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康复训练联合阿托伐他汀对 SIVD 患者认知功能及日常行为能力的影响 *

韩 晶[1] 成 娜[2] 徐 海[1] 单梓梅[2] 陶 静[1]

（新疆维吾尔自治区人民医院 1 康复医学科;2 干部保健中心三病区 新疆 乌鲁木齐 830001）

摘要 目的:研究康复训练联合阿托伐他汀对 SIVD 患者认知功能及日常行为能力的影响。**方法:**选取 97 例确诊为 SIVD 的患者，根据随机数表法将所有患者分为观察组(n=48)和对照组(n=49)，对照组给予口服多奈哌齐，观察组给予口服阿托伐他汀和康复训练。**结果:**治疗 1 个月后，观察组和对照组的 MMSE、MoCA、BI 评分与治疗前差异均无统计学意义(P>0.05)；治疗 6 个月后，观察组的 MMSE、MoCA、BI 评分显著高于治疗前(P<0.05)；观察组的 MMSE、MoCA、BI 评分显著高于对照组(P<0.001)；观察组治疗 1 个月与 6 个月后总有效分别为 16.6%与 87.5%，高于同期对照组的 12.24%(x^2=0.363，P=0.547）与 53.06%(x^2=27.523，P<0.001)，差异无统计学意义。**结论:**康复训练联合阿托伐他汀能有效治疗 SIVD，值得在临床中推广。

关键词:康复训练；多奈哌齐；阿托伐他汀；皮质下缺血性血管性痴呆

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Effect of Rehabilitation Training Combined with Atorvastatin on Cognitive Function and Daily Behavior of Patients with SIVD*

HAN Jing[1], CHENG Na[2], XU Hai[1], SHAN Zi-mei[2], TAO Jing[1]

(1 Department of rehabilitation medicine, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang, 830001, China; 2 Center of Healthy Care for Cadres, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang, 830001, China)

ABSTRACT Objective: To study the effect of rehabilitation training combined with atorvastatin on cognitive function and daily behavior of patients with subcortical ischemic vascular dementia (SIVD). **Methods:** In our hospital from October 2013 to May 2016, 97 cases were diagnosed as SIVD patients, and they were divided into observation group (n=48) and control group (n=49) according to random number table method. Patients in the control group were given oral donepezil, and those in observation group were given oral atorvastatin and rehabilitation training. Montreal Cognitive Assessment (MoCA), Simple mental state examination (MMSE) and Barthel Index (BI) were adopted to record the changes after treatment. **Results:** After one month of treatment, the MMSE, MoCA and BI scores in observation group and control group showed no significant difference, as compared with before treatment (P>0.05). After 6 months of treatment, the MMSE, MoCA and BI scores in observation group were significantly higher than those before treatment (P<0.05). As well, the MMSE, MoCA and BI scores were also significantly higher in observation group than in control group (P<0.001). In the observation group, the total effective rate was 16.6% after one month and 87.5% after 6 months. Both were respectively higher than those in the control group (12.24%, x^2=0.363, P=0.547; 53.06%, x^2=27.523, P<0.001). **Conclusion:** Rehabilitation training combined with atorvastatin can effectively treat SIVD, so it is worth promoting in clinic.

Key words: Rehabilitation training; Donepezil; Atorvastatin; Subcortical ischemic vascular dementia

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前言

随着我国人口老龄化进程不断加快，老年疾病所占的比例也不断上升，其中心脑血管为主要危机病症，对老年患者的生命健康造成极大威胁[1]。在反复发生中风偏瘫等疾病后，老年患者开始出现获得性智力功能障碍，未得到及时治疗将使得病情越来越严重，导致血管性痴呆(vascular dementia，VD)，而皮质下缺血性血管性痴呆（subcortical ischemic vascular dementia，SIVD)为 VD 最常见类型。相关研究统计表明我国老年性痴呆仅为 3.9%，而血管性痴呆比例高达 68.5%[2]，对我国老年患者家庭造成极大的精神负担及经济负担。目前临床针对 SIVD 并未有显效的治疗方案，药物治疗对患者认知功能改善极为有限，对病情无明显缓解作用。本实验研究康复训练联合阿托伐他汀对 SIVD 患者认知功能及日常行为能力的影响，为临床治疗提供一定参考价值。

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作者简介:韩晶(1981-)，女，硕士，主治医师，主要从事神经系统疾病的康复治疗，

电话:099185644100，E-mail:417955104@qq.com

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1 资料与方法

1.1 一般临床资料

选取我院 2013 年 10 月 -2016 年 5 月我院住院部确诊为 SIVD 的患者 97 例。其中男性 50 例,女性 47 例。年龄为 56～86 岁,病程为 1.5 年～4.3 年。根据随机数表法将所有患者分为观察组(n=48)和对照组(n=49),观察组男性 25 例,女性 23 例,平均年龄为(67.2± 5.7)岁,病程为(3.1± 1.7)年;对照组男性 25 例,女性 24 例,平均年龄为(67.8± 5.4)岁,病程为(3.2± 1.7)年。两组患者临床资料具有差异无统计学意义(P>0.05),具有可比性。

1.2 病例选择标准

患者纳入标准:1) 诊断符合 VD 标准;2) 诊断符合 SIVD 标准。排除标准:1)伴有严重器官病变;2)存在行动障碍;3)机体过于虚弱或生命体征较弱。

1.3 方法

1.3.1 对照组 给予口服多奈哌齐,5 mg,1 次 / 天。观察组:给予口服阿托伐他汀,20 mg,1 次 / 天,并给予康复训练。

1.3.2 康复训练 以提高患者日常生活能力量表 (Ability of daily living,ADL)分数为中心的训练方法。1)床上翻身训练、上下床能力及室内外移动能力训练;2)细化生活自理能力,包括自主进食,控制二便及沐浴更衣;3)随着训练效果渐进可给予家务活动指导训练和社交指导[3];4)使用外物进行记忆辅助工具,例如名片、日历、闹钟等提示患者自身环境,针对性训练患者智商障碍及意识障碍[5];5)积极发现患者兴趣爱好,鼓励参与各自喜好,例如下棋唱歌跳舞等。每次治疗 2 小时,4 次 / 周,治疗持续 6 个月。

1.4 观察治疗及评价标准

◎ 蒙特利尔认知评估量表 (Montreal Cognitive Assessment,MOCA):总分 30 分,评价指标包括注意力集中、记忆、语言、抽象思维、计算和执行能力,分数低于 26 为异常。◎ 简易智力状况检查法(Simple mental state examination,MMSE):总分为 30 分,,评价指标包括时间地点的定向能力,同时包括语言理解、自我表达、注意力和记忆力等。正常与不正常的分界值与受教育程度有关,划分痴呆的标准:文盲(未受教育)≤ 17 分;小学程度(受教育年限≤ 6 年)≤ 20 分;中学(包括中专)程度≤ 22 分;大学(包括大专)程度≤ 23 分。◎ ADL 评定使用 Barthel 指数 (Barthel Index,BI):评测指标为日常自理能力和执行能力。25～45 分为重度残疾,50～70 分为中度残疾,75～95 分为轻度残疾,100 分完全自理[6-8]。

组内治疗先后 MMSE 评分差异≥ 5 分为显效;MMSE 评分差异 2～4 为有效;MMSE 评分差异≤ 2 分为无效。显效和有效为总有效例数。

记录 2 组治疗过程中出现的不良事件,包括血常规、尿常规、肝肾功能、心电图、凝血功能等。

1.5 统计学方法

计数资料行 x^2 检验或确切概率法,计量资料用 ($\bar{x}$± s)表示,组间比较采用两样本 t 检验,以 P<0.05 提示差异具有统计学意义。

2 结果

两组治疗前 MMSE、MoCA、BI 评分差异均无统计学意义(P>0.05);观察组和对照组治疗 1 个月后 MMSE、MoCA、BI 评分与治疗前差异均无统计学意义(P>0.05);治疗 6 个月后,观察组的 MMSE、MoCA、BI 评分与治疗前差异有统计学意义(P<0.05),观察组的 MMSE、MoCA、BI 评分与对照组差异有统计学意义(P<0.001)(表 1)。

表 1 两组患者治疗前后 MMSE、MoCA、BI 评分比较($\bar{x}$± s,分)

Table 1 Comparison of the MMSE, MoCA and BI scores between the two groups before and after treatment ($\bar{x}$± s, score)

Groups	Time	MMSE	MoCA	BI
Observation group	Before treatment	16.23± 2.33	14.35± 2.24	48.66± 12.43
	After 1 month	17.42± 3.02	15.02± 2.44	55.17± 14.31
	After 6 months	20.14± 3.13◎◎	20.67± 3.15◎◎	69.36± 17.29◎◎
Control group	Before treatment	16.08± 2.37	14.03± 2.09	50.34± 12.72
	After 1 month	17.27± 3.44	15.18± 2.23	54.94± 13.81
	After 6 months	18.25± 3.06◎	17.19 ± 3.04◎	60.25± 14.26◎

Note: ◎ compared with before treatment, P<0.05; ◎ compared with control group, P<0.001.

观察组治疗 1 个月后总有效为 16.6%,高于对照组的 12.24%,差异无统计学意义(x^2=0.363,P=0.547);观察组治疗 6 个月后显效为 29.16%,高于对照组的 4.08%,差异有统计学意义(x^2=22.681,P<0.001);观察组治疗 6 个月后有效为 58.34%,高于对照组的 8.16%,差异有统计学意义(x^2=56.535,P<0.001);观察组治疗 6 个月后总有效为 87.5%,高于对照组的 53.06%,差异有统计学意义(x^2=27.523,P<0.001)(表 2)。

两组均未出现明显不良反应。观察组出现 1 例恶心和腹泻,给予适当药物治疗后症状消失。

3 讨论

SIVD 为综合症,其病理特点为皮质下多发性腔隙性梗死和白质病变,主要病因是以小血管病变型缺血性脑血管病。临床症状包括运动和认知执行速度下降、构音障碍、情绪改变、日常生活能力减退、排尿障碍和步态异常等。目前有 2 种临床类型:腔隙状态和皮质下动脉硬化性白质脑病。CM 和 MRI 是 SIVD 的重要诊断途径,SIVD 患者可能存在一定程度的海马和皮质萎缩[9]。也有研究发现皮质下型 VCI 中的小血管性轻度认

知损害与皮质下血管性痴呆的皮质萎缩存在显著差异,认知功能下降与前额叶背外侧和颞叶皮质的萎缩有关[10]。目前临床药物如多奈哌齐被证实有一定疗效,但无法有效缓解 SIVD 的疾病进程。停药后症状立即复发,长期服用还会对记忆力造成更严重损伤[11]。

表 2 两组患者治疗后临床疗效比较(n/%)

Table 2 Comparison of the clinical curative effect between the two groups after treatment (n / %)

Groups	Time	Significantly effective	Effective	Invalid	Total effective
Observation group	After 1 month	4(8.3)	4(8.3)	40(83.4)	8(16.6)
	After 6 months	14(29.16)◎	28(58.34)◎	6(12.5)	42(87.5)◎
Control group	After 1 month	2(4.08)	4(8.16)	43(87.76)	6(12.24)
	After 6 months	4(8.16)	22(44.90)	23(46.94)	26(53.06)

Note: ◎ compared with control group, P<0.05.

由实验数据可得，观察组和对照组治疗 1 个月后 MMSE、MoCA、BI 评分与治疗前差异均无统计学意义(P>0.05),观察组治疗 1 个月后总有效为 16.6%,高于对照组的 12.24%,差异无统计学意义,表明在治疗前期阿托伐他汀配合康复训练并不能带来显著疗效,但同时评分均为提升,证明治疗仍然是有效的。猜测为短期内未生成新的血管,神经也未重组再生[12]。治疗 6 个月后,观察组的 MMSE、MoCA、BI 评分与治疗前差异有统计学意义(P<0.05),观察组的 MMSE、MoCA、BI 评分与对照组差异有统计学意义(P<0.001),观察组治疗 6 个月后总有效为 87.5%,高于对照组的 53.06%,差异有统计学意义,在治疗半年后治疗开始出现显著的效果,康复训练联合阿托伐他汀的治疗下患者出现明显的康复,且较纯多奈哌齐组更有效。相关文献认为他汀类药物的多靶点的药理特点相关,而多奈哌齐作用机制为单一乙酸胆碱释放抑制[13-15]。国内研究得出[16],他汀类药物在 3 个月到 6 个月的治疗时间内能有效改善血管,对痴呆患者有显著疗效,且他汀类药物不需要强化降脂 80 mg/d,且能降低血脂,对动脉粥样硬化和内皮脱落等有一定作用,促进侧循环的建立。

康复训练对预防痴呆也具有重要作用,康复训练能加快血液流动，促进脑血管再生 [17]。同时康复训练能减少脑卒中和 TIA 的发生率,合理的运动可提高患者记忆力和认知力[18],有实验证实,将 39 例痴呆患者分为实验组和对照组,分别为 19 例和 20 例,在无药物为期 6 个月的治疗下,实验组在认知、记忆和推理能力上均有较大程度的恢复,而对照组恢复效果并不理想,甚至病情更加严重。在康复训练中应注意以下 3 点[19,20]:1）首先给予患者体力训练，尝试独立步行及擦桌子等日常活动,在达到生活自理的情况下,才开始给予智力训练,给予扑克牌训练数字记忆;2)鼓励患者阅读报纸和书刊,防止智力退化;3)禁止患者单独外出,在恢复期间应对患者严加照顾。

综上所述，血管恢复和再生是治疗 SIVD 的主要目标,包括其他心脑血管疾病均应该以血管康复为主。康复训练在治疗 SIVD 中也有极大作用，肢体的运动也能起到预防大脑痴呆的作用,将机体作为一个整体治疗。康复训练联合阿托伐他汀的疗效显著,临床值得推广。

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