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匹伐他汀钙与阿托伐他汀钙治疗冠心病的临床疗效及安全性比较 *

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摘要 目的:观察和比较匹伐他汀钙与阿托伐他汀钙治疗冠心病的临床疗效及安全性。**方法:**选取 2016 年 3 月到 2018 年 12 月于我院就诊的冠心病患者共 100 例,将其按照入院编号随机分为两组,匹伐他汀钙组(50 例)与阿托伐他汀钙组(50 例)。在服药前及服药后第 6、12 个月,检测和比较两组血糖(Glu)、糖化血红蛋白(HbA1c)、超敏 C 反应蛋白(hsCRP)、总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)、谷丙转氨酶(ALT)、谷草转氨酶(AST)、肌酐(Cr)、肌酸激酶(CK)水平的变化。**结果:**治疗后 6、12 个月,匹伐他汀钙组血清 HDL-C 水平较治疗前显著升高($P<0.05$),而血清 hsCRP 水平明显降低($P<0.05$),阿托伐他汀钙组 HDL-C、hsCRP 与治疗前比较差异均没有统计学意义($P>0.05$)。治疗后 12 个月,阿托伐他汀钙组 HbA1c 较治疗前显著升高($P<0.05$),而匹伐他汀钙组与治疗前比较差异没有统计学意义($P>0.05$)。治疗后 6、12 个月,两组患者血清 TC、LDL-C 水平均较治疗前明显降低($P<0.05$),两组患者血清 TG、Glu、ALT、AST、Cr、CK 水平较治疗前差异无明显统计学意义($P>0.05$)。**结论:**匹伐他汀钙和阿托伐他汀钙治疗均能够降低冠心病患者的血清 LDL-C、TC、TG 水平,而匹伐他汀钙同时可升高 HDL-C,降低血清 hsCRP 水平,并且不增加新发糖尿病的风险。

关键词:匹伐他汀钙;阿托伐他汀钙;冠心病

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Comparison of the Efficacy and Safety of Pitavastatin Calcium and Atorvastatin Calcium in the Treatment of Coronary Heart Disease*

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ABSTRACT Objective: To comparison the efficacy and safety of pitavastatin calcium and atorvastatin calcium in the Treatment of Coronary Heart Disease. **Methods:** 100 patients with coronary heart disease from March 2016 to December 2018 were divided into the pitavastatin calcium group($n=50$) and the atorvastatin calcium group ($n=50$). The blood glucose(Glu), Glycated hemoglobin(HbA1c), Ultra-sensitive C reaction protein (hsCRP), Total cholesterol (TC), Triglycerides (TG), Low density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol(HDL-C), Acetyltransferase(ALT), Valley grass transaminase(AST), Creatinine(Cr), Creatine kinase (CK) were monitored and compared before treatment and after treatment of 6,12 months. **Results:** After 6months and 12months treatment the pitavastatin calcium group HDL-C were significantly elevated ($P<0.05$), hsCRP were significantly lower($P<0.05$). After 6months and 12months the atorvastatin calcium group HDL-C and hsCRP compared to before treatment the difference were not statistically($P>0.05$). The atorvastatin calcium group HbA1c were elevated after 12months treatment with statistically differences($P<0.05$), but the pitavastatin calcium were not elevated($P>0.05$). The two groups TC, LDL-C were lower with statistically significant differences($P<0.05$). The differences between Glu, ALT, AST, Cr, CK before treatment and after treatment were without statistically differences ($P>0.05$), 1 patient was removed because of transaminase elevated. **Conclusions:** Both pitavastatin calcium and atorvastatin calcium can lower LDL-C, TC, TG in Coronary Heart Disease patients, Moreover, the pitavastatin calcium can elevate HDL-C level and lower hsCRP level. Meanwhile, the pitavastatin calcium had no evidence in new diabetes, it was efficacy and safety in long-term treatment.

Key words: Pitavastatin calcium; Atorvastatin calcium; Coronary heart disease

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前言

随着人们生活方式的改变,冠心病患者的数量逐年增加,而其高致残率、致死率严重影响患者的生活质量。冠心病可调

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节危险因素包括血脂异常、高血压病、超重和肥胖以及吸烟^[1],其中,血脂异常是动脉粥样硬化的重要危险因素,可直接导致冠心病的发生。随着经济条件的改善和饮食结构的改变,我国血脂异常患病率明显上升,总体患病率高达 40.40%^[2],良好的控制血脂对于降低心血管疾病的患病率起着至关重要的作用^[3]。

他汀类药物除了能显著降低血脂作用外^[4],其独立于调脂作用以外的多效性也在更多的领域得到了证实^[5-10]。但随着对他汀药物治疗的深入研究,除了其肝、肾、肌肉毒性之外,其对血糖代谢的影响也越来越受到重视^[11-15]。本研究旨在通过检测糖脂代谢相关指标的变化,观察和比较匹伐他汀钙与阿托伐他汀钙治疗冠心病的临床疗效和安全性,结果报道如下。

1 资料与方法

1.1 一般资料

选取 2016 年 3 月到 2018 年 12 月于我院就诊的冠心病患者共 100 例,性别不限。将患者按照入院编号随机分为两组。匹伐他汀钙组 50 例,包括男性 31 例,女性 19 例,平均年龄(60.50± 8.45);阿托伐他汀钙组 50 例(1 例中途因转氨酶升高排除),包括男性 29 例,女性 21 例,平均年龄(62.84± 10.23)。两组患者在一般资料对比均无显著性差异($P>0.05$),具有可比性。

1.2 入选标准

冠状动脉 CT 血管成像狭窄中度以上及冠状动脉造影血管狭窄 50%以上及 PCI 的患者,入院前 3 个月未接受任何他汀药物治疗的患者。

1.3 排除标准

① 活动性肝病、AST、ALT 升高 3 倍以上;② CK 升高超过 3 倍以上或伴有肌痛;③ 妊娠、哺乳或产后 6 个月;④ 近 6 个月激素、免疫抑制剂治疗患者;⑤ 合并血液病、恶性肿瘤患者;⑥ 肾上腺皮质疾病患者;⑦ 甲状腺疾病患者。

1.4 治疗方法

匹伐他汀钙组患者入院后每日睡前给予匹伐他汀钙(2 mg/片装,国药准字 H20080736)。阿托伐他汀钙组入院后每晚服用阿托伐他汀钙(20 mg/片装,国药准字 H20051408)。两组患者在服药前及服药后第 6 个月,第 12 个月,检测血糖 (Blood glucose, Glu)、糖化血红蛋白(Glycated hemoglobin, HbA1c)、超敏 C 反应蛋白(Glycated hemoglobin, hsCRP)、总胆固醇(Total cholesterol, TC)、甘油三酯(Triglycerides, TG)、低密度脂蛋白胆固醇 (Low density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇 (High-density lipoprotein cholesterol, HDL-C)、谷丙转氨酶 (Acetyltransferase, ALT)、谷草转氨酶(Valley grass transaminase, AST)、肌酐(Creatinine, Cr)、肌酸激酶(Creatine kinase, CK)。在接受治疗期间,根据患者实际病情给予控制血糖、降压、抗血小板聚集等治疗。

1.5 统计学方法

数据采用 SPSS 23.0 统计学软件进行处理。计量数据以均数± 标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验,计数数据采用 χ^2 检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

治疗后 6、12 个月,匹伐他汀钙组血清 HDL-C 水平较治疗前显著升高($P<0.05$),而血清 hsCRP 水平明显降低($P<0.05$),阿托伐他汀钙组 HDL-C、hsCRP 与治疗前比较差异均没有统计学意义($P>0.05$)。治疗后 12 个月,阿托伐他汀钙组 HbA1c 较治疗前显著升高($P<0.05$),而匹伐他汀钙组与治疗前比较差异没有统计学意义($P>0.05$)。治疗后 6、12 个月,两组患者血清 TC、LDL-C 水平均较治疗前明显降低($P<0.05$),两组患者血清 TG、Glu、ALT、AST、Cr、CK 水平较治疗前差异无明显统计学意义($P>0.05$)。详见表 1。阿托伐他汀钙组有一例患者因转氨酶升高剔除。

表 1 两组患者治疗前后生化指标的比较

Table 1 Comparison of the biochemical indexes before and after treatment between two groups

	Pitavastatin			Atorvastatin		
	Before treatment	At 6 months after treatment	At 12 months after treatment	Before treatment	At 6 months after treatment	At 12 months after treatment
Glu(mmol/l)	5.97± 2.14	5.83± 0.71	5.84± 0.72	6.54± 3.72	6.30± 1.05	6.48± 1.51
HbA1c%	6.02± 1.29	5.73± 0.61	5.90± 0.98	6.48± 2.30	6.46± 1.09	6.77± 1.13
hsCRP/(mg/L)	3.54± 1.74	2.49± 1.20**	2.69± 3.47**	2.69± 1.50	2.60± 1.07	2.35± 1.33
TC(mmol/l)	5.05± 1.15	4.02± 0.63*	4.04± 0.77**	4.50± 1.26	3.82± 0.77*	3.72± 0.76**
TG(mmol/l)	2.06± 1.45	1.58± 0.46	1.60± 0.51	1.67± 0.89	1.46± 0.48	1.38± 0.52
LDL-C(mmol/l)	3.15± 0.13	2.50± 0.46**	2.48± 0.57**	2.80± 0.91	2.34± 0.64**	2.22± 0.54**
HDL-C(mmol/l)	1.25± 0.31	1.39± 0.36*	1.38± 0.28*	1.35± 0.63	1.34± 0.38	1.21± 0.25
ALT(U/l)	19.71± 8.31	22.36± 6.90	21.59± 6.55	26.41± 15.01	28.71± 13.08	29.74± 22.86
AST(U/l)	23.34± 9.00	24.65± 6.88	24.39± 6.22	34.14± 28.64	29.60± 12.25	32.09± 37.28
Cr(mmol/l)	69.0± 23.06	68.13± 17.61	65.99± 18.73	70.20± 19.65	70.23± 12.84	68.65± 15.03
CK(U/l)	46.26± 14.52	47.12± 12.05	48.82± 13.29	47.69± 17.17	45.07± 13.29	49.61± 14.70

* $P<0.05$ ** $P<0.01$.

3 讨论

动脉粥样硬化的防治是预防冠心病的关键环节,血脂异常和炎症反应是动脉粥样硬化的重要危险因素,TC、TG、LDL-C

升高及 HDL-C 降低是冠心病、高血压和脑血管疾病等心脑血管事件最重要的独立危险因素之一^[16],降低 LDL-C 可显著减少心血管事件的发生^[17,18]。在一项日本的随机对照双盲三组剂量的试验中,匹伐他汀钙 1、2 和 4 mg 组 TC 分别降低 23.0%、29.1% 和 32.5%,LDL-C 分别降低 33.6%、41.8% 和 47.2%,TG 分别降低 7.7%、13.6% 和 14.7%^[19]。Angela Pirillo 等的研究显示匹伐他汀钙能够升高 HDL-C^[16],这与本研究一致,两组患者 LDL-C 较治疗前明显降低,匹伐他汀钙组患者 HDL-C 升高。血清 hsCRP 作为血管炎性的重要标记物,是动脉粥样硬化发生发展过程相关的重要炎症因子,也是冠心病发生的独立危险因素,其对心血管事件预测价值甚至超过 LDL-C^[20],因此在调脂治疗的同时,降低 hsCRP、降低血管炎性反应也是治疗冠心病的重要环节。最新研究显示他汀类药物能够降低炎症因子起到免疫调节作用,炎症反应的减轻起到稳定粥样硬化斑块、减少斑块破裂脱落风险,能够减少急性冠脉综合征患者发生心肌梗死及心源性猝死等心血管事件的发生^[21-25]。

本研究结果显示匹伐他汀钙能够降低冠心病患者血清 TC、TG、LDL-C 和 hsCRP 水平,升高血清 HDL-C 水平,具有显著的调脂与抗炎作用,与以往的报道一致^[26,27]。近年来,相关研究显示他汀类药物可影响 2 型糖尿病患者的血糖代谢,增加新发糖尿病的风险^[28]。匹伐他汀钙作为新一代的合成他汀药物,目前没有证据表明其会引起新发糖尿病风险^[29-31]。本研究结果显示匹伐他汀钙并没有升高冠心病患者血糖及糖化血红蛋白水平。与其他引起血糖升高的他汀类药物不同,匹伐他汀影响胰岛素抵抗与胰岛素分泌的可能机制如下:(1)辅酶 Q10 为线粒体 ATP 生成所必需,大多数他汀可能使 β 细胞中辅酶 Q10 表达降低,导致胰岛素分泌降低,而匹伐他汀不影响胰岛 β 细胞辅酶 Q10 的表达,因此不降低胰岛素分泌;(2)葡萄糖转运体 4(GLUT-4)是肌肉和脂肪细胞中介导胰岛素依赖的葡萄糖摄取的主要跨膜蛋白,大多数他汀可能导致 GLUT-4 表达降低,使胰岛素敏感性降低,而匹伐他汀不影响 GLUT-4 表达,不引起外周组织中胰岛素依赖的葡萄糖摄取,不影响胰岛素敏感性;(3)脂联素是由脂肪细胞分泌的一种胰岛素增敏激素,大多数他汀可能导致脂联素水平降低,而匹伐他汀可导致脂联素水平升高,从而改善胰岛素敏感性;(4)瘦素是脂肪细胞分泌的一种促 β 细胞增殖和胰岛素分泌的激素,大多数他汀可降低瘦素表达,而匹伐他汀不影响瘦素表达,从而保护 β 细胞和不引起胰岛素分泌降低。

综上所述,匹伐他汀钙和阿托伐他汀钙均能够降低冠心病患者的 LDL-C、TC、TG 水平,而匹伐他汀钙同时升高 HDL-C,降低 hsCRP,并且不增加新发糖尿病的风险。由于本研究样本量较小,观察时间有限,匹伐他汀钙的使用安全性和临床疗效尚需要更多的临床实践以明确。

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(上接第 3292 页)

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