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Diagnostic value of analysis of H-FABP, NT-proBNP, and cTnI in heart function in children with congenital heart disease and pneumonia

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Abstract. – AIM: To analyze the expression of heart-fatty acid-binding protein (H-FABP), N-terminal pro-brain natriuretic peptide (NT-proBNP), and cTnI in children with congenital heart disease (CHD) and pneumonia, and evaluate its diagnostic value in heart failure (HF).

PATIENTS AND METHODS: The levels of serum H-FABP, NT-proBNP, and cardiac troponin 1 (cTnI) were measured by immunoassays in 22 children with CHD, pneumonia, and HF (group I), 25 children with CHD and pneumonia (group II), and 25 healthy children without CHD or pneumonia (control group).

RESULTS: The concentration and positive rate of serum H-FABP, NT-proBNP, and cTnI were significantly higher in group I than those in group II. Compared to control group, these indexes were increased in both group I and group II. There were statistical significant differences in the positive rate of NT-proBNP and cTnI but not H-FABP between groups of patients with different classes of heart function.

CONCLUSIONS: The levels of H-FABP, NT-proBNP, and cTnI were correlated with heart function, and can be used for the diagnosis of early-stage HF in children with CHD.

Key Words:
Congenital heart disease, Heart failure, H-FABP, NT-proBNP, cTnI, Child.

Introduction

Heart failure (HF) is a common complication in children with congenital heart disease (CHD). Early interference or treatment can effectively improve the prognosis. However, clinical features are lacking for the diagnosis of HF at early stage, which hindered the delivery of early interference. Therefore, early diagnosis is critical for effective treatment. Recent studies suggest that the aberrant expression of cytokines contributes to the onset of CHD with HF[1]. Heart-type fatty acid-binding protein (H-FABP) is a soluble protein localized in cytoplasm. It was recently found to be enriched in myocardial cells[2]. N-terminal pro-brain natriuretic peptid (NT-proBNP), a cardiac hormone, is secreted by ventricular myocytes and has protective effects on heart. Cardiac troponin I (cTnI) controls the calcium-mediated interactions between actin and myosin in cardiac and skeletal muscles. It has been widely used in clinical practice as a gold standard for diagnosis of myocardial injury. Although clinical application of individual cytokines in the diagnosis of heart function is common, evaluation of heart function by combined examination of the above three cytokines is rare. In this study, we compared the expression of H-FABP, NT-proBNP, and cTnI in children with CHD and pneumonia, and analyzed the correlation between different levels of the three cytokines and heart function.

Patients and Methods

Subjects

A total of 47 cases (27 males, 20 females, mean age 3.49 ± 0.23 years) from Jan 2009 to Jan 2012 were included in this study. This study conducted in accordance with the Declaration of Helsinki, obtained the approval from the Ethics Committee of the Third Affiliated Hospital of Xinxiang Medical University. Written informed consent was recruited from all participants. Of these patients, 19 had ventricular septal defect (VSD), 24 had atrial septal defect (ASD), and 4 had complete transposition of great arteries (CTGA). The patients were classified as follows. Group I: 22 patients with CHD, pneumonia, and HF, in which there were 8 cases of New York Heart Association (NYHA)

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class II, 9 cases of class III, and 5 cases of class IV. Group II: 25 patients with CHD and pneumonia but without HF. 25 cases of healthy children (13 males, 12 females, age range from 6 months to 7 years, mean age 3.84 ± 0.42 years) were selected as control group. All patients had complete clinical data. There were no significant differences in age and sex between groups as determined by *t* test ($p > 0.05$).

Methods

Venous blood samples were obtained from children in those three groups within 1-3 days after their entry to hospital. The levels of serum H-FABP, NT-pro BNP, and cTnI were measured by immunoassays using commercial kits purchased from SYM-BIO LifeScience Co., Shanghai, China) (for detection of H-FABP) and Roche Diagnostics, Indianapolis, IN, USA (for detection of NT-proBNP and cTnI). Procedures were performed according to the manufacturer's instruction. Values were considered to be positive when the concentration of serum H-FABP > 7 ng/ml (normal range 0-7 ng/ml), NT-pro BNP > 200 pg/ml (normal range 0-200 pg/ml), and cTnI > 0.8 ng/ml[3].

Statistical Analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All values were expressed as x ± s. Wilcoxon rank sum test was used to test a difference between two groups. The chi-square test (χ^2), trend χ^2, and Fisher's exact test were used to compare positive rate between groups. Statistical significance was defined as $p < 0.05$.

Results

The Levels and Positive Rate of H-FABP, NT-pro BNP, and cTnI in Different Groups

We compared the levels of H-FABP, NT-pro BNP, and cTnI among group I, group II, and control group. As shown in Table I, the levels and positive rate of H-FABP, NT-pro BNP, and cTnI were significantly higher in group I than those in group II ($p < 0.001$). Compared to control group, the levels and positive rate of H-FABP, NT-pro BNP, and cTnI were increased in both group I and group II ($p < 0.05$).

The Positive Rate of H-FABP, NT-proBNP, and cTnlin Patients with Different Classes of Heart Function

As shown in Table II, the positive rate of NT-proBNP and cTnI increased with the increasing level of heart function classification (from class II to class IV) ($p < 0.05$). There was no significant difference in the positive rate of H-FABP between groups ($p > 0.05$).

Discussion

Evaluation of heart function in children with HF relies on electrocardiogram, ultrasonic cardiogram, and nonspecific clinical performance. The clinical features of HF include weight gain or edema, dysphoria, cyanosis, poor response, pale complexion, and reduction in milk consumption. All these features can be used for early diagnosis of HF[4]. However, these symptoms can also be observed in children with CHD. Therefore, these clinical performances were not specific for HF and not suitable for accurate diagnosis. Increased heart load, pneumonia, or respiratory tract infection that often accompany CHD can induce HF. Furthermore, neonates are easily attacked by HF because of limited cardiac reparative ability, low left ventricular reserve, reduced content of retractor muscle, or immature sympathetic nervous system[5]. At pre-

Table I. Comparison of H-FABP, NT-pro BNP, and cTnI levels.

		Concentration (x ± s)			Positive rate n (%)		
	n	H-FABP (ng/ml)	NT-proBNP (ng/ml)	cTnI (ng/ml)	H-FABP	BNP	cTnI
Group I	22	35.73 ± 10.45	378.14 ± 10.45	0.84 ± 0.20	18 (81.8)	20 (90.9)	13 (59.1)
Group II	25	4.15 ± 5.22	142.53 ± 5.22	0.53 ± 0.11	9 (36.0)	7 (28.0)	3 (12.0)
Control	25	1.23 ± 0.15	0.74 ± 0.15	0.18 ± 0.04	0 (0.0)	0 (0.0)	0 (0.0)
		H = 78.44	H = 143.67	H = 30.47	$\chi^2 = 33.46$	$\chi^2 = 47.49$	$\chi^2 = 45.62$
p		< 0.001	< 0.001	< 0.001	< 0.005	< 0.005	< 0.005

Table II. Comparison of the positive rate of H-FABP, NT-proBNP, and cTnI in group I with different classes of heart function.

	n	Positive rate n (%)		
		H-FABP	NT-pro BNP	cTnI
Class II	8	6 (75.0)	6 (75.0)	3 (37.5)
Class III	9	8 (88.9)	9 (100.0)	7 (77.8)
Class IV	5	5 (100.0)	5 (100.0)	5 (100.0)
χ^2		1.72	3.85	6.18
p		> 0.05	< 0.05	< 0.05

sent, a gold standard for diagnosis of HF in children and laboratory indexes for evaluation of heart function are still lacking.

H-FABP is a soluble protein which is present in cardiocytes[6]. It participates in the absorption and transport of fatty acids, and released to the blood from cell membranes within 0-3 h after HF. The concentration of H-FABP in the serum was elevated after HF and can maintain for 12-14 h. The level of H-FABP is positively correlated with lasting time of HF, the severity of myocardial damage, and the progress of myocardial ischemia, suggesting that H-FABP level can be used for early diagnosis of HF[7]. It is also an early, sensitive, and specific biomarker for evaluation of ischemia-reperfusion injury in the surgical correction of deformities in children with CHD[8,9]. Our results showed that the level of H-FABP was significantly higher in children with HF than that in children without HF. The positive rate of H-FABP was up to 81.8%, and no significant difference was observed in patients with different classes of heart function. This indicates that H-FABP level is upregulated during the early stage of HF and can be used as a biomarker for early-stage HF.

NT-proBNP is mainly distributed in heart tissues and is enriched in the left ventricular. Its synthesis and expression were influenced by tension and traction of left ventricular. When HF occurs, NT-proBNP is secreted instantly. Because of its rapid synthesis and relatively long half-life, NT-proBNP level can reflect the severity of HF and is significantly upregulated in children with HF[10-11]. Our data showed that the level of NT-proBNP was significantly higher in children with HF than that in children without HF. The positive rate of NT-proBNP also increased in patients with HF. Notably, the positive rate of NT-proBNP was up to 100% in children with heart function above class II, suggesting a positive correlation between NT-proBNP level and the severity of HF. Thus, it is a valuable index for the clinical diagnosis of HF and is useful for the evaluation of prognosis[12].

At normal condition, cTnI is anchored to muscle mass fiber as a structural protein. A small portion of cTnI is free in the cytosol. When HF occurs, free cTnI was released first, followed by the release of cTnI from muscle mass fiber. The concentration of cTnI in serum is elevated within 4-6 h and peaks at 18-24 h after the attack of HF. This elevation of cTnI can last for relatively long time. Recent years, cTnI has gained considerable attention for its use as biomarker in the diagnosis of HF. Because of its sensitivity and specificity, cTnI is valuable in the diagnosis of the disease and evaluation of the prognosis. However, at early stage of heart failure, cTnI exists as a protein complex and is susceptible for degradation. Therefore, it is not sensitive in the diagnosis of early-stage HF[13]. The results present in this study suggest that the level and positive rate of serum cTnI are increased in children with HF. They were positively correlated with the severity of HF and showed low specificity in patients with class II heart function.

Compared to H-FABP and NT-proBNP, cTnI is not suitable for early diagnosis of HF due to its lack of sensitivity at early stage of HF[14].

Conclusions

Our results indicate that the levels and positive rate of H-FABP, NT-proBNP, and cTnI were significant higher in children with CHD, pneumonia, and HF than those in children with CHD and pneumonia but without HF. This consistent increase of the three biomarkers in HF patients suggests that combined use of them in the diagnosis of HF in children with CHD may obtain more accurate results and increase clinical cure rate[15,16].

Conflict of Interest

The Authors declare that they have no conflict of interests.

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