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CK-MB、hs-CRP 和 cTnI 联合检测病毒性心肌炎患儿的临床价值研究

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摘要 目的:探讨肌酸激酶同工酶(CK-MB)、超敏 C 反应蛋白(hs-CRP)和心肌肌钙蛋白 I(cTnI)联合检测病毒性心肌炎(VMC)患儿的临床价值。**方法:**选取 2015 年 7 月-2017 年 3 月在本院确诊的 70 例 VMC 患儿为观察组,选取同期在本院体检的 70 例健康儿童为对照组,在入院后第 2d、第 3d、第 5d、第 7d、第 9d 和第 11d 分别测定所有儿童血清 CK-MB、cTnI 和 hs-CRP 水平,分析比较三项指标联合检测和单独检测的灵敏度、特异性和准确性。**结果:**观察组患儿血清 CK-MB、cTnI、hs-CRP 水平均高于对照组,差异有统计学意义($P<0.05$)。观察组患儿 CK-MB、cTnI 和 hs-CRP 联合检测的灵敏度和准确性分别为 90.12%、93.62%,均高于单独检测,差异有统计学意义($P<0.05$),三项指标联合检测的特异性高于 hs-CRP 单独检测,差异有统计学意义($P<0.05$)。检测结果显示,hs-CRP 阳性率最高,但在血清中也最先消失,CK-MB 次之,cTnI 最慢。差异有统计学意义($P<0.05$)。**结论:**采用 CK-MB、cTnI 和 hs-CRP 的联合检测,可提高检测 VMC 患儿的灵敏度和准确性,更具有临床诊断价值。

关键词:病毒性心肌炎;心肌肌钙蛋白 I;肌酸激酶同工酶;超敏 C 反应蛋白;临床价值

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Clinical Value Study of Combined Detection of CK-MB, hs-CRP and cTnI in Children with Viral Myocarditis

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ABSTRACT Objective: To study the clinical value of combined detection of creatine kinase-MB (CK-MB), hypersensitivity C reactive protein (hs-CRP) and cardiac troponin I (cTnI) in children with viral myocarditis (VMC). **Methods:** 70 children diagnosed with VMC in our hospital from July 2015 to March 2017 were selected as the observation group, and 70 healthy children in the same period were selected as the control group. The serum levels of CK-MB, cTnI and hs-CRP were measured in the 2d, 3d, 5d, 7d, 9d, 11d after admission. The sensitivity, specificity and accuracy of combined detection and single detection of three indicators were analyzed and compared. **Results:** The serum levels of CK-MB, cTnI and hs-CRP in the observation group were higher than those in the control group, the differences were statistically significant ($P<0.05$). The sensitivity and accuracy of the combined detection of CK-MB, cTnI and hs-CRP in the observation group were 90.12% and 93.62% respectively, which were higher than those of the single detection, the differences were statistically significant ($P<0.05$). The specificity of combined detection of three indicators was higher than that of hs-CRP single detection, the differences were statistically significant ($P<0.05$). The detection results showed that the positive rate of hs-CRP was the highest, but it disappeared first in the serum, followed by CK-MB, and cTnI was the slowest. The levels of CK-MB, cTnI and hs-CRP and the positive rate of the observation group showed downward trend, the differences were statistically significant ($P<0.05$). **Conclusion:** The combined detection of CK-MB, cTnI and hs-CRP can improve the sensitivity and accuracy of detection of VMC, and it has clinical diagnostic value.

Key words: Viral myocarditis; Cardiac troponin I; Creatine kinase-MB; Hypersensitivity C reactive protein; Clinical value

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前言

病毒性心肌炎(viral myocarditis, VMC)是一种感染性心肌疾病^[1],通常其临床症状描述较为宽泛,比如心肌梗死、伴急性胸痛、心律失常、完全性心脏传导阻滞发病相关的猝死综合征等,使其临床诊断具有挑战性,目前临床检查缺乏专业的实验

设备,导致该病真实的发病率是未知的^[2-4]。VMC 是学龄前及学龄儿童常见的心血管疾病之一,分析患儿感染史、临床症状及体征、采用传统的超声心动图或选择性冠状动脉造影在大多数情况下不能够确诊病情,通常临床上采用心内膜心肌活检(endomyocardial biopsy, EMB)是作为诊断的金标准,但因成本高、风险高、依从性低、创伤大等原因未得到普遍推广^[5-7]。近年许多学者提出肌酸激酶同工酶(creatine kinase-MB, CK-MB)和心肌肌钙蛋白 I(cardiac troponin I, cTnI)可反应 VMC 患者在病毒感染后心肌细胞病变或坏死程度,并且超敏 C 反应蛋白(hy-

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persensitivity C reactive protein,hs-CRP)在 VMC 发病过程中具有重要临床检测意义^[8-10],但是这三项指标的单独检测易造成误诊或漏诊,所以本文联合这三项指标共同检测,旨在探讨这三项指标联合检测能否更加准确地诊断小儿 VMC。

1 材料与方法

1.1 一般资料

选取 2015 年 7 月-2017 年 3 月在本医院确诊的 VMC 患儿 70 例为观察组,纳入标准:(1)参照小儿《病毒性心肌炎诊断标准(修订草案)》中相关标准^[11];(2)年龄 <14 岁;(3)患儿或家属知情同意并签署知情同意书;(4)配合检查者。排除标准:(1)急慢性感染者;(2)合并严重肝、肾、肺功能缺陷者;(3)恶性肿瘤者;(4)精神失常者。其中男 37 例,女性 33 例;年龄 4-14 岁,平均(7.39±2.51)岁。另选取同期在本院体检的健康儿童 70 例作为对照组,其中男 36 例,女性 34 例,年龄 5-13 岁,平均(8.19±2.68)岁。两组儿童的一般资料比较无统计学差异($P>0.05$),具有可比性。本研究的内容符合医院伦理委员会的相关条例,并已批准通过。

1.2 检测方法

对照组儿童于体检当日抽取空腹肘静脉血 5 mL,观察组患儿与入院后第二天抽取空腹肘静脉血 5 mL,均进行离心运动(2500 r/min,30 min),保存分离得到的血清(-40℃),待检。采

用双位点酶免法(上海诊断技术有限公司)检测 CK-MB 水平,采用酶联免疫夹心法(上海伯易生物科技有限公司)检测 cTnI 水平,采用胶乳增强免疫透射比浊法(上海捷门生物技术合作公司)检测 Hs-CRP 水平,检测仪器均为日立 7100 自动生化分析仪。判断标准:CK-MB 大于 25U/L 为阳性,cTnI 大于 1.5ng/L 为阳性,hs-CRP 大于 2 mg/L 为阳性,阳性率=(阳性例数/总例数)*100%。根据公式计算诊断方法的灵敏度、特异性和准确性。计算公式:SE=TP/(TP+FN),SP=TN/(TN+FP),AC=(TP+TN)/(TP+FN+TN+FP),其中 SE 为灵敏度,SP 为特异性,AC 准确性,TP 为真阳性,FP 为假阳性,TN 为真阴性,FN 为假阴性。

1.3 统计学方法

采用 SPSS22.0 软件进行统计分析,CK-MB、cTnI 等计量资料以($\bar{x}\pm s$)表示,用 t 检验或重复测量方差分析比较,特异性、灵敏度等计数资料用[n(%)]表示,行 χ^2 检验分析,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组儿童三项指标水平的比较

观察组患儿血清 CK-MB、cTnI、hs-CRP 水平均高于对照组,差异有统计学意义($P<0.05$)。见表 1。

表 1 两组儿童三项指标水平的比较($\bar{x}\pm s$)

Table 1 Comparison of three indicators in the two groups($\bar{x}\pm s$)

Groups	n	CK-MB(U/L)	cTnI(ng/L)	hs-CRP(mg/L)
Observation group	70	29.51±4.64	6.51±1.72	6.24±2.17
Control group	70	15.85±3.52	1.19±0.58	1.48±1.06
t		19.623	12.2212	10.1234
P		0.000	0.000	0.000

2.2 观察组患儿三项指标灵敏度、特异性和准确性比较

观察组患儿三项指标联合检测的灵敏度和准确性均高于

CK-MB、cTnI、hs-CRP 单独检测,三项指标联合检测的特异性高于 hs-CRP 单独检测,差异有统计学意义($P<0.05$)。见表 2。

表 2 观察组患儿三项指标灵敏度、特异性和准确性比较(%)

Table 2 Comparison of sensitivity, specificity and accuracy of three indexes in the observation group(%)

Indexes	Sensitivity	Specificity	Accuracy
CK-MB	59.82*	95.74	72.16*
cTnI	55.95*	90.53	82.18*
hs-CRP	65.46*	80.28*	72.14*
Combined detection	90.12	95.77	93.62

2.3 观察组患儿三项指标检测结果的动态变化

根据检测结果显示,hs-CRP 阳性率最高,但在血清中也最先消失,CK-MB 次之,cTnI 最慢。观察组患儿 CK-MB、cTnI 和 hs-CRP 水平和阳性率均呈下降趋势,差异有统计学意义($P<0.05$)。见表 3。

3 讨论

VMC 是在感染病毒后由于病毒复制和碎片外泄漏的变化引起的弥漫性或局限性的炎症反应,可导致心室重构或心肌细胞的变化,在人的生命全过程均可发生,但多见于 14 以下的患儿^[12-14]。小儿 VMC 若未得到及时的治疗,会导致患儿心脏扩大甚至心肌病,大多数患儿心电图发生改变,从而给患儿和家庭带来严重的身心压力和经济负担^[15]。目前虽然没有治疗的特效药,但是经过恰当的对症护理治疗,是可以痊愈的,诊断小儿

表 3 观察组患儿三项指标检测结果的动态变化

Table 3 Dynamic changes of three indicators in the observation group

Times	CK-MB(U/L)	Positive rate(%)	cTnI(ng /L)	Positive rate(%)	hs-CRP(mg/L)	Positive rate(%)
2d after admission	32.5± 4.6	59.8	6.5± 1.7	55.9	6.2± 2.1	65.4
3d after admission	26.5± 3.3	37.3	5.5± 2.7	44.2	5.1± 1.0	30.4
5d after admission	20.4± 2.6	23.0	5.0± 1.4	33.2	4.3± 1.1	10.5
7d after admission	17.5± 2.8	18.1	4.2± 1.1	24.3	3.2± 1.3	0.0
9d after admission	12.4± 1.6	0.0	3.5± 1.0	15.3	2.0± 1.2	0.0
11d after admission	8.3± 3.1	0.0	2.0± 1.7	8.2	0.8± 1.1	0.0
F_{x^2}	7.547	9.887	6.947	11.947	12.576	10.587
P	0.002	0.001	0.005	0.000	0.000	0.000

VMC 需借助多种辅助检查,其中血清学指标检测是实验室检查的方法之一,优点较多,包括无创伤、操作方便、患儿依从性高等,可作为多种疾病诊断及预后判断^[16-18]。

CK-MB 在临床上早有研究,血液中含量甚低,但是能够在心肌细胞损伤或坏死时检测出来,浓度随着病情的发展逐渐升高,在 9-30h 间达高峰,然后逐渐恢复到原来的水平^[19,20]。cTn 分为 cTnT、cTnI 两类,可以反应心肌损伤的微小改变,许多学者已研究了关于诊断 VMC 的价值^[21]。cTnI 只存在于心肌损伤过程中,cTnT 存在于非心脏的其他器官的肌肉中,并且健康人群血液中 cTnI 甚少,特异性高。C 反应蛋白(C reactive protein, CRP)是一种体内急性期炎症活动或组织损伤的应答蛋白,与炎症反应程度呈正相关^[22,23]。对 CRP 研究主要集中在心脑血管的损伤,特异性低,且需要炎症反应达到一定强度才可检测到,因此轻症患者需要更高灵敏的检测方法。近年来,有研究提出敏感性高的测量物即 hs-CRP,其检测水平为 0.1-10 mg/L,是所有炎症反应检测的标志物^[24,25]。

由本次研究结果可知,观察组患儿血清 CK-MB、cTnI 和 hs-CRP 水平均高于对照组 ($P<0.05$),提示观察组患儿的 CK-MB、cTnI 和 hs-CRP 水平比健康儿童的偏高,所以 CK-MB、cTnI 和 hs-CRP 水平可作为小儿 VMC 的诊断指标。本研究结果显示,观察组患儿三项指标联合检测的灵敏度和准确性均高于 CK-MB、cTnI、hs-CRP 单独检测,三项指标联合检测的特异性高于 hs-CRP 单独检测($P<0.05$),说明三项指标联合检测具有更高的准确性。可能的原因是 CK-MB 作为心肌损伤的诊断指标物,检测出现真阳性的机会较多,同时真阴性的概率大,但其临床表现差异大,且当其他器官有损伤也有检出较高含量的 CK-MB,单独由 CK-MB 浓度偏高一项指标诊断心肌损伤易造成误诊、漏诊^[26,27]。CK-MB 的分子量高于 cTnI 的分子量,则心肌损伤时 cTnI 分子更易从细胞中释放出来,但在临床诊断 VMC 时血清 cTnI 的灵敏度并不高,因此不能作为诊断 VMC 的唯一指标,需要寻找更加敏感和特异的指标物^[28,29]。hs-CRP 可检测炎症反应,但单一指标检测易导致误诊,因此需进行联合检测。本次检测结果显示,hs-CRP 阳性率最高,但在血清中也最先消失,CK-MB 次之,cTnI 最慢。观察组患儿 CK-MB、cTnI 和 hs-CRP 水平和阳性率均呈下降趋势($P<0.05$)。分析得出,VMC 患儿 hs-CRP 灵敏度比较高,但是也是最先消失,并且在其他心脑血管损害中也可检测到,特异性低,CK-MB、

cTnI 在血清中停留时间较长,特异性高,但是灵敏度不够理想,对诊断患病初期的患儿有一定的误差,这与李友邕^[30]等人的研究结果一致。所以要确诊 VMC 需要结合血清三项指标联合检查,并且进行综合判断,以确保准确性,避免漏诊误诊。

综上所述,CK-MB、cTnI、hs-CRP 三项指标联合检测的灵敏度和准确性均高于单独检测,并且特异性高于 hs-CRP 单独检测,可提高临床准确度,值得推广应用。

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