

57例急性重度敌敌畏中毒患者的临床特征和救治体会

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【摘要】目的 总结急性重度敌敌畏中毒的临床特征和救治体会。**方法** 回顾性分析2014年7月至2019年12月厦门大学附属东南医院暨联勤保障部队第九〇九医院收治的57例急性重度敌敌畏中毒患者的临床资料,其中男性23例、女性34例,年龄38(18~80)岁,均为口服中毒。在重症监护下,给予基础救治措施,包括清除毒物、特效解毒剂、血液净化、呼吸支持、循环支持等;针对顽固性低血压和严重心律失常在积极给予容量复苏、纠正酸中毒、稳定内环境的同时,增加保护心肌药、血管活性药和抗心律失常药的使用,必要时安装临时起搏器。观察患者心脏损害发生情况、转归和预后,分析影响患者预后的相关因素。采用多因素Logistic回归分析影响患者预后的独立危险因素。**结果** 本组73.7%(42/57)的患者合并不同程度心脏损害,表现为心肌酶谱不同程度升高42例(100.0%)、心电图改变39例(92.9%)、心律失常25例(59.5%)、低血压14例(33.3%)、高血压2例(4.8%)。本组患者重症监护病房(ICU)住院时间2~10 d,平均(5.6 ± 1.7)d;总住院时间2~14 d,平均(9.5 ± 2.4)d。本组患者治愈45例,好转5例,死亡7例(12.3%),其中4例死于心搏骤停或严重室性心律失常,2例死于多器官功能衰竭,1例死于中枢性呼吸循环功能衰竭。单因素分析显示,死亡患者入院时格拉斯哥昏迷评分(GCS)较存活者低(分: 3.4 ± 0.6 比 4.3 ± 1.1 , $P=0.039$),严重心律失常发生率较存活者高[57.1%(4/7)比20.0%(10/50), $P=0.033$]。安装临时起搏器的严重心律失常患者存活率显著高于未安装临时起搏器者[20.0%(10/50)比0(0/7), $P<0.01$]。存活和死亡患者年龄比较差异无统计学意义(岁: 36.8 ± 10.4 比 39.5 ± 11.2 , $P=0.526$)。Logistic回归多因素分析显示,入院时GCS评分≤6分[优势比(OR)=2.417, 95%可信区间(95%CI)为1.853~4.692, $P=0.028$]、伴严重心律失常($OR=1.438$, 95%CI为1.072~3.739, $P=0.031$)是急性重度敌敌畏中毒患者死亡的独立危险因素,安装临时起搏器是患者死亡的独立保护因素($OR=0.896$, 95%CI为0.657~0.964, $P=0.015$)。**结论** 心脏损害在急性重度敌敌畏中毒中常见,继发严重心律失常与患者死亡相关。在使用保护心肌药和血管活性药的同时,合理选择抗心律失常药,必要时安装临时起搏器能稳定血压、保证循环灌注,提高救治成功率。

【关键词】 敌敌畏；急性有机磷农药中毒；心脏损害；心律失常；临时起搏器

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Clinical characteristics and rescue therapeutic experience of 57 patients with acute severe dichlorvos poisoning Shi Conghui, Wu Xiancong, Zheng Zhipeng, Yu Yigang, Shen Qingyin, Zhuang Jiayi, Liu Huina

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【Abstract】Objective To summarize the clinical characteristics and experiences in rescue treatment in patients with acute severe dichlorvos poisoning. **Methods** The clinical data of 57 patients with acute severe dichlorvos poisoning admitted to the department of emergency of Affiliated Hospital of Xiamen University from July 2014 to December 2019 were retrospectively analyzed, including 23 males and 34 females aged 38 (18~80) years old, and all of them took the dichlorvos orally. Under severe case monitoring, the basic rescue and treatment measures included toxic cleaning, using specific antidotes, blood purification, respiratory support, circulatory support, etc. For obstinate hypotension and severe arrhythmia, the patients were given volume resuscitation, correcting acidosis, stabilizing the internal environment, adding drug for protecting myocardia, vasoactive drugs and anti-arrhythmic drugs, and implanting temporary pacemakers if necessary. The occurrence of cardiac damage, outcome and prognosis and the related factors affecting the patients' prognosis were observed. The multivariate Logistic regression analysis was used to analyze the independent risk factors of prognosis. **Results** In this group of patients, there were 73.7% (42/57) of them associated with different degrees of cardiac damage, including 42 cases (100.0%) of myocardial enzymes increasing, 39 cases (92.9%) with abnormal electrocardiogram, 25 cases (59.5%) with arrhythmia, 14 cases (33.3%) with hypotension, and 2 cases (4.8%) with hypertension. The patients stayed in intensive care unit (ICU) for 2~10 days, with an average of (5.6 ± 1.7) days and their total length of hospital stay was 2~14 days, with an average of (9.5 ± 2.4) days. The 45 cases were cured, 5 cases were improved and 7 cases (12.3%) died; among the dead ones, 4 cases died of cardiac arrest or severe ventricular arrhythmia, 2 cases of multiple organ failure and 1 case of central respiratory and circulatory failure. Univariate analysis showed that the Glasgow Coma Scale (GCS) score at admission of patients in death group was lower than that in survivors (3.4 ± 0.6 vs. 4.3 ± 1.1 , $P = 0.039$) and the incidence of severe arrhythmia of death group was higher than that of survivors [57.1% (4/7) vs. 20.0% (10/50), $P = 0.033$]. For patients with severe arrhythmia, the survival

rate of patients with temporary pacemaker was significantly higher than that of patients without temporary pacemaker [20.0% (10/50) vs. 0 (0/7), $P < 0.01$]. There was no significant difference in age between survival and death groups (age: 36.8 ± 10.4 vs. 39.5 ± 11.2 , $P = 0.526$). Logistic regression multivariate analysis showed that GCS score ≤ 6 [odds ratio (OR) = 2.417, 95% confidence interval (95%CI) was 1.853–4.692, $P = 0.028$] and combination with severe arrhythmia (OR = 1.438, 95%CI was 1.072–3.739, $P = 0.031$) were independent risk factors for death of patients with acute severe dichlorvos poisoning, and temporary pacemaker installation was an independent protective factor for death (OR = 0.896, 95%CI was 0.657–0.964, $P = 0.015$). **Conclusions** Cardiac damage is commonly seen in acute severe dichlorvos poisoning, and the secondary severe arrhythmia is related to the patients' death. At the same time of using vasoactive drugs, rational select of antiarrhythmic drugs combined with installation of temporary pacemaker if necessary can stabilize blood pressure, ensure circulatory perfusion and improve the successful rate of rescue and treatment.

【Key words】 Dichlorvos; Acute organophosphorus pesticide poisoning; Cardiac damage; Arrhythmia; Temporary pacemaker

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急性敌敌畏中毒可引发一系列毒蕈碱样、烟碱样和中枢神经系统症状,严重者出现多器官损害,表现为以神经系统损害为主的全身性疾病^[1-2]。口服敌敌畏达到较大量则可导致重度中毒,出现肺水肿、昏迷、呼吸衰竭(呼衰)和脑水肿等^[3-4]。临幊上,大多数急性重度敌敌畏中毒患者都继发了不同程度的心脏损害,且部分患者在救治过程中死于严重心律失常、顽固性低血压和(或)心搏骤停。因此,救治上除了常规基础方案外,仍需合理使用保护心肌药、血管活性药和抗心律失常药,必要时及时安装临时起搏器,进而提高临床救治成功率。

1 资料与方法

1.1 病例选择:回顾性分析2014年7月至2019年12月本院收治的57例急性重度敌敌畏中毒患者的临幊资料。诊断标准为有敌敌畏明确接触史、典型临幊表现(胆碱能兴奋或危象)、胆碱酯酶活性降低,必要时行毒物检测来诊断。纳入符合诊断标准且病情分级属于重度(合并肺水肿、呼衰、昏迷或脑水肿中至少1项)的患者。排除合并其他毒物[如乙醇、地西洋(安定)等]中毒、中毒前明确存在严重心血管疾病史、中途放弃治疗或转院的患者。

1.2 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(审批号:20200420),对患者采取的治疗和检测得到过患者或家属知情同意。

1.3 一般资料:最终入选57例急性重度敌敌畏中毒患者,男性23例,女性34例;中位年龄38(18~80)岁;均为口服途径中毒(故意吞服);敌敌畏摄入量40~200 mL,平均(75.4 ± 20.8)mL;服毒至就诊时间15~120 min,平均(58.7 ± 24.6)min。首发症状表现为胃肠道41例、全身性37例、中枢或外周神经系统32例、呼吸系统28例。全血胆碱酯酶活性均<正常参考值30%。入院时格拉斯哥昏迷评分(GCS)3~8分,

平均(4.2 ± 1.2)分;急性生理学与慢性健康状况评分II(APACHE II)8~30分,平均(18.4 ± 4.9)分。

1.4 救治原则和方案:入院后常规进行生命体征和器官功能监测,建立中心静脉通路,尽早入住急诊重症监护病房(ICU)。救治原则和方案如下。

1.4.1 基础救治措施:①清除毒物^[5-7]:中毒6 h内或明确胃内毒物残留者,使用温清水或2%碳酸氢钠反复洗胃,洗胃后或直接使用聚乙二醇电解质散进行导泻;②特效解毒剂^[8]:早期、联合、足量、重复使用解毒剂氯磷定和阿托品,氯磷定首次剂量1.5~3.0 g,30 min内静脉滴注(静滴),维持剂量每24 h 6.0~8.0 g;阿托品2~4 mg,间隔10 min静脉注射1次直至阿托品化,之后根据病情变化调整剂量及给药时间,1周后改为盐酸戊乙奎醚,维持剂量1~2 mg,每8 h 1次;③血液净化^[9]:中毒24 h内早期使用瑞典金宝PrismaFLEX ADSORBA 300C一次性使用活性炭吸附器,进行血液灌流2~3次;④呼吸功能支持:一旦出现呼衰,立即建立人工气道进行机械通气;⑤循环支持:在补液、容量复苏、纠正酸中毒、稳定内环境的同时,使用保护心肌药物,一旦血压降至90/60 mmHg(1 mmHg≈0.133 kPa)以下,使用血管活性药物维持目标血压在90~120/60~80 mmHg;⑥中成药:联合使用参附注射液(每次60~80 mL静滴,每12 h 1次)和血必净注射液(每次50 mL静滴,每12 h 1次)改善循环灌注,清除炎性介质。

1.4.2 顽固性低血压和(或)严重心律失常的处理:在积极给予容量复苏、纠正酸中毒、稳定内环境的基础上,患者仍出现顽固性低血压和(或)严重心律失常,则加强保护心肌药、纠正水电解质及酸碱失衡、血管活性药和抗心律失常药的使用,必要时及时植入临时起搏器。室性心律失常者给予胺碘酮,

初始剂量为24 h内1 000 mg静滴,先行负荷滴注,再行维持滴注,用法和用量遵循药品说明书。

1.5 指标收集:观察患者心脏损害发生情况、转归和预后,并分析影响预后的因素。

1.6 统计学分析:使用SPSS 21.0软件分析数据,符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,采用t检验;非正态分布的计量资料以中位数(范围)表示;计数资料以例(%)表示。采用多因素Logistic回归分析影响患者预后的独立危险因素。 $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 心脏损害发生情况(表1):本组73.7%(42/57)的患者合并不同程度的心脏损害,表现为心肌酶谱不同程度升高42例(100.0%),心电图改变39例(92.9%)、心律失常25例(59.5%)、低血压14例(33.3%)、高血压2例(4.8%)。14例严重心律失常患者中,有10例及时安装临时起搏器。

表1 57例敌敌畏中毒患者心脏损害的表现情况

项目	例数 (例)	百分比 (%)	项目	例数 (例)	百分比 (%)
心电图改变			心律失常		
QT间期延长	18	31.6	窦性心动过速	9	15.8
ST-T改变	13	22.8	窦性心动过缓	7	12.3
T波倒置	4	7.0	室性心动过速	4	7.0
传导阻滞	2	3.5	室性期前收缩	2	3.5
PR间期延长	2	3.5	心室纤颤	2	3.5
血压变化			室上性心律失常	1	1.8
低血压	14	24.6			
高血压	2	3.5			

2.2 转归和预后:本组患者ICU住院时间2~10 d,平均(5.6 ± 1.7)d;总住院时间2~14 d,平均(9.5 ± 2.4)d。治愈45例,好转5例,死亡7例,其中4例(57.1%)死于心搏骤停或严重心律失常(室性)、2例(28.6%)死于多器官功能衰竭、1例(14.3%)死于中枢性呼吸循环功能衰竭。

2.3 影响敌敌畏中毒患者预后的单因素分析(表2):单因素分析表明,与存活者比较,死亡者入院时GCS评分较低,严重心律失常比例更高(均 $P < 0.05$)。对于存在严重心律失常患者,安装临时起搏器可以显著降低病死率($P < 0.05$)。

2.4 影响敌敌畏中毒患者预后的多因素分析(表3):多因素Logistic回归分析显示,入院时GCS评分、伴严重心律失常是急性重度敌敌畏中毒患者死亡的独立危险因素(均 $P < 0.05$),安装临时起搏器是急性重度敌敌畏中毒患者死亡的独立保护因素($P < 0.05$)。

表2 影响敌敌畏中毒患者预后的单因素分析

预后	例数 (例)	性别(例)		年龄 (岁, $x \pm s$)	入院时GCS (分, $x \pm s$)
		男性	女性		
存活	50	22	28	36.8 ± 10.4	4.3 ± 1.1
死亡	7	1	6	39.5 ± 11.2	3.4 ± 0.6
χ^2/t 值		0.253		0.638	
P 值		0.133		0.526	
预后	例数 (例)	严重心律失常 [%(例)]		安装临时起搏器 ^a [%(例)]	
		有	无	有	无
存活	50	20.0(10)	80.0(40)	20.0(10)	0(0)
死亡	7	57.1(4)	42.9(3)	0(0)	57.1(4)
χ^2/t 值		4.572		14.000	
P 值		0.033		<0.001	

注:GCS为格拉斯哥昏迷评分,a代表此处仅统计严重心律失常患者

表3 影响患者预后的 Logistic 回归多因素分析

变量	OR值	95%CI	P值
入院时GCS评分≤6分	2.417	1.853~4.692	0.028
伴严重心律失常	1.438	1.072~3.739	0.031
安装临时起搏器	0.896	0.657~0.964	0.015

注:GCS为格拉斯哥昏迷评分,OR为优势比,95%CI为95%可信区间

3 讨 论

近年来,尽管农药中毒的发生率似乎有所下降,但重度农药中毒患者的病死率仍较高。调查显示,有机磷农药尤其是敌敌畏是导致重度农药中毒的主要毒物种类之一^[10-11]。因此,加强对急性重度敌敌畏中毒患者的救治能力的研究有重要意义。

急性敌敌畏中毒具备有机磷农药中毒的共性特点,中毒后由于副交感神经末梢过度兴奋最早出现毒蕈碱样症状,随着农药与体内胆碱酯酶的不断结合,导致大量乙酰胆碱蓄积,随之出现烟碱样症状,整体表现为以神经系统损害为主的全身性疾病,可造成以肺、脑和心脏为主的全身多器官损害^[12]。临幊上,肺、脑损害容易被发现和受到重视,而心脏损害表现相对隐匿,常被掩盖和忽视^[13]。笔者在临幊上也发现,部分急性重度敌敌畏中毒患者尽管采取了清除毒物、特效解毒剂、呼吸支持以及血液净化等一系列及时有效的抢救措施,最终却意外死于心搏骤停和严重心律失常。有研究表明,急性有机磷农药中毒可对心脏产生直接和间接毒性作用,造成心肌损害和电生理活动异常,中毒程度越严重,心脏损害程度越大,严重者可导致恶性心律失常、心力衰竭(心衰)和猝死^[14]。本研究显示,绝大多数重度敌敌畏中毒患者合并不同程度的心脏损害,可表现为心肌酶谱异常、心电图改变、心律失常和血压改变。因此,临幊上应加强对敌敌畏中毒后心脏损害的防治,常规进行心电图检查、心电监护和心肌酶谱检测,必要时检测心衰标志物脑钠肽,重视保护心肌药物的

使用。有学者提出,地西洋(安定)和盐酸维拉帕米(异搏定)早期联合使用可能起到减轻心脏损害、降低病死率的作用,但尚缺乏循证医学证据^[15-16]。患者一旦发生严重心律失常,出现血流动力学不稳定(合并休克或心衰),应根据心律失常的类型选择合理的抗心律失常药和恰当的处理措施,室性心动过速、心室纤颤可使用胺碘酮或电复律,治疗过程中出现严重房室传导阻滞、心动过缓时应及时安装临时起搏器。Chen等^[17]报道称,心脏损害在急性有机磷农药中毒中的发生率为52.0%,心脏损害的发生及其严重程度与服毒剂量、毒物种类、口服到就诊时间间隔等因素有关。Aghabiklooei等^[18]认为,导致急性有机磷农药中毒患者死亡的重要原因是心脏损害。本研究则进一步表明,重度敌敌畏中毒患者心脏损害的发生率高达73.7%,其中继发严重心律失常与急性重度敌敌畏中毒患者死亡相关,对于药物和电复律治疗心律失常无效或不宜使用者,及时安装临时起搏器有助于降低患者病死率,提高救治成功率。另外,有研究显示,血必净注射液^[19-20]、参附注射液^[21]等中成药在急性重度敌敌畏中毒救治中可能起到清除炎性介质、保护重要器官功能、降低循环灌注不足、纠正心律失常等作用,临幊上可合理选择应用。

利益冲突 所有作者均声明不存在利益冲突

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