The Relationship between Liver Injury and Serum Levels of C-Reactive Protein and Procalcitonin in Patients with Acute Pancreatitis

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ABSTRACT

Acute pancreatitis (AP) can cause damage to multiple organs in the whole body, and the liver is one of the most frequently affected by AP. Ninety-six AP patients, consisting 67 patients with liver injury, were enrolled. They were classified as mild AP (MAP) and severe AP (SAP), according to the Atlanta Revised Classification, with 50 healthy subjects serving as the controls. The serum levels of C-reactive protein (CRP) and procalcitonin (PCT) were measured by ELISA. Serum levels of alanine aminotransferase (ALT), alkaline phosphatase (AKP) and aspartate aminotransferase (AST) were also analysed. AP patients had high incidence of liver injury which was greater in SAP than in MAP patients, the levels of serum CRP and serum PCT were positively correlated to ALT, AKP and AST levels in AP patients with liver injury. Serum levels of CRP and PCT may be used as indicators of liver injury in the AP patients.

Key Words: *Acute pancreatitis, Liver injury, C-reactive protein, Procalcitonin.*

Acute pancreatitis (AP), which are classified as mild AP (MAP), moderately-severe AP (MSAP) and severe AP (SAP), is a disease with a high mortality rate.[1] However, organ failure, which is caused by AP, is concerned not merely with pancreatic tissue; but with other tissues, such as liver, renal, cardiovascular, and pulmonary.[2] The researchers find that the first tissue injury induced by AP is liver; but there is a few systematic and comprehensive research whether the biomarker of the diagnosis of AP is suitable to detect liver injury which is caused by AP? Therefore, the aim of this investigation was to assess whether the serum levels of C-reactive protein and procalcitonin were able to predict liver injury in acute pancreatitis?

From January 2014 to December 2016, 96 patients were enrolled into this study due to an AP attack; 29 were excluded, 10 suffered from fatty liver, 16 suffered from primary viral hepatitis, and 3 patients were diagnosed with schistosomiasis. Finally, 67 liver injury patients caused by AP were included in this study. Therefore, a total of 146 subjects comprising of 96 patients and 50 healthy people were enrolled into the study. There were statistical differences among the different groups in age, Ranson score, APACHE II score, and Balthazar CT score in the initial stage of hospitalization, except for gender (Table IA).

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Compared to the control group, the SAP group and MAP group showed significantly higher ALT, AKP and AST before the treatment as well as the post-treatment of SAP group. However, there were no statistical differences in the MAP after treatment. ALT, AKP and AST levels were significantly lower in both SAP group and MAP group before and after treatment ($p < 0.01$, Table IB).

A. Clinical characteristics of the patients with acute pancreatitis and control group, B. Comparison of liver function between SAP group and MAP group, C. The change of the serum level of CRP and PCT, D. Comparison of the serum level of CRP and PCT between AP with liver injury. $^{###}p<0.001$, AP group *vs.* control by paired t-test; $^{***}p<0.001$, comparison between AP-induced liver injury group and AP without liver injury group by paired t-test; $^{\$\$\$}p<0.001$, comparison between MAP group and SAP group by paired t-test; $^{!!!}p<0.001$, comparison between pre-treatment and post-treatment of MAP group by paired t-test; $^{\&\&\&}p<0.001$, comparison between pre-treatment and post-treatment of SAP group by paired t-test. M, male; F, female; APACHE-II, acute physiology and chronic health examination-II. AP, acute pancreatitis; MAP, mild acute pancreatitis; SAP, severe acute pancreatitis; ALT, alanine amino-transferase; AST, aspartate amino-transferase; AKP, alkaline phosphatase. CRP, C-reactive protein; PCT, procalcitonin.

Compared to the control group, the AP group showed significantly higher CRP and PCT before the treatment, and the SAP group was more obvious than the MAP group ($p < 0.001$, Table IC). The serum levels of CRP and PCT in AP combined liver injury group were higher than those without liver damage group, after treatment

Table I: The biomarker of liver injury in the acute pancreatitis patients.

A	Baseline data	SAP group (n=52)	MAP group (n=44)	Control group (n=50)	p-value
	Sex (M/F)	52(27/25)	44(20/24)	50(29/21)	0.383
	Age (year)	50±6.4	47±5.1	44±5.8	<0.001
	Ranson score ≥3,N (%)	52(54.17%)	44(45.83%)	0	<0.001
	Admission APACHE Ⅱ score≥ 8,N (%)	52(54.17%)	44(45.83%)	0	<0.001
	Balthazar CT score D,N (%)	52(54.17%)	44(45.83%)	0	<0.001

B	SAP			MAP		
Liver fuctiong index	Before treatment	After treatment	*p-value*	Before treatment	After treatment	*p-value*
ALT (U/L)	123.54±41.02	83.75±57.19	<0.001	53.27±30.95	33.74±19.01	0.002
AST (U/L)	93.88±51.82	48.65±31.30	<0.001	48.32±17.93	21.08±13.37	<0.001
AKP (U/L)	175.35±62.33	73.27±48.17	<0.001	96.20±58.77	62.01±39.87	0.001

C					
AP	n	CRP (mg/L)	*p-value*	PCT (ng/mL)	*p-value*
AP	96	118.38 ± 12.79	<0.001(###)	1.04±0.75	<0.001(###)
MAP	44	81.39 ± 12.43		1.86±0.91	
SAP	52	164.75 ± 25.87	<0.001($$$)	3.61±1.30	<0.001($$$)
AP-induced liver injury	67	154.48 ± 28.32	<0.001(***)	2.82±0.77	<0.001(***)
AP without liver injury	29	62.86 ± 29.43		0.93±0.62	
Control	50	14.10 ± 3.73		0.19±0.08	

D					
Group	n	CRP (mg/L)	*p-value*	PCT (ng/mL)	*p-value*
MAP with liver injury					
Before treatment	17	114.78±13.55		2.32± 1.26	
After treatment	17	18.61± 3.97	<0.001(!!!)	0.90± 0.68	<0.001(!!!)
SAP with liver injury					
Before treatment	50	162.75±29.21		3.60±1.39	
After treatment	50	93.12± 17.55	<0.001(&&&)	1.27± 0.97	<0.001(&&&)

the serum levels of CRP and PCT in MAP combined with liver injury significantly lower than before treatment. Similarly, the serum levels of CRP and PCT in SAP combined with liver injury were significantly lower between before and after treatment, but the serum levels of CRP and PCT were still higher than the control group in SAP combined with liver injury after treatment (p <0.001, Tables IC and ID).

There was a strong positive correlation in ALT, AKP, AST, PCT and CRP levels between the two groups. Correlation analysis found that ALT, AKP and AST levels were positively correlated with serum CRP (ALT: r=0.80, p<0.01; AKP: r=0.88, p<0.01; AST: r=0.86, p<0.01) and serum PCT (ALT: r=0.89, p<0.01; AKP: r=0.85, p<0.01; AST: r=0.88, p<0.01).

The effect of serum CRP and PCT were used for diagnosing liver injury caused by AP in the corresponding reference range. The sensitivity of serum CRP was 89.55% and the specificity was 88%; the sensitivity of serum PCT was 94.03% and the specificity was 92%.

Because of the liver's special position, it becomes the first target organs for extra-pancreatic damage of SAP, and the pathological changes also can be observed in liver injury patients caused by AP.[3] The premature activation of pancreatic proteases unlocks the progression of SAP, resulting in the release of various inflammatory mediators *via* the portal vein. Subsequently, various inflammatory cytokines released to inflammatory cells are strongly activated and greatly amplify the release of cytokines into the bloodstream, which results in systemic complications and ultimately leads to liver injury. Conversely, liver injury is in a position to accelerate the progression of AP. Unfortunately, there was no effective evaluation index system that was rapidly used to confirm progressive multiple system organ dysfunction.

In view of this, procalcitonin (PCT) and C-reactive protein (CRP) levels, which are the most recognized biomarkers used for the prediction of AP in the routine diagnostic procedure, were used to estimate AP.[4] In these cases, it was found that the serum level of CRP and PCT in AP group could be markedly higher than control group, and the SAP group was more obvious than the MAP group. This result was in agreement with

the conclusions of other researchers.[5] In a considerable degree, the results showed that the serum levels of CRP and PCT in AP combined liver injury group were higher than those without liver damage group. After treatment, the serum levels of CRP and PCT in MAP combined with liver injury were significantly lower than before treatment. The same result was found before treatment and after treatment in SAP combined with liver injury, but the serum levels of CRP and PCT were still higher than the control group in SAP combined with liver injury after treatment. The reasons for this phenomenon might be associated with the degree of organ damage. It was found out that the liver injury caused by SAP could secrete more inflammatory factors, and the tissue damage is more serious. Up to 96% suffered from liver injury in SAP group; however, only 39% suffered from liver injury in MAP group. It might indicate that the serum levels of CRP and PCT were able to provide more accurate diagnoses in SAP-induced liver injury. The expression of ALT, AKP and AST was similar to the expression trend of CRP and PCT. There was a positive correlation between CRP, PCT and ALT, AKP, AST by correlation analysis, and the result was consistent with other reports. Moreover, the results showed that the serum levels of CRP and PCT were enough sensibility and specificity for diagnosing liver injury caused by SAP, which suggested that CRP and PCT might be used as a indicator of predicting liver injury in acute pancreatitis.

REFERENCES

1. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al*. Classification of acute pancreatitis – 2012: Revision of the Atlanta classification and definitions by international consensus. *Gut* 2013; **62**:102-11.
2. Dumnicka P, Kusnierz-Cabala B, Sporek M, Mazur-Laskowska M, Gil K, Kuzniewski M, *et al*. Serum concentrations of angiopoietin-2 and soluble FMS-Like tyrosine kinase 1 (sFlt-1) are associated with coagulopathy among patients with acute pancreatitis. *Int J Mol Sci* 2017; **18**:E753.
3. Folch-Puy E. Importance of the liver in systemic complications associated with acute pancreatitis: the role of Kupffer cells. *J Pathol* 2007; **211**:383-8.
4. Lee KJ, Kim HM, Choi JS, Kim YJ, Kim YS, Cho JH. Comparison of predictive systems in severe acute pancreatitis according to the revised Atlanta classification. *Pancreas* 2016; **45**:46-50.
5. Sporek M, Dumnicka P, Gala-Bladzinska A, Mazur-Laskowska M, Walocha J, Ceranowicz P, *et al*. Determination of serum neutrophil gelatinase-associated lipocalin at the early stage of acute pancreatitis. *Folia Med Cracov* 2016; **56**:5-16.