Tumor necrosis factor-α and procalcitonin level variations in the serum and their effects on organ function in patients with severe acute pancreatitis during infected stage

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Abstract: To investigate the changes of tumor necrosis factor-α (TNF-α) and procalcitonin (PCT) in the serum and their effects on organ function in patients with severe acute pancreatitis (SAP) during infected stage, aiming to provide a reference to individual treatment. 32 patients with SAP during infected stage admitted to the Digestive Department of The Second Affiliated Hospital of Zhengzhou University from April 2014 to May 2015 and also 30 volunteer normal people were recruited in this study. And 26 patients detected with positive pathogenic bacteria were grouped into group A and another 6 patients with negative pathogenic bacteria into group B and 30 normal people into group C. And TNF-α and PCT level in the serum and the liver, kidney and lung function and the relationship between them of all the included people were compared and analyzed. the serum TNF-α level detected in the bile, urine and the surface of wound in group A was much higher than that in group B ($P<0.05$); and there was no significant difference in PCT between group A and group B; and TNF-α and PCT level in the serum in group A and group B were remarkably higher than group C ($P<0.05$). In addition, the organ function (the liver, kidney and lung) in the patients with high TNF-α level (High TNF-α group) was significantly different from the patients with low TNF-α level (Low TNF-α group) ($P<0.05$). And various organ functional indexes increased significantly in the patients with high PCT level ($P<0.05$). There were two kinds of TNF-α level (high level and low level) in the patients during SAP general infection stage, and the high level may reduce various organ function, the low level can contribute to the regular inflammatory response. And there is a high PCT level in the early SAP infection stage, which can be used to predict the patients' condition.

Keywords: Severe pancreatitis; Infection stage; TNF-α, PCT; Organ function.

INTRODUCTION

Severe acute pancreatitis (SAP) is a common emergent and severe disease, with complex pathogenesis, frequent changes in disease condition, high mortality. With the mechanism study on SAP, more and more people paid attention to the influence of inflammatory cytokines on SAP, and TNF-α and PCT released during the SAP infection stage were of significance to judge the condition and development of the disease in the patients (Luan *et al*, 2013; Zhu Q and Gong ZH, 2011). And in this study, 32 patients with SAP from April 2014 to May 2015 were recruited to explore the effect of TNF-α and PCT on the organ functions.

MATERIALS AND METHODS

General information

32 patients with severe pancreatitis who were treated in our hospital from April 2014 to May 2015 were selected as study subjects. Among the 32 patients, there was 19 males, aged between 32-71 years old and average aged (51.2±10.5) tears old; there was 13 females, aged between 35-78 years old, and average aged (51.2±10.5) years old.

Inclusion criteria: Patients who conform to the Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China in 2003 (Luan *et al*, 2013); patients with acute pancreatitis with local complications (such as pancreatic necrosis, pancreatic abscess) or organ failure (such as respiratory failure, circulatory failure); the PACHE-II ≥ 8 or Balthazar CT ≥ II.

Exclusion criteria: Patients with hypocalcemia and acute abdomen caused by other disease; patients with vague awareness and without language communication skills

All patients voluntarily joined this study with informed consents and the study had been approved by the Medical Ethics Committee of The Second Affiliated Hospital of Zhengzhou University.

Methods

Among32 patients were underwent drainage operation of necrosis, infectious tissues or pseudo cyst, 9 cases were underwent biliary drainage. Bacterial strains (bacteria or fungi) from the bile, urine, sputum and surgery wound surface in the patients during the general infection stage were collected and cultured every one day and the TNF-α and PCT in serum were detected. TNF-α and PCT level in the serum in 30 normal people were also detected.

Grouping

There were 26 cases who had been detected the bacterial strain (bacteria or fungi) in the bile, urine, sputum, or surgical wound surface divided into group A; and group B

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included 6 cases with negative bacterial strains in the various tissue fluids; and group C referred to the TNF-α and PCT level in 30 normal people. The activity of TNF-α and PCT between group A and group were compared and the level of TNF-α and PCT in the serum among group A, group B and group C. And organ function (the liver, kidney, lung) between High TNF-α group (>55U/ml) and low TNF-α group (≤55U/ml) were compared and analyzed.

Detection of TNF-α and PCT

Double Antibody- immunofluoresent assay (DAB-IFA) was used to detect PCT level in the serum, and Enzyme Linked Immunosorbent Assay (DAB-ELISA) was used to check TNF-α level in the serum (Cheng *et al*, 2012).

STATISTICAL ANALYSIS

SAPSS19.0 software was used to analyze the data, measurement data was expressed by Standard Deviation ($x \pm s$) and checked by T-test. Enumeration data was checked by χ^2. And $P<0.05$ was statistically significant.

RESULTS

TNF-α and PCT level changes in the patients

The findings in this study showed that the TNF-α level detected from the fluids (except the sputum) in group A was much higher than group B ($P<0.05$) and it had no significant difference in the serum PCT levels between group A and group B ($P>0.05$) and the serum TNF-α and PCT during SAP infectious stage in group A and group B were significant higher than group C. Seen in table 1.

The influence of TNF-α and PCT on various organ functions

The indicators of liver, kidney, lung in High TNF-α level group was significant different from Low TNF-α level group ($P<0.05$), taking on a contingent negative variation. And the functional parameter of various organs also significantly decreased in patients with high PCT level ($P<0.05$). And the organ function changes were mainly hepatic cell synthesis decrease and permeability increase, and the decrease of renal filtration function and pulmonary gas exchange function, as shown in the table 2.

DISCUSSION

TNF-α is a kind of peptide hormone generated by mononuclear macrophages, which is a must substance of inflammatory response, participating in the normal inflammatory reaction and immune response. However, it will damage various organs if over a certain level in the serum. Therefore, low level of TNF-α is the basis to the local inflammation response, while a high level might injury organ function (Mao *et al*, 2001). PCT is the precursor of calcitonin, which is a kind of inflammatory mediator generated by macrophagus induced by bacterial endotoxin during infectious stage. And it will maintain a low level in the normal condition, but will increase at the early infectious stage. Therefore, the high PCT level can be taken as the sensitive index to detect the bacterial infection in the early stage. And the pathogenesis of pancreatitis is not yet clear, which is generally believed to be related to the interaction of microcirculatory disturbance of pancreas and inflammatory cytokines.

This study comprehensively discussed the changes of TNF-α and PCT level in the serum in the patients with SAP during infected stage. And the results showed that the TNF-α level in the patients who had been detected negative focal bacteria during infected stage was much higher than the normal people, but significantly lower than the patents who had been detected positive bacteria, indicating that there was a certain level of TNF-α in the serum regardless of the bacteria in the patents during infected stage (Wu *et al*, 2013). While it had no difference in the PCT level in the patients during infected stage with or without bacteria. The patients during infected stage could be divided into the high TNF-α level group and low TNF-α level group, and the TNF-α level in the serum was closely related to the prognosis that the low level would promote inflammatory response and the high level would damage various organ functions. And in this study, the PCT level in group A and B were much higher than group C, indicating that it changed a lot in PCT level in the early infectious stage and it was closely related to the infectious degree, that the PCT level could be taken as an effective monitoring index in the early SAP infection stage.

The organ function failure induced by infection is the primary cause resulting in death of the patients during the SAP infectious stage, relating to the over release of the inflammatory factors (TNF-α, IL-1 and IL-12 etc.) (Norman, 2008; Kusske *et al*, 1996; Montravers *et al*, 1995). And the excessive release of TNF-α can also induce the body to generate more PCT. And during the general infectious stage, the TNF-α level was divided into the high level and low level, and the high level is related to the organ failure. And some researches had showed that the TNF-α generated in the liver will damage the liver function obviously (Davis and Hagen, 1997). And in this study, the albumin in the high TNF-α level group decreased obviously, and transaminase increased obviously, suggesting the damage mainly presents with the increase of permeation across liver cell and decrease of synthetic ability of liver cells. And the renal function in group A obviously decreased, indicating that the urinary system infection will harm to the renal function, which might because that TNF-α will effect the renal microcirculation. And the TNF-α generated by macrophage in the lung will damage the respiratory system directly, and also damage the distant organs with

Table 1: Changes of TNF-α and PCT level in the serum of three groups (x±s)

Groups	Samples (cases)	Serum TNF-α level (U/ml)	Serum PCT level (μg/l)
Group A	Positive pathogenic bacteria in the bile (n=15)	76.83±16.42[a]	12.54±3.61
	Positive pathogenic bacteria in the urine (n=13)	72.39±15.17[a]	11.19±2.78
	Positive pathogenic bacteria in the sputum (n=7)	79.14±13.09	13.87±4.06
	Positive pathogenic bacteria on the surface (n=11)	67.83±12.12[a]	13.39±3.57
Group B	Positive pathogenic bacteria in the bile (n=7)	40.54±11.09	13.48±3.92
	Positive pathogenic bacteria in the urine (n=9)	51.63±16.29	12.88±4.57
	Positive pathogenic bacteria in the sputum (n=6)	65.15±12.87	14.03±3.98
	Positive pathogenic bacteria on the surface (n=7)	51.32±9.73	13.25±4.94
Group C	Serum (n=30)	22.54±5.28[b]	2.94±0.83[c]

Note: [a]Comparison of TNF-α level between group A and group B, P<0.05; [b]TNF-α level in group A and group B, compared with group C, P<0.05; [C]PCT level in group A and group B, compared with group C, P<0.05.

Table 2: Effects of TNF-α and PCT level in serum on organ function (x±s)

Organ function		High TNF-α group (n=26)	Low TNF-α group (n=6)	High PCT group (n=32)
Liver	Glutamic-pyruvic transaminase (IU/L)	29.6±9.3[a]	66.5±15.8	31.5±8.6[a]
	Glutamic oxalacetic transaminase (IU/L)	31.4±11.1[a]	83.2±25.6	34.7±9.4[a]
	Albumin (mg/L)	375.8±101.3[a]	225.6±85.4	368.2±99.5[a]
	Total bilirubin (μmol/L)	30.2±15.4[a]	67.5±21.3	31.1±16.8[a]
	Alkaline phoSAPhatase (IU/L)	166.5±48.2[a]	278.2±57.3	179.2±56.9[a]
	Glutamyl tranSAPeptidase (IU/L)	126.9±23.4[a]	251.7±45.6	144.1±33.7[a]
Kidney	Creatinine (μmol/L)	99.8±15.7[a]	145.6±27.5	96.4±11.2[a]
	Urea nitrogen (μmol/L)	7.1±2.6[a]	13.2±4.3	6.6±3.1[a]
	Urine protein (mg/d)	134.1±6.8[a]	193.5±15.4	151.9±13.6[a]
Lung	$AaDO_2$ (KPa)	101.3±28.4[a]	155.7±29.2	95.0±24.7[a]
	PaO_2/FiO_2 (KPa)	49.9±11.3[a]	31.5±8.4	55.9±13.5[a]

Note: [a]Compared with the Low TNF-α group, P<0.05.

the blood circulation. And its mechanism was that TNF-α activates on the pulmonary vascular endothelial cells to activate thrombus adjusting factors, promoting the release of IL-1 in the endothelial cells, neutrophil aggregation and migration, causing neutrophils adherent to the wall. And the elastase released by neutrophils will damage the lung tissue, causing the reduce of the pulmonary ventilation and diffusion (Grewal *et al*, 1994).

CONCLUSION

As mentioned above, low TNF-α level during SAP infectious stage will increase with the infection degree, and the serum PCT level has a high sensitivity in the monitoring infection. Therefore, it is very important to monitor the TNF-α level and PCT level in the serum during different infectious period, providing a reference to the individualized treatment.

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