磷酸肌酸钠治疗重度颅脑损伤合并心肌损害的临床观察

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摘要 目的：观察磷酸肌酸钠对重度颅脑损伤合并心肌损害患者的心肌、脑组织保护作用。**方法：**选择 60 例重度颅脑损伤合并心肌损害需要手术治疗的患者随机分为治疗组 30 例，对照组 30 例，对照组采用常规治疗，治疗组加用磷酸肌酸钠至术后 3 天，观察两组颅内压（ICP），脑氧分压（PbrO₂），心功能及心肌酶的变化情况。**结果：**治疗组颅内压及心肌酶明显低于对照组（P<0.05），治疗组脑氧分压心功能明显优于对照组（P<0.05）。**结论：**应用磷酸肌酸钠可明显改善心脑组织微循环及能量代谢，具有良好的保护作用。

关键词：磷酸肌酸钠；颅脑损伤；心肌损害；能量代谢

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Clinical Observation on Patients with Severe Head Injury Combined with Myocavdial Damage Treated by Creatine Phosphate

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ABSTRACT Objective: To explore the protective effect of creatine phosphate on patients with severe head injury combined with myocavdial damage. Methods: 60 Patients with severe head injury combined with myocavdial damage were divided into treatment group (30 patients)and control group(30 patients)randomly. Patients in treatment group were treated by creatine phosphate into three days,while patients in control group adopted routine treatment. Comparing the cardiac enzymes levels before and after treatment, there were intracranial pressure, brain partial pressure of oxygen, cardiac function between two groups. Results: Intracranial pressure and cardiac enzymes levels in were statistically lower in treatmet group than in control group. Brain partial pressure of oxygen and cardiac function were significant increased in treatment group than in control group (P<0.05). Conclusion: Creatine phosphate can significant increase microcirculation and energy metabolism of the heat and brain constitutions and promote the rehabilitation of patients.

Key words: Creatine Phosphate; Severe Head Injury; Myocavdial Damage; Energy Metabolism

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前言

重度颅脑损伤合并心肌损害后最早出现的病理生理改变就是能量代谢障碍，缺氧时能量只能依靠葡萄糖无氧酵解产生，其生成的 ATP 远低于有氧代谢，同时产生大量乳酸，使心肌、脑组织等高耗能细胞功能受损，结构破坏。磷酸肌酸钠（creatine phosphate,cp）是一种外源性能量供应源，能直接透过细胞膜进入细胞，减少心肌、脑组织缺血再灌注性损伤，是保护心肌细胞和心肌线粒体膜完整的重要物质[1]，同时为脑组织供能，改善脑组织能量代谢，对颅脑损伤后脑细胞结构及功能恢复有益[2]。

1 资料与方法

1.1 病例选择

选择本院 2009 年 1 月至 2011 年 10 月收治的 60 例重度颅脑损伤合并心肌损害患者，所有患者均有一侧脑挫裂伤伴脑出血，既往心功能差，心电图检查 ST 段压低≥0.05 mV，需要手术治疗，随机分为两组，治疗组 30 例使用磷酸肌酸钠，对照组点滴生理盐水。

1.2 实验方法

治疗组入手术室后将磷酸肌酸钠（海口奇力制药厂生产）2g 溶于生理盐水 100 mL 并在 30 分钟内静点完毕，并于术后前三天各输注磷酸肌酸钠 2g，对照组点滴生理盐水 100 mL。

1.3 麻醉方法

入室前肌注东莨菪碱 0.3 mg，入室后监测 ECG、有创桡动脉压和 CVP、SPO_2、$PECO_2$，麻醉诱导：咪唑安定 0.05mg·Kg^{-1}，舒芬太尼 0.5 μg·Kg^{-1}，丙泊酚 1 mg·Kg^{-1}，维库溴铵 0.1 mg·Kg^{-1}，3 分钟后气管插管，行麻醉机控制呼吸，术中麻醉维持用瑞芬太尼 0.2 μg·Kg^{-1}·min^{-1}，吸入 1%七氟醚，间断静推维库溴铵。

1.4 外科治疗

60 例患者手术均行去骨瓣减压脑内血肿清除术，术后带气

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管导管回重症监护室，在丙泊酚镇静状态下接呼吸机支持治疗。

1.5 监测方法

心功能测定采用 GE 公司生产的 Vivid7 彩色超声心动图仪，心功能指标包括：每搏输出量（SV, mL/ 次），射血分数（EF,%），左室收缩末容积（LVESD），左室舒张末容积（LVEDD）。两组患者均于术后 1 小时及治疗后 3 天取静脉血，用 Beckman CX9 全自动生化分析仪进行心肌酶谱活性测定，包括磷酸肌酸激酶（CPK）及同工酶（CK-MB），乳酸脱氢酶（LDH），α- 羟丁酸脱氢酶（HBDH）。行 Camino 脑实质内置管经压力换能器，持续监测颅内压（ICP），探头直接插入无损伤的脑组织内测定脑氧分压（PbrO），并于术中硬脑膜切开（T1），输注磷酸肌酸钠后 2 小时（T2）及术后（T3）3 个时点记录数值。

1.6 统计学处理

数据均通过 SPSS 13.0 软件包进行处理，计量资料以均数± 标准差（$\bar{X}\pm S$）表示，不同时点组间及组内采用双因素重复测量数据方差分析，计数资料采用 X^2 检验，P<0.05 为差异有统计学意义。

2 结果

2.1 两组一般资料比较

两组性别、年龄、体重，手术时间等一般情况差异无统计学意义。

2.2 两组患者心肌酶谱测定结果比较

术后 1 小时，术后第三天治疗组心肌酶均明显低于对照组，（P<0.05），见表 1。

表 1 两组心肌酶水平比较（$\bar{X}\pm S$，U/L）

Table 1 Comparison with two groups of myocardial enzymes level

Group	AST	CK-MB	CK	HBDH	LDH
术后 1 小时（One hour after operation）					
Creatine phosphate	46.7± 7.8	45.6± 28.6	438.2± 273.5	371.6± 152.9	427.6± 186.1
Control	53.7± 11.2	61.1± 29.1	516.8± 247.1	427.5± 175.8	505.5± 178.5
术后三天(Three days after operation)					
Creatine phosphate	30.9± 8.8	21.6± 8.3	377.2± 88.6	207.6± 76.3	267.3± 150.6
Control	48.6± 9.6	39.2± 9.7	426.7± 195.2	376.5± 98.4	389.5± 186.1

2.3 两组治疗前后心功能水平比较

两组用药前基本情况无显著性差异。治疗组治疗后心功能指标明显优于对照组（P<0.05），见表 2。

2.4 两组患者不同时点 ICP 和 $PbrO_2$ 值比较

治疗组 ICP 明显低于对照组，治疗组 $Pbro_2$ 明显高于对照组，（P<0.05），见表 3。

表 2 两组治疗前后心功能水平（$\bar{X}\pm S$）

Table 2 Two groups before and after treatment level of cardiac function

观察指标(Items)	SV（mL/ 次）	EF（%）	LVESD（mm）	LVEDD（mm）
Creatine phosphate				
Befor treat	55.82± 3.06	0.50± 0.03	30.2± 3.3	50.2± 5.5
After treat	59.68± 4.07	0.55± 0.05	30.5± 2.1	46.9± 5.5
Control				
Befor treat	55.78± 3.47	0.51± 0.03	30.3± 4.7	50.6± 6.9
After treat	46.06± 3.81	0.45± 0.06	35.3± 4.7	53.4± 5.2

表 3 两组患者各时间点 ICP 和 $PbrO_2$ 值的比较

Table 3 Comparison of patients'ICP and $PbrO_2$ between two groups at different time points (n=30, $\bar{X}\pm S$, P/mmHg)

Group		T1	T2	T3
ICP	Creatine phosphate	25.07± 3.68	16.56± 3.28	18.45± 3.17
	Control	25.67± 3.57	18.56± 3.39	21.78± 3.11
$PbrO_2$	Creatine phosphate	12.78± 4.87	13.06± 6.78	18.62± 7.16
	Control	12.51± 5.36	12.63± 6.67	12.68± 8.21

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3 讨论

重度颅脑损伤是临床神经外科常见疾病之一，易并发严重的颅内高压，由于脑血管出血或闭塞引起其支配区域的脑血流减少，脑组织快速进入缺血缺氧状态，导致脑细胞能量代谢障碍，产生脑水肿及脑组织坏死[3,4]，故应及时手术解除压迫。如术前合并心肌损害，加之手术创伤和麻醉应激反应，使围手术期心肌细胞能量储备更加匮乏，易引发心律失常，甚至心衰[5,6]，有较高的病死率和致残率。磷酸肌酸分子中含高能量的氨基磷酸键，是人体内源性能量活性物质[7]，当它大量耗竭时，外源性能量支持非常必要[8,9]。

外源性磷酸肌酸钠可穿透缺血细胞直接供能，除应用于心脏保护外，对神经系统也起一定的保护作用。其产生能量的途径为[10,11,12]，在磷酸肌酸肌酸激酶（CPK）催化下，磷酸肌酸+ADP=肌酸+ATP 上述反应过程存在四种不同区域：(1) 胞浆膜，此处磷酸肌酸供应钙离子通透所需的能量；(2) 胞浆网，此处磷酸肌酸为通道提供能量；(3) 线粒体的膜间隙，此处肌酸负载细胞能量；(4) 肌原纤维，其作用机制主要是进入细胞参与高能磷酸键的维持，可补充因脑缺血乏氧或葡萄糖减少造成的 ATP 缺乏，细胞死亡可以降至原来最大量的一半，可见其显有明显的神经保护作用[13,14]。

本临床研究显示，减少 CP 的损失或增加 CP 的供应，可保护细胞膜的完整，进而维持血管功能壁的完整性，增强毛细血管前扩约肌对局部血压的调节，有利于维持血脑屏障和改善间质性脑水肿[15,16]。同时，随着 CP 的补充，$PbrO_2$(脑氧分压)也逐步改善，有利于脑损伤的预后[17]。研究还发现，CP 通过为 Na^+—K^+—ATP 泵与 Ca^{2+} 泵供能，使心肌收缩力迅速恢复，提高左室射血分数[18]。提高 CP 的含量可明显降低左室舒张末压并增加再灌注后冠状动脉流量，也证实了 Feng 等[19]提出的心肌内 CP 和 ATP 含量与左室形成压呈线性关系。治疗组心肌酶谱恢复明显优于对照组，证实补充 CP 后心肌受损程度轻，心肌功能恢复迅速[20]。说明 CP 对心肌短期及长期改善缺血缺氧状况都有明显作用。

综上所述，CP 具有安全、高效、低毒特点，对受损的心肌、脑组织有明显的保护作用，对于重度颅脑损伤合并心肌损害的患者，在手术治疗的基础上，尽早使用 CP 既有助于心功能的恢复，并促进脑损伤更快恢复，提高预后生活质量，值得进一步推广应用。

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