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血浆置换联合血液灌流治疗急性重度有机磷农药中毒的疗效 及对患者肝功能的影响

强 浩 安小峰[△] 解 岗 胡守芹 唐 科

(皖北煤电集团总医院急救中心 安徽 宿州 234000)

摘要 目的: 探讨血浆置换联合血液灌流治疗急性重度有机磷农药中毒的临床疗效及对患者肝功能的影响。**方法:** 选择我院于2014年1月至2017年9月收治的66例急性重度有机磷农药中毒患者,按照随机原则分为血液灌流组(n=30)、联合治疗组(n=36),两组均接受急性重度有机磷农药中毒常规治疗,在此基础上血液灌流组和联合治疗组分别接受血液灌流、血浆置换联合血液灌流治疗。观察两组治疗效果,治疗前、治疗1周后血浆丙氨酸转氨酶(ALT)、天门冬氨酸氨基转移酶(AST)、总胆红素水平。观察治疗过程中的不良反应发生情况。**结果:** 与血液灌流组比较,联合治疗组胆碱酯酶(CHE)恢复时间较短,而长托宁用量较少,住院时间较短,且抢救成功率较高($P<0.05$)。治疗1周后联合治疗组血浆ALT、AST、总胆红素显著低于血液灌流组($P<0.05$)。治疗过程联合治疗组出现1例皮疹,不良反应发生率为2.78%,血液灌流组无不良反应发生,两组不良反应发生率比较无差异($P>0.05$)。**结论:** 血浆置换联合血液灌流能明显提高急性重度有机磷中毒患者的抢救成功率,同时改善患者肝功能,且安全性良好,值得临床推广。

关键词: 有机磷农药中毒;血浆置换;血液灌流;肝功能;疗效

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Effect of Plasma Exchange combine with Hemoperfusion on Acute Severe Organophosphorus Pesticide Poisoning and Its Influence on Liver Function

QIANG Hao, AN Xiao-feng[△], XIE Gang, HU Shou-qin, TANG Ke

(Emergency Medical Center, Wanbei Coal - Electricity Group General Hospital, Suzhou, Anhui, 234000, China)

ABSTRACT Objective: To investigate the clinical efficacy of plasma exchange combine with hemoperfusion on acute severe organophosphorus pesticide poisoning and its influence on liver function. **Methods:** 66 patients with acute severe organophosphorus pesticide poisoning who were treated in our hospital from January 2014 to September 2017 were selected, according to the principle of randomization, the patients were divided into hemoperfusion group (n=30) and combined treatment group (n=36), the two groups received conventional treatment of acute severe organophosphorus pesticide poisoning, on this basis, hemoperfusion group and combined treatment group were treated with hemoperfusion, plasma exchange combined with hemoperfusion. The treatment effects between the two groups, plasma alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin levels before and after 1 weeks of treatment were observed, the adverse reactions during the treatment were observed. **Results:** Compared with hemoperfusion group, the cholinesterase (CHE) recovery time in the combined treatment group were shorter, the amount of penicyclidine hydrochloride was less, the hospitalization time was shorter, while the success rate of rescue was higher ($P<0.05$). The plasma levels of ALT, AST and total bilirubin in the combined treatment group were significantly lower than those in the hemoperfusion group ($P<0.05$). There were 1 case of rash in the combined treatment group, the incidence of adverse reactions was 2.78%, and there were no adverse reactions occurred in the hemoperfusion group, there was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Plasma exchange combine hemoperfusion can significantly improve the successful rate of salvage in patients with acute severe organophosphorus pesticide poisoning, can improve the liver function of patients and have good safety, which is worthy of clinical promotion.

Key words: Organophosphorus pesticide poisoning; Plasma exchange; Hemoperfusion; Liver function; Curative effect

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前言

有机磷农药是农业常用的杀虫剂,对人、畜均有强烈的毒

性。据统计,全球每年发生急性有机磷农药中毒人数超过300万,其中口服有机磷农药自杀人数超过30万,约占自杀人群的30%^[1]。目前,临床上对于急性有机磷农药中毒主要是以清除体

作者简介:强浩(1982-),男,本科,主治医师,从事急诊急救方面的研究,E-mail: xbsobq@163.com

[△] 通讯作者:安小峰(1978-),男,本科,副主任医师,从事急诊急救方面的研究,E-mail: qtdpvr@163.com

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内及体外毒物、应用阿托品与解磷定等解毒剂、支持治疗等方法,具有一定治疗效果,但急性有机磷中毒的死亡率仍高达10%以上,尤其是急性重度有机磷农药中毒死亡率更高达30%以上^[2-4]。肝脏是人体代谢的重要器官,具有解毒的功能,发生有机磷农药中毒后,农药可聚集于肝脏,造成肝功能损伤^[5]。检测有机磷农药中毒患者的肝功能,有助于了解患者病情。近年来,随着医疗技术的不断发展,血液灌流等技术也逐渐被用于急性有机磷中毒抢救中。为观察血浆置换联合血液灌流治疗急性重度有机磷农药中毒的临床疗效及对患者肝功能的影响,笔者进行了对照研究,现作如下报道。

1 资料和方法

1.1 临床资料

选择我院于2014年1月至2017年9月收治的66例急性重度有机磷农药中毒患者,男24例、女42例;年龄20~69岁。纳入标准:(1)所有患者均符合《急性有机磷农药中毒诊断及处理原则》中的诊断标准^[6],且入院时血清胆碱酯酶(cholinesterase, CHE)定量水平<500 U/L;(2)所有患者均为口服中毒,服药至就诊时间<4h;(3)发病后先行血液灌流,1-2次,再行血浆置换。排除标准:(1)肝肾功能不全或衰竭者;(2)不能配合治疗者;(3)治疗过程中转院、放弃治疗者。应用随机数字表法将患者分为血液灌流组30例和联合治疗组36例,两组一般资料比较见表1。本研究经医院伦理委员会同意。

1.2 治疗方法

两组患者入院后应用日立7180全自动生化检测仪检测血清CHE,试剂盒购自北京万泰德瑞诊断公司。同时接受急性重度有机磷农药中毒常规治疗,包括:迅速开通呼吸道,保持呼吸道通畅,清除衣服、皮肤黏膜等尚未吸收的有机磷农药,给予洗胃、导泻和利尿治疗,患者静脉滴注碘解磷定CHE复能剂和抗胆碱药阿托品(静脉注射至阿托品化)及肌注长托宁(维持长托宁化),并给予对症治疗。

1.2.1 血液灌流组 在常规治疗基础上进行血液灌流治疗:患者入院后尽快建立外周静脉通道,应用健帆HA230树脂血液

灌流器进行血液灌流治疗,参数设定为:血流量120~160 mL/min,应用普通肝素抗凝治疗,首次应用剂量为0.3~0.5 mg/kg,每60 min给予5~10 mg/kg维持,灌流时间90~120 min/次,入院排除禁忌症后尽快实施血液灌流,次日进行第二次血液灌流。

1.2.2 联合治疗组 在常规治疗基础上给予血浆置换联合血液灌流治疗,第二次血液灌流结束后进行血浆置换,应用美国Hermeneutics MCS+LN9000220E血浆分离机进行体外血液循环,分离并移除废血浆同时输入替换血浆,首选置换量为2000 mL,当不足时应用羟乙基淀粉、白蛋白和平衡液代替,血浆置换过程中应用枸橼酸钠抗凝,置换速度为30~40 mL/min。血浆置换后进行血液灌流,治疗方法与血液灌流组一致。

1.3 观察指标

收集并对比两组患者年龄、中毒剂量、CHE水平、服药至就诊时间等情况。分别于治疗前采集两组患者10 mL静脉血,治疗1周后采集存活患者10 mL清晨空腹外周静脉血,经4000 r/min离心8 min(离心半径6 cm)分离血浆,应用日立5300全自动生化检测仪检查各组患者血浆丙氨酸转氨酶(Alanine aminotransferase, ALT)、天门冬氨酸氨基转移酶(Aspartate aminotransferase, AST)、总胆红素水平。观察比较各组存活患者CHE恢复时间、抗胆碱药物(长托宁)用量、住院时间、不良反应等。计算抢救成功率,抢救成功率=组内存活患者/组内所有患者×100%。

1.4 统计学方法

本研究所有数据应用SPSS25.0软件进行统计学分析,计数资料以[n(%)]表示,应用 χ^2 检验。计量资料以($\bar{x} \pm s$)表示,两组间数据比较应用t检验,将 $P < 0.05$ 记作差异有统计学意义。

2 结果

2.1 两组患者一般资料比较

两组患者性别、年龄、中毒剂量、CHE水平、服药至就诊时间比较均无统计学差异($P > 0.05$),具有可比性,详见表1。

表1 两组患者一般资料比较

Table 1 Comparison of general data between the two groups

Groups	n	Male:Female	Age(years)	Toxic dose(mL)	CHE(U/L)	Medication to visit time(h)
Combined treatment group	36	13:23	48.19± 19.81	135.00± 105.00	269.00± 146.00	1.38± 0.38
Hemoperfusion group	30	11:19	45.00± 19.00	105.00± 70.00	290.00± 80.00	1.50± 0.50
t/χ^2	-	0.002	0.664	1.336	-0.704	-1.107
P	-	0.963	0.509	0.186	0.484	0.272

2.2 两组治疗情况比较

与血液灌流组比较,联合治疗组CHE恢复时间较短,而长托宁用量较少,住院时间较短,且抢救成功率较高($P < 0.05$),见表2。

2.3 两组治疗前、治疗1周后血浆ALT、AST、总胆红素比较

治疗前两组血浆ALT、AST、总胆红素比较差异无统计学意义($P > 0.05$);治疗1周后联合治疗组血浆ALT、AST、总胆红

素显著低于血液灌流组($P < 0.05$),见表3。

2.4 两组不良反应比较

治疗过程中两组均无严重不良反应,联合治疗组出现1例皮疹,经抗过敏治疗后消退,不良反应发生率为2.78%(1/36),血流灌流组无不良反应发生,两组不良反应发生率比较无差异($P > 0.05$)。

表 2 两组围术期指标及抢救成功率比较($\bar{x} \pm s$)Table 2 Comparison of perioperative indexes and rescue success rate of salvage between the two groups ($\bar{x} \pm s$)

Groups	n	CHE recovery time(d)	Dosage of penicyclidine hydrochloride(mg)	Hospitalization time (d)	Success rate of salvage [n(%)]
Combined treatment group	36	4.20± 1.20	45.00± 17.00	11.20± 8.20	33(91.67)
Hemoperfusion group	30	9.20± 3.20	58.00± 16.00	15.00± 3.00	22(73.33)
t/ χ^2	-	-8.682	-3.177	-2.405	3.960
P	-	0.000	0.002	0.019	0.047

表 3 两组治疗前、治疗 1 周后血浆 ALT、AST、总胆红素比较($\bar{x} \pm s$)Table 3 Comparison of the plasma levels of ALT, AST, and total bilirubin before and after 1 weeks of treatment between the two groups ($\bar{x} \pm s$)

Groups	Time	n	ALT(U/L)	AST(U/L)	Total bilirubin(μ mol/L)
Combined treatment group	Before treatment	36	27.00± 18.00	34.00± 26.00	12.70± 10.70
	After 1 weeks of treatment		50.00± 42.00 [#]	30.70± 20.70 [#]	11.40± 8.00 [#]
Hemoperfusion group	Before treatment	30	24.00± 12.00	36.00± 19.00	13.60± 4.60
	After 1 weeks of treatment		75.00± 45.00	55.00± 30.00	26.00± 10.00

Note: compared with hemoperfusion group, [#] $P < 0.05$.

3 讨论

急性有机磷农药中毒具有发病急、病情进展迅速、死亡率高特点,尤其是急性重度有机磷农药中毒更是临床救治的难点。有机磷农药可以通过消化道、呼吸道和皮肤三种途径进入体内,并与体内的 CHE 结合,形成稳定的磷化 CHE,使 CHE 活性降低,导致体内大量的乙酰胆碱蓄积,并引发一系列的毒蕈碱样症状^[7-9]。目前,临床上对急性重症有机磷农药中毒的常规治疗方法虽然有一定治疗效果,但急性重度有机磷农药中毒的救治仍存在很大的瓶颈。其主要问题在于有机磷农药吸收迅速,进入体内可在肝脏、肾脏和脂肪组织蓄积,即使采用洗胃仍无法清除体内吸收的农药^[10-12]。同时在治疗过程中患者病情变化迅速,阿托品用量也不易掌握。近年来,随着血液净化技术的不断发展,应用血液净化对急性重度有机磷农药中毒得以实现。血浆置换和血液灌流是目前临床上常用的血液净化技术。血液灌流主要是将患者血液引入固态吸附器的灌流器中,通过固态吸附装置将体内毒素清除,并将净化的血液回输患者体内^[13-15]。有研究表明^[16],血液灌流对已与有机磷结合的 CHE 无作用,但可以有效的降低抗胆碱药物用量,提高患者生存率。血浆置换则是在体外通过血浆膜分离技术将血浆分离,并补充新鲜的血浆,实现清除毒物的作用^[17-19]。

本研究对我院收治的急性重度有机磷农药中毒患者进行对照研究,结果显示,与血液灌流组比较,联合治疗组 CHE 恢复时间较短,而长托宁用量较少,住院时间较短,且抢救成功率较高($P < 0.05$),证实血浆置换联合血液灌流治疗急性重度有机磷农药重度患者效果优于血液灌流治疗。推测其原因,血液灌流可以在体外通过固态吸附装置将体内毒素清除,对急性重度有机磷农药中毒患者有良好的治疗效果,因而成为急性有机磷中毒抢救的重要方法,但血液灌流对已与有机磷结合的 CHE 无作用^[20,21]。而血浆置换则可以弥补血液灌流这一缺陷,与血液

灌流结合可以发挥很好的治疗作用^[22-24]。而治疗 1 周后,联合治疗组血浆 ALT、AST、总胆红素显著低于血液灌流组。ALT、AST 主要存在于肝细胞中,当肝细胞受损时,细胞内的 ALT、AST 释放到血液中,导致血浆 ALT、AST 水平升高,其水平变化是临床上反映肝功能的主要指标^[25,26]。而肝脏是人体最大的解毒器官,当有机磷农药进入体内后会造成肝脏的损伤,导致 ALT、AST 水平升高。本研究中治疗 1 周后联合治疗组血浆 AST 水平降低,证实联合治疗组患者肝功能恢复较好。比较不良反应情况发现,联合治疗组仅出现 1 例皮疹,而血液灌流组无不良反应发生,两组不良反应发生率比较无统计学意义,表明血浆置换联合血液灌流治疗急性重度有机磷中毒安全有效。综上所述,血浆置换联合血液灌流能明显提高急性重度有机磷中毒患者的抢救成功率,同时改善患者肝功能,且安全性良好,值得临床推广。

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