doi: 10.13241/j.cnki.pmb.2014.20.035

阿托伐他汀钙联合阿司匹林治疗短暂性脑缺血发作的疗效及对颈动脉粥样硬化斑块和血脂水平的影响研究

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摘要 目的:探讨阿托伐他汀钙联合阿司匹林对短暂性脑缺血发作的治疗疗效及其对颈动脉粥样硬化斑块和血脂水平的影响。**方法:**选择我院80例短暂性脑缺血发作患者,按入院顺序随机平均分为两组,研究组40例患者给予阿托伐他汀钙联合阿司匹林治疗,对照组40例患者仅使用阿司匹林治疗。比较两组患者治疗后的治疗有效率,6个月后分别对两组患者颈动脉粥样硬化斑块及血脂水平进行检测。**结果:**研究组患者治疗总有效率为92.5%,明显高于对照组75%,比较差异具有统计学意义(P<0.05);治疗6个月后研究组患者IMT及斑块面积较治疗前明显降低,且降低程度明显高于对照组,比较差异具有统计学意义(P<0.05);研究组血清中LDL、TC、TG水平较治疗前显著下降,且下降程度明显高于对照组,同时HDL水平显著上升,而上升程度也明显高于对照组,比较差异具有统计学意义(P<0.05)。**结论:**阿托伐他汀钙联合阿司匹林对短暂性脑缺血发作的治疗疗效显著,可明显减轻或消除颈动脉粥样硬化斑块并明显降低血脂水平,值得推广应用。

关键词: 阿托伐他汀钙;阿司匹林;短暂性脑缺血;颈动脉粥样硬化;血脂

中图分类号:R743 **文献标识码:**A **文章编号:**1673-6273(2014)20-3931-04

Efficacy of Atorvastatin Calcium Combined with Aspirin in Treatment of Transient Ischemic Attacks and its Effects on Carotid Atherosclerotic Plaques and Blood lipid Levels

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ABSTRACT Objective: To evaluate the efficacy of atorvastatin calcium combined with aspirin in treatment of transient ischemic attacks and its effects on carotid atherosclerotic plaques and blood lipid levels. **Methods:** 80 cases of patients with transient ischemic attacks in our hospital were randomly divided into two groups according to the order of admission. The study group was treated with atorvastatin calcium in combination with aspirin while the control group of 40 patients used aspirin only. Efficiency of two groups was compared after the treatment and carotid atherosclerotic plaque and lipid levels were detected respectively after 6 months. **Results:** The total effective rate of the study group was 92.5% significantly higher than 75% of the control group, the difference was statistically significant (P<0.05); 6 months later after treatment the study group's IMT and plaque area were significantly reduced, and they were significantly higher than the control group, the difference was statistically significant (P<0.05); The study group's serum LDL, TC, TG levels were significantly decreased as compared with before and the degree of decline was significantly higher than that of the control group. Meanwhile, the HDL levels of study group was significant increased, and the difference was statistically significant (P<0.05). **Conclusion:** Atorvastatin calcium combined with aspirin has a significant therapeutic effect on transient ischemic attack. It could significantly reduce or eliminate atherosclerotic plaque in the carotid artery and significantly reduce blood lipid levels, so it should be widely applied.

Key words: Atorvastatin calcium; Aspirin; Transient cerebral ischemia; Carotid atherosclerosis; Lipids

Chinese Library Classification(CLC): R743 Document code: A

Article ID: 1673-6273(2014)20-3931-04

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(收稿日期:2013-12-19 接受日期:2014-01-16)

前言

短暂性脑缺血发作(TIA)是临床常见多发性脑血管疾病,其主要发病原因为颈动脉粥样硬化以及其导致的颈动脉狭窄,发生该类症状的患者在 2 年内出现卒中的几率达 40%,频繁发作者 48 h 内脑卒中发生率甚至高达 50%[1,2]。因而对 TLA 的有效预防是目前广大医患人员关注的热点,有研究证实[3],他汀类药物对心脑血管疾病的预防作用日益凸现,并将他汀类药物作为冠心病、缺血性脑卒中防治的基础用药。阿托伐他汀钙是一种疗效确切的调脂药物[4],但对短暂性脑缺血发作息者的颈动脉斑块能的影响作用的报道不多,本研究使用阿托伐他汀钙联合阿司匹林对我院 40 例短暂性脑缺血发作患者进行治疗,疗效显著,现报告如下。

1 资料与方法

1.1 一般资料

选择我院 2012 年 1 月至 2013 年 1 月收治的 80 例短暂性脑缺血发作患者,均符合全国第四届脑血管病学术会议修订的诊断标准[5],并经 CT 及 MRI 等扫描检查确诊,经颈部血管超声检查证实有颈动脉粥样硬化斑块形成。其中男 47 例,女 33 例;年龄 43～76 岁,平均(63.2± 8.9)岁;病程 1 周至 6 个月,平均(3.2± 1.4)个月;颈动脉病变单侧 32 例,双侧 48 例。所有入选患者均经知情同意,并排除脑梗死、脑出血、严重高血压(≥ 180/110 mmHg)及全身严重合并症,就诊前未有脑卒中史,未使用抗血小板、抗凝、溶栓等药物治疗,按入院顺序随机平均分为两组,研究组及对照组各 40 例,两组患者在性别、年龄、病程、病变位置及程度等方面比较差异无统计学意义(P＞0.05),具有可比性。

1.2 方法

两组患者入院后给予常规尼莫地平、胞二磷胆碱、丹参或低分子右旋糖酐等药物静脉滴注,治疗 2 周,研究组患者在此基础上使用阿托伐他汀钙联合阿司匹林进行治疗,阿托伐他汀钙口服 10 mg,每天 1 次,同时服用阿司匹林 100 mg,每天 1 次, 连续服用 6 个月。对照组患者每天仅口服阿司匹林 100 mg,连续服用 6 个月。

1.3 评价标准

疗效评价标准[6]:①治愈:发作能快速终止,未见复发;②有效:仍发作,但发作频率及持续时间均得到控制;③无效:发作未控制,发作频率及持续时间未见好转;④进展:发生脑梗死或其他不良转归。

颈动脉粥样硬化检测:所有患者于治疗前及治疗后 6 个月使用 acuson 公司生产 Sequoia-520 型彩色多普勒血流超声诊断仪,由专业人员检测其两侧颈动脉,分别检测患者颈总动脉、颈内动脉、颈外动脉及颈动脉分叉部,同时检测有无斑块及斑块厚度,取最厚处记录为颈动脉内膜中层厚度(IMT),局部动脉粥样硬化区域 IMT≥ 1.1 mm,称之为动脉粥样硬化斑块。

血脂检测:所有患者于治疗前及治疗后 6 个月,清晨取血清使用全自动生化仪酶法测定血清总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白(HDL)和低密度脂蛋白(LDL)水平。

1.4 统计学处理

应用 SPSS16.0 分析数据,计量资料以平均数($\bar{x}$± s)表示,组间比较进行 t 检验, 组内比较进行配对 t 检验, 计数资料用 X^2 检验,以 P＜0.05 表示差异有统计学意义。

表 1 两组患者治疗疗效比较(n,%)

Table 1 Comparison of efficacy of two groups (n, %)

组别 Groups	例数 (n)	治愈 Cure	有效 Response	无效 Invalid	进展 Evolve	总有效率(%) Total effective rate (%)
研究组 Study group	40	19	18	2	1	92.5▲
对照组 Control group	40	11	19	6	4	75.0

注:与对照组比较, X^2=4.501,▲P<0.05。

Note: Compared with the control group, X^2=4.501, ▲P<0.05.

2 结果

2.1 两组患者治疗后疗效比较

研究组患者总治疗有效率为 92.5%明显高于对照组的 75%,比较差异具有统计学意义(P＜0.05),见表 1。

2.2 两组患者治疗前后颈动脉内中膜厚度(IMT)及斑块面积比较

两组患者治疗 6 个月后 IMT 及斑块面积较治疗前明显降低,且研究组降低程度明显高于对照组,比较差异具有统计学意义(P＜0.05),详见表 2。

2.3 两组患者治疗前后血脂变化

两组患者治疗 6 个月后 LDL、TC、TG 水平较治疗前均明显下降, 研究组患者 3 项血脂指标下降程度较对照组明显,比较差异具有统计学意义(P＜0.05);同时两组患者治疗后 HDL 水平均明显上升, 且研究组患者 HDL 的上升程度明显高于对照组,比较差异具有统计学意义(P＜0.05),详见表 3。

3 讨论

短暂性脑缺血发作造成缺血性脑卒中最重要的危险因素,主要动脉粥样硬化、动脉狭窄、心脏疾患、血液成分异常及血流动力学等多因素共同作用造成[7]。有研究报道显示[8],发作频繁、持续时间较长的短暂性脑缺血发作患者,其发生脑梗死的概率明显增高且发生时间早。因此,对于短暂性脑缺血发作的早期防治是减少缺血性脑卒中发生的重要手段。另有研究表明[9],颈动脉粥样硬化是造成短暂性脑缺血发作的最重要原因之一,TIA 患者颈动脉粥样硬化的发生率明显高于同龄的健康人群,

表 2 两组患者治疗前后 IMT 及斑块面积比较($\bar{x}\pm s$)

Table 2 Comparison of IMT and plaque area in two groups before and after treatment ($\bar{x} \pm s$)

组别 Groups	例数 n	颈动脉中膜厚度(mm)IMT(mm)				斑块面积(mm²)Plaque area(mm2)			
		治疗前 Prior treatment	治疗后 Post treatment	t	P	治疗前 Prior treatment	治疗后 Post treatment	t	P
研究组 Study group	40	1.54± 0.63	1.25± 0.34	2.89	＜0.05	26.53± 11.45	18.95± 9.23	3.48	＜0.05
对照组 Control group	40	1.55± 0.65	1.47± 0.46	0.75	＞0.05	27.12± 12.04	25.12± 10.35	0.81	＞0.05
t		0.07	2.43			0.22	2.82		
P		＞0.05	＜0.05			＞0.05	＜0.05		

表 3 两组患者治疗前后血脂变化情况比较(mmol/L, $\bar{x}\pm s$)

Table 3 Comparison of lipid levels in two groups before and after treatment (mmol/L, $\bar{x}\pm s$)

组别 Groups	例数(n)	时间	LDL	HDL	TC	TG
研究组 Study group	40	治疗前 Prior treatment	4.98± 0.64	1.03± 0.35	5.42± 1.21	2.89± 0.58
		治疗后 Post treatment	3.75± 0.54△▲	1.52± 0.42△▲	4.23± 1.04△▲	2.12± 0.45△▲
对照组 Control group	40	治疗前 Prior treatment	4.89± 0.63	1.10± 0.34	5.35± 1.06	3.01± 0.75
		治疗后 Post treatment	4.65± 0.61△	1.21± 0.35△	5.10± 1.23△	2.76± 0.65△

注:与治疗前比较,△P<0.05,与对照组同期比较,▲P<0.05。

Note: Compared with before treatment, △P<0.05, compared with same period of the control group, ▲P<0.05 .

且颈动脉狭窄程度和粥样硬化斑块的形态、状况都与短暂性脑缺血发作和完全性脑卒中的发生有关。目前，微栓子学说是TIA 发病机制最贴切的解释[10,11]:① 颈动脉狭窄处附壁血栓以及动脉粥样硬化斑块脱落形成微栓子将颅内动脉栓塞,同时刺激其产生痉挛,最终可形成梗死灶;② 斑块可使动脉变得狭窄,造成狭窄区远端形成脑血流低灌注状态。③ 斑块脱落使血管内皮下胶原暴露造成白细胞浸润、吸附血小板及纤维蛋白原导致新的微血栓形成,进而引起 TIA 的反复发作。对于 TIA 反复发作的有效防治手段即对动脉血栓进行抗凝、抗血小板治疗,已有研究报道[12],对高血压病患者的降脂治疗可有效降低其缺血性心脏病及心脑血管事件的发生率。

他汀类药物即为三羟基三甲基戊二酰辅酶还原酶抑制剂,主要通过与该酶的天然底物结合来抑制体内内源性胆固醇的生物合成，并刺激细胞表面的 LDL 受体数目增加，通过 LDL 受体与 LDL 结合进入其介导的脂质讲解途径来降低血清中 LDL 含量,同时清除斑块内脂质达到降脂的目的[13,14]。另外有研究证实[15,16],该类药物可抑制血小板功能、减少血小板血栓形成,同时具有抗炎、抗氧化、稳定及逆转粥样斑块、保护血管内皮功能的作用。目前,他汀类药物是临床治疗心脑血管疾病的主要用药,可明显降低动脉血栓的发生率[17]。阿托伐他汀钙是防止血栓形成的最强效他汀类药物,其所具有的调脂及抗动脉粥样硬化斑块的作用可同时起到降低 LDL、TC、TG 并升高 HDL 的作用,多种途径降低 TIA 发作的发生率[18-20]。本研究中,使用阿托伐他汀钙联合阿司匹林进行治疗的研究组治疗后的有效率为 92.5%，明显高于仅使用阿司匹林治疗的对照组 75%,比较差异具有统计学意义(P＜0.05)。治疗后 6 个月检测两组患者 IMT 及斑块面积发现，两组患者检测值均较治疗前明显下降,但研究组下降程度明显高于对照组,比较差异具有统计学意义(P＜0.05)。另外,通过对两组患者治疗前及治疗后 6 个月 LDL、HDL、TC、TG 水平检测发现，两组患者治疗后 LDL、TC、TG 水平均明显较治疗前下降，而 HDL 较治疗前明显上升,且研究组各血清标志物下降及上升程度均明显高于对照组,比较差异具有统计学意义(P＜0.05)。该结果充分说明,阿托伐他汀钙具有减轻或消除颈动脉粥样硬化斑块、抑制血小板功能及显著降脂的作用。

综上所述,阿托伐他汀钙具有调脂及抗动脉粥样硬化的作用，可显著减轻或消除 TIA 患者的颈动脉粥样硬化斑块,对 TIA 的治疗疗效显著,值得临床推广应用。

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