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急性重度敌敌畏中毒患者血清儿茶酚胺水平与其心脏损伤的关系*

汪波 林保冠 石挺慧 陈志丘 吴世畅 何成毓

(海南省农垦三亚医院急诊科 海南 三亚 572000)

摘要 目的:探讨急性重度敌敌畏中毒患者血清儿茶酚胺水平与其心脏损伤的关系。**方法:**选取我院 2009 年 12 月至 2011 年 12 月收治的急性重度敌敌畏中毒患者 40 例,接受阿托品和氯解磷定等常规治疗,检测患者入院第 1、3、5 天血清肌酸激酶(CK-MB)、心肌肌钙蛋白(CTNI)、胆碱酯酶(AchE)、乙酰胆碱(Ach)、肾上腺素(EPI)和去甲肾上腺素(NorP)等指标,分析患者血清儿茶酚胺水平与其心脏损伤的关系。**结果:**40 例患者中,34 例存活,6 例死亡;窦性心动过速 35 例,心电图(ECG)ST-T 改变 36 例;血清 CK-MB、CTNI 入院第 1、3、5 天相比,先升高后降低,出院时降至正常,变化差异有统计学意义(CK-MB: $H=8.782, P=0.002$; CTNI: $H=5.017, P=0.024$)。Ach 入院第 1 天时最高,逐渐降低,出院时恢复到正常水平,变化差异有统计学意义($H=9.235, P=0.002$); AchE 入院第 1 天时最低,逐渐升高至正常,变化差异有统计学意义($H=46.891, P=0.001$)。肾上腺素(EPI)和去甲肾上腺素(NorP)代表儿茶酚胺的变化,入院当天为峰值,其后均逐渐下降,出院恢复正常,变化差异有统计学意义(EPI: $H=16.031, P=0.021$; NorP: $H=57.913, P=0.025$)。进一步分析显示 EPI 和 NorP 水平分别与 CK-MB 和 CTNI 呈显著正相关,差异均具有统计学意义($P<0.05$)。**结论:**敌敌畏中毒时,儿茶酚胺与乙酰胆碱的释放增多,可能引起心肌损害或加重心肌缺血的严重程度。

关键词:重度急性敌敌畏中毒;心脏损伤;儿茶酚胺

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Relationship between the Heart Injury and Catecholamine Level of Patients with Severe Acute Dichlorvos Poisoning*

WANG Bo, LIN Bao-guan, SHI Ting-hui, CHEN Zhi-qiu, WU Shi-chang, HE Cheng-yu

(Department of Emergency of the Third People's Hospital of Hainan, Sanya, Hainan, 572000, China)

ABSTRACT Objective: To study the relationship between the heart injury and catecholamine level of patients with severe acute dichlorvos poisoning. **Methods:** 40 patients with severe acute dichlorvos poisoning admitted in our hospital from December 2009 to December 2012 were selected. The alteration of creatine kinase-MB (CKMB), cardiac troponin I (CTNI), acetylcholinesterase(AchE), acetylcholine (Ach), epinephrine (EPI) and norepinephrine(NorP) levels were detected for patients with atropine and chlorine phosphate solubilizing sst routine therapy on the 1st, 3rd and 5th day after admission. And the relationship between the catecholamine levels and the heart damage was analyzed. **Results:** In 40 patients, 34 patients lived and 6 cases died. 35 patients had sinus tachycardia and 36 patients with ST-T change. Serum CK-MB, CTNI increased at first and then dropped to normal. The difference was statistically significant (CK-MB: $H=8.782, P=0.002$; CTNI: $H=5.017, P=0.024$). Ach admission by 1 supreme, and gradually reduce, the hospital returned to normal level. The difference was statistically significant ($H=9.235, P=0.002$). AchE admission minimum, and gradually rise to normal. The difference was statistically significant($H=46.891, P=0.001$). EPI and NorP on behalf of catecholamine changes, to the hospital for the peak, then decreased gradually and at last returned to normal. The difference was statistically significant(EPI: $H=16.031, P=0.021$; NorP: $H=57.913, P=0.025$). **Conclusion:** Dichlorvos poisoning could increase the release of catecholamines and acetylcholine, which may cause myocardial damage or worsen the severity of myocardial ischemia.

Key words: Severe acute dichlorvos poisoning; Heart damage; Catecholamine

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前言

据统计,全球每年因农药中毒的死亡人数高达 20 万,其中 2/3 死亡患者为有机磷农药中毒 (acute organophosphorus poisoning, AOPP)所致。有机磷农药中毒的表现多样,其主要死亡

原因为急性呼吸衰竭。多数患者在及时抢救之后可脱离生命危险,但是病情稳定之后,部分患者会突然死亡,其原因尚不清楚。临床推测可能与心脏损伤有直接关系,其机理可能与儿茶酚胺异常、心肌缺血、心肌坏死有关^[1,2]。因此,本研究通过检测急性重度敌敌畏中毒患者的肌酸激酶同工酶(CK-MB)、心肌肌

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作者简介:汪波(1971-),男,本科,主治医师,研究方向:心肺复苏,电话:13876598155,

E-mail:wangbo_1971@126.com

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钙蛋白(CTNI)、胆碱酯酶(AchE)、乙酰胆碱(Ach)、肾上腺素(EPI)和去甲肾上腺素(NorP)水平并记录各指标变化,旨在分析其儿茶酚胺水平与心脏损伤的关系,为临床治疗急性敌敌畏中毒提供重要依据。

1 资料与方法

1.1 一般资料

选取 2009 年 12 月 31 日至 2011 年 12 月 31 日于我院急诊科就诊的急性重度敌敌畏中毒(SADP)患者 40 例。入选标准按照 SADP 诊断标准^[1]:(1)短时间内摄入敌敌畏;(2)昏迷;(3)需机械通气支持呼吸;(4)休克;(5)血清胆碱酯酶活性下降大于 30%。有其他有机磷中毒或合并有敌敌畏中毒者,及确诊患有心脏病、糖尿病、高血压者予以排除。40 例患者中,男 16 例,女 24 例,年龄范围 16-60 岁,平均年龄 37.17 ± 10.02 岁。

1.2 方法

所有患者均行常规 ICU 监护,给予阿托品、氯解磷定、血管活性药物、营养支持剂等治疗,根据需要配合机械通气,于静脉推注阿托品,使患者保持阿托品化,即维持血压 $>90/60$ mm

Hg,心率 >100 次/min,腋部无汗,瞳孔扩大。肌肉注射氯解磷定 1.5 g,每 3 h 一次,逐渐减量直至患者乙酰胆碱酯酶(AchE)恢复正常。

所有患者均于入院第 1、3、5 天检测,肌酸激酶同工酶(CK-MB)、心肌肌钙蛋白(CTNI)、胆碱酯酶(AchE)、乙酰胆碱(Ach)、肾上腺素(EPI)和去甲肾上腺素(NorP)。

1.3 统计学分析

所有资料用 SPSS17.0 进行统计,AchE、Ach、CK-MB、EPI 和 NorP 用重复测量的方法进行分析。计量资料用均数 $\pm$ 标准差表示,组间比较采用 t 检验,计数资料用例数和百分率表示,组间比较采用 χ^2 检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 患者的临床表现和结局

40 例 SADP 患者入院时均表现为昏迷、肌颤、心动过速、小便失禁,以及胆碱能样、烟碱样和中枢神经系统症状。其中,34 例好转出院,6 例死亡,2 名为男性(见表 1)。

表 1 入院时患者的临床症状和体征(n=40)

Table 1 Clinical signs and symptoms of patients on admission(n=40)

Cholinergic	Case(n, %)	Nicotinic	Case(n, %)	Central	Case(n, %)
Miosis	6(15.0)	Muscular Twitching	39(97.5)	Convulsions	25(62.5)
Vomiting	8(20.0)	Polycardia	30(75.0)	Coma	37(92.5)
Salivation	19(47.5)	Hypertension	19(47.5)		
Hyperhidrosis	10(25.0)				
Frothy Sputum	12(30.0)				
Gatism	15(37.5)				
Bradycardia	12(30.0)				
hypotension	3(7.5)				

2.2 患者 ECG 的变化

入院后行心电图(ECG)检测,窦性心动过速 30 例,窦性心动过缓 8 例,室早 3 例,PR 间期延长 6 例,右束支传导阻滞 2 例,入院时 ST-T 改变 35 例,其中 19 例 ST 段抬高,16 例压低。6 例患者 V1-V2 导联 T 波倒置;12 例 T 波高尖。3 例患者出现 u 波。出院时,患者心电图各项指标都趋于正常,部分患者有 1-2 项指标异常。

2.3 患者血清学指标的变化

入院第 1 天,患者血清乙酰胆碱酯酶(AchE)出现最低值,为 (1456.23 ± 352.04) U/L,之后逐渐升高,出院时已恢复到正常水平,变化差异有统计学意义($H=46.891$, $P=0.001$)。心肌损伤标志物 CK-MB 和 CTNI 在第 3 天达到峰值(27.89 ± 1.32) ng/ml,

(7.05 ± 4.85) ng/ml,随后下降,出院前基本恢复正常,变化差异有统计学意义(CK-MB: $H=8.782$, $P=0.002$; CTNI: $H=5.017$, $P=0.024$)。乙酰胆碱(Ach)入院时达峰 (17.47 ± 1.86) ng/ml,出院时恢复正常,变化差异有统计学意义($H=9.235$, $P=0.002$)。肾上腺素(EPI)和去甲肾上腺素(NorP)代表儿茶酚胺的变化,入院当天为峰值分别为 (163.85 ± 18.34) pg/ml 和 (1087.29 ± 257.05) pg/ml,其后均逐渐下降,出院恢复正常,变化差异有统计学意义(EPI: $H=16.031$, $P=0.021$; NorP: $H=57.913$, $P=0.025$)(见表 2)。进一步分析显示 EPI 和 NorP 分别与 CK-MB 和 CTNI 呈显著正相关,差异均具有统计学意义 (EPI: $r_{CK-MB}=5.329$, $P_{CK-MB}=0.000$; $r_{CTNI}=8.637$, $P_{CTNI}=0.000$; NorP: $r_{CK-MB}=12.748$, $P_{CK-MB}=0.000$; $r_{CTNI}=14.358$, $P_{CTNI}=0.000$)。

表 2 患者 AchE、CK-MB、CTNI、Ach、EPI 和 NorP 的变化(MEAN $\pm$ SD)

Table 2 Changes of AchE, CK-MB, CTNI, Ach, EPI and NorP of patients(MEAN $\pm$ SD)

Indicators	1d	3d	5d	Leaving hospital	H value	P value
AchE(IU/L)	1456.32 $\pm$ 352.04	1697.77 $\pm$ 858.93	4127.26 $\pm$ 1009.64	7032 $\pm$ 13.86	46.891	0.001
Ach(ng/ml)	17.47 $\pm$ 1.86	15.76 $\pm$ 1.39	13.49 $\pm$ 1.83	9.86 $\pm$ 1.83	9.235	0.002
EPI(pg/ml)	163.85 $\pm$ 18.34	150.84 $\pm$ 14.20	85.39 $\pm$ 21.73	70.27 $\pm$ 4.12	16.031	0.021
NorP(pg/ml)	1087.54 $\pm$ 257.83	877.11 $\pm$ 244.84	411.59 $\pm$ 284.53	264 $\pm$ 11.84	57.913	0.025
CK-MB(ng/ml)	13.04 $\pm$ 9.01	27.89 $\pm$ 1.32	10.92 $\pm$ 2.85	11.35 $\pm$ 2.78	8.782	0.002
CTNI(ng/ml)	4.05 $\pm$ 3.67	7.05 $\pm$ 4.85	5.08 $\pm$ 2.94	2.95 $\pm$ 2.05	5.017	0.024

3 讨论

敌敌畏是最常见的有机磷农药之一,可经皮肤接触、呼吸道吸入及误服、误用而导致中毒^[46]。敌敌畏中毒的机制系由于毒性物质抑制了胆碱酯酶的活性,使乙酰胆碱在体内积蓄,胆碱能神经持续冲动而引发机体出现一系列症状^[7,8]。临床常用的解毒药为胆碱酯酶复活剂和抗胆碱药,胆碱酯酶复活剂如氯解磷定,通过化学作用恢复胆碱酯酶的活性。抗胆碱药如阿托品,通过阻断乙酰胆碱对副交感神经和中枢神经系统受体的作用,从而减轻患者的中毒症状^[9-11]。另外,有文献报道,敌敌畏所致的心律失常和心肌损害,是由于儿茶酚胺分泌增多刺激交感神经或由于使用胆碱酯酶复活剂及阿托品治疗所引起^[12]。因此,本研究通过检测敌敌畏中毒患者 ECG、血清 CK-MB、CTNI、胆碱酯酶、乙酰胆碱、肾上腺素和去甲肾上腺素等指标的变化,旨在分析儿茶酚胺与心脏损伤在敌敌畏中毒患者中的关系。

临床根据中毒症状分为轻度、中度、重度和中间型综合征,轻度仅有头晕头痛、恶心呕吐、多汗、胸闷等;中度还会出现肌纤维颤动、瞳孔缩小、轻度呼吸困难,但意识尚清楚;重度中毒,除上述症状外,可出现昏迷、肺水肿等危象;中间型综合征是一组以肌无力为突出表现的综合征,可在急性中毒后 1~4 天突发死亡。敌敌畏中毒损害最终并非单脏器或组织受损,其病理机制较为复杂,本研究用 ECG 的检测值代表心脏的总体受损状态,CK-MB、CTNI 数值分析心肌的受损情况,肾上腺素和去甲肾上腺素的水平反应患者体内儿茶酚胺的波动,进而分析各项指标代表的脏器之间的相关性^[13-15]。

本研究 40 例患者的 Ach 入院时均为峰值,经过治疗后逐渐降低,到出院时恢复正常,代表从敌敌畏重度中毒到机体恢复正常的整个过程。在此过程中,大量血清 Ach 诱导交感神经活跃,产生儿茶酚胺入血,使得肾上腺素和去甲肾上腺素水平升高,最终出现了心肌的损伤^[16]。本研究认为引起心脏功能紊乱的主要原因可能是内源性儿茶酚胺增多所致。40 例患者中都出现了不同程度的心肌损害,并且当儿茶酚胺释放增多时损伤更为严重,由此可以推测敌敌畏中毒与心血管系统受损有密切关系,其机制可能与乙酰胆碱作用于中枢神经系统和心脏有关系^[17-19]。从敌敌畏中毒患者 ECG 的变化发现,30 例患者出现心动过速,可能与中毒后乙酰胆碱大量释放有关,但也不排除是电解质紊乱、低氧血症、代谢性酸中毒所引起。研究敌敌畏中毒患者心肌缺血的症状发现,有 35 例出现 ST-T 改变,其中 19 例 ST 段抬高,16 例压低,并且随病情的好转发生变化,出院时可恢复正常,这就与乙酰胆碱、肾上腺素和去甲肾上腺素的变化趋势有着很好的相关性。临床观察表明,敌敌畏中毒患者,心脏均有严重损害,可能是由于机体自身产生的儿茶酚胺作用于中枢系统刺激分泌乙酰胆碱有关,也可能是儿茶酚胺直接刺激心脏所致^[20]。

综上所述,重度急性敌敌畏中毒可导致心脏损伤,儿茶酚胺分泌增加可能是重要原因之一,这可能为以后临床治疗急性敌敌畏中毒提供了有效的参考依据。

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