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【临床研究】

中药联合辛伐他汀治疗急性脑梗死的临床疗效

罗利俊,陈玲,苟玉兰,梅俊华,刘兵舰,吕晓强

(武汉市第一医院神经内科,湖北 武汉 430022)

摘要: 目的 观察中药联合辛伐他汀治疗急性脑梗死的近期及远期效果。方法 150例急性脑梗死患者随机分为对照组、辛伐他汀组和联合治疗组,每组50例。对照组采用脑梗死规范药物治疗,包括抗血小板积聚、调整血糖和血压、改善循环、保护神经细胞、降低脑水肿及相关营养支持治疗,并给予健康教育及早期综合康复治疗,出院后常规口服药物治疗;辛伐他汀组在对照组治疗基础上每日1次加用辛伐他汀40 mg口服,出院后在常规药物治疗的基础上继续坚持每日1次口服辛伐他汀40 mg;联合治疗组在辛伐他汀组治疗的基础上,按中医辨证论治加用中草药方剂。3组患者于入组时和治疗4、8、24周后分别进行美国国立卫生院神经功能缺损评分(NIHSS)及生活质量评分(BI),并比较血总胆固醇(TC)、三酰甘油(TG)、低密度脂蛋白(LDL)及高密度脂蛋白(HDL)水平。3组患者均定期随访,共随访4 a,观察比较再发急性脑梗死、心肌梗死、脑出血及死亡情况。结果 治疗前3组患者的血脂水平、NIHSS和BI比较差异均无统计学意义($P > 0.05$)。治疗4、8、24周后,与治疗前比较,对照组患者血脂水平无明显变化($P > 0.05$),NIHSS明显降低($P < 0.05$),BI明显提高($P < 0.05$);辛伐他汀组和联合治疗组患者TC、TG、LDL水平和NIHSS与治疗前及对照组的同时间点相比较均明显降低($P < 0.05$),而BI均明显提高($P < 0.05$);联合治疗组患者的TC、LDL水平明显低于辛伐他汀组($P < 0.05$)。治疗8、24周后,联合治疗组患者的NIHSS显著低于辛伐他汀组($P < 0.05$),BI均显著高于辛伐他汀组($P < 0.05$)。随访4 a,辛伐他汀组和联合治疗组患者心肌梗死的发病率和脑梗死再发率均低于对照组($P < 0.05$);辛伐他汀组患者心肌梗死发病率和脑梗死再发率与联合治疗组比较差异无统计学意义($P > 0.05$);3组患者的脑出血发病率及病死率比较差异无统计学意义($P > 0.05$)。结论 中药联合辛伐他汀防治急性脑梗死更有利于降低血脂水平,改善患者预后并提高其生活质量,联合治疗安全有效。

关键词: 脑梗死;中药;辛伐他汀

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Clinical curative effect of integrated traditional Chinese medicine combined with simvastatin treatment on acute cerebral infarction

LUO Li-jun, CHEN Ling, GOU Yu-lan, MEI Jun-hua, LIU Bing-jian, LYU Xiao-qiang

(Department of Neurology, the First Hospital of Wuhan, Wuhan 430022, Hubei Province, China)

Abstract: **Objective** To observe the short-term and long-term effect of integrated traditional Chinese medicine combined with simvastatin on acute cerebral infarction patients. **Methods** A total of 150 patients with acute cerebral infarction were randomly divided into control group ($n = 50$), simvastatin group ($n = 50$) and integrated treatment group ($n = 50$). The patients in control group were treated with standardized drug including anti-platelet aggregation, adjusting blood sugar and blood pressure, improving cerebral blood circulation, protecting the nerve cells, reducing brain edema and other related nutritional support treatment, and were given health-education and early comprehensive rehabilitation, who were given routine oral drug treatment after discharge. On the basis of the treatment of control group, the patients in the simvastatin group had received simvastatin (40 mg, once a day). Patients in the integrated treatment group additionally took Chinese medicine apart from receiving the same treatment as the simvastatin group. The rating scales such as National Institutes of Health Stroke Scale (NIHSS) and barthel index (BI) were used to evaluate all patients at pre-therapy, after 4, 8 and 24 weeks of treatment. At the same time, the levels of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) were measured and compared among the three groups. All patients were followed up for 4 years on a regular basis, and the incidence of the cerebral infarction, the myocardial infarction, intracerebral hemorrhage and death were observed and compared. **Results**

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作者简介:罗利俊(1971-),女,湖北浠水人,硕士,副主任医师,研究方向:脑血管病的中西医结合治疗,神经免疫学。

通信作者:陈玲(1977-),女,湖北天门人,硕士,主治医师,研究方向:脑血管病的中西医结合治疗,癫痫。

There were no statistically significance difference about lipid levels and the scores of NIHSS and BI among the three groups before treatment ($P > 0.05$) . After 4, 8 and 24 weeks of treatment, the lipid levels in the control group had no obvious change compared with those before treatment ($P > 0.05$), while the scores of NIHSS were significantly lower ($P < 0.05$), and the scores of BI were increased significantly ($P < 0.05$). In the simvastatin group and the integrated treatment group, the levels of TC, TG, LDL-C and the scores of NIHSS were significantly lower than before treatment and the same time of the control group ($P < 0.05$), but the scores of BI were increased significantly ($P < 0.05$). In the integrated treatment group, the levels of TC and LDL-C were obviously lower than those in the simvastatin group ($P < 0.05$). After 8 and 24 weeks of treatment, the scores of NIHSS of the integrated treatment group were significantly lower and the scores of BI were increased obviously than those of the simvastatin group ($P < 0.05$). After 4 years, the incidence of cerebral infarction and myocardial infarction in the two treatment groups were obviously lower than those of the control group ($P < 0.05$), but there was no obviously difference between the two treatment groups ($P > 0.05$); and there was no obviously difference in the intracerebral hemorrhage and deathly event rate among the three groups ($P > 0.05$). There was no obviously difference comparing the adverse reaction between the simvastatin group and the integrated treatment group ($P > 0.05$). **Conclusion** Integrated traditional Chinese medicine and simvastatin can significantly reduce the blood lipid level and perfect the prognosis, improve the life qualities of stroke patients, and the integrated treatment is safety.

Key words: cerebral infarction; traditional Chinese medicine; simvastatin

研究表明,中药及他汀类药物在脑梗死的治疗中均具有重要作用^[1-4]。作者根据中医辨证,联合应用辛伐他汀和中草药方剂治疗急性脑梗死,以进一步观察中草药方剂联合辛伐他汀治疗急性脑梗死的近期、远期疗效及安全性,现报道如下。

1 资料与方法

1.1 一般资料 选择2007年7月至2008年3月在武汉市第一医院卒中单元病房住院的急性脑梗死患者150例,均符合以下入选标准:(1)急性脑梗死患者,发病7 d内入院,经临床、颅脑计算机断层扫描/磁共振成像证实;(2)年龄40~80岁;(3)小学以上文化程度,检查合作者;(4)患者及家属均知情同意。排除标准:(1)各种意识障碍、昏迷、失语、严重认知功能障碍、严重心肝肾功能障碍、既往有精神疾病史者、依从性差者;(2)既往对他汀类药物过敏者;(3)正在参加其他试验者;(4)有自杀行为者。按随机抽签的方法分为3组,其中对照组50例,男31例,女19例;年龄41~80岁,平均(61.6±9.8)岁;小学文化9例,初中24例,高中及以上17例;治疗前患者美国国立卫生院神经功能缺损评分(National Institutes of Health Stroke Scale, NIHSS)平均为12.7±3.3。辛伐他汀组50例,男29例,女21例;年龄40~79岁,平均(61.2±10.7)岁;小学文化7例,初中27例,高中及以上16例;患者治疗前NIHSS平均为12.9±3.6。联合治疗组50例,男34例,女16例;年龄41~79岁,平均(62.3±11.4)岁;小学文化10例,初中25例,高中及以上15例;患者治疗前NIHSS为13.0±3.5。治疗前3组患者性别、年龄、文化程度、NIHSS比较差异均无统计学意义

($P > 0.05$)。

1.2 治疗方法

1.2.1 对照组 对照组给予脑梗死规范药物治疗,包括抗血小板积聚、调整血糖和血压、改善循环、保护神经细胞、降低脑水肿及相关营养支持治疗,并给予健康教育及早期综合康复治疗,疗程2~3周,出院后常规口服药物治疗,随访4 a。

1.2.2 辛伐他汀组 辛伐他汀组在对照组常规药物治疗及早期综合康复治疗的基础上加用辛伐他汀(杭州默沙东制药有限公司,国药准字H19990366)40 mg口服,每日1次,睡前口服,疗程2~3周,出院后在常规药物治疗的基础上坚持应用辛伐他汀40 mg口服,每日1次,睡前口服,用药随访4 a。

1.2.3 联合治疗组 联合治疗组在辛伐他汀组基础上根据脑卒中中医辨证分型将患者分为5个证型进行论治:(1)风痰阻络型:治宜熄风化痰通络,方药化痰通络汤加减,法半夏10 g、橘红10 g、枳壳10 g、川芎10 g、红花10 g、远志10 g、石菖蒲10 g、茯神15 g、党参15 g、丹参15 g、炙甘草10 g;(2)痰热腑实型:治宜化痰泄热通腑,方药星蒌承气汤加减,生大黄10 g、芒硝10 g、全瓜蒌30 g、胆南星6 g;(3)气虚血瘀型:治宜益气活血,方药补阳还五汤加减,黄芪生125 g、当归尾6 g、赤芍5 g、地龙3 g、川芎3 g、红花3 g、桃仁3 g;(4)肝阳上亢型:治宜平肝泻火,方药天麻钩藤饮加减,天麻9 g、梔子9 g、黄芩9 g、杜仲9 g、益母草9 g、桑寄生9 g、夜交藤9 g、朱茯神9 g、川牛膝12 g、钩藤(后下)12 g、石决明(先煎)18 g;(5)阴虚风动型:治宜滋阴熄风,方药镇肝熄风汤加减,怀牛膝30 g、生赭石30 g、川楝子6 g、生龙骨15 g、生牡蛎15 g、生龟板15 g、生杭芍

0.05);3组患者的脑出血发病率及病死率比较差异无统计学意义($P > 0.05$)。

2.4 不良反应比较 对照组中,有2例因明显消化道症状退出观察,有3例因依从性差退出。辛伐他汀组有2例出现明显消化道不良反应退出;有1例出现乏力感退出,停药后症状消失;有1例丙氨酸氨基转移酶(alanine aminotransferase, ALT)明显升高,超过正常高值的3倍,退出研究,停用辛伐他汀并给予护肝治疗,后复查肝功能正常;另有2例ALT升高,但未超过正常上限的2倍,坚持用药,后复查肝功能正常,仍继续观察,未退出。联合治疗组有3例出现明显消化道不良反应退出;1例出现明显乏力感退出,停药后症状消失;1例ALT明显升高超过正常上限3倍退出,停用辛伐他汀并给予护肝治疗,后复查肝功能正常。4a中3组患者均未发生肾损害、骨骼肌损害等严重不良反应,联合治疗组与辛伐他汀组不良反应比较差异无统计学意义($P > 0.05$)。

3 讨论

中医学认为,急性缺血性中风属本虚标实之证,在本为肝肾阴虚,气血衰少,在标为痰浊、邪热、风火、气血郁阻,治疗应注重标本兼顾,应用辨证施治,依风、虚、瘀、痰、火等5大病机,分别予熄风、化痰、逐瘀、通络、益气、活血、泻火、镇肝潜阳、滋阴补肝肾等^[1,5],本研究中的中药辨证论治正是以上述中医学理论为基础。脑动脉硬化是急性中风的主要病理基础^[6],TC、LDL等沉积于血管壁是典型的痰浊形成,可诱发血小板聚集,淤血闭塞经脉而中风^[7]。本研究中药方剂中的红花、枳壳可使心脏收缩和扩张增加,可降低血清TC含量;瓜蒌、胆南星、地龙、钩藤、水蛭、川芎、丹参等能抑制血小板聚集,增强大脑耐缺氧能力,保护血管内皮细胞。

他汀类药物是临床最常用、效果最肯定的调脂药,辛伐他汀作用机制为选择性竞争抑制3-羟基-3-甲基戊二酰辅酶A,降低肝细胞TC合成,明显抑制LDL的生成及促进其向细胞内的转入,提升LDL清除率,有效降低血脂水平,同时通过稳定动脉粥样硬化斑块、抑制炎症反应、抑制巨噬细胞、改善血管内皮功能、抑制血小板聚集等多向效应的协同作用来改善心脑血管功能^[8,9]。在西方发达国家,他汀类降脂药已被广泛应用于心脑血管病的治疗及预防中,但在我国他汀类药物在临床的使用率较低,缺乏对该类药物的足够认识、过分担心该类药物的不良反应、缺乏临床应用经验等均干扰了他汀类药物在临床上的应用。基于以上临床现状,作者开展了本研究,以观察中药联合辛伐他汀治疗急性脑梗死的近

期及远期疗效和安全性。研究结果表明,在近期临床疗效方面,中药联合辛伐他汀治疗急性脑梗死,能更好地改善患者的血脂水平,明显改善患者的NIHSS及BI,提高其生活质量,与既往相关研究^[8-11]相符,可能与诸多中药联用能明显改善血脂异常指标、降低血小板聚集、降低血液黏稠度、改善微循环障碍、减轻氧自由基的损害、保护脑细胞及减少细胞凋亡等作用有关^[10-11]。在远期临床疗效方面,辛伐他汀组和联合治疗组急性脑梗死再发率、急性心肌梗死发病率均明显下降,而脑出血发病率差异无统计学意义,提示中药及辛伐他汀能明显改善脑梗死患者的远期预后,观察结果与国内相关研究^[7,12]类似;但本研究中,4a后3组患者病死率差异无统计学意义,与以往研究^[13]不符,考虑可能与观察病例数较少及观察时间较短有关。同时研究表明,中药与辛伐他汀联合应用未发现明显不良反应,安全有效,值得临床推广应用。

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