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奥拉西坦联合高压氧治疗重度一氧化碳中毒的疗效及对血清 LPA、H-FABP 及认知功能的影响 *

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摘要 目的:探讨奥拉西坦联合高压氧治疗重度一氧化碳中毒的疗效及对血清溶血磷脂酸(LPA)、心型脂肪酸结合蛋白(H-FABP)及认知功能的影响。**方法:**选择 2016 年 1 月-2018 年 1 月我院收治的重度一氧化碳中毒患者 90 例进行研究,以随机数表法分为观察组(n=48)和对照组(n=42)。对照组给予高压氧治疗,观察组在对照组的基础上加用奥拉西坦治疗。比较两组患者的临床疗效、血清 LPA、H-FABP、认知能力、住院时间、迟发性脑病发生率。**结果:**两组总有效率分别为 93.75%、76.19%,差异显著($P<0.05$);治疗前,两组血清 LPA、H-FABP 水平无显著性差异;治疗后,两组血清 LPA、H-FABP 均显著下降,且观察组血清 LPA、H-FABP 水平低于对照组, ($P<0.05$);治疗前,两组患者认知功能无显著性差异;治疗后,两组认知功能较治疗前均显著升高($P<0.05$),且观察组定向力、记忆力、注意力、语言能力水平均明显高于对照组($P<0.05$);观察组患者住院时间、迟发性脑病发生率均显著低于对照组,差异显著($P<0.05$)。**结论:**在重度一氧化碳中毒患者中应用奥拉西坦联合高压氧效果显著,可有效改善患者血清 LPA、H-FABP 水平及认知功能。

关键词:奥拉西坦;高压氧;重度一氧化碳中毒;溶血磷脂酸;心型脂肪酸结合蛋白;认知功能

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Curative Efficacy of Olactam Combined with Hyperbaric Oxygenin Treatment of Severe Carbon Monoxide Poisoning and its Effects on Serum LPA, H-fabp and Cognitive Function*

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ABSTRACT Objective: To study Curative efficacy of olactam combined with hyperbaric oxygenin treatment of Severe carbon monoxide poisoning and its effects on serum lysophosphatidic acid (LPA), heart-type fatty acid binding protein (H-FABP) and cognitive function. **Methods:** 90 cases of severe carbon monoxide poisoning admitted to our hospital from January 2016 to January 2018 were selected for the study, divided into observation group(n=48) and control group(n=42) by random number table method. The control group was treated with hyperbaric oxygen, and the observation group was treated with olracitam on the basis of the control group. The clinical efficacy, serum LPA, h-fabp, cognitive ability, length of stay and incidence of delayed encephalopathy were compared between the two groups. **Results:** After treatment, the total effective rate of the two groups was 93.75% and 76.19%, respectively, with significant difference ($P<0.05$). Before treatment, there was no significant difference in serum LPA and h-fabp levels between the two groups. After treatment, serum LPA and h-fabp in both groups decreased significantly, and serum LPA and h-fab P levels in the observation group were lower than those in the control group ($P<0.05$). Before treatment, there was no significant difference in cognitive function between the two groups. After treatment, the cognitive functions of the two groups were significantly increased compared with those before treatment ($P<0.05$), and the levels of orientation, memory, attention and language ability in the observation group were significantly higher than those in the control group ($P<0.05$). The length of stay and the incidence of delayed encephalopathy in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** Olracetam combined with hyperbaric oxygen has a significant effect in patients with severe carbon monoxide poisoning, and can effectively improve serum LPA, h-fabp levels and cognitive function.

Key words: Olactam; Hyperbaric oxygen; Severe carbon monoxide poisoning; Lysophosphatidic acid; Heart-type fatty acid binding protein; Cognitive function

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前言

一氧化碳中毒俗称煤气中毒,是指含碳物质燃烧不完全时的产物经呼吸道吸入引起的中毒,具有较高的危险性,多数患者在入院时已处于昏迷状态^[1,2]。重度一氧化碳中毒当发现时时间多已过晚,由于在短时间内吸入过多高浓度一氧化碳,病人呈现深度昏迷、大小便失禁、血压下降、呼吸急促,因此应在极大程度上缩短治疗时间,减少病症对患者身体机能的影响,提高患者的生存率^[3,4]。

有研究显示,缺氧状态下组织细胞的氧合及代谢功能障碍,机体可发生损伤,而通过检测患者 LPA 可有效评估其缺氧状态缓解情况^[5,6]。H-FABP 是一种存在于细胞内的蛋白质,主要分布于心肌组织,为机体提供能量,有研究显示,重度一氧化碳中毒患者 H-FABP 水平明显升高,对疾病的预后评估有重要意义^[7,8]。临床通常使用高压氧治疗该病,能够提高血氧分压,增加脑组织内氧的弥漫半径,但是其单一治疗效果并不明显,仍有部分患者昏迷时间较长,或苏醒后出现痴呆等并发症;奥拉西坦属吡拉西坦类似物,可透过血脑屏障,分布于颅内,刺激特异性中枢神经通路,为大脑提供充足的能量^[9,10]。但是其对患者血清 LPA、H-FABP 及认知功能的作用机制尚不明确,因此,本研究对奥拉西坦联合高压氧治疗重度一氧化碳中毒的疗效进行研究,并观察其对血清 LPA、H-FABP 及认知功能的影响,现报告如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月-2018 年 1 月我院收治的重度一氧化碳中毒患者 90 例进行研究。采用简单随机分组法分为 2 组,观察组中途脱离研究 2 名,完成研究 48 例,其中男 29 例,女 19 例,年龄 21~59 岁,平均(45.68±4.12)岁,中毒至就诊时间(7.15±3.51)h,高压氧仓治疗次数(11.86±4.53)次,中度昏迷 29 例,重度昏迷 19 例;对照组中途脱离研究 8 名,完成研究 42 例,其中男 28 例,女 14 例,年龄 20~60 岁,平均(46.02±4.26)岁,中毒至就诊时间(7.21±3.47)h,高压氧仓治疗次数(11.91±4.54)次,中度昏迷 24 例,重度昏迷 18 例。两组基线资料无显著差异($P>0.05$),存在可比性。病情分级标准:轻度:头痛、头晕、恶心、

乏力,无异常体征;中度:浅昏迷状态,伴烦躁、大小便失禁,膝腱反射亢进或消失,腹壁反射减弱或消失,可出现病理征;重度:多呈深度昏迷状态,无言语、运动反应,可有去大脑强直性抽搐,生理、病理反射消失,可合并脑水肿、肺水肿、心肌损伤、肝肾功能损伤、上消化道出血及脑梗死等。

纳入标准:(1)均有明确一氧化碳接触史;(2)伴有恶心、呕吐及昏迷症状;(3)实验室检查血中碳氧血红蛋白呈阳性,浓度 $>30\%$;(4)患者知情同意。排除标准:(1)其他有毒物质或神经系统疾病引起昏迷症状者;(2)高压氧禁忌症者;(3)伴有恶性肿瘤患者。

1.2 方法

对照组采用高压氧治疗:压力为 0.20~0.25 MPa,氧浓度为 $<23\%$,稳定吸氧 80 mi 一天一次。观察组在对照组的基础上加用奥拉西坦:奥拉西坦(规格:5 mL:1.0 g,生产厂家:广东世信药业有限公司,国药准字 H20050860)3 g 加入 100 mL 生理盐水静脉滴注,1 天 1 次。两组均连续治疗 2 周。

1.3 观察指标

采集治疗前后空腹静脉血 5 mL,以 $3000\text{ r}\cdot\text{min}^{-1}$ 的速度进行离心,时间 10 min,提取上层血清后,置于零下 20℃ 的冷冻箱内存储以备检测,血清 LPA、H-FABP 的测定采用双抗体夹心酶联免疫吸附法(ELISA);采用 MMSE 量表评定患者认知功能:最高 30 分,正常:27~30 分;认知功能障碍: <27 分;观察记录住院时间和迟发性脑病发生率。

疗效评定标准^[12]:显效:神志清楚,无后遗症;有效:神志清楚,但无自理生活能力;无效:临床症状无改善或加重。总有效率=(显+有效)/总例数 $\times 100\%$ 。

1.4 统计学分析

以 spss18.0 软件包处理,计量资料均用均数 $\pm$ 标准差($\bar{x}\pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示, χ^2 检验, $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组疗效比较

两组总有效率分别为 93.75%、76.19%,差异显著($P<0.05$),见表 1。

表 1 两组疗效比较[n(%)]

Table 1 Comparison of efficacy between the two groups[n(%)]

Groups	n	Excellent	Valid	Invalid	Total effective rate
Observation group	48	26(54.17)	19(39.58)	3(6.25)	45(93.75)
Control group	42	18(42.86)	14(33.33)	10(23.81)	32(76.19)
χ^2 value					5.589
P value					0.018

2.2 两组血清 LPA、H-FABP 水平比较

治疗前,两组血清 LPA、H-FABP 水平无显著性差异;治疗后,两组血清 LPA、H-FABP 均显著下降,且观察组血清 LPA、H-FABP 水平低于对照组,($P<0.05$),见表 2。

2.3 两组认知功能比较

治疗前,两组患者认知功能无显著性差异;治疗后,两组认

知功能较治疗前均显著升高($P<0.05$),且观察组定向力、记忆力、注意力、语言能力水平平均明显高于对照组($P<0.05$),见表 3。

2.4 两组住院时间、迟发性脑病发生情况比较

观察组患者住院时间、迟发性脑病发生率均显著低于对照组,差异显著($P<0.05$),见表 4。

表 2 两组血清 LPA、H-FABP 水平比较($\bar{x} \pm s$)Table 2 Comparison of serum LPA and h-fabp levels between the two groups($\bar{x} \pm s$)

Groups	n	LPA($\mu\text{mol/L}$)		H-FABP($\mu\text{g/L}$)	
		Before the treatment	After treatment	Before the treatment	After treatment
Observation group	48	3.68 $\pm$ 0.17	2.01 $\pm$ 0.22	22.84 $\pm$ 4.52	12.27 $\pm$ 5.15
Control group	42	3.71 $\pm$ 0.19	3.15 $\pm$ 0.23	23.01 $\pm$ 4.63	18.35 $\pm$ 4.26
t value		0.791	24.010	0.176	6.050
P value		0.431	0.000	0.861	0.000

表 3 两组认知功能比较($\bar{x} \pm s$,分)Table 3 Comparison of cognitive functions between the two groups($\bar{x} \pm s$, points)

Groups	n	Directional force		Memory		Attention		Language ability	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	48	2.17 $\pm$ 0.33	9.05 $\pm$ 0.78	0.52 $\pm$ 0.07	2.26 $\pm$ 0.25	1.16 $\pm$ 0.17	4.09 $\pm$ 0.45	2.12 $\pm$ 0.33	7.95 $\pm$ 0.87
Control group	42	2.19 $\pm$ 0.35	6.23 $\pm$ 0.71	0.54 $\pm$ 0.08	1.51 $\pm$ 0.23	1.15 $\pm$ 0.19	3.17 $\pm$ 0.42	2.11 $\pm$ 0.34	5.21 $\pm$ 0.54
t value		0.279	17.838	1.265	14.736	0.264	9.980	0.141	17.645
P value		0.781	0.000	0.209	0.000	0.793	0.000	0.888	0.000

表 4 两组住院时间、迟发性脑病发生情况比较

Table 4 Comparison of hospital stay and delayed encephalopathy between the two groups

Groups	n	The length of time(d)	Tardy encephalopathy(n)
Observation group	48	10.14 $\pm$ 5.41	2(4.17)
Control group	42	13.52 $\pm$ 6.82	9(21.43)
Statistics		2.619	6.221
P value		0.010	0.013

3 讨论

一氧化碳重度对患者机体损害很大,严重危害人们健康,重度一氧化碳中毒是机体吸入过量一氧化碳气体后引起的全身中毒性疾病,这类患者在短时间内吸入高浓度一氧化碳,血液碳氧血红蛋白浓度达到 50%以上,患者呈深度昏迷,各种反射消失,若得不到及时治疗则会发生死亡^[12,13]。

临床通常使用高压氧治疗重度一氧化碳中毒,高压氧能够极大地提高血氧分压,增加血氧含量,纠正组织缺氧,改善脑缺氧,降低颅内压,对一氧化碳中毒具有迅速的廓清作用。但是其单一治疗重度一氧化碳中毒疗效并不确切,较多患者仍遗留严重神经功能损伤,需联合其他脑保护药物以扩大疗效^[14-17]。奥拉西坦能激活腺苷酸激酶,有利于蛋白质在大脑中的合成,增加大脑皮质乙酰胆碱的转运,促进脑代谢,具有保护、激活神经细胞的作用^[18-20]。有研究显示,奥拉西坦用于治疗一氧化碳中毒有较好的疗效,能够增加海马部位的运转,增强大脑对葡萄糖及氧的利用,从而修复、保护细胞的作用^[21-24]。本研究结果显示,联合奥拉西坦治疗的患者总有效率为 93.75%,明显高于单独使用高压氧治疗的患者,且住院时间、迟发性脑病发生率也显著低于单独使用高压氧的患者,与上述文献基本相似。提示,奥拉西坦联合高压氧治疗重度一氧化碳中毒效果确切,能明显提高患者的临床疗效,降低住院时间及迟发性脑病发生情况。分析是因为高压氧能够增高脑组织氧浓度,改善患者脑组织内供

氧,减少渗出和脑水肿,从而阻断脑缺氧和脑水肿的恶性循环;奥拉西坦属于脑代谢调节药,能够促进大脑合成蛋白质,提高大脑摄取胆碱能力,提高了大脑利用氧和葡萄糖,两种方式联合治疗以提高患者的临床疗效。

有研究表明,LPA 水平可作为一氧化碳中毒迟发性脑病患者氧自由基氧化状态的观测指标^[25-27]。LPA 是脑部损伤的标志性监测指标,在缺氧状态下可导致低密度脂蛋白氧化和磷脂酶活性增高,从而参与血栓的形成;H-FABP 是一种能与长链脂肪酸可逆的蛋白质,是组织细胞缺血和坏死的敏感标志物,有研究显示,重度一氧化碳中毒后患者组织细胞缺氧,使脂肪酸大量增加,为了转移脂肪酸,H-FABP 水平升高,与疾病的发生存在密切关系^[28,29]。本研究结果显示,治疗后,患者 LPA、H-FABP 水平明显改善,且使用奥拉西坦联合高压氧治疗的患者改善情况优于单独使用高压氧的患者。结果提示,当患者一氧化碳中毒后组织细胞出现损伤,LPA、H-FABP 水平升高,经奥拉西坦联合高压氧治疗后降低,改善患者血液循环,降低组织损害程度,促进患者缺氧后神经功能的恢复。另外,联合治疗的患者定向力、记忆力、注意力、语言能力水平均明显高于单独使用高压氧治疗的患者,提示,奥拉西坦联合高压氧治疗重度一氧化碳中毒有较好的效果,能明显改善患者认知功能。Pasquier M^[30]等研究也认为,奥拉西坦能改善一氧化碳中毒患者的认知功能。分析是因为高压氧能够减少脑血流量,减轻脑水肿,降低颅内压,同时改善脑代谢,恢复患者脑功能;奥拉西

坦对于特异性中枢神经通路具有刺激作用,增加大脑中核酸及蛋白质的合成,为大脑提供充足的能量,从而改善患者的认知功能。

综上所述,在重度一氧化碳中毒患者中应用奥拉西坦联合高压氧效果显著,可有效改善患者血清 LPA、H-FABP 水平及认知功能。

参考文献(References)

- [1] Rose J J, Nolley E, Gladwin M T. A 53-Year-Old Woman with Severe Carbon Monoxide Poisoning [J]. *Ann Am Thorac Soc*, 2017, 14(9): 1475-1478
- [2] Fan D, Lv Y, Hu H, et al. Severe pulmonary edema following hyperbaric oxygen therapy for acute carbon monoxide poisoning: a case report and clinical experience [J]. *Undersea & Hyperbaric Medicine Journal of the Undersea & Hyperbaric Medical Society Inc*, 2017, 44(3): 287
- [3] Bicilioglu Y, Anil M, Yilmaz I, et al. Clinical and laboratory characteristics of unintentional carbon monoxide poisoning due to coal stove in children [J]. *Journal of Toxicology Toxin Reviews*, 2017, 36(1): 33-38
- [4] Ji J. Acute Compartment Syndrome Which Causes Rhabdomyolysis by Carbon Monoxide Poisoning and Sciatic Nerve Injury Associated with It: A Case Report[J]. *Hip & Pelvis*, 2017, 29(3): 204-209
- [5] QuickStats: Number of Deaths Resulting from Unintentional Carbon Monoxide Poisoning, by Month and Year - National Vital Statistics System, United States, 2010-2015 [J]. *Mmwr Morbidity & Mortality Weekly Report*, 2017, 66(8): 234-234
- [6] Gozubuyuk A A, Dag H, Kacar A, et al. Epidemiology, pathophysiology, clinical evaluation, and treatment of carbon monoxide poisoning in child, infant, and fetus[J]. *North Clin Istanbul*, 2017, 4(1): 100-107
- [7] Santos L R, Alvescorreia M, Câmara M, et al. Multiple Victims of Carbon Monoxide Poisoning in the Aftermath of a Wildfire: A Case Series[J]. *Acta Médica Portuguesa*, 2018, 31(3): 146
- [8] Hara S, Kobayash M, Kuriwa F, et al. Gene expression in rat striatum following carbon monoxide poisoning [J]. *Genomics Data*, 2017, 12(C): 74-75
- [9] Abideen Z U, Mahmud S N, Rasheed A, et al. Central Diabetes Insipidus and Hyperglycemic Hyperosmolar State Following Accidental Carbon Monoxide Poisoning[J]. *Cureus*, 2017, 9(6): e1305
- [10] Dos E S, Villa A, Garnier R, et al. Surveillance and Analysis of Occupational Carbon Monoxide Poisoning in the Paris Region [J]. *Annals of Work Exposures & Health*, 2017, 61(8): 986
- [11] Ge Huan, Gao Chunjin, Zhao liming, et al. Guidelines for clinical treatment of carbon monoxide poisoning (2) [J]. *Chinese Journal of navigation medicine and hyperbaric medicine*, 2012, 19(5): 315-317
- [12] AsgharianRezaee M, Moallem S A, Mohammadpour A H, et al. Histopathological study of erythropoietin protective effect on carbon monoxide-induced cardiotoxicity in rat [J]. *Iranian Journal of Basic Medical Sciences*, 2017, 20(11): 1189-1193
- [13] Caroncantin M, Abbott M, Brookslim E, et al. Intracoronary thrombus formation following carbon monoxide poisoning [J]. *Journal of Forensic Sciences*, 2017, 59(3): 830-832
- [14] Moon J M, Chun B J, Lee S D, et al. Serum neuron-specific enolase levels at presentation and long-term neurological sequelae after acute charcoal burning-induced carbon monoxide poisoning [J]. *Clinical Toxicology*, 2017, 56(8): 1-8
- [15] Sobhakumari A, Poppenga R H, Pesavento J B, et al. Pathology of carbon monoxide poisoning in two cats[J]. *Bmc Veterinary Research*, 2018, 14(1): 67
- [16] Irem G, Çevik Y, Keskin A T, et al. Copeptin levels in carbon monoxide poisoning [J]. *Turkish Journal of Medical Sciences*, 2017, 47(2): 653-657
- [17] Marchewka J, Gawlik I, Dębski G, et al. Cardiological aspects of carbon monoxide poisoning[J]. *Folia Medica Cracoviensia*, 2017, 57(1): 75
- [18] Trepels-Kottek S, Orlikowsky T, Wagner N. Treatment of carbon monoxide poisoning in children [J]. *Monatsschrift Kinderheilkunde*, 2018, 166(3): 1-2
- [19] Huang C C, Ho C H, Chen Y C, et al. Demographic and clinical characteristics of carbon monoxide poisoning: nationwide data between 1999 and 2012 in Taiwan [J]. *Scand J Trauma Resusc Emerg Med*, 2017, 25(1): 70
- [20] Chang Y C, Lee H Y, Huang J L, et al. Risk Factors and Outcome Analysis in Children with Carbon Monoxide Poisoning [J]. *Pediatrics & Neonatology*, 2017, 58(2): 171-177
- [21] Hampson N B, Moon R E, Weaver L K. Another perspective on ACEP policy on critical issues in carbon monoxide poisoning: Invited commentary [J]. *Undersea & Hyperbaric Medicine Journal of the Undersea & Hyperbaric Medical Society Inc*, 2017, 44(2): 89
- [22] Huang C C, Ho C H, Chen Y C, et al. Increased risk for diabetes mellitus in patients with carbon monoxide poisoning [J]. *Oncotarget*, 2017, 8(38): 63680-63690
- [23] Siskind E, Jonsson J. Successful Kidney Transplant from Donor with Carbon Monoxide Poisoning[J]. *Transplantation*, 2018, 102(8): 1
- [24] Huang CC, Ho CH, Chen YC, et al. Hyperbaric Oxygen Therapy Is Associated with Lower Short- and Long-Term Mortality in Patients with Carbon Monoxide Poisoning[J]. *Chest*, 2017, 152(5): 943-953
- [25] Kumarihamy P, Kularatne S A M, Pathirage M, et al. A case of delayed neurological manifestation following carbon monoxide poisoning in Sri Lanka: epidemiology of exposure and literature review[J]. *BMC Pharmacology and Toxicology*, 2019, 20(1): 17
- [26] Watt S, Prado C E, Crowe S F. Immediate and delayed neuropsychological effects of carbon monoxide poisoning: a meta-analysis [J]. *Journal of the International Neuropsychological Society*, 2017, 24(4): 1-11
- [27] Huang C C, Ho C H, Chen Y C, et al. Increased risk for diabetes mellitus in patients with carbon monoxide poisoning. [J]. *Oncotarget*, 2017, 8(38): 63680-63690
- [28] Jankowska D, Palabindala V, Salim S A. Non-ST elevation myocardial infarction secondary to carbon monoxide intoxication[J]. *Journal of Community Hospital Internal Medicine Perspectives*, 2017, 7(2): 130-133
- [29] AsgharianRezaee M, Moallem S A, Mohammadpour A H, et al. Histopathological study of erythropoietin protective effect on carbon monoxide-induced cardiotoxicity in rat [J]. *Iranian Journal of Basic Medical Sciences*, 2017, 20(11): 1189-1193
- [30] Pasquier M, Dami F, Carron P N, et al. Mass Casualty Triage in the Case of Carbon Monoxide Poisoning: Lessons Learned [J]. *Disaster Medicine & Public Health Preparedness*, 2017, 12(3): 1-6