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不同剂量阿伐他汀联合阿司匹林治疗原发性高血压 并动脉粥样硬化的临床研究 *

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摘要 目的:探讨不同剂量阿托伐他汀联合阿司匹林治疗原发性高血压并动脉粥样硬化的临床疗效。**方法:**选取 2015 年 1 月-2016 年 12 月在我院治疗的原发性高血压并动脉粥样硬化患者 80 例,随机分为对照组和实验组,每组 40 例。实验组给予口服高剂量阿托伐他汀(40 mg/d)联合阿司匹林肠溶片(100 mg/d)治疗,对照组给予口服高剂量阿托伐他汀(20 mg/d)联合阿司匹林肠溶片(100 mg/d) 治疗,疗程均为 3 个月。观察和比较两组患者治疗前后的总胆固醇 (total cholesterol, TC)、高密度脂蛋白胆固醇 (high-density lipoprotein cholesterol, HDL-C)、甘油三酯(triglyceride, TG)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)以及颈动脉斑块分级。**结果:**两组治疗后的 SBP、DBP、血清 TC、TG 和 LDL-C 水平均较治疗前显著降低,血清 HDL-C 水平较治疗前明显升高,且实验组 SBP、DBP、血清 TC、TG 和 LDL-C 水平均显著低于对照组($P<0.05$),血清 HDL-C 水平明显高于对照组($P<0.05$)。实验组颈动脉斑块 0- I 级的比例显著高于对照组($P<0.05$)。**结论:**口服高剂量阿托伐他汀(40 mg/d)联合阿司匹林肠溶片(100 mg/d) 治疗原发性高血压并动脉粥样硬化较较低剂量阿托伐他汀(20 mg/d)联合阿司匹林肠溶片(100 mg/d)疗效更好,可以有效降低血压,调节血脂并改善患者预后。

关键词:阿托伐他汀;阿司匹林;原发性高血压;动脉粥样硬化

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A Clinical Study on Different Doses of Atorvastatin and Aspirin in the Treatment of Essential Hypertension with Atherosclerosis*

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ABSTRACT Objective: To explore the clinical efficacy of different doses of atorvastatin combined with aspirin in the treatment of primary hypertension with atherosclerosis. **Methods:** The clinical data of patients with essential hypertension treated by atorvastatin and aspirin in our hospital from January 2015 to December were randomly divided into the control group and the experimental group, 40 cases in each group. The experimental group was given oral high dose of atorvastatin (40 mg/d) combined with aspirin enteric-coated tablet (100 mg/d), while the control group was given low dose of atorvastatin (20 mg/d) combined with aspirin enteric-coated tablet (100 mg/d), the course of treatment was 3 months. The levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP) and carotid plaque grade were observed and compared before and after the treatment between two groups. **Results:** After treatment, the levels of SBP, DBP, serum TC, TG and LDL-C in the two groups were significantly lower than those before treatment, the serum HDL-C levels were significantly higher than before treatment ($P<0.05$). The levels of SBP, DBP, serum TC, TG and LDL-C in the experimental group were significantly lower than those in the control group ($P<0.05$), serum HDL-C level was significantly higher than that in the control group ($P<0.05$). The proportion of carotid plaque 0-I in the experimental group was significantly higher than that of the control group ($P<0.05$). **Conclusions:** High dose of atorvastatin (40 mg/d) combined with aspirin enteric-coated tablets (100 mg/d) is more effective than low dose atorvastatin (20 mg/d) combined with aspirin enteric-coated tablets (100 mg/d) in the treatment of primary hypertension with atherosclerosis, it can reduce the blood pressure, regulate the blood lipids and improve the prognosis of patients.

Key words: Atorvastatin; Aspirin; Essential hypertension; Atherosclerosis

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前言

高血压病是一种常见病和多发病,长期血压升高会损害内皮功能,对重要的脏器心脑肾的结构和功能产生影响,最终引起这些脏器的功能衰竭,而原发性高血压也是动脉粥样硬化的最重要危险因素^[1]。高血压可由多种因素引发,是一种处于不断进展状态的心血管综合征,使心脏、血管功能与结构发生异常。基于目前的医学发展水平和检查手段,对于能发现导致血压升高的确切病因,我们称之为继发性高血压,反之则称为原发性高血压^[2]。

阿托伐他汀是羟甲基戊二酰辅酶 A 还原酶的竞争性及选择性的抑制剂,可逆转、延缓患者动脉粥样硬化的进展速度,有效调节患者的血脂及血管内皮功能^[3]。作为一种调节血脂的药物,其经常和其他降血脂药物(如阿司匹林)一起使用^[4]。本研究探讨了不同剂量阿托伐他汀(40 mg/d)/(20 mg/d)联合阿司匹林治疗原发性高血压并动脉粥样硬化的临床疗效,即比较两种方案在降低血压和调节血脂方面的效果,旨在为临床选择合理的治疗方案提供合理依据,结果报道如下。

1 资料与方法

1.1 临床资料

选取 2015 年 1 月-2016 年 12 月在我院治疗的原发性高血压并动脉粥样硬化患者 80 例,随机分为对照组和实验组,每组 40 例。对照组男 22 例,女 18 例,年龄 65-69 岁,平均年龄(67.8±6.6)岁,BMI 24-28 kg/m²,平均 BMI (26.2±3.8) kg/m²;实验组中男 21 例,女 19 例,年龄 64-68 岁,平均年龄(66.8±5.6)岁,BMI 23-27 kg/m²,平均 BMI (26.4±3.4) kg/m²。两组患者的性别、年龄、体重、BMI、病程和 IMT 均没有显著性差异(P>0.05),具可比性,见表 1。

表 1 两组患者的一般资料比较

Table 1 Comparison of the general data between two groups

Project	Experimental group	Control group
Gender(male/female)	21/19	22/18
Age(years)	66.8±5.6	67.8±6.6
Weight (kg)	71.5±7.1	68.5±8.8
BMI (kg/m ²)	26.2±3.4	26.4±3.8
Duration (years)	5.3±1.4	5.2±1.2
IMT(mm)	2.7±0.8	2.8±0.9

排除标准:既往有心肌梗死病史或者脑卒中病史;患者合并肝病或者肾病;患者一个月内使用过其他的他汀类药物。纳入标准:患者为原发性高血压,排除其他继发原因引起的高血压;患者的具体临床情况符合 2010 年颁布的《中国高血压防治指南》中的对于高血压的诊断标准,即:140 mmHg ≤ SBP<160 mmHg,95 mmHg ≤ DBP<110 mmHg,并且颈动脉超声检查显示患者的颈动脉内膜和中膜厚度的总和(IMT)≥1.2 mm。

1.2 治疗方法

2 组患者入院后均给予常规降压处理,包括钙离子拮抗类

及血管紧张素转化酶抑制剂药物。在此基础上,实验组治疗方案为:口服高剂量阿托伐他汀(40 mg/d)联合阿司匹林肠溶片(100 mg/d),疗程 3 个月;对照组治疗方案为:口服低剂量阿托伐他汀(20 mg/d)联合阿司匹林肠溶片(100 mg/d),疗程 3 个月。

1.3 仪器和药品

仪器:ROCHE 702 全自动生化分析仪;西门子 S2000 彩超仪。

药品:阿司匹林肠溶片:中国(北京)拜耳制药有限公司,批号:BJ32328,规格:每片 100 mg;阿托伐他汀片:中国(大连)辉瑞制药有限公司,批号:R42103,规格:每片 20 mg。

1.4 观察指标

1.4.1 两组患者治疗前后 SBP 和 DBP

1.4.2 两组患者治疗前后颈动脉斑块分级 颈动脉斑块分级标准:Ⅲ级:存在多个斑块,IMT≥4.0 mm。Ⅱ级:存在多个或 1 个斑块,2.0 ≤ IMT<4.0 mm; I 级:仅有 1 个斑块或 1.2 ≤ IMT<2.0 mm;0 级:IMT<1.2 mm。

1.4.3 两组患者治疗前后的血清 TC、HDL-C、TG 和 LDL-C 检测前 3 d 禁高脂饮食,抽取清晨空腹肘静脉血 5 mL,采用酶法在罗氏全自动生化分析仪上检测血清 TC、HDL-C、TG 和 LDL-C 水平。

1.5 统计学分析

采用 SPSS 20.0 软件进行统计学分析,计量资料组间比较采用 t 检验,计数资料组间比较采用 χ^2 检验,以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗前后的血压变化比较

两组患者治疗前的 SBP 和 DBP 对比差异无统计学意义(P>0.05),两组治疗后的 SBP 和 DBP 均较治疗前显著降低,且实验组 SBP 和 DBP 均显著低于对照组(P<0.05),见表 2。

2.2 两组患者治疗前后的血清 TC、HDL-C、TG 和 LDL-C 水平的比较

治疗前,两组血清 TC、TG、LDL-C 和 HDL-C 水平比较差异无统计学意义(P>0.05)。治疗后,两组血清 TC、TG 和 LDL-C 水平均较治疗前显著降低,而血清 HDL-C 水平明显高于治疗前,且实验组血清 TC、TG 和 LDL-C 水平均显著低于对照组,而血清 HDL-C 水平明显高于对照组(P<0.05),见表 3。

2.3 两组患者治疗后的颈动脉斑块分级比较

两组患者治疗后的颈动脉斑块分级比较差异有统计学意义(P=0.020),实验组颈动脉斑块 0-Ⅰ级的比例显著高于对照组(P<0.05),见表 4。

3 讨论

原发性高血压的病因目前尚未完全明确,与遗传因素、环境因素均具有显著相关性^[5,6]。原发性高血压是一种处于不断变化状态的心血管疾病综合征,会对患者的血管和心脏的功能造成严重影响^[7,8]。相关研究结果表明动脉粥样硬化的发生与原发性高血压患者心脑血管疾病的发生密切相关^[9]。因此,在临床上对于原发性高血压的治疗中十分重视动脉粥样硬化的治疗^[10,11]。

表 2 两组患者治疗前后的血压变化比较($\bar{x} \pm s$)Table 2 Comparison of the changes of blood pressure between two groups before and after treatment($\bar{x} \pm s$)

Group	Time	Control group	Experimental group
SBP (mmHg))	Before treatment	151.6 $\pm$ 5.2	151.2 $\pm$ 4.8
	After treatment	136.2 $\pm$ 3.8*	129.5 $\pm$ 3.4* [#]
DBP (mmHg)	Before treatment	106.5 $\pm$ 4.5	107.5 $\pm$ 5.4
	After treatment	94.2 $\pm$ 3.8*	80.4 $\pm$ 3.5* [#]

Note: compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

表 3 两组治疗前后血清 TC、HDL-C、TG 和 LDL-C 水平的比较($\bar{x} \pm s$)Table 3 Comparison of the serum TC, HDL-C, TG and LDL-C levels between two groups before and after treatment ($\bar{x} \pm s$)

Group	Time	Control group	Experimental group
TC	Before treatment	5.8 $\pm$ 1.5	5.7 $\pm$ 1.9
	After treatment	4.3 $\pm$ 1.1*	3.5 $\pm$ 1.0* [#]
TG	Before treatment	2.5 $\pm$ 0.6	2.4 $\pm$ 0.5
	After treatment	1.8 $\pm$ 0.4*	1.0 $\pm$ 0.3* [#]
LDL-C	Before treatment	4.4 $\pm$ 0.4	4.3 $\pm$ 0.7
	After treatment	3.2 $\pm$ 0.3*	2.3 $\pm$ 0.2* [#]
HDL-C	Before treatment	0.8 $\pm$ 0.2	0.7 $\pm$ 0.2
	After treatment	1.1 $\pm$ 0.2*	1.5 $\pm$ 0.2* [#]

Note: compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

表 4 两组患者治疗后的颈动脉斑块分级比较

Table 4 Comparison of the carotid plaques classification between two groups after treatment

Classification	Control group(n=40)	Experimental group (n=40)
0	2	10
I	14	18
II	16	8
III	8	4

原发性高血压患者发生动脉粥样硬化是一个比较复杂的过程,主要机理是血压处于很高状态时会对血管壁造成冲击,进而破坏患者的血管内膜稳定性,导致内皮细胞受到严重损害,血液中的脂质会借机沉积在血管壁上,加速了动脉粥样硬化的发生与发展^[12]。动脉硬化以后,高血压患者血管的正常舒张功能会受到抑制,导致患者血管壁僵硬化,进而血压升高得更明显^[13]。高血压和动脉粥样硬化是一个恶性循环,想要控制高血压,就要治疗患者的动脉粥样硬化,想要患者动脉粥样硬化减轻,就需积极控制高血压^[14]。

阿司匹林用药范围十分广泛,具有消炎、止痛和解热的效果,还可以抑制血小板的释放和聚集,可以抵抗患者血栓的形成,有效预防心脑血管疾病的发生和进一步发展^[15-17]。口服阿司匹林后,很大一部分会水解成为水杨酸,还有小部分水杨酸被氧化为胆酸,最终的代谢产物是葡萄糖醛酸与水杨酸的结合物^[18,19]。阿司匹林的药理效果是通过环氧化酶中的环氧化酶-1活性部位多肽链 530 位丝氨酸的羟基发生乙酰化形成的,进而使

环氧化酶活性丧失,阻断了血小板的聚集^[20,21]。有研究表明阿司匹林虽然可以部分降低高血压患者心脑血管疾病的发生率,但是效果并不是十分理想^[22]。

阿托伐他汀是羟甲基戊二酰辅酶 A 还原酶的竞争性和选择性的抑制剂^[23,24]。羟甲基戊二酰辅酶 A 在转化成为甲羟戊酸的过程中需要羟甲基戊二酰辅酶 A 还原酶的参与^[25]。阿托伐他汀可以抑制患者体内胆固醇和羟甲基戊二酰辅酶 A 还原酶的合成,进而降低脂蛋白和胆固醇的浓度,增加肝细胞表面的低密度脂蛋白受体,增强低密度脂蛋白的分解代谢和摄取^[26,27]。而动脉粥样硬化的加重和患者血液中低密度脂蛋白胆固醇以及总胆固醇浓度的增加息息相关,是高血压患者发生心脑血管疾病的高危因素^[28];而高密度脂蛋白的浓度增高可以降低心脑血管疾病发生的危险性^[29]。且研究显示阿托伐他汀可以显著增高患者血液中高密度脂蛋白的浓度,同时降低患者血液中低密度脂蛋白胆固醇浓度和总胆固醇浓度,有效缓解患者病情^[30]。本研究结果显示阿司匹林联合高剂量阿托伐他汀的降血压、降脂效果较阿司匹林联合低剂量阿托伐他汀更加显著,且患者治疗后颈动脉斑块分级明显改善,提示其临床效果更优。

综上所述,口服高剂量阿托伐他汀(40 mg/d)联合阿司匹林肠溶片(100 mg/d)较低剂量阿托伐他汀(20 mg/d)联合阿司匹林肠溶片(100 mg/d)疗效好,可以有效降低血压,调节血脂并改善患者预后。

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