CLINICAL ASSESSMENT OF HIGH-SENSITIVITY C-REACTIVE PROTEIN, MYOCARDIAL ZYMOGRAM AND ELECTROCARDIOGRAM CHANGE IN EARLY DIAGNOSIS OF HFMD

Yu Zhang, Yuan-Da Zhang, Li-Po Han, Haobin Song
Department of Pediatrics, Baoding Children's Hospital, Key Laborary of Clinical Research on Respiratory Digestive Disease, Hebei Baoding 071000, China

ABSTRACT

Introduction: *HFMD (hand-foot-and-mouth disease) is an acute intestinal infectious disease. Early discovery, early diagnosis and early treatment have important significance.In this study, we discuss clinical significance of high-sensitivity C-reactive protein (hs-CRP), myocardial zymogram level and the changes of Electrocardiogram in early diagnosis of hand-foot-and-mouth disease (HFMD).*

Case Presentation: *80 child patients clinically diagnosed with HFMD were selected. 39 patients were brought in the severe disease group, and the remaining 41 patients were included in the mild disease group. WBC, hs-CRP, FPG and myocardial zymogram level of all child patients were detected and recorded, and electrocardiogram changes were monitored and recorded.WBC, hs-CRP, FPG, and myocardial zymogram level of severe disease group were higher than that of mild disease group, and the differences had statistical significance (P<0.05). Electrocardiogram change appeared for both groups. Compared with the mild disease group, the heart rate of patients in severe disease group sped up obviously, and anomalous change occurrence rate at ST-T section significantly increased. The differences had statistical significance (P<0.05).*

Conclusion: *The hs-CRP, myocardial enzyme level and electrocardiogram detection can early diagnosis, timely treatment, reduce mortality and improve the prognosis of children in the study. Thus, these detection are helpful in the diagnosis of severe HFMD. And it has high clinical value in the early diagnosis of HFMD complicated with myocardial injury.*

Keywords: *HFMD, WBC, hs-CRP, myocardial zymogram, electrocardiogram, FPG, early diagnosis.*

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Introduction

HFMD(hand-foot-and-mouth disease) is an acute intestinal infectious disease caused by ribonucleic acid enterovirus. It is a common disease of pediatric department[1-2]. In recent years, HFMD outbreak and prevalence have appeared in multiple regions in China. Mild patients can recover within 1 week, but a few patients will develop to severe HFMD[3]. Severe HFMD progresses rapidly, causing heart damage and even death[4]. Thus, early discovery, early diagnosis and early treatment have important significance. In this paper, clinical significance of patients' WBC, hs-CRP, blood glucose, myocardial zymogram level and electrocardiogram change in early diagnosis of HFMD analyzed as follows.

Materials and methods

Ethical approval

The study was approved by the Institutional Ethics Committee of our hospitals, and written informed consent was obtained from all participants.

Data and method

General data:

80 child patients clinically diagnosed with HFMD from January 2016 to December 2017 were chosen.

Inclusion criteria:

Complies with the diagnostic criteria for severe and mild of HFMD in 2010 Guidelines for HFMD Diagnosis and Treatment[5]. Patients' parents or main guardians cooperated in blood sample collection, and signed the informed consent form.

Exclusion criteria:

• Those misdiagnosed with HFMD;

• Congenital diseases;

• Organ system diseases such as liver, lung, kidney and blood coagulation.

According to disease severity, the child patients were further classified into severe disease group and mild disease group. 39 patients with one or more complications such as encephalitis, meningitis, encephalomyelitis, pulmonary edema and circulatory failure were brought in the severe disease group, and the remaining 41 patients with clinical manifestations of fever, stomatalgia and herpes or anabrosis in oral mucosawere included in the mild disease group. The differences of both groups in gender, age and disease course had no statistical significance (P>0.05), so they had comparability, as shown in Table 1.

Group	No.	Gender (male/female, No.)	Age (x±s, years old)	Course of disease (x±s, d)
Severe disease group	39	21/18	2.7±1.3	7.3±1.4
Mild disease group	41	23/18	2.9±1.1	7.5±1.1
t/X^2 value		0.211	0.639	0.731
P value		0.900	0.529	0.389

Table. 1: Comparison of general data (n=80).

Sample collection:

3ml venous blood was drawn on an empty stomach from all patients on the day of treatment or in the morning of the next day. The upper serum was taken and kept in the -20° C refrigerator for detection after centrifuged.

Detection method:

• Microscope count method was used to detect WBC. The detailed operating steps refer to operation instruction of the counter.

• Immune scatter turbidity was applied to detect serum hs-CRP level by referring to descriptions of the kit and relevant materials provided by the manufacturer.

• Glucose oxidase method was used to detect FPG level.

• 7180 fully automatic biochemical analyzer of Hitachi was adopted to detect serum myocardial zymogram level.

• Electrocardiographic examination: 12 lead electrocardiogram was used to examine the patients. The values of P-QRS-T multiple heart beats were measured and recorded, and the average value was taken[6].

Statistical method:

SPSS22.0 statistical software was applied for analysis. Measurement data were expressed with mean ± standard deviation (x±s). t test was used for inter-group comparison. Enumeration data were expressed with %. X^2 test was used for intra=group comparison. P<0.05 means the difference has statistical significance.

Results

Comparison of WBC, hs-CRP and FPG indexes

WBC, hs-CRP and FPG level of severe disease group were higher than that of mild disease group. Inter-group comparison difference had statistical significance (P<0.05), as shown in Table 2.

Group	No. (n)	WBC $*10^9$/L	hs-CRP (mg/L)	FPG (mmol/L)
Mild disease group	41	8.9±2.9	10.4±3.7	5.3±1.9
Severe disease group	39	10.6±3.9	12.5±4.8	8.7±2.0
t value		2.023	2.136	14.299
P value		0.027	0.024	0.000

Table. 2: Comparison of WBC, hs-CRP and FPG (x±s).

Comparison of myocardial zymogram index

Aspartate aminotransferase (AST), CK-MB, CK, LDH, LDH-1 and α-HBDH of severe disease group were higher than that of mild disease group, and the differences had statistical significance (P<0.05).

Group	No.	Aspartate aminotransferase (AST)	CK-MB	CK	LDH
Mild disease group	41	45.8±6.1	52.9±10.6	128.4±82.5	457.2±84.7
Severe disease group	39	55.4±7.6	67.4±14.2	148.9±99.4	494.5±99.3
t value		2.673	3.226	3.148	3.685
P value		0.011	0.000	0.001	0.000

Group	No.	LDH-1	α-HBDH	ALT	Glutamic oxalacetic transaminase (AST)
Mild disease group	41	94.5±41.2	379.6±81.2	48.7±10.0	43.6±8.8
Severe disease group	39	117.9±51.2	415.8±99.7	49.8±9.4	45.3±9.3
t value		2.897	4.105	0.911	1.544
P value		0.007	0.000	0.363	0.124

Table. 3: Comparison of myocardial zymogram index (x±s) (U/L).

ALT and glutamic oxalacetic transaminase (AST) increased little, and the differences had no statistical significance (P>0.05), as shown in Table 3.

Comparison of electrocardiographic features

The heart rate of severe disease group was obviously faster than that of mild disease group. Abnormal change occurrence rate of ST-T section in severe disease group increased significantly, and the differences had statistical significance (P<0.05). Occurrence rate differences of RBBB, VT, VF and VPC in both groups had no statistical significance (P>0.05), as shown in Table 4.

Group	No.	Heart rate (次/min)	Abnormal change of ST-T section [n(%)]	RBBB [n(%)]	VT [n(%)]	VF [n(%)]	VPC [n(%)]
Mild disease group	41	117.0±22.0	4(9.75)	5(12.19)	6(14.63)	2(4.87)	4(9.75)
Severe disease group	39	144.0±19.0	14(34.14)	6(14.63)	10(24.39)	3(7.31)	6(14.63)
t/ X^2 value		10.854	24.18	0.030	2.940	0.036	1.090
P value		0.000	0.000	0.862	0.086	0.850	0.297

Table. 4: Comparison of electrocardiographic features [n(%)].

Discussion

HFMD is a common global infectious disease caused by enterovirus. After the virus invades in the body through respiratory tract or intestinal tract, it is replicated on the epithelial cell of pharyngeal and small intestine and nearby lymphocytes, enters blood and triggers viremia. The common HFMD viruses include A16 coxsackie virus and 71 enterovirus. The disease has selfconfinement property, and the patients with mild symptoms can heal by themselves. The state of individual patients with severe symptoms develops fast, and severe complications may occur such as pulmonary edema, myocarditis and aseptic meningitis. Further, the disease may develop to severe HFMD which brings great threat to patients' life[7-9].

Severe HFMD is mostly infected by EV71 enterovirus which belongs to picornaviridae and enterovirus category. It is a kind of highly neurotropic virus. It can cause the primary viremia. The minority of viruses may invade in reticuloendothelium, deep lymph node and marrow, propagate in quantity and then are discharged into blood circulation to lead to the secondary viremia. The secondary viremia will transport EV71 enterovirus to each organ of the body for mass propagation, thus leading to organ lesion and severe HFMD. The onset of severe HFMD is acute, and the clinical manifestations are not obvious, so missed diagnosis may happen easily. Severe encephalitis and neurogenic pulmonary edema often occur to cause death within a short time. The case fatality rate is high[10]. Clinically, patients' symptoms, signs, rash distribution feature, throat swab or excrement specimen virus detection are used to make a definite diagnosis of HFMD. However, it usually takes 2-4w for virus detection[11], so the optimal opportunity for treatment is often missed.

This study shows WBC level of severe disease group is obviously higher than that of mild disease group, indicating WBC level of HFMD patients rises obviously and the rising degree is related to the state of disease. Consistent with the results of Ben-Chetrit et al.[12]. hs-CRP is acute time phase response protein synthesized by liver, which is a sensibility index to evaluate inflammation level. This study shows that, hs-CRP level of severe disease group is obviously higher than that of mild disease group, indicating hs-CRP rising of HFMD patients is positively correlated with infection degree and hs-CRP is in the high level[13]. Besides, hs-CRP level of high-risk patients is higher than that of general patients[14]. Early hs-CRP level detection can serve as an important reference index for early diagnosis of HFMD and disease severity. FPG level of severe disease group is higher than that of mild disease group. At present, it is mostly believed that hyperglycemia in severe HFMD is mostly transient and irritable, and is caused by the rise of epinephrine and glucagon, so it is the most important predictive index of pulmonary edema caused by HFMD[15]. Myocardial zymogram activity has close relationship with cardiac damage. Myocardial enzyme index detection can reflect myocardial damage[16].

This study shows that, various indexes of myocardial zymogram in the severe disease group are higher than that in the mild disease group. This conclusion prompts that, most severe HFMD patients have myocardial damage, and myocardial damage has close relationship with HFMD severity. This means early myocardial zymogram detection can provide effective information for judging HFMD-combined myocardial damage. WBC, hs-CRP, FPG and myocardial zymogram of severe HFMD patients are higher than that of mild HFMD patients. Their joint detection contributes to early diagnosis and severity evaluation of HFMD and combined

myocardial damage. A lot of researches indicate that[17-18], myocardial cells of EV71 severe HFMD patients have different degrees of edema or necrosis. This may be because virus proliferation in myocardial tissues induces immunoreaction mechanism and leads to myocardial damage. Heart rate change also will reflect the degree of myocardial damage. More severe myocardial damage is, faster the heart rate is. Myocardial damage will lead to multiple kinds of arrhythmia, and specific changes appear to electrocardiogram[19-20].

The study shows that, the heart rate of patients in the severe disease group speeds up obviously, and abnormal change occurrence rate of ST-T section increases significantly. But, the occurrence rates of RBBB, VT, VF and VPC in both groups are close. This prompts that, electrocardiogram and heart rate contribute to early diagnosis of HFMD.

Conclusion

In conclusion, the rise of WBC, hs-CRP, FPG, and myocardial zymogram, heart rate acceleration and abnormal changes of ST-T section have important significance in early diagnosis of HFMD. Thus, it is required to keep an eye on patients' clinical symptoms, electrocardiogram and laboratory examination for early diagnosis, timely treatment, reduction of case fatality rate and prognosis improvement.

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Corresponding Author:
Yu Zhang
Department of Pediatrics,Baoding Children's Hospital, Key Laboratory of Clinical Research on Respiratory Digestive Disease, Hebei Baoding 071000, China
Email: 282@163.com
(China)