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Original Article

Dynamic changes and clinical significance of serum IMD and PCT in patients with acute pancreatitis

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Abstract: To explore dynamic changes and clinical significance of serum IMD and PCT in patients with acute pancreatitis. According to acute pancreatitis guide, patients with acute pancreatitis were divided into mild acute pancreatitis (MAP group, n = 60) and severe acute pancreatitis (SAP group, n = 30). Serum IMD and serum PCT contents in MAP group and SAP group were detected in 24 hours, 48 hours, 72 hours and 7 days after admission, meanwhile APACHE II score was recorded within 24 hours; Healthy people in the same period were taken as the control group (NS group, n = 30); changes and differences in serum IMD and serum PCT were compared. Correlation analysis of serum IMD and PCT, IMD and APACHE II scores, PCT and APACHE II scores was performed. In MAP group and SAP group, PCT content increased over time, and the difference was significant ($P < 0.05$); PCT content in SAP group was significantly higher than that in MAP group; IMD content in MAP group and SAP group decreased over time; the difference was significant (P); IMD content in SAP group was significantly lower than that in the MAP group, and the difference was significant ($P < 0.05$); serum IMD content had a negative correlation with PCT, with a certain value for acute pancreatitis diagnosis; serum IMD content was negatively correlated with APACHE II score in MAP group and SAP group ($rs < 0$, $P < 0.05$). Serum PCT content showed a positive correlation with APACHE II score in MAP group and SAP group ($rs > 0$, $P < 0.05$). Serum IMD and PCT can be used as indicators of early diagnosis of acute pancreatitis, and also have a certain value in severe pancreatitis diagnosis.

Keywords: Acute pancreatitis, IMD, PCT

Introduction

Acute pancreatitis (AP) is the pancreatic self-digestion caused by many factors, further leading to pancreatic edema, hemorrhage, local necrosis and systemic inflammatory response. According to China's acute pancreatitis treatment guidelines (2013, Shanghai) [1], the clinical acute pancreatitis is divided into mild pancreatitis (MAP) and severe acute pancreatitis (SAP). Clinically MAP is more common, with (or without) local or systemic complications, mainly performing edematous pancreatitis in pathology, with stable condition and good prognosis; severe acute pancreatitis (SAP) is often accompanied by organ dysfunction or multiple organ failure, with a mortality rate of 36% to 50%, and the mortality rate is even higher when combined with SAP infection [2]. Early SAP diagnosis and appropriate treatment programs are important ways to reduce the mortality of severe pancreatitis. Early evaluation methods for acute pancreatitis include univariate evaluation system and multivariate evaluation system. Single factor evaluation system: IL-6, CRP and so on. Multi-factor evaluation system: Ranson score, APACHE II score and AP severity bedside index score (BISAP). Multifactorial scoring system is more complex, which cannot give a reasonable evaluation index within a short time. Therefore, a rapid detection indicator is needed in clinic, which can give a guidance indicator within a short period of time. Intermedin (IMD), as a newly discovered member of the calcitonin gene-related peptide superfamily, is similar to adrenomedullin (ADM) in biological function, also known as adrenal gland [2]. Studies have shown that, IMD can improve vascular endothelial barrier in inflammation and hypoxia-induced vascular leakage process, and plays an important role in improving human umbilical vein endothelial function [3]. In addition, studies have shown that IMD1-53 also plays an important role in improving rat acute lung injury and

Table 1. Acute pancreatitis patients and healthy population general information

Group	Gender (male/female)	Age (years)
MAP group	35/25	45.3 ± 10.6
SAP group	15/5	40.7 ± 12.5
NS group	15/15	43.2 ± 10.8

reducing inflammatory mediators [4]. Regarding the conclusion obtained from the animal experiment of this study: IMD may have a protective effect on rat pancreatic vascular endothelial cells, and play some role in improving pancreatic microcirculation; this experiment intends to study dynamic changes in serum IMD in patients with acute pancreatitis as well as to explore the role of serum IMD in the diagnosis of acute pancreatitis. Calcitonin is a common indicator of infection in clinical; it can assess clinical infectious diseases [5]. Some research confirmed that: PCT, CRP and APACHE II score played important roles in SAP diagnosis; in 24 hours the sensitivity was 56%, 69% and 46%, respectively; while in 48 h, the sensitivity of PCT, CRP and APACHE II score in the diagnosis of SAP was 67%, 100% and 49%. Therefore, PCT has an important value for the diagnosis of acute pancreatitis, particularly for the diagnosis of severe acute pancreatitis [6]. Therefore we want to study the role of serum PCT combined with IMD in the diagnosis of acute pancreatitis, and perform APACHE II score in patients with acute pancreatitis, in order to explore the correlation between the IMD and the PCT, IMD and APACHE II, and PCT and APACHE II, expecting to help the early diagnosis and treatment of severe pancreatitis.

Material and method

Patient selection

Inclusion criteria: One of the diagnostic criteria was as follows: acute abdominal pain; related changes in blood chemistry, serum AMS (amylase) and (or) serum Lipase activity at least three times higher than the value of their own; related imaging changes. Meanwhile collect the serum of healthy human accepting physical examination in HaiCi Hospital in the morning. In accordance with acute pancreatitis Guide [7], the acute pancreatitis patients were divided into two groups: mild acute pancreatitis group (MAP group) and severe pancreatitis group (SAP group).

Exclusion criteria: Exclusion criteria: exclude people suffering from infectious diseases; exclude people with acute infectious disease. Exclude people with chronic diseases.

General data

Statistical analysis of general data: General data of three groups of clinical populations were as follows: age and gender had no significant difference, which cannot indicate statistical significance ($P < 0.05$, **Table 1**).

The main testing laboratory parameters and clinical data: The disease data of clinical populations were collected: The main test data included AMS, serum IMD, serum PCT, routine blood test and other test indicators. The clinical data to be recorded: surface temperature measurements, heart rate, systolic and diastolic blood pressure, blood PH value and other important numeric manifestations of the crisis value. In accordance with APACHE II scores of critically ill patients, the sorting and statistics of clinical data were performed.

The main testing instruments and equipment as well as reagents and testing process

High-speed centrifuge (Shanghai sophisticated surgical instrument factory); microplate reader (US SUNRISE Company); PCT immunohistochemistry kit; IMD immunohistochemistry kit.

IMD testing process: IMD testing process: IMD detection principle: ELISA method, using double-antibody sandwich assay to measure serum IMD content; Testing process: the sample, standard product, and HRP antibodies were added in one time; after incubation and washing, TMB coloring was performed, and finally sample absorbance (OD) was detected at 450 nm on a microplate reader, and the sample concentration was calculated.

PCT testing process: PCT testing process: PCT detection principle: ELISA method, using double-antibody sandwich assay to measure the PCT content; Testing process: the sample, standard product, and HRP antibodies were added in one time; after incubation and washing, TMB coloring was performed, and finally sample absorbance (OD) was detected at 450 nm on a microplate, and the sample concentration was calculated.

Table 2. Serum IMD content in each group ($\bar{x}$ ± s, pg/ml)

Group	IMD serum content (pg/ml)			
	24 hours	48 hours	72 hours	7 days
MAP group	697.2 ± 421.7	427.7 ± 263.1	302 ± 226.9	526.4 ± 345.2
SAP group	597.2 ± 421.7	427.7 ± 26.1	226.1 ± 237.9	104.5 ± 55.9
NS group	809.5±206.4	-	-	-

Table 3. Test results of serum PCT ($\bar{x}$ ± s, pg/ml)

Group	Serum PCT content (pg/ml)			
	24 hours	48 hours	72 hours	7 days
MAP group	311.4 ± 58.8	265.5 ± 87.0	254.7 ± 63.1	173.8 ± 50.4
SAP group	1860.0 ± 1446.6	4586.4 ± 7006.1	4419.5 ± 6619.1	2986.9 ± 3233.18
NS group	80.4 ± 20.5	-	-	-

Statistical methods

SPSS17.0 statistical software was used for statistical analysis. The resulting data are presented as mean ± standard deviation ($\bar{x}$ ± s); single-factor analysis of variance was used for statistical analysis, test level = 0.05. Between the groups, pairwise comparisons were performed using the t test. Correlation analysis was performed using Pearson correlation analysis; $P < 0.05$ was considered statistically significant.

Results

IMD dynamic test results

Serum IMD level in severe pancreatitis group was significantly lower than that in mild pancreatitis group; serum IMD level in normal control group was higher than that in mild pancreatitis group and severe pancreatitis group; the difference was statistically significant ($P < 0.05$); serum IMD level in mild pancreatitis group gradually decreased with time, especially in 24 h and 48 h after admission; but serum IMD significantly increased in 7 d after admission, which was significantly higher than that in the 24 h and 48 h, with statistically significant differences ($P < 0.05$). The above conclusions were summarized: When mild acute pancreatitis patients admitted to hospital, serum IMD content decreased as the disease worsened; serum IMD content increased as the disease was alleviated (**Table 2**).

PCT dynamic test results

Serum PCT content in SAP group was significantly higher than that in MAP group and NS control group, and serum PCT content in MAP group was higher than that in NS control group; the difference was statistically significant ($P < 0.05$); serum PCT level in mild pancreatitis group gradually increased with time, especially in 24 h and 48 h after admission; but serum PCT decreased in 7 d after admission, which was significantly lower than that in the 24 h and 48 h, with statistically significant differences ($P < 0.05$). The above results were summarized: in MAP group, when patients were more sicker, serum PCT content increased; when the disease was relieved, the serum PCT content would be significantly reduced; while in SAP Group, the content of serum PCT increased as the disease worsened at the early stage, particularly in the 7th day, serum PCT content abnormally increased (**Table 3**).

APACHE II score

After patients accepted treatment in 24 h after admission, medical staff could conduct scoring: score results of MAP group and SAP group after 24 h of admission were respectively: 4.5 ± 1.8 and 15.2 ± 3.8; the scores of the two groups were compared; the score of SAP group was significantly higher than that of mild pancreatitis group, and the difference was statistically significant ($P < 0.05$).

Correlation analysis between APACHE II score and PCT, APACHE II score and IMD

In 24 h of admission, correlation coefficients between APACHE II score and IMD in MAP group and SAP group were respectively: -0.088, -0.117; correlation coefficients between

APACHE II score and PCT in MAP group and SAP group were respectively: 0.192, 0.231.

Correlation analysis between IMD and PCT

Correlation analysis between serum IMD and PCT in MAP group: There was a correlation between IMD and PCT in 24 h, 48 h, 72 h and 7 d; the correlation coefficients were: 0.713, 0.482, -0.106, -0.94.

Correlation analysis between serum IMD and PCT in SAP group: There was a correlation between IMD and PCT in 24 h, 48 h, 72 h and 7 d; the correlation coefficients were: -0.241, -0.456, 0.863, 0.3440.

Discussion

AP is a common acute abdomen in clinical; its clinical outcomes have large differences, which is mainly due to the different disease condition in clinical categories. MAP occupies a large proportion in the clinical classification, mainly because of mild local and systemic inflammatory response; while SAP is a more difficult case in clinical, with serious local and systemic inflammatory response, some multiple organ damage, and high mortality rate; its early diagnosis and treatment has been a serious problem. Accurate disease prediction and diagnosis and detailed analysis ideas require us to explore the index of accuracy. IMD is the newly discovered member of CGRP superfamily (CGRP), and has some similarities with adrenomedullin in function [8], so its biological function has been one focus of research. The researchers found that IMD was often expressed in human pituitary gland, kidney, lungs and other organs, and the researchers also confirmed that its concrete expression in these systems was associated with their biological function [9]. Studies have shown that: IMD has a protective effect on myocardial cells; exogenous IMD can significantly improve myocardial ischemia and restore heart function [10]. Similar situation was also found in the circulatory system: IMD can increase blood flow in renal blood vessels, meanwhile IMD can promote glomerular to produce the original urine, and repair the damage to the kidneys caused by a variety of inflammatory cytokines [11]. The biological functions of IMD in the digestive system also have been reported and confirmed: in SAP rat model, the researchers found that the expression of IMD has obvious relevance with cardiac metabolism; when exogenous IMD was injected, SAP rat mortality was significantly reduced and heart function significantly recovered [12]. The experiment showed that: IMD had obvious expression in pancreatic tissue, and serum IMD level in rats with severe pancreatitis was significantly lower than that in rats with mild pancreatitis; serum IMD level had a negative correlation with animal pancreatitis tissue score. This is also confirmed that rat endogenous IMD expression had a negative correlation with the severity of pancreatitis, which may have a protective effect on rat pancreatitis. Clinical studies of this experiment also showed that: serum IMD content in patients with pancreatitis decreased along with the aggravation and progression of pancreatitis, indicating that IMD change and changes in disease were contrary. This also indicated that: IMD may play an important protective role in the occurrence and development of the disease, especially bring important tool for the early diagnosis of clinical SAP. Acute Physiology and Chronic Health Evaluation (APACHE II score) is an important means to evaluate the condition of critically ill patients for ICU clinicians. Research has confirmed that: APACHE II score played an important role in early assessment of SAP especially systemic inflammation and clinical prognosis; With the score increased, SAP condition became worse. APACHE II score has the highest accuracy in 24 h after admission, so early evaluation is necessary. In this study, serum IMD content in 24 hours of admission was negatively correlated with APACHE II score, indicating that IMD played an important protective role for patients with acute pancreatitis, and brought hope to the clinical diagnosis.

PCT is the bioactive peptide secreted by thyroid C cells; it is secreted and released into the blood when the body has infectious disease, which is an indicator of inflammation and infection in clinic. Studies have shown that: serum PCT detection gives the type of pathogen infection, and clinicians often use it as the basis for medication [13]. In addition, animal studies showed that: SAP combined with infection can trigger the release of inflammatory mediators and serum PCT generation; dynamic serum PCT, as an important marker of the early diagnosis of severe pancreatitis with infection, has important clinical value [14]. Pancreatic necro-

sis infection is a major factor of the death in advanced patients, so early detection of serum PCT is very necessary [15]. In this clinical study, the serum PCT in SAP group was significantly higher than that in MAP group, and increased with disease aggravation; and it had a positive correlation with APACHE II score. This fully confirmed the important role of PCT in reflecting disease severity. This experiment cannot collect a large number of SAP patients in a short time, which brought a trouble to clinical studies. And the problem was not discussed at the genetic level; however, the studies in animal and clinical level confirmed the important role of IMD in reflecting the development and progression of acute pancreatitis. I believe that combined detection of serum IMD and PCT deserves more profound research and promotion.

Conclusion

IMD was expressed in the serum of patients with pancreatitis and normal human. IMD may have anti-inflammatory effect. Early detection of serum IMD has some significance.

Serum PCT: serum PCT has important meaning for the early detection of infectious diseases, and in the detection of acute pancreatitis, serum PCT also has statistical significance, indicating that serum PCT is important for predicting the prognosis of acute pancreatitis.

Serum IMD and PCT were positively and negatively correlated with APACHE II score in 24 h after admission respectively, indicating that serum PCT and IMD have obvious advantages at the early stage of disease.

There was a negative correlation between serum IMD and PCT; the two combination had a theoretical basis for early diagnosis of severe acute pancreatitis.

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Disclosure of conflict of interest

None.

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