

参麦注射液治疗心肺复苏后患者心肌损伤的临床观察

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DOI: 10.3969/j.issn.1008-9691.2017.06.009

【摘要】 目的 观察参麦注射液对心肺复苏(CPR)患者心肌损伤的影响,并探讨其可能的作用机制。**方法** 选择青岛市海慈医院 2010 年 1 月至 2016 年 12 月就诊的心搏呼吸骤停患者 62 例,将患者按简单随机方法分为常规治疗对照组 30 例和参麦治疗组 32 例。两组患者均给予 CPR 基本生命支持,同时给予复苏常用药物治疗;参麦治疗组在常规治疗基础上静脉滴注(静滴)参麦注射液 100 mL,每日 1 次。治疗 7 d 进行疗效评价。于治疗前和治疗 1、3、7 d 取血测定两组患者心肌损伤标志物肌酸激酶同工酶(CK-MB)、心肌肌钙蛋白 T(cTnT)、N 末端 B 型钠尿肽前体(NT-proBNP)水平,并观察两组室性心动过速、心室纤颤(室颤)及房室传导阻滞等心律失常发生率;采用床旁二维超声心动图测定两组患者左室射血分数(LVEF)、每搏量(SV)、心排血量(CO)。**结果** 常规治疗对照组治疗 1 d CK-MB、cTnT 表现为一过性升高,治疗 3 d 后较治疗前明显降低,治疗 7 d 达到最低水平;NT-proBNP 治疗后持续降低,LVEF、SV、CO 治疗后持续升高;参麦治疗组治疗后 CK-MB、NT-proBNP 持续降低,cTnT 先升高后逐渐降低,治疗后 7 d 达到最低水平,LVEF、SV、CO 先降低后逐渐升高,治疗后 7 d 达到最高水平;参麦治疗组治疗后 3、7 d CK-MB、cTnT、NT-proBNP 均明显低于常规治疗对照组[治疗 3 d: CK-MB(U/L)为 51 ± 1 比 82 ± 3 , cTnT($\mu\text{g/L}$)为 2.5 ± 0.3 比 3.9 ± 0.2 , NT-proBNP(ng/L)为 5810 ± 103 比 15965 ± 152 ;治疗 7 d: CK-MB(U/L)为 27 ± 2 比 56 ± 3 , cTnT($\mu\text{g/L}$)为 1.2 ± 0.3 比 2.9 ± 0.2 , NT-proBNP(ng/L)为 2834 ± 123 比 4832 ± 76], LVEF、SV、CO 均明显高于常规治疗对照组[治疗 3 d: LVEF 为 0.47 ± 0.03 比 0.45 ± 0.02 , SV(mL)为 45 ± 5 比 39 ± 4 , CO(L/min)为 3.7 ± 0.2 比 3.6 ± 0.2 ;治疗 7 d: LVEF 为 0.59 ± 0.02 比 0.51 ± 0.03 , SV(mL)为 55 ± 4 比 45 ± 2 , CO(L/min)为 5.3 ± 0.3 比 4.6 ± 0.4 , 均 $P < 0.05$]。两组患者 CPR 后均有心律失常发生,参麦治疗组治疗 1 d 心律失常发生率与治疗前比较差异均无统计学意义(均 $P > 0.05$),治疗 3、7 d 后心律失常发生率均较治疗前明显下降,治疗 7 d 达最低水平,且参麦治疗组治疗后降低程度较对照组更显著[室性心动过速: 9.4%(3/32)比 20.0%(6/30),室颤: 9.4%(3/32)比 20.0%(6/30),房室传导阻滞: 18.8%(6/32)比 36.7%(11/30),均 $P < 0.05$]。**结论** 参麦注射液对 CPR 后患者心肌损伤有一定保护作用,其机制可能与降低 CK-MB、cTnT、NT-proBNP 水平,进而改善 LVEF、SV、CO 有关。

【关键词】 心肺复苏; 心肌损伤; 缺血/再灌注; 参麦注射液

基金项目: 山东省青岛市医药科研指导计划(2007-WSZD-068)

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【Abstract】 Objective To observe the curative effect of Shenmai injection on patients with myocardial injury after cardiopulmonary resuscitation (CPR) and to explore its possible mechanism. **Methods** Sixty-two patients with cardiac arrest and respiratory arrest admitted to Qingdao Hiser Hospital from January 2010 to December 2016 were enrolled, they were randomly divided into a conventional therapy control group (30 cases) and a Shenmai treatment group (32 cases) and both groups were also treated by conventional treatment. The patients in the two groups were given basic life support of CPR and its commonly used drugs simultaneously. In Shenmai treatment group, the patients were additionally infused intravenously with 100 mL of Shenmai injection once per day. The therapeutic effect was evaluated after treatment for 7 days. On the day before treatment and 1, 3 and 7 days after treatment, the patient's blood was collected to determine the levels of myocardial injury landmarks, serum creatine kinase isoenzyme (CK-MB), cardiac troponin T (cTnT) and N-terminal B-type natriuretic peptide (NT-proBNP), and the incidences of arrhythmia of ventricular tachycardia, ventricular fibrillation (VF) and atrioventricular block were observed in the two groups; the left ventricular ejection fraction (LVEF), stroke volume (SV) and cardiac output (CO) were measured at bedside by two-dimensional echocardiography for the patients of two groups. **Results** In conventional therapy control group, the levels of CK-MB, cTnT showed a temporary increase after 1 day of treatment, after 3 days of treatment, CK-MB and cTnT were significantly lower than those before treatment, and reached the lowest levels after 7 days of treatment; the level of NT-proBNP after treatment showed a continuous decrease, the levels of LVEF, SV, CO were persistently increased after treatment; in Shenmai treatment group, the levels of CK-MB, NT-proBNP were decreased continuously after treatment, cTnT was firstly increase and then decrease, and reached to the lowest levels after 7 days of treatment while the levels of LVEF, SV and CO were firstly decreased and then increased gradually, and reached to the highest levels after 7 days of treatment; compared with those of conventional therapy control group, the levels of CK-MB, cTnT, NT-proBNP in Shenmai treatment group were significantly lower after 3 and 7 days of treatment [3 days of treatment: CK-MB (U/L)

was 51 ± 1 vs. 82 ± 3 , cTnT ($\mu\text{g/L}$) was 2.5 ± 0.3 vs. 3.9 ± 0.2 , NT-proBNP (ng/L) was $5\,810 \pm 103$ vs. $15\,965 \pm 152$; 7 days of treatment: CK-MB (U/L) was 27 ± 2 vs. 56 ± 3 , cTnT ($\mu\text{g/L}$) was 1.2 ± 0.3 vs. 2.9 ± 0.2 , NT-proBNP (ng/L) was $2\,834 \pm 123$ vs. $4\,832 \pm 76$, while LVEF, SV and CO were significantly higher than those in conventional therapy control group [3 days of treatment: LVEF was 0.47 ± 0.03 vs. 0.45 ± 0.02 , SV (mL) was 45 ± 5 vs. 39 ± 4 , CO (L/min) was 3.7 ± 0.2 vs. 3.6 ± 0.2 ; 7 days of treatment: LVEF was 0.59 ± 0.02 vs. 0.51 ± 0.03 , SV (mL) was 55 ± 4 vs. 45 ± 2 , CO (L/min) was 5.3 ± 0.3 vs. 4.6 ± 0.4 , all $P < 0.05$]. After CPR, arrhythmia developed in the patients of two groups, and compared with that before treatment, there was no statistical significant difference in the incidence of arrhythmia after 1 day of treatment in Shenmai treatment group (all $P > 0.05$); the incidence of arrhythmia was decreased significantly after 3 and 7 days of treatment compared with those before treatment, reached to the lowest level on the 7th day of treatment, and the degree of decrease of incidence of arrhythmia in Shenmai treatment group was more obvious than those of the conventional therapy control group [ventricular tachycardia: 9.4% (3/32) vs. 20.0% (6/30), VF: 9.4% (3/32) vs. 20.0% (6/30), atrial ventricular block: 18.8% (6/32) vs. 36.7% (11/30), all $P < 0.05$]. **Conclusions** Shenmai injection has certain protective effect on injured myocardium in patients undergoing CPR, the mechanism is possibly related to reducing the levels of CK-MB, cTnT, NT-proBNP and further improving the LVEF, SV and CO.

[Key words] Cardiopulmonary resuscitation; Myocardial injury; Ischemia/reperfusion; Shenmai injection

Fund program: Guiding Program of Medical and Pharmaceutical Scientific Research of Qingdao, Shandong Province (2007-WSZD-068)

心肺复苏后综合征(PCAS)是指心搏骤停(CA)复苏成功后出现的严重全身系统性缺血后多器官功能障碍或衰竭,又称为复苏后多器官功能障碍综合征(PMODS)^[1]。有研究表明,PCAS或PRMODS是CA患者最终复苏失败和整体预后不良的重要原因^[2]。心肺复苏(CPR)后,由于各器官血流灌注不足和缺氧,引起组织功能不同程度损伤以及再灌注损伤,进而出现心、肺、肝、肾及大脑等多器官功能不全或衰竭。CA患者死亡的重要原因是CPR后心功能障碍^[3]。复苏后心功能障碍是患者死亡的主要原因之一^[4],因此,加强复苏后续治疗,改善患者心肌功能,进而可以降低病死率。参麦注射液源于明代秦景明《症因脉治》中的参麦饮,主要由红参、麦冬组成。现代药理学研究表明,参麦注射液化学成分主要为人参皂苷、人参多糖、甾苷、有机酸等,具有加强机体器官抗应激能力的作用,目前临床多用于治疗休克气阴两虚证、冠心病、病毒性心肌炎、慢性肺源性心脏病(肺心病)、粒细胞减少症等^[5]。本研究观察参麦注射液对CPR后患者心功能的影响,现报告如下。

1 资料与方法

1.1 病例的选择:选择2010年1月至2016年12月在本院急诊就诊的心搏呼吸骤停患者62例,其中男性34例、女28例,年龄33~74岁、平均(55.1 ± 15.2)岁;心搏呼吸骤停原因为心源性猝死、药物过敏、溺水、电击伤、休克、其他如不明原因猝死等。

1.1.1 纳入标准:临床诊断为猝死;年龄 <18 岁或 >75 岁;起病30 min内入院。

1.1.2 排除标准:原有慢性呼吸道疾病、恶性肿瘤、严重肝肾疾病、血液系统疾病等;既往有卒中史。

1.1.3 伦理学:本研究符合医学伦理学标准,并经本院医学伦理委员会批准,取得患者或家属知情同意。

1.2 研究分组:将62例患者按简单随机方法分为常规治疗对照组30例和参麦治疗组32例。两组性别、年龄、原发病比较差异均无统计学意义(均 $P > 0.05$;表1),说明两组资料均衡,有可比性。

1.3 治疗方法:常规治疗对照组采用西医常规治疗,严格按照2010版CPR指南给予胸外心脏按压、气管插管、电除颤和经静脉使用常规CPR药物^[6];参麦治疗组在西医常规治疗基础上给予参麦注射液(由大理药业股份有限公司生产)100 mL+生理盐水500 mL静脉滴注(静滴),每日1次,治疗7 d进行疗效评价。

1.4 观察指标:观察两组室性心动过速、室颤(室颤)及房室传导阻滞等心律失常的发生率;于治疗前和治疗1、3、7 d取两组患者静脉血,采用光电比色法、化学发光法、双向测流免疫法分别测定心肌损伤标志物肌酸激酶同工酶(CK-MB)、心肌肌钙蛋白T(cTnT)、N末端B型钠尿肽前体(NT-proBNP)水平;采用床旁二维超声心动图测定两组左室射血分数(LVEF)、每搏量(SV)、心排血量(CO)水平。

表1 两组一般资料比较

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)	原发病(例)					
		男性	女性		溺水	电击伤	药物过敏	心源性猝死	休克	其他
常规治疗对照组	30	17	13	57.2 ± 13.2	2	3	1	6	15	3
参麦治疗组	32	17	15	53.3 ± 14.1	1	2	1	9	17	2

1.5 统计学处理: 使用 SPSS 17.0 统计软件处理数据,符合正态分布的计量资料以均数 $\pm$ 标准差 ($\bar{x} \pm s$) 表示,组间比较采用 LSD-*t* 检验;计数资料以例数表示,采用 χ^2 检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组心律失常发生率比较(表 2): 两组患者 CPR 后均有心律失常发生,治疗 1 d 心律失常发生率无明显变化,治疗 3、7 d 后心律失常发生率均较治疗前明显下降,治疗 7 d 达最低水平,且参麦治疗组治疗后的降低程度较对照组更显著(均 $P < 0.05$)。

表 2 两组心律失常发生率比较

组别	例数	治疗时间	心律失常 [% (例)]		
			室性心动过速	室颤	房室传导阻滞
常规治疗对照组	30	治疗前	50.0 (15)	53.3 (16)	90.0 (27)
	30	治疗 1 d	43.3 (13)	50.0 (15)	83.3 (25)
	30	治疗 3 d	33.3 (10) ^a	43.3 (13) ^a	53.3 (16) ^a
	30	治疗 7 d	20.0 (6) ^a	20.0 (6) ^a	36.7 (11) ^a
参麦治疗组	32	治疗前	37.5 (12)	56.3 (18)	87.5 (28)
	32	治疗 1 d	43.8 (14)	56.3 (13)	87.5 (26)
	32	治疗 3 d	18.8 (6) ^{ab}	21.9 (7) ^{ab}	37.5 (12) ^{ab}
	32	治疗 7 d	9.4 (3) ^{ab}	9.4 (3) ^{ab}	18.8 (6) ^{ab}

注:与治疗前比较,^a $P < 0.05$;与常规治疗对照组比较,^b $P < 0.05$

2.2 两组心肌损伤标志物及心功能指标的变化比较(表 3): 常规治疗对照组治疗 1 d CK-MB、cTnT 表现为一过性升高,治疗 3 d 后较治疗前明显降低,治疗 7 d 达到最低水平,NT-proBNP 治疗后持续降低,LVEF、SV、CO 治疗后持续升高;参麦治疗组治疗后 CK-MB、NT-proBNP 持续降低,cTnT 先升高后逐渐降低,治疗后 7 d 达到最低水平,LVEF、SV、CO 先降低后升逐渐升高,治疗后 7 d 达到最高水平;且参麦治疗组治疗后 3、7 d CK-MB、cTnT、NT-proBNP 均明显低于常规治疗对照组,LVEF、SV、CO 均明显高于常规治疗对照组(均 $P < 0.05$)。

3 讨论

部分患者或动物在缺血后实施再灌注,不仅不能使组织器官功能恢复,反而使代谢紊乱、功能及结构破坏进一步加重^[7]。CPR 后心肌功能障碍主要与心肌缺血以及再灌注损伤有关^[8],再灌注是治疗缺血性心脏病的常用措施,但再灌注常导致心律失常、心肌舒缩功能障碍及心肌细胞不可逆损伤加重,引起心肌缺血/再灌注(I/R)损伤^[9];心肌 I/R 时可以产生大量氧自由基,而氧自由基可使代谢酶活性丧失,加重心肌能量和抗氧化储备的缺乏,这些氧自由基中的超氧阴离子能与一氧化氮(NO)结合,生成过氧化亚硝酸盐,进而生成一种强氧化剂过氧化硝酸损害心功能。也有研究表明,炎症反应参与了动脉粥样硬化的发生发展^[10],CPR 后患者肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β) 水平明显升高^[11],这些炎症因子与心功能的下降有一定相关性。现代药理学研究证明,参麦注射液能通过减少 IL-6、TNF- α 等细胞因子水平,减轻炎症反应^[12]。研究显示,CA 后,心肌细胞缺血、缺氧,使有氧氧化转变为无氧氧化,能量供给不足,导致细胞功能障碍,心功能受损,能量缺乏使细胞质内游离 Ca^{2+} 持续升高,诱发心律失常,加重心肌缺血、缺氧损伤,ATP 酶活性的降低亦参与了 CPR 后的心肌损伤^[13]。研究表明,凋亡是缺血性心肌细胞死亡的重要方式之一^[14]。此外,CPR 中,电除颤本身也会损伤心肌,需要中断胸外按压^[15]。因此,重视胸外按压,避免中断,可使心肌得到持续有效的血流灌注^[16]。

而《内经》记载“正气存内,邪不可干”“邪之所凑,其气必虚”。CPR 自主循环刚刚恢复以阴阳俱亡、心阳暴脱、亡阳为主,治宜温经回阳^[17],通过扶助正气,进而使正气盛,邪气有所制,谓之扶正祛邪。参麦注射液源于祖国医学参麦饮,具有益气固

表 3 两组心肌损伤标志物及心功能指标比较 ($\bar{x} \pm s$)

组别	例数 (例)	治疗时间	CK-MB (U/L)	cTnT (μ g/L)	NT-proBNP (ng/L)	LVEF	SV (mL)	CO (L/min)
常规治疗对照组	30	治疗前	107 $\pm$ 3	4.6 $\pm$ 0.3	23 623 $\pm$ 98	0.36 $\pm$ 0.03	28 $\pm$ 2	2.2 $\pm$ 0.5
	30	治疗 1 d	116 $\pm$ 2	4.7 $\pm$ 0.1	21 687 $\pm$ 236	0.39 $\pm$ 0.02	30 $\pm$ 4	2.5 $\pm$ 0.3
	30	治疗 3 d	82 $\pm$ 3 ^a	3.9 $\pm$ 0.2 ^a	15 965 $\pm$ 152 ^a	0.45 $\pm$ 0.02 ^a	39 $\pm$ 4 ^a	3.6 $\pm$ 0.2 ^a
	30	治疗 7 d	56 $\pm$ 3 ^a	2.9 $\pm$ 0.2 ^a	4 832 $\pm$ 76 ^a	0.51 $\pm$ 0.03 ^a	45 $\pm$ 2 ^a	4.6 $\pm$ 0.4 ^a
参麦治疗组	32	治疗前	112 $\pm$ 2	4.5 $\pm$ 0.4	19 870 $\pm$ 169	0.39 $\pm$ 0.03	32 $\pm$ 3	2.9 $\pm$ 0.3
	32	治疗 1 d	107 $\pm$ 3	4.9 $\pm$ 0.1	17 357 $\pm$ 201	0.36 $\pm$ 0.02	30 $\pm$ 3	2.7 $\pm$ 0.2
	32	治疗 3 d	51 $\pm$ 1 ^{ab}	2.5 $\pm$ 0.3 ^{ab}	5 810 $\pm$ 103 ^{ab}	0.47 $\pm$ 0.03 ^{ab}	45 $\pm$ 5 ^{ab}	3.7 $\pm$ 0.2 ^{ab}
	32	治疗 7 d	27 $\pm$ 2 ^{ab}	1.2 $\pm$ 0.3 ^{ab}	2 834 $\pm$ 123 ^{ab}	0.59 $\pm$ 0.02 ^{ab}	55 $\pm$ 4 ^{ab}	5.3 $\pm$ 0.3 ^{ab}

注:与治疗前比较,^a $P < 0.05$;与常规治疗对照组比较,^b $P < 0.05$

脱、养阴生津的功效,是体现扶正祛邪法的代表药物。现代临床多将其用于气阴两虚之休克、冠心病、病毒性心肌炎等的治疗。现代药理学研究显示,参麦注射液对受损心肌有抗 I/R 损伤和保护的作用,可逆转心肌重塑,改善心功能^[18]。体外实验表明,参麦注射液可改善心肌细胞的能量代谢,抑制心肌细胞凋亡^[19]。在临床上将参麦注射液用于 CPR 患者的后续治疗中,对于改善 CPR 后患者心功能有一定疗效。而且,中药多靶点的作用往往会收到良好的效果^[20]。

近年来研究发现,血清 cTnT 是一个反映心肌损伤及心肌细胞坏死的标志物^[21],是心脏的特异性抗原,当心肌受损后可以快速、持久释放入血^[22]。研究显示,参麦注射液对其升高无明显抑制作用,但对心肌细胞 cTnT 的脱失有明显抑制作用,说明参麦注射液对心肌损伤有一定的保护作用。本研究显示,治疗 1 d 参麦治疗组 CK-MB、cTnT 与常规治疗对照组比较差异无统计学意义,治疗 3、7 d 参麦治疗组 CK-MB、cTnT 较常规治疗对照组明显降低,其作用机制是通过抑制心肌细胞损伤标志物释放,还是通过抑制心肌细胞 cTnT 的脱失进而发挥作用有待于进一步研究。心脏不仅具有泵血功能,而且还是一个内分泌腺体,当心肌被拉伸时 NT-proBNP 释放入血^[23],其水平高低与心肌负荷水平直接相关。临床上将其作为诊断心衰的指标,同时 LVEF、SV、CO 亦是评估心功能的重要指标,本研究显示,参麦治疗组治疗后 NT-proBNP 水平明显低于常规治疗对照组,LVEF、SV、CO 明显高于常规治疗对照组。因此,参麦注射液可以改善 CPR 后患者的心肌损伤,进而增加了 CPR 的成功率,其机制可能与清除自由基、抑制某些促炎因子的释放及改善心肌能量代谢等有关,其减少心律失常发生的机制可能是通过稳定细胞膜电位,延长受损心肌细胞的动作电位时程,降低 L 型钙通道电流活性,减少 Ca^{2+} 内流,降低细胞内 Ca^{2+} 浓度,减少细胞内钙超载,从而减轻 I/R 损伤,但其保护心肌的具体机制尚有待进一步研究。

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(收稿日期: 2017-05-03)

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(收稿日期: 2017-02-13)