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Original Research

Significant changes in the levels of myocardial enzyme in the child patients with Mycoplasma pneumoniae pneumonia

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Abstract: Mycoplasma is a gram-negative with thin wall bacterium that in humans, *Mycoplasma pneumoniae* causes pneumonia. This experiment was designed to explore the changes of myocardial enzymes in the mycoplasma pneumoniae pneumonia (MPP) child patients, and analyze the clinical value of these changes, in combination with the relevant indicators, symptoms and signs, in the evaluation of the pneumonia mycoplasma infection. For this aim, a total of 120 child patients with MPP in the acute phase,120 child patients with MPP in the recovery phase and 120 healthy children were simultaneously enrolled into this study to detect the levels of aspartate aminotransferase (AST), creatine kinase (CK), Creatine Kinase Isoenzyme (CK-MB) and lactic dehydrogenase (LDH) in blood. Results showed that MPP patients in the acute phase had higher levels of LDH, CK, CK-MB, AST, PCt, CRP, MPV, PDW, PCt, percentage of neutrophils, WBC count in the peripheral blood and ESR than those of the patients in the recovery patients and healthy children, while the level of PLT was lower (all $P<0.05$). In the acute phase, the level of CK-MB correlated to the fever, fever duration, extrapulmonary organ damage (except for the myocardial damage) and the antibody titer of MP (all $P<0.05$). It was concluded that in the acute phase of MMP, the level of CK-MB could not only reflect the myocardial damage readily but also the infection of MP as well as the resultant inflammation and disease progression, which could effectively guide the diagnosis and treatment of MPP.

Key words: Mycoplasma pneumoniae; Mycoplasma pneumoniae pneumonia; Myocardial enzymes; Myocardial damage.

Introduction

Recently, Mycoplasma pneumoniae (MP) has gradually become the major cause of pediatric pneumonia. According to a large-scale survey, among the in-hospital pediatric patients aged 5 years old or below, MP infection has taken up nearly 29.01% (1). Mycoplasma pneumoniae pneumonia (MPP) occurs mostly in the school-age children, resulting in the damage to the gastrointestinal, cardiac and urinary systems of the patients and threatening the mental and physical health of the children (2). A study shows that among the extrapulmonary complications of MPP, the involvement of cardiovascular disease occupies almost 27.91% of the patients (3). Manifestations in the cardiovascular system include myocarditis and pericarditis, and in some severe cases, patients may suffer from heart failure or cardiac shock; thus, cardiovascular complications are believed to be one of the criteria for recognizing the critical MPP (4). Factors of myocardial damage are significant for the early diagnosis and prophylaxis of cardiac complications. The change of activity of creatine kinase isoenzymes (CK-MB), as the specific myocardial enzymes, is closely associated with the necrosis of myocardial cells (5, 6). In this study, we aimed to explore the clinical value of CK-MB, as the indicator of myocardial damage in MPP pediatric patients, in combination with the relevant indicators, symptoms and signs, in treatment of the MP infection.

Materials and Methods

Subjects

A total of 120 child patients with MPP in the acute phase, consisting of 69 males and 51 females aged between 2 months and 12 years old with an average of (5.77±1.44) years old, 120 child patients with MPP in the recovery phase, consisting of 67 males and 53 females aged between 2 months and 12 years old with an average of (5.47±1.56) years old, and 120 healthy children, consisting of 66 males and 54 females aged between 2 months and 12 years old with an average of (5.85±1.57) years old were simultaneously enrolled into this study. Comparisons of the general data, including age and gender, showed that the differences among the three groups showed no statistical significance ($P>0.05$). Inclusion criteria: 1) patients with symptoms conforming to the diagnostic criteria of *Zhu Futang: Textbook of Pediatrics* (7th edition), simultaneously showing the typical symptoms including fever, cough, shortness of breath or wheezing; 2) patients in the acute phase in the onset time of 0.5 d to 8 d, without any recovery prior to the admission; 3) patients in the recovery phase with no clinical symptoms after 2 to 8 weeks of treatment, and X-ray or physical examination shows significant alleviation or no symptoms; 4) patients with no history of infection within 1 month; 5) patients with perfect clinical data; 6) patients or their family that gained the informed con-

sent. Exclusion criteria: 1) patients with a history of the MP infection, myocarditis, or congenital heart disease; 2) patients with other conditions in heart, liver or lung; 3) patients with the autonomous immune diseases; 4) patients with the metabolic disturbance. This study had been approved by the Ethic Committee of the hospital prior to the implementation.

Methods

From the enrolled children, 3 mL peripheral blood was drawn for the detections of levels of aspartate aminotransferase (AST), creatine kinase (CK), CK-MB, lactate dehydrogenase (LDH), C-reactive protein (CRP) and procalcitonin (PCt) in the blood by using the automatic biochemical analyzer (Erba, Germany). The automatic blood cell analyzer was utilized to measure the levels of white blood cells (WBCs), percentage of the neutrophils, erythrocyte sedimentation rate (ESR), blood platelet (PLT), mean platelet volume (MPV), platelet distribution width (PDW) and platelet hematocrit (PCt). The level of anti-MP antibody in the serum of patients was detected by using the colloidal gold's method with the detection kit provided by Chengdu Kanghua Biological Products Co., Ltd.

Statistical analysis

SPSS 20.0 software was utilized for the data analysis, and all data underwent the test of normality. For enumeration data, they were presented by means ± standard deviation and compared using the one-way analysis of variance (One-way ANOVA) followed by least significant difference (LSD) or Student-Newman-Keuls (SNK) test for pairwise test. Count data were expressed by the rate (%), and compared by the chi-square test. $P<0.05$ suggested that the difference had statistical significance.

Results

Comparison of the levels of myocardial enzymes in children patients among three groups

In comparison with the control group, LDH, CK, CK-MB and AST levels were significantly elevated in the children patients in recovery or acute phase ($P<0.05$), while the children in acute phase had more evident increases than those in the recovery phase ($P<0.05$, Table 1).

Comparison of the inflammatory factors in children patients among three groups

In comparison with the control group, children patients had obvious increases in the levels of CRP and PCt in both of the recovery and acute phases ($P<0.05$), while the levels in the acute phase were much higher than those in the recovery phase ($P<0.05$; Table 2).

Comparison of the platelet parameters in children patients among three groups

In comparison with the control group, the levels of PLT in the children patients in the recovery phase and acute phase were decreased, with significant increases in the levels of MPV, PDW and PCt ($P<0.05$). However, when compared with the children patients in the recovery phase, the level of PLT in the acute phase was decreased, with increases in the levels of MPV, PDW and PCt ($P<0.05$; Table 3).

Comparison of the laboratory parameters of children patients among three groups

Compared to the control group, the percentage of neutrophils, WBC count and ESR were all elevated ($P<0.05$) in the children patients in the acute and recovery phases, and the children patients in the acute phase had a much higher percentage of neutrophils,

Table 1. Comparisons of the levels of myocardial enzymes in children patients among three groups.

Myocardial enzymes	Control group (n=120)	Recovery phase (n=120)	Acute phase (n=120)
LDH (U/L)	199.37±29.48	294.63±29.77*	338.58±30.63$^{*\#}$
CK (U/L)	211.44±20.66	312.77±32.49*	353.75±36.90$^{*\#}$
CK-MB (U/L)	15.20±3.09	30.18±6.19*	48.70±8.35$^{*\#}$
AST (U/L)	23.90±3.77	52.16±5.64*	71.50±10.18$^{*\#}$

Note: $^{*}P<0.05$ *vs.* the control group; $^{\#}P<0.05$ *vs.* the recovery phase.

Table 2. Comparison of the inflammatory factors in children patients among three groups.

Inflammatory factors	Control group (n=120)	Recovery phase (n=120)	Acute phase (n=120)
CRP (mg/L)	2.17±0.54	11.10±1.43*	24.19±2.07$^{*\#}$
PCt (μg/mL)	0.44±0.05	0.63±0.05*	0.81±0.07$^{*\#}$

Note: $^{*}P<0.05$ *vs.* the control group; $^{\#}P<0.05$ *vs.* the recovery phase.

Table 3. Comparisons of the platelet parameters in children patients among three groups.

Parameters	Control group (n=120)	Recovery phase (n=120)	Acute phase (n=120)
PLT ($\times 10^9$/L)	290.59±10.35	241.27±8.26*	149.09±5.33$^{*\#}$
MPV (fl)	8.70±0.85	9.74±0.94*	11.06±1.13$^{*\#}$
PDW (%)	12.51±2.56	24.02±2.59*	29.34±2.18$^{*\#}$
PCt (%)	0.21±0.03	0.33±0.04*	0.42±0.05$^{*\#}$

Note: $^{*}P<0.05$ *vs.* the control group; $^{\#}P<0.05$ *vs.* the recovery phase.

Table 4. Comparison of the laboratory parameters of children patients among three groups.

Parameters	Control group (n=120)	Recovery phase (n=120)	Acute phase (n=120)
Neutrophils (%)	65.33±1.64	73.18±2.75*	84.69±6.37*#
WBC count in peripheral blood	6157.65±268.75	10306.84±2009.29*	11596.76±1998.33*#
ESR (%)	6.33±1.49	13.54±3.86*	19.95±5.24*#

Note: *P<0.05 *vs.* the control group; #P<0.05 *vs.* the recovery phase.

Table 5. Correlation between the CK-MB level and the condition of children patients in the acute phase.

Signs	n	CK-MB (U/L)	t	*P*
Infection sites				
Upper respiratory tract	102	48.72±8.23	0.048	0.96
Lower respiratory tract	34	48.64±8.42		
Fever				
Moderate or low-grade fever	48	45.33±8.20	3.325	0.001
High fever	88	50.54±9.02		
Fever duration				
< 7d	31	44.41±8.22	3.22	0.002
≥ 7d	105	49.96±8.52		
Extrapulmonary damage (except the myocardial damage)				
No	44	45.64±8.34	2.947	0.004
Yes	92	50.17±8.42		
MP antibody titers				
≤ 1:160	21	45.25±8.45	2.167	0.031
> 1:160	115	49.57±8.40		

WBC count and ESR than those in the recovery phase (P<0.05; Table 4).

Correlation between the level of CK-MB and the condition of children patients in the acute phase

Evidence showed no relevance between the infection site and the level of CK-MB in children patients in the acute phase (P>0.05). Higher levels of CK-MB were identified in the children with fever, duration of fever longer than 7 d, extrapulmonary damages (except the myocardial damage) as well as the MP antibody titers higher than 1:160 (all P<0.05; Table 5).

Discussion

MP, as one of the mycoplasmas that are in close relation with the human beings, is spread mainly through the droplet transmission to induce the acute inflammation in the lung, concomitant with the multiple extrapulmonary organ damages (7). Almost all organs and systems are involved in the extrapulmonary damages, among which the cardiovascular system is the most vulnerable, especially the myocardium. Currently, pathogenesis regarding to how MP infection results in the myocardial damage remains unknown, and people have put forward the following hypotheses (8-10):1) MP and the cells in lung and heart share the same antigens, and MP infection causes the release of corresponding antibodies in the myocardial tissues, resulting in the lesions in targeted organs and the emergence of the symptoms in myocardial tissues; 2) MP infection increases the sensitivity to the pathogens, further triggering the Type III allergic reactions; 3) MP infection also causes the viremia, which further contributes to the myocardial injury; 4) MP can invade into the epithelial cells directly in the respiratory tract, increasing the vascular permeability, stimulating the T cells and the macrophage to induce the infiltration of myocardial matrix, and inducing the secretion of pro-inflammatory cytokines from the inflammatory cells to cause the myocardial damage; 5) Inflammation and pulmonary edema caused by MPP can further reduce the gas exchange area, leading to the ischemia and hypoxia, and the abnormal energy metabolism in myocardium, thereby causing the myocardial damage. These results suggest that myocardial damage caused by the MP infection is contributed commonly by direct invasion and/or indirect immune damages.

Among the majority of children patients, myocardial damage is mild, without any evident clinical signs, and, thus, the diagnosis should be made by using the myocardial enzymes and electrocardiogram examination. Myocardial enzymes, including CK, LDH, CK-MB and AST, are the major serum enzymes used for the clinical diagnosis of MPP complicated with the myocardial damage (11). It has been confirmed that increases in the myocardial enzymes are commonly found in the MPP children patients who, thus, are diagnosed as the myocardial damage or myocarditis (12). In this study, we found that the levels of CK, LDH, CK-MB and AST in the myocardial enzymes of the children patients in the acute phase were higher than those in the recovery phase or the healthy volunteers. Thus, MP infection results in the myocardial damage in children's patients, but the fact that AST and LDH are detected in a variety of tissues causes a lack of specificity. Besides, abnormal increases of AST and LDH are identified in various situations, including the erythrocytes hemolysis, myocardial infarction, or arrhythmia. Hence, the application of AST and LDH should be limited in the diagnosis of myocardial damage. As a myocardium-specific enzymatic

indicator, CK-MB is scarcely found in other tissues. Any damage to the myocardial cells and the resultant change in the permeability of the cell membrane, thus facilitating the increases of CK-MB in the blood. Additionally, due to the high sensitivity (97.5%) and specificity (100%) of CK-MB in the diagnosis of myocardial damage, it serves as a golden indicator in the diagnosis of myocardial damages (13, 14).

It has been reported that extrapulmonary damage caused by the MP infection, like myocardial damage, is relevant with the titers of MP antibody and the temperature of the children patients: Degree of infection is reflected by the antibody dilution, which further indicates the possibility of extrapulmonary damage (15). Thomas et al. reported that CK-MB is associated with the fever, fever duration, extrapulmonary damage (except the myocardial damage) and titers of MP antibody, and any emergence of clinical symptoms above caused by MP infection may induce the myocardial damage (16). Consistently, we also noted that in the children patients with fever, CK-MB was also up-regulated, and the duration of fever also contributed to the elevation of CK-MB. Also, among the children patients with extrapulmonary damages, except for the myocardial damage, CK-MB was also higher than that in those with no extrapulmonary damage. He Chao et al. found that MPP-triggered myocardial damage is correlated with the WBC count and the titer of MP antibody, instead of the percentage of neutrophils or ESR (17, 18). Therefore, MP could trigger the myocardial damage directly or indirectly through the immune damage; the persistent fever, increases in WBC count and the titer of the MP antibody in MP-infected children patients remind us of the necessity of measurement of CK-MB (19). Similarly, WBC count, neutrophil percentage, ESR and titer of MP antibody are elevated in the children patients in the acute phase, and CK-MB is correlated with the WBC count in peripheral blood and the titer of MP antibody. Thus, the level of CK-MB in the MP-infected children patients in the acute phase could reflect the myocardial damage, and the correlation with the extrapulmonary damage also displays the severity of the disease.

PCt, as a key indicator reflecting the infection, inflammation and organ failure, is associated with the types, inflammation and immune responses in the infected organs. Research has shown that the effects of lipopolysaccharide and endotoxin of MP can induce the secretion of PCt after infection (20, 21). Dynamic monitoring of the PCt level in the MPP children patients can help us figure out the severity of the disease to guide the rational administration of biotics. CRP can activate the inflammatory cells, like macrophages or lymphocytes, to induce the secretion of inflammatory cytokines, and further trigger the inflammatory responses. Thus, it can reflect the progression of the disease. Besides, for MP-infected children patients in the acute phase and complicated with the myocardial damage, TNF-α, IL-6 and CRP are acutely increased, and the variations are closely correlated with the disease condition (22). In this study, PCt and CRP levels are also increased in the acute phase, which are higher than those in the recovery phase, suggesting that MP infection does trigger the severe inflammatory responses. Correlation analysis also reveals that PCt and CRP are positively correlated with the level of CK-MB, indicating that in the acute phase of MPP, myocardial infection is also related to the MP infection-caused inflammatory responses. CK-MB level can reflect the inflammatory responses, thereby helping us to know the severity of the disease.

In conclusion, in the acute phase of MPP, CK-MB level can reflect not only the myocardial damage but also MP infection, inflammatory and severity of the disease. Thus, it is useful in guiding the prompt treatment of MPP.

The myocardium is the middle layer of the heart wall. It is a muscular and contractile layer, also the thickest layer of the heart wall. Myocardium is an exception in terms of its ability to perform continuous contractions throughout a person's life, and human survival depends on it (23). Enzymes and related genes need to be identified and managed about each complication and disease (24, 25). In this research, we explore the changes of myocardial enzymes in the mycoplasma pneumoniae pneumonia (MPP) child patients.

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