Exclusion criteria:

• Exclusion of primary liver, kidney and endocrine diseases;

• Patients with other malignant tumors, organ dysfunction and systemic complications were excluded. 41 healthy adults were selected as the control group.

In the MAP group, there were 20 males and 21 females, with an average age of 41.15±1.05 years old. There were 22 males and 19 females in SAP group, with an average age of 40.85±1.35 years old. In the control group, there were 21 males and 20 females, with an average age of 41.05±1.09 years old. There was no significant difference in gender and age between the three groups (P>0.05). See table 1.

Group	*n*	Gender		Age/years old
		Male	Female	
MAP	41	20	21	41.15±1.05
SAP	41	22	19	40.85±1.35
Control	41	21	20	41.05±1.09
χ^2/F		0.195		0.700
P		0.907		0.500

Table. 1: Comparison of three groups of general data.

Methods

Obestatin, PAF, M30 and M65 in the control group and AP patients were determined by solid phase sandwich ELISA in a professional laboratory and in accordance with the ELISA kit instructions. In the early morning of the first day of admission, 6mL peripheral venous blood of AP patients was extracted, centrifuged at 2000 r/min for 20 min, and placed in anticoagulant tubes. Serum was separated and stored in a refrigerator at -30 °C for centralized detection. The treatment measures of the control group were consistent with the above.

Observation Indexes

• Changes in serum indicators: obestatin levels were determined by Enzyme Linked Immuno Sorbent Assay(ELISA), and Radioimmunoassay(RIA) was used to determine changes in interleukin-1β and Tumor Necrosis Factor(TNF-α) levels.

• Changes in PAF, M30 and M65 levels: changes in PAF, M30 and M65 levels were determined by enzyme-linked immunosorbent assay.

• The assay value of interleukin-17 (IL-17) and M65 levels in acute pancreatitis patients was analyzed.

• Analyze the correlation of Obestatin, PAF, M30 and M65 in SAP patients.

Statistical methods

SPSS13.0 software package was used for statistical analysis of the data. Measurement data were represented by ($\bar{x}\pm s$) and t-test was adopted.One-way anova and χ^2 test were used for comparison among multiple groups, P<0.05 was considered as statistically significant difference. The specificity and sensitivity of M65 and IL-17 were analyzed by ROC curve, and the diagnostic threshold value of specificity index was calculated by yoden index. P<0.05 was considered as statistically significant difference. Pearson correlation test was used for correlation analysis.

Results

Three groups of Obestatin, IL-1β and TNF-α levels

The levels of Obestatin, IL-1β and TNF-α in the MAP group and SAP group were significantly higher than those in the control group, and the levels of Obestatin, IL-1β and TNF-α in the MAP group were significantly lower than those in the SAP group, and the difference was statistically significant (P<0.05); See table 2.

Group	*n*	Time/Day	Obestatin/ng/mL	IL-1β/ng/mL	TNF-α/ng/mL
Control	41	1	4.88±1.50	1.53±1.30	2.53±1.30
MAP	41	1	6.90±1.49*	2.84±1.46*	4.65±1.75*
SAP	41	1	9.99±1.64#△	4.77±1.73#△	7.52±1.96#△

Table. 2: Comparison of three levels of Obestatin, IL-1β and TNF-α.

*Note: *,#indicates comparison with the control group, P<0.05; △indicates that compared with the MAP group at the same time, P<0.05.*

Comparison of three groups of PAF levels

The PAF level of patients in MAP group and SAP group was significantly higher than that in the control group, and the PAF level in SAP group was significantly higher than that in MAP group (P<0.05), see Table 3.

Group	*n*	Time/Day	PAF/pg/mL
Control	41	1	3.19±2.28
MAP	41	1	13.07±1.58
SAP	41	1	26.11±1.06

Table. 3: Comparison of three groups of PAF levels.

Comparison of three groups of M30, M65 level and M30/M65 ratio

The levels of serum M30 and M65 in the MAP group and SAP group were significantly higher than those in the control group. The M30/M65 ratio was significantly lower than that in the control group, and the M30 and M65 levels in the SAP group were significantly higher than those in the MAP group. The difference was statistically significant (P<0.05). The ratio of M30/M65 in SAP group was lower than that in MAP group, the difference was not statistically significant (P>0.05), see Table 4.

Group	Time/Day	M30/ng/L	M65/ng/mL	M30/M65
Control (*n*=41)	1	117.79±22.53	425.57±73.49	0.277±0.032
MAP(*n*=41)	1	188.15±35.38[a]	1001.27±92.35[a]	0.188±0.022[a]
SAP(*n*=41)	1	235.58±42.94[ab]	1559.34±114.57[ab]	0.151±0.009[ab]

Table. 4: Comparison of three groups of M30, M65 levels and M30/M65 ratio.
Note: a means P<0.05 compared with the control group; B means P<0.05 compared with MAP group.

To analyze the detection value of Obestatin, PAF, M30 and M65 levels in AP patients

Obestatin, PAF, M30 and M65 curves have an area under the curves of 0.784 (95%CI: 0.713~0.804), 0.798 (95%CI: 0.704~0.893), 0.839 (95%CI: 0.767~0.844) and 0.756 (95%CI: 0.678~0.835), respectively, with the optimal cut-off point of 3780.61U/L. Obestatin, PAF, M30, and M65 test showed specificity of 93.21%, 93.20%, 96.40%, and 100% of AP patients, respectively, and sensitivity of 89.30%, 83.30%, 86.41%, and 26.70%, respectively. All four patients showed good specificity and sensitivity in the diagnosis of acute pancreatitis, as shown in table 5.

Serum indexes	Specificity/%	Sensitivity/%	Positive predictive value /%	Negative predictive value /%
Obestatin	93.21	89.3	90.36	93.26
PAF	93.2	83.3	90.21	84.61
M30	96.4	86.41	95.57	86.77
M65	100	26.7	93.61	79.2

Table. 5: Detection value of IL-17 and M65 levels in patients with acute pancreatitis.

Correlation analysis of Obestatin, PAF, M30 and M65 in SAP patients

Pearson analysis showed that Obestatin was positively correlated with PFA, M30 and M65 levels in SAP patients (P<0.05), as shown in table 6.

Serum indexes	Obestatin	PAF	M30	M65
Obestatin	-	0.651	0.762	0.534
PAF	0.568	-	0.544	0.568
M30	0.645	0.68	-	0.836
M65	0.873	0.738	0.721	-

Table. 6: Correlation of Obestatin, PAF, M30 and M65 in SAP patients.

Discussion

AP is a common pancreatic disease in clinic, which is mainly manifested as systemic inflammatory reaction. In the initiation and development of AP, about 25% of MAP patients developed into SAP[8]. Compared with MAP, SAP has a high incidence of complications, combined with local or systemic complications, resulting in sepsis, multiple organ failure, and a mortality rate of up to 40%. According to research, SAP is associated with inflammatory reactions, cell apoptosis and necrosis, and oxidative stress. Therefore, exploring the changes of serum levels of AP patients is crucial to improve the cure rate and reduce the mortality rate.

Obestatin is a new type of ghrelin related peptide extracted from the stomach. Its pharmacological and physiological effects are different from or even opposite to ghrelin, which can antagonize ghrelin's appetite stimulation, reduce jejunal contraction frequency and body mass, and slow down gastric empitation[9]. Obestatin inhibits the development of AP, improves the survival of islet B cells, and protects the pancreas. As a member of the Interleukin 1(IL-1) family, IL-1β is an inflammatory factor with immunomodulatory effects[10]. TNF-α is an important immune regulator in human body, which is mainly involved in inflammatory response and immune response[11]. The secretion of IL-1β and TNF-α can induce a cascade of inflammatory mediators and stimulate the development of AP. In this study, Obestatin, IL-1β, and TNF-α levels in MAP group and SAP group were significantly higher than those in control group on the first day after admission, P<0.05 was considered as statistically significant difference. PAF is a key mediator involved in inflammatory response, mainly located on the membranes of platelets, monocytes, endothelial cells and other cells, and increases its production through positive feedback[12].

It can mediate a series of signal transduction in cells, and have a chain reaction with other inflammatory factors and cytokines, forming neutrophils and platelets aggregation, causing endothelial injury, microcirculation disorder, and systemic inflammatory response syndrome[13]. In this study, on the first day after admission, PAF levels of patients in the MAP group and SAP group were significantly higher than those in the control group, with statistically significant differences (P<0.05). Moreover, PAF level of patients in SAP group was significantly higher than that in MAP group, indicating that PAF level was correlated with SAP severity. Cell Keratin 18(CK18) is a component of the hepatic cytoskeleton, a member of the intermediate filament protein family, and also serves as a tumor marker[14]. CK18 can be cleaved by the caspase system and enter the peripheral blood, which can be recognized by M30 in serum, reflecting the apoptosis of cells; M65 can detect the content of CK18 in serum, which can reflect the total amount of cell necrosis and apoptosis[15]; The ratio of M30/M65 reflects the ratio of the total amount of apoptotic cells to the total amount of necrosis and apoptosis. In the present study, on the first day of admission, the serum M30 and M65 levels in the MAP group and the SAP group were significantly higher than those in the control group, and the M30/M65 ratio was significantly lower than that in the control group (P<0.05). The levels of M30 and M65 in patients were significantly higher than those in MAP group, and the difference was statistically significant (P<0.05). Therefore, M30 and M65 have good diagnostic value for SAP. The specificity of Obestatin, PAF, M30 and M65 in detecting AP patients were 93.21%, 93.20%, 96.40% and 100%, respectively. The sensitivity was 89.30%, 83.30%, 86.41% and 26.70%, respectively. They have good specificity and sensitivity in the diagnosis of acute pancreatitis. Pearson analysis showed that Obestatin was positively correlated with PFA, M30 and M65 levels in ASP patients (P <0.05). Therefore, the levels of Obestatin, PAF, M30 and M65 in SAP patients have important diagnostic value in determining the severity of ASP patients, which is conducive to the selection of early treatment measures, effective control of inflammatory response, prevention and treatment of complications, and reduction of mortality.

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