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叶酸、甲钴胺对脑血管病患者同型半胱氨酸水平及认知障碍疗效观察*

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摘要 目的:探讨叶酸、甲钴胺对脑血管病患者血清同型半胱氨酸水平、以及认知障碍的疗效。**方法:**112例脑血管病患者,用随机表法,将患者分为三个叶酸组、甲钴胺组和联合治疗(叶酸+甲钴胺)组。叶酸组口服叶酸5 mg(1次/天)。甲钴胺组予以甲钴胺口服500 μg(3次/天)。联合治疗组联合用药,连续口服6个月。评价治疗前后的血清同型半胱氨酸及认知障碍评分。**结果:**治疗后,三组间血清同型半胱氨酸水平差异有统计学意义($P<0.05$)。联合治疗组血清同型半胱氨酸水平明显低于叶酸组和甲钴胺组($P<0.05$)。三组间认知障碍MMSE评分差异有统计学意义($P<0.05$)。甲钴胺组和联合治疗组治疗前后MMSE评分差异有统计意义($P<0.05$),但叶酸组治疗前后MMSE评分差异无统计学意义($P>0.05$)。联合治疗组认知障碍MMSE评分水平明显高于叶酸组和甲钴胺组($P<0.05$)。**结论:**叶酸联合甲钴胺能够改善脑血管病患者认知障碍评分,降低血清同型半胱氨酸水平,但叶酸对认知障碍无明显疗效。

关键词:脑血管病;叶酸;甲钴胺;认知障碍;同型半胱氨酸

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Observation on the Effects of Folic Acid and Mecobalamin on Homocysteine Levels and Cognitive Impairment of Patients with Cerebrovascular Disease*

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ABSTRACT Objective: To study the curative effects of folic acid, mecobalamin on serum homocysteine levels and cognitive impairment of cerebrovascular patients. **Methods:** A total of 112 patients with cerebrovascular disease in our hospital were randomly divided into three groups, namely, folic acid group, mecobalamin group and combination group (folic acid + mecobalamin). Patients in folic acid group had oral folic acid 5 mg once per day. Patients in mecobalamin group had mecobalamin orally 500 μg (3 times/day). Patients in combination group had the combination of two. All had treatment for 6 consecutive months. The evaluation on serum homocysteine levels and cognitive impairment scores were carried out before and after treatment. **Results:** After treatment, the serum homocysteine levels had significant differences between the three groups ($P<0.05$). The serum homocysteine levels in combination group were significantly lower than in the folic acid group and mecobalamin group ($P<0.05$). The cognitive impairment MMSE score also showed statistically significant difference between three groups ($P<0.05$). The MMSE score had statistical differences between before and after treatment in mecobalamin group and combination group ($P<0.05$), but no statistical difference in MMSE score was found between before and after treatment in folic acid group ($P>0.05$). The cognitive impairment MMSE score in combination group was obviously higher than in folic acid group and mecobalamin group ($P<0.05$). **Conclusions:** Folic acid combined with mecobalamin can reduce serum homocysteine levels, and improve cognitive impairment score in patients with cerebrovascular disease. But folic acid had no obvious curative effects on cognitive impairment.

Key words: Cerebrovascular disease; Folic acid; Mecobalamin; Cognitive impairment; Homocysteine

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前言

随着我国人口老龄化速度的加快,生活水平的提高,饮食结构的不断改变,以及高血压、高血糖、高血脂等,脑血管疾病发生率居高不下,成为导致我国老年人死亡的主要原因之一^[1]。脑卒中起包括缺血性卒中和出血性卒中,脑局部血液循环发生

障碍从而导致脑功能细胞缺血坏死引起的一系列神经功能缺损综合征,易导致认知精神障碍,其发病率、致残率、死亡率均较高^[2]。大量的研究发现,同型半胱氨酸和脑血管病的发病密切相关^[3,4]。本研究主要探讨叶酸、甲钴胺对降低脑血管病患者同型半胱氨酸效果,以及对认知障碍的改善的效果。

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1 材料与方法

1.1 研究对象

2014年1月到2016年4月我院就诊的脑血管病患者112例。采用随机表法,将所有病例分为三个亚组,即叶酸组,其中男23例,女17例,年龄 56.3 ± 7.9 岁;甲钴胺组,其中男19例,女18例,年龄 56.6 ± 8.2 岁;联合治疗(叶酸+甲钴胺)组,其中男20例,女15例,年龄 56.8 ± 8.7 岁。纳入标准:①既往有慢性脑血管病发作病史,且已由两位副主任医师以上专科医生明确诊断;②伴有一定程度认知障碍,简易智能精神状态检查量表评分 ≤ 24 分以下;③排除急性脑出血、脑栓塞、脑肿瘤、各类感染、严重心肝肾疾病、外伤、非器质性精神病、有意识障碍等患者。

1.2 治疗方案

叶酸组口服叶酸5 mg,1次/天。甲钴胺治疗组,予以甲钴胺口服500 μg ,3次/天。联合治疗组,予以叶酸5 mg,1次/天,甲钴胺口服500 μg ,3次/天。连续口服6个月。

1.3 血清学指标检测

清晨空腹8小时以上,采集受试者外周肘静脉血,离心沉淀,采集上清液标本用于测定血清同型半胱氨酸水平。采用循环酶法在340 nm波长下检测血清同型半胱氨酸水平,采用同型半胱氨酸检测试剂盒,完全按照试剂盒说明书操作。所有患者在干预实施前测定一次,同样干预6个月后再测定血清同型半胱氨酸水平。

1.4 认知障碍水平评定

认知障碍水平评估采用简易智能精神状态检查量表,该量表是于1975年由美国Folstein设计应用,是目前最具影响力的认知功能评价和筛选工具,该量表具有良好的信度和效度。其内容包括以下7个领域:地点定向力、时间定向力、即刻记忆、延迟记忆、注意及计算力、语言及视空间7个方面的内容,一共有30个小项。判定标准:受教育年限 <4 年者加2分,受教育年限为4~8年加1分,认知功能正常为25~30分;轻度认知障碍为21~24分;中度认知障碍为14~20分;13分以下为重度认知障碍。所有患者在干预实施前进行认知障碍评分,同样干预6个月后再进行认知障碍评分。

1.5 统计学方法

所有数据采用SPSS 15.0统计软件进行分析,计量资料采用均值 $\pm$ 标准差($\bar{x} \pm s$),应用t检验;P值均小于0.05,认为有统计学意义。

2 结果

2.1 不同组间治疗前后血清同型半胱氨酸水平比较

由表1看出,治疗前叶酸组、甲钴胺组和联合治疗组间血清同型半胱氨酸水平无统计学差异($P>0.05$)。治疗后,三组间血清同型半胱氨酸水平差异有统计学意义($P<0.05$)。联合治疗组血清同型半胱氨酸水平明显低于叶酸组和甲钴胺组($P<0.05$)。

表1 三组间治疗前后血清同型半胱氨酸水平比较($\mu\text{mol/L}$)

Table 1 Comparison of serum homocysteine levels before and after treatment between three groups ($\mu\text{mol/L}$)

	Case number	Before the treatment	After treatment	t	P
Folic acid group	40	17.39 $\pm$ 3.56	16.22 $\pm$ 4.13	2.29	0.01
mecobalamin group	37	18.16 $\pm$ 3.63	15.09 $\pm$ 3.37	4.23	0.00
Combination group	35	17.64 $\pm$ 4.02	12.45 $\pm$ 2.74	7.68	0.00
E		3.15	23.43		
p		0.16	0.00		

Note: Compared with the combination group, there was statistical difference, $P<0.05$.

2.2 不同组间治疗前后认知障碍水平评分

由表2看出,治疗前叶酸组、甲钴胺组和联合治疗组间认知障碍MMSE评分水平无统计学差异($P>0.05$)。治疗后,三组间认知障碍MMSE评分水平有统计学意义($P<0.05$)。甲钴胺组

和联合治疗组治疗前后MMSE评分差异有统计意义($P<0.05$),但叶酸组治疗前后MMSE评分差异无统计学意义($P>0.05$)。联合治疗组认知障碍MMSE评分水平明显高于叶酸组和甲钴胺组($P<0.05$)。

表2 三组间治疗前后认知障碍MMSE评分水平比较

Table 2 Comparison of cognitive impairment MMSE score before and after treatment between the three groups

	Case number	Before the treatment	After treatment	t	P
Folic acid group	40	14.23 $\pm$ 5.16	14.52 $\pm$ 4.62	1.29	0.11
mecobalamin group	37	15.05 $\pm$ 4.62	15.64 $\pm$ 4.17	1.93	0.01
Combination group	35	14.74 $\pm$ 4.73	16.46 $\pm$ 4.37	3.82	0.00
E		2.15	13.27		
p		0.37	0.00		

3 讨论

随着社会城市化的发展,脑血管病逐渐成为威胁我国居民健康的主要疾病之一,社会造成了十分巨大的经济支出,给人

民的健康带来的巨大的危害^[5]。根据我国现有的流行病学的调查,脑血管病的发病率为130-300/10万人^[6],死亡率居高不下,达80-120/10万人^[7]。对脑血管病的治疗效果不理想,认为对其预防的重要性远高于治疗^[8]。大量的流行病学调查已证实,同型

半胱氨酸 (Homocysteine, Hcy) 是一种可以导致血管损伤氨基酸, 高同型半胱氨酸血症被证实是心、脑血管等疾病的独立危险因素, 且血浆 Hcy 每升高 $1 \mu\text{mol/L}$, 发生脑血管病的相对危险度升高 1.079^[9]。研究认为, Hcy 能够促进氧自由基生成和脂质过氧过程, 导致血管内皮损伤, 促进动脉管壁中平滑肌细胞增殖, 同时能够聚血小板的粘附的功能, 最终使得管壁增厚, 官腔狭窄, 导致微循环血管血栓形成^[10,11]。

临床观察发现, 卒中患者在发生卒中后 3 天到 2 周内并发不同程度的认知障碍^[12]。其基本理论认为, 卒中患者的脑血流灌注量及血流速度均较正常人降低, 使脑功能细胞及组织缺血缺氧, 影响脑细胞正常的认知判断功能, 导致认知障碍的发生, 脑局部血流没有及时得到恢复的患者, 其认知障碍很难恢复至卒中前水平^[13]。患者表现为记忆力障碍, 尤其近期记忆力减退为主要临床表现, 部分患者最终发展成为痴呆^[14]。

许多研究表明: 维生素 B6、B12、叶酸等水平降低将明显增加 Hcy 血症的危险性, 其中以叶酸关系最为密切, 肾功能障碍患者肾脏清除能力降低, 将引起高 Hcy 血症, 导致一系列的血管病变^[15]。Kamat P K 等研究发现, Hc 每增加 $5 \mu\text{mol/L}$, 其微量尿蛋白出现的危险性增加 30%, 肾功能障碍加速了体内高 Hcy 的累及, 同时高 Hcy 增加了肾脏微血管的病变速度, 二者呈现恶性循环, 加速了病程的进展^[16]。本研究发现, 叶酸具有降低脑血管病患者血清同型半胱氨酸的功能, 三组间治疗前后血清同型半胱氨酸水平明显降低, 认为叶酸能够促进 Hcy 的代谢过程, 降低体内的 Hcy 水平。

甲钴胺是水溶性 B 族维生素, 是体内 Hcy 合成蛋氨酸的辅酶, 但体内甲钴胺及其衍生物水平升高, 参与 Hcy 合成过重中竞争性抑制 Hcy 的合成, 引起高同型半胱氨酸血症, 最终氧自由基损伤血管内皮细胞, 促进动脉硬化及血栓形成^[17]。同样, 脑缺血后神经传导束脱髓鞘, 髓鞘受损, 神经传导束的结构稳定性下降^[18]。甲钴胺提供神经髓鞘修复的所需的维生素 B12, 促进髓鞘形成, 促进神经功能的恢复^[19,20]。本研究发现, 甲钴胺组和联合治疗组治疗前后 MMSE 评分差异有统计意义, 联合治疗组认知障碍 MMSE 评分水平明显高于叶酸组和甲钴胺组, 说明甲钴胺具有修复神经的功能, 改善脑缺血病患者认知障碍的水平。

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