doi: 10.13241/j.cnki.pmb.2014.35.030

阿托伐他汀治疗冠心病合并脑梗死的临床研究 *

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摘要 目的:研究阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死的临床效果。**方法:**从 2011 年 1 月到 2013 年 1 月,在我院共有 96 例病患被诊断为冠心病合并脑梗死。以数字法随机分成观察组(48 例)和对照组(48 例)。对照组每天口服苯磺酸氨氯地平，观察组在对照组的基础上口服阿托伐他汀钙片。对比两组疗效及病患血脂水平。**结果:** 观察组疗效为优者占比 62.50 %(30/48),优良率为 91.67 %(44/48),均显著高于对照组的 39.58 %(19/48),75.00 %(36/48),差异均有统计学意义(均 P＜0.05);观察组治疗后 TC (4.74± 1.20)mmol/L，显著性低于对照组 (5.22± 1.15)mmol/L,TG (1.06± 0.30)mmol/L，显著性低于对照组(1.51± 0.28)mmol/L,LDL-C (3.19± 0.51)mmol/L,显著性低于对照组(3.87± 0.25)mmol/L,上述差异均有统计学意义(P＜0.05)。**结论:**阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死,不仅可明显提升治疗效果,还可减少病患的并发症的发生。方便安全,值得临床推荐。

关键词:阿托伐他汀;苯磺酸氨氯地平;冠心病;脑梗死

中图分类号:R541.4;R743 **文献标识码:**A **文章编号:**1673-6273(2014)35-6913-03

Clinical Research of Atorvastatin Combined Amlodipine Combined in Treatment of Coronary Heart Disease and Cerebral Infarction*

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ABSTRACT Objective: To study the therapeutic effect of combined atorvastatin amlodipine besylate in treatment of coronary heart disease and cerebral infarction. **Methods:** 96 patients in our hospital who were diagnosed coronary heart disease and cerebral infarction from January 2011 to January 2013 were selected and were digitally randomly divided into observation group (48 cases) and control group (48 cases) . The control group was treated with amlodipine besylate daily, and the observation group was treated with atorvastatin calcium on the basis of the control group. The therapeutic effect and the blood lipid levels of two groups of patients was compared. **Results:** The patients of the observation group were excellent accounting for 62.50% (30/48), good for 91.67% (44/48), which were significantly higher than that of control group, which were 39.58% (19/48),75.00% (36/48), respectively. The differences was statistically significant (P<0.05). TC in observation group was (4.74± 1.20) mmol/L, which was significantly lower than that of control group (5.22± 1.15) mmol/L, and TG was (1.06± 0.30) mmol/L, LDL-C was (3.19± 0.51) mmol/L, which were significantly lower than control group's (1.51 ± 0.28) mmol/L and (3.87 ± 0.25) mmol/L. Differences above all showed statistically significant (P<0.05). **Conclusions:** Atorvastatin combined amlodipine in treatment of coronary heart disease and cerebral infarction can significantly improve the therapeutic effect, also can reduce the occurrence of complications in patients.

Key words: Atorvastatin; Amlodipine Besylate Tablet; Coronary artery disease; Cerebral infarction

Chinese Library Classification(CLC): R541.4; R743 Document code: A

Article ID: 1673-6273(2014)35-6913-03

前言

脑梗死又名血性脑卒中,发病原因主要是由于供应脑部血液的动脉出现粥样硬化和血栓形成，使管腔狭窄甚至闭塞,导致局灶性急性脑供血不足;也有因异常物体(固体、液体、气体)沿血液循环进入脑动脉或供应脑血液循环的颈部动脉,造成血流阻断或血流量骤减而产生相应支配区域脑组织软化坏死者[1-3]。冠心病又名冠状动脉粥样硬化性心脏病,是冠状动脉血管发生动脉粥样硬化病变而引起血管腔狭窄或阻塞,造成心肌缺血、缺氧或坏死而导致的心脏病。但是冠心病的范围可能更广泛,还包括炎症、栓塞等导致管腔狭窄或闭塞[4-6]。冠心病合并脑梗死病患,轻者表现为突然的失声,高血压和局部瘫痪等症状。重者表现为全瘫甚至死亡等症状。以往的治疗方法尽管能减轻其症状,但效果并不十分显著[7,8]。鉴于此,本文研究阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死的临床效果。现报道如下。

1 资料和方法

1.1 临床资料

从 2011 年 1 月到 2013 年 1 月，在我院共有 96 例病患被

* 基金项目:教育部留学回国人员科研启动基金(教外司留(2011)1568 号)

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(收稿日期:2014-07-28 接受日期:2014-08-25)

诊断为冠心病合并脑梗死。其中男性 63 例，女性 33 例。年龄在 38 至 77 岁之间，平均年龄为 53.5± 9.5 岁。以数字法随机分成观察组（48 例）和对照组（48 例）。其中观察组男性 30 例，女性 18 例。年龄在 38 至 75 岁之间，平均年龄在 52.3± 9.3 岁。对照组男性 33 例，女性 15 例。年龄在 39 至 77 岁之间，平均年龄在 53.4± 9.7 岁。两组在性别，年龄以及病况等方面比较，差异无统计学意义（P＞0.05）。具有可比性。

1.2 研究方法

治疗前，两组病患先停止使用抗高血压的药品。每日晚饭后对照组服用苯磺酸氨氯地平 5 mg，观察组在对照组的基础上加服阿托伐他汀钙片。在治疗前第 6 周和治疗后第 6 周上午，病患空腹抽血，用离心法分离血清，检测 TC，TG，LDL-C 的含量。比较两个组别治疗前后的血脂水平变化。

1.3 疗效评价

临床疗效评定标准 [4]：相对于原来，病患病发次数少于 20%，静息心电图恢复正常为优；病发次数及药物消耗量少于 20%～50%，静息心电图改善一半以上为良；病发次数以及药物消耗量多于一半，静息心电图无变化为差。

1.4 统计学方法

采用 SPSS13.0 统计软件分析。数据比较采用 x^2 检验，计量数据以均数± 标准差（$\bar{x}$± s）表示，实施 t 检验。P<0.05 为差异有统计学意义。

2 结果

2.1 两个组别治疗前和治疗后的血脂水平变化对比

治疗前，两组患者血脂指标 TC、TG 及 LDL-C 浓度接近，差异无统计学意义（P＞0.05）；治疗后观察组上述三指标显著性下降，差异有统计学意义（P＜0.05），对照组上述三指标无显著性变化，差异无统计学意义（P＞0.05）；治疗后观察组 TC、TG 及 LDL-C 均显著性低于对照组，差异具备统计学意义（P＜0.05）。表明阿托伐他汀联合苯磺酸氨氯地平治疗可明显缓解病患的并发症；具有积极意义。见表 1。

表 1 两组治疗前后的血脂水平变化比较（$\bar{x}$± s）

Table 1 Comparison of blood lipid of patients in the two groups before and after the treatment($\bar{x}$± s)

Group	TC（mmol/L）				TG(mmol/L)				LDL-C(mmol/L)			
	Before	After	t	P	Before	After	t	P	Before	After	t	P
Observation group	5.23± 1.07	4.74± 1.20	2.112	<0.05	1.53± 0.24	1.06± 0.30	8.476	<0.05	3.89± 0.78	3.19± 0.51	5.204	<0.05
Control group	5.25± 1.05	5.22± 1.15	0.133	>0.05	1.52± 0.22	1.51± 0.28	0.195	>0.05	3.89± 0.71	3.87± 0.52	0.157	>0.05
t	0.092	-2.001			0.042	2.039			0	2.697		
P	P>0.05	P<0.05			P>0.05	P<0.05			P>0.05	P<0.05		

2.2 两组患者的疗效对比

观察组疗效优比率 62.50%，显著性高于对照组 39.58%，差异有统计学意义（卡方值 5.044，P＜0.05）；且总优良率 91.67%，显著性高于对照组 75.00%，差异亦有统计学意义（卡方值 4.800，P＜0.05），表明阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死的临床效果显著。见表 2。

表 2 两个组别治疗后疗效对比（例，%）

Table 2 Comparison of therapeutic efficacy between two groups before and after treatment(n,%)

Group	Case	Efficacy	Good	Invalid	Total effective rate
Observation group	48	30(62.50)	14(29.17)	7(14.58)	44(91.67)
Control group	48	19(39.58)	17(35.42)	12(25.00)	36(75.00)
x^2	-	5.044	0.429	1.640	4.800
P	-	P<0.05	P>0.05	P>0.05	P<0.05

3 讨论

脑梗死和冠心病是中老年人瘫痪率和死亡率升高的主要原因之一，还伴随着多种类似于心绞痛，高血压等的并发症[8-10]。其病因多为脑动脉粥样硬化导致血管闭塞，致使脑供血不足而造成脑细胞坏死。阿托伐他汀钙片是应用最为广泛的临床降低血脂防治动脉粥样硬化疾病的药物。不仅能够降低血浆胆固醇和脂蛋白水平，而且减少低密度脂蛋白的生成。临床上用于家族性高胆固醇血症、混合性高脂血症等症[11,12]。该药物为 HMG-CoA 还原酶选择性抑制剂，通过抑制 HMG-CoA 还原酶和胆固醇在肝脏的生物合成而降低血浆胆固醇和脂蛋白水平，并能通过增加肝细胞表面低密度脂蛋白（LDL）受体数目而增加 LDL 的摄取和分解代谢。它对肝脏中的还原酶及胆固醇的生物合成起抑制作用从而调节血脂[13]。阿托伐他汀在抗炎方面也具有明显作用，其可与单个核细胞上的相关抗原上的特殊表位结合促使参与炎症反应的炎性细胞因子，内皮细胞粘附分子，组织相容性复合物等表达下调，上调一氧化氮合成酶，增加一氧化氮合成，抑制血小板，白细胞粘附，发挥抗炎，逆转或延缓粥样硬化病变的作用[14,15]。阿托伐他汀钙片虽在心血管治疗中有不可忽视的作用，但是长时间服用可能引起肠胃的不适和肝肾部分功能的下降。且由于每个人的身体素质不同，阿托伐他汀钙片的治疗效果还是存在缺陷[16]。苯磺酸氨氯地平在体内

的作用机制主要是阻滞细胞外钙离子通道进入血管平滑肌细胞内,但不影响血浆钙离子浓度,达到减弱兴奋耦连减轻血管紧张素 II 和 I 肾上腺素能受体的缩血管效应和降低阻力血管的反应收缩性,从而能够有效的逆转左心室肥厚,降低心血管的发生率[17]。钙离子拮抗剂同样具有降低血脂的作用,故阿托伐他汀与苯磺酸氨氯地平联合治疗是较为完善的治疗方法[18]。

本文通过对阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死的临床效果的研究。结果发现,观察组疗效为优者占比 62.50%(30/48),优良率为 91.67%(44/48),均显著高于对照组的 39.58%(19/48),75.00%(36/48)。表明阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死的临床效果显著。此外,观察组血脂指标浓度下降量明显多于对照组。这与既往研究一致[19]。表明阿托伐他汀联合苯磺酸氨氯地平治疗可明显缓解病患的并发症。这可能与阿托伐他汀及苯磺酸氨氯地平能有效的抑制胆固醇合成过程中所需的酶,使得胆固醇的合成量减少,小密度脂蛋白受体的合成量增多等因素有关。有报道表明,冠心病及脑梗死病患伴随有高血压,故可以通过降低血脂来减缓冠心病和脑梗死的发生[20]。

综上所述,阿托伐他汀联合苯磺酸氨氯地平治疗冠心病合并脑梗死,不仅可以提高治疗效果,还可以减缓并发症的发生。

参 考 文 献(References)

[1] 马志伟, 徐南飞, 陈萍, 等. 阿托伐他汀治疗阿尔茨海默病疗效观察[J]. 现代生物医学进展,2012,12(28): 5530-5532
Ma Zhi-wei, Xu Nan-fei, Chen Ping, et al. Atorvastatin Efficacy of Treatment of Alzheimer's Disease [J]. Progress in Modern Biomedicine,2012,12(28):5530-5532

[2] Li J, Zhang L, Xie NZ, et al. Relationship between the cholesterol ester transfer protein TaqIB polymorphism and the lipid-lowering effect of atorvastatin in patients with coronary atherosclerotic heart disease[J]. Genet Mol Res, 2014,24,13(1):2140-2148

[3] 罗望珍.静脉滴注头孢曲松后饮酒致休克 1 例[J]. 中华医院感染学杂志,2013,23(4):909-910
Luo Wang-zhen. Intravenous drip ceftriaxone in 1 case after drinking to shock[J]. Chinese Journal of Nosocomiology,2013,23(4):909-910

[4] Foody JM, Toth PP, Tomassini JE, et al. Changes in LDL-C levels and goal attainment associated with addition of ezetimibe to simvastatin, atorvastatin, or rosuvastatin compared with titrating statin monotherapy[J]. Vasc Health Risk Manag,2013,9(28):719-727

[5] Ghia CJ, Panda AS, Khobragade LR, et al. Alternate Day versus Once Daily Atorvastatin for Primary Prevention of (CHD) in Naïve Patients of Dyslipidemia[J]. J Clin Diagn Res,2014,8(3):27-31

[6] He BX, Shi L, Qiu J, et al. The effect of CYP3A4*1G allele on the pharmacokinetics of atorvastatin in Chinese Han patients with coronary heart disease[J]. J Clin Pharmacol,2014,54(4):462-467

[7] Sever PS, Poulter NR, Chang CL, et al. Evaluation of C-reactive protein before and on-treatment as a predictor of benefit of atorvastatin: a cohort analysis from the Anglo-Scandinavian Cardiac Outcomes Trial lipid-lowering arm[J]. J Am Coll Cardiol,2013,20, 62 (8):717-729

[8] Bays HE, Conard SE, Leiter LA, et al. Influence of age, gender, and race on the efficacy of adding ezetimibe to atorvastatin vs. atorvastatin up-titration in patients at moderately high or high risk for coronary heart disease[J]. Int J Cardiol,2011,153(2):141-147

[9] Li J, Sun YM, Wang LF, et al. Comparison of effects of simvastatin versus atorvastatin on oxidative stress in patients with coronary heart disease[J]. Clin Cardiol,2010,33(4):222-227

[10] Conard S, Bays H, Leiter LA, et al. Ezetimibe added to atorvastatin compared with doubling the atorvastatin dose in patients at high risk for coronary heart disease with diabetes mellitus, metabolic syndrome or neither[J]. Diabetes Obes Metab,2010,12(3):210-218

[11] Azizi M, Perdrix L, Bobrie G, et al. Greater efficacy of aldosterone blockade and diuretic reinforcement vs. Dual renin-angiotensin blockade for left ventricular mass regression in patients with resistant hypertension[J]. J Hypertens,2014[Epub ahead of print]

[12] Li J, Tie CR, Li QX, et al. Amlodipine prevents adriamycin-induced toxicity in cultured rat mesangial cells by up-regulation of Smad6, Smad7 expression [J]. Environ Toxicol Pharmacol,2014,22,38 (1): 251-256

[13] Mori Y, Aritomi S, Niinuma K, et al. Additive effects of cilnidipine, an L-/N-type calcium channel blocker, and an angiotensin II receptor blocker on reducing cardiorenal damage in Otsuka Long-Evans Tokushima Fatty rats with type 2 diabetes mellitus [J]. Drug Des Devel Ther,2014,8(12):799-810

[14] Muntner P, Levitan EB, Lynch AI, et al. Effect of chlorthalidone, amlodipine, and lisinopril on visit-to-visit variability of blood pressure: results from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial [J]. J Clin Hypertens (Greenwich),2014,16(5):323-330

[15] Jadhav U, Hiremath J, Namjoshi DJ, et al. Blood pressure control with a single-pill combination of indapamide sustained-release and amlodipine in patients with hypertension: the EFFICIENT study [J]. PLoS One,2014,9(4):e92955

[16] Sharif-Kashani B, Hamraghani A, Salamzadeh J, et al. Effect of Amlodipine and Sildenafil on the NT-ProBNP Level of Patients with COPD-Induced Pulmonary Hypertension [J]. Iran J Pharm Res,2014, 13(Suppl):161-168

[17] 陈慧慧, 赵勇, 李丛, 等. 氨氯地平与阿托伐他汀联合应用的研究进展[J].中国老年学杂志,2013, 8:4652-4655
Chen Hui-hui, Zhao Yong, Li Cong, et al. Amlodipine and atorvastatin combined application of research progress [J]. Chinese Journal of Gerontology,2013,18:4652-4655

[18] 齐丽彤, 孙跃民, 李树仁, 等. 苯磺酸氨氯地平 / 阿托伐他汀钙复合制剂治疗高血压病合并高脂血症的有效性和安全性[J]. 中国新药杂志,2013,18:2159-2163
Qi Li-tong, Sun Yue-min, Li Shu-ren, et al. Benzene sulfonic acid amlodipine/atorvastatin calcium compound preparation efficacy and safety of the treatment of hypertension with hyperlipidemia [J]. Chinese Journal of New Drugs,2013,18:2159-2163

[19] Chang-Jiang Ge, Shu-Zheng Lu, Yun-Dai Chen, et al. Synergistic effect of amlodipine and atorvastatin on blood pressure, left ventricular remodeling, and C-reactive protein in hypertensive patients with primary hypercholesterolemia [J]. Heart and Vessels, 2008,8(2):91-95

[20] 潘庭荣, 许庆元, 成克铭, 等. 急性脑梗死患者血清中 Lp(a)CRP D- 二聚体及纤维蛋白原水平变化及意义[J].河北医学, 2014, 1(1): 12-15
Pan Ting-rong, Xu Qing-yuan, Cheng Ke-ming, et al. Lp (a) in acute cerebral infarction patients serum CRP D - dimer and fibrinogen level change and meaning[J]. Hebei Medicine,2014,1(1):12-15