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阿托伐他汀联合参松养心胶囊治疗老年心力衰竭患者临床疗效及安全性研究*

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摘要 目的:探讨阿托伐他汀联合参松养心胶囊对老年心力衰竭患者的临床疗效及安全性。**方法:**选取我院心血管内科治疗的老年慢性心力衰竭患者 121 例,按治疗药物不同分为两组,对照组 46 例采用西医常规治疗,研究组 75 例常规治疗基础上给予阿托伐他汀联合参松养心胶囊治疗,记录两组 12 个月后的临床疗效,治疗后 3、6 及 12 个月后的总胆固醇(Total cholesterol, TC)、甘油三酯(Triglyceride, TG)、高密度脂蛋白胆固醇(High density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)水平的变化及不良反应的发生情况。**结果:**与治疗 3 个月时相比,两组治疗 12 个月时临床有效率均显著提高,研究组治疗 6、12 个月临床有效率均显著高于对照组(85.33% vs. 76.09%, 88% vs. 80.43%, $P < 0.05$)。两组治疗后血清 TC、TG、LDL-C 水平逐步下降,血清 HDL-C 水平逐步上升,研究组治疗第 12 月后血清 TC、TG 及 LDL-C 水平较对照组显著降低($P < 0.05$),血清 HDL-C 水平较对照组明显升高($P < 0.05$)。两组在 1 年观察期内均未见明显肝肾功能损伤及肌溶解,不良反应发生率比较差异无统计学意义($P > 0.05$)。**结论:**长期使用阿托伐他汀联合参松养心胶囊治疗老年性心力衰竭的临床效果明显优于西医常规治疗,其可有效降低血脂水平,安全性高。

关键词:阿托伐他汀;参松养心胶囊;老年心力衰竭;临床疗效;安全性

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A Study on the Clinical Effect and Safety of Atorvastatin Combined with Shensongyangxin Capsule on the Elderly Patients with Heart Failure*

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ABSTRACT Objective: To investigate the clinical effect and safety of atorvastatin combined with Shensongyangxin Capsule on the elderly patients with heart failure. **Methods:** 121 cases of elderly patients with chronic heart failure were selected and divided into two groups according to the different therapeutic agents, 46 cases in the control group were treated with routine treatment, 75 cases in the experiment group were treated with Atorvastatin combined with Shensongyangxin capsule, both groups were treated for 12 months. The clinical efficacy at 12 months after treatment and the changes of total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) levels at 3, 6 and 12 months after treatment and the incidence of adverse reaction were compared between two groups. **Results:** Compared with those at 3 months after treatment, the clinical effective rate of both groups at 12 months after treatment were significantly improved, and the clinical effective rates of experimental group at 6 and 12 months after treatment were significantly higher than those of the control group (85.33% vs. 76.09%, 88% vs. 80.43%, $P < 0.05$). After treatment, the levels of serum TC, TG and LDL-C levels were gradually decreased, and the level of serum HDL-C increased gradually in the two groups, the serum TC, TG and LDL-C levels in the experiment group were significantly lower than those of the control group at 12 months after treatment ($P < 0.05$); the serum HDL-C level was significantly higher than that of the control group ($P < 0.05$); there was no significant hepatic and renal dysfunction and myolysis in the two groups during the observation period of one year, there was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). **Conclusion:** Atorvastatin combined with Shensong Yangxin Capsule is significantly better than the routine western medicine in the treatment of senile heart failure, which can effectively reduce the blood lipid levels with high safety.

Key words: Atorvastatin; Shensongyangxin Capsule; Elderly; Heart failure; Clinical efficacy; Safety

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前言

慢性心力衰竭是危害老年人健康的重要疾病,也是临床医师重点关注的问题^[1,2]。有研究显示人体血清低密度脂蛋白胆固醇(LDL-C)水平每增加 1%,冠状动脉粥样硬化性心脏病的发生机率则可增加 2%~4%,甚至更高^[3,4]。他汀类药物是目前临床上最常用的降脂类药物,其不仅具有令人满意的降脂效果,且具有抑制炎症反应、调节血管内皮功能、抵抗血小板聚集、稳定斑块的作用,降低心血管事件发生率的效果已被多项研究报道证实^[5]。

中成药参松养心胶囊具有养阴益气、安神清心、通络活血等效果,既往多用于气阴两虚、心络瘀阻证等治疗中,近年来有研究发现,其在临床上也具有协助降低心力衰竭患者不良事件的发生率的作用^[6,7]。然而,目前关于阿托伐他汀长期联合参松养心胶囊服用对老年心力衰竭患者临床疗效及安全性并不完全明确。本研究主要探讨了阿托伐他汀长期服用对老年心力衰

竭患者临床疗效及安全性:

1 资料与方法

1.1 临床资料

选取自 2013 年 4 月到 2015 年 1 月来我院心血管内科治疗的老年慢性心力衰竭患者 121 例,纳入标准:①符合慢性心力衰竭诊断标准^[8],并通过 X 线检查、心电图、超声心动图等检查得以确诊;②知情同意此研究。排除标准:①合并肺源性心脏病、先天性心脏病、败血症、心肌梗死、急性肺栓塞等疾病;②合并严重肝肾功能障碍、恶性肿瘤及全身免疫系统疾病者;③合并多发性皮炎、横纹肌溶解症等肌肉疾病者。按治疗药物不同进行分组,对照组 46 例采用西医常规治疗,研究组 75 例在常规治疗基础上给予阿托伐他汀联合参松养心胶囊治疗,疗程为 1 年。两组基本临床资料比较差异均无统计学意义,具有可比性($P < 0.05$),详见表 1。

表 1 两组患者一般资料对比($\bar{x} \pm s$)
Table 1 Comparison of the general data between the two groups($\bar{x} \pm s$)

Item		Control group(n=46)	Experiment group(n=75)
Gender	Male	28(60.87%)	44(58.67%)
	Female	18(37.13%)	31(41.33%)
Age(years)		62.79 $\pm$ 10.79	62.79 $\pm$ 10.38
Course of disease(years)		4.35 $\pm$ 3.28	4.29 $\pm$ 3.64
NYHA cardiac functional grading	II	20(43.48%)	30(40%)
	III	26(56.52%)	45(60%)
Blood lipid(mmol/L)	TC	5.11 $\pm$ 1.21	5.13 $\pm$ 1.19
	TG	1.65 $\pm$ 0.98	1.63 $\pm$ 0.95
	HDL-C	1.24 $\pm$ 0.45	1.23 $\pm$ 1.47
	LDL-C	3.60 $\pm$ 1.02	3.58 $\pm$ 1.01
Primary disease	Ischemic cardiomyopathy	31(67.39%)	49(65.33%)
	Dilated cardiomyopathy	15(32.61%)	26(34.67%)

1.2 治疗方法

对照组给予心力衰竭常规治疗,包括利尿剂、血管紧张素转换酶抑制剂(ACEI)及 β 受体阻滞剂等应用,必要时可给予加洋地黄类强心剂。

研究组在对照组的基础上给予阿托伐他汀(北京嘉林药业股份有限公司,国药准字 H19990258)20 mg, 1 次/d,参松养心胶囊(北京以岭药业有限公司,国药准字 Z20103032),2-4 粒/次,3 次/d。

1.3 观测指标

1.3.1 临床疗效 参照《中药新药临床研究指导原则》:显效为心功能改善 2 级以上,心脏指数(CI)升高 1.0 L/(min $\cdot$ m²),肺毛细血管楔压(PCWP)<12 mmHg;有效为心功能改善 1 级,CI 升高 0.5 L/(min $\cdot$ m²),PCWP<18 mmHg;无效为未达到有效标准。

1.3.2 血脂水平 观察两组间治疗 3、6 及 12 个月后的血清总胆固醇(Total cholesterol, TC)、甘油三酯(Triglyceride, TG)、高

密度脂蛋白胆固醇(High density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)水平。

1.3.3 不良反应的发生情况 观察两组心血管事件的发生率以及肝肾功能、肌酸磷酸的变化情况。

1.4 统计学分析

所有统计数据采用 spss17.0 软件包分析,符合正态分布的计量资料采用均数 $\pm$ 标准差表示,两组间治疗前后及组间血脂水平对比采用 t 检验,计数资料采用卡方检验, $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者治疗后不同时间点临床疗效分析

与治疗 3 个月时相比,两组治疗 12 个月时临床有效率均显著提高,研究组治疗 6、12 个月后临床有效率均显著高于对

照组(85.33% vs. 76.09%, 88% vs. 80.43%, $P<0.05$)。

表 2 两组患者不同时间点临床疗效分析[例(%)]

Table 2 Comparison of the clinical effect at different time points between the two groups[n(%)]

Groups	Points	Effective	Valid	Invalid	Total effective rate
Control group(n=46)	At 3 months after treatment	11(23.92%)	19(41.30%)	16(34.78%)	65.22%
	At 6 months after treatment	17(36.96%)	18(39.13%)	11(23.91%)	76.09%*
	At 12 months after treatment	19(41.30%)	18(39.13%)	9(19.57%)	80.43%*
Experimental group (n=75)	At 3 months after treatment	23(30.67%)	31(41.33%)	21(28%)	72%
	At 6 months after treatment	35(46.66%)	29(38.67%)	11(14.67%)	85.33%*#
	At 12 months after treatment	46(61.33%)	20(26.67%)	9(12%)	88%*#

Note: Compare with same group after treatment 3 months, * $P<0.05$, Comparison with the control group # $P<0.01$.

2.2 两组患者不同时间点血脂水平比较

与治疗前比较, 两组患者治疗后 12 个月血清 TC、TG 及 LDL-C 水平呈下降趋势, 血清 HDL-C 水平呈上升趋势; 与对照

组同期相比较, 实验组治疗后 12 个月血清 TC、TG 及 LDL-C 水平较低, 血清 HDL-C 水平较高($P<0.05$)。

表 3 两组患者不同时间点血脂水平比较($\bar{x}\pm s$, mmol/L)

Table 3 Comparison of the blood lipid levels at different time points between the two groups($\bar{x}\pm s$, mmol/L)

Groups	Points	TC	TG	HDL-C	LDL-C
Control group(n=46)	At 3 months after treatment	5.01 $\pm$ 0.47	1.57 $\pm$ 1.14	1.25 $\pm$ 0.90	3.51 $\pm$ 0.27
	At 6 months after treatment	4.85 $\pm$ 0.36	1.45 $\pm$ 0.12	1.30 $\pm$ 0.12	3.42 $\pm$ 0.25
	At 12 months after treatment	4.57 $\pm$ 0.43	1.43 $\pm$ 1.03	1.32 $\pm$ 0.98	3.33 $\pm$ 0.25
Experimental group (n=75)	At 3 months after treatment	3.67 $\pm$ 0.35	1.31 $\pm$ 0.10	1.43 $\pm$ 0.12	2.54 $\pm$ 0.24
	At 6 months after treatment	3.41 $\pm$ 0.33	1.22 $\pm$ 0.10	1.52 $\pm$ 0.12	1.86 $\pm$ 0.17
	At 12 months after treatment	3.12 $\pm$ 0.30#	1.11 $\pm$ 0.10#	1.61 $\pm$ 0.15#	1.32 $\pm$ 0.11#

Note: the same time point ratio with the control group, # $P<0.05$.

2.3 两组患者不同时间点不良反应发生状况比较

两组均未出现严重肝肾功能损伤, 肌溶解等不良反应, 仅为转氨酶增高或轻度恶心、呕吐等胃肠道反应。治疗 3 个月时, 对照组 2 例轻度转氨酶升高, 2 例胃肠道反应, 研究组 5 例口干, 2 例 CK-MB 升高; 治疗 6 个月时, 对照组 3 例轻度转氨酶升高, 2 例胃肠道反应, 1 例 CK-MB 升高, 研究组 5 例口干, 3

例头痛, 2 例 CK-MB 升高, 1 例恶心; 治疗 12 个月时, 对照组 3 例轻度转氨酶升高, 2 例胃肠道反应, 2 例 CK-MB 升高, 研究组 5 例口干, 3 例头痛, 3 例 CK-MB 升高, 2 例恶心。两组治疗 3、6、12 个月后不良反应发生率比较差异无统计学意义 ($P>0.05$), 见表 4。

表 4 两组患者不同时间点不良反应发生情况比较[例(%)]

Table 4 Comparison of the incidence of adverse reaction at different time points between the two groups[n(%)]

Groups	After treatment 3 months	After treatment 6 months	After treatment 12 months
Control group(n=46)	4(8.70%)	6(13.04%)	7(15.22%)
Experimental group(n=75)	7(9.33%)	11(14.67%)	13(17.33%)

3 讨论

慢性心力衰竭是各类心脏病的终末阶段, 其发病率可随着年龄的增长而不断增加, 若患者得不到及时的治疗, 心功能不全的症状也会随之加重^[9]。相关数据显示, 在 65 岁的人群中, 慢性心力衰竭的发病率高达 50%^[10,11], 且患者通常合并心功能降低、运动耐力减弱等表现, 心肌重构过程中常合并局部性心肌细胞凋亡、坏死、性间质细胞纤维化等病理改变。已有较多报道

指出血脂紊乱是冠心病、动脉粥样硬化、脑血管疾病中的一大重要致病因素。而他汀类药物仍是目前降脂治疗的首选药物^[12,13], 可通过对肝细胞表面低密度脂蛋白受体的抑制作用, 促进胆固醇的消除, 降低 TC、TG、LDL-C 的表达及升高 HDL-C 的表达^[14,15]。有研究指出, 他汀类药物不仅在降低血脂中效果显著, 且不会对肌酐、转氨酶、尿微量蛋白等指标产生较大影响。

参松养心胶囊的组成主要包括由人参、麦冬、山茱萸、丹参、炒酸枣仁、桑寄生、赤芍、土鳖虫、甘松、黄连、南五味子、龙

骨等,在现代药理学中显示其可抗心律失常,对气短乏力、心悸、失眠等症状均具有改善效果,不仅可用于治疗快速性心律失常,且对缓慢性心律失常例如窦性心律过缓等均具有满意的效果,且药物不良反应少,安全性高。已有较多大型临床实验证实了他汀类降脂药物用于治疗心力衰竭中的优势。本次研究结果显示患者在阿托伐他汀联合参松养心胶囊治疗 3、6、12 个月后血清 TC、TG、LDL-C 下降,HDL-C 上升,且改善程度均优于常规西医治疗,表明了长期应用阿托伐他汀的有效性。

血脂异常是心血管疾病最主要的危险因素之一,通过改善血脂紊乱在预防动脉粥样硬化病变发生、发展中具有极为重要的意义。阿托伐他汀作为一种羟甲基戊二酸单酰辅酶 A (HMG-CoA)还原酶抑制剂,可通过对 HMG-CoA 还原酶产生竞争性抑制作用,改善血脂水平。近 20 年来,多项大规模临床试验的结果显示他汀类药物在冠心病的一级和二级预防中均能显著降低心血管事件的危险。本研究结果显示长期应用他汀类药物联合参松养心胶囊并未导致患者出现较多不良反应,提示该方案是安全可靠的。

综上所述,本次研究显示长期使用阿托伐他汀联合参松养心胶囊治疗老年慢性心力衰竭的临床治疗效果显著优于常规西医治疗,对血脂控制水平控制能达到临床满意,而且安全性高。然而,本次试验患者例数有限,随访时间较短,而且患者对阿托伐他汀药物联合参松养心胶囊的依从性均会对研究结果产生一定程度影响。另一方面,对于长期应用阿托伐他汀对神经内分泌因素、免疫和炎症激活等热点研究尚需要进一步探索。

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