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中西医结合治疗对 T2DM 合并 CHD 患者血糖、血脂及血管内皮功能的影响 *

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摘要 目的:探讨中西医结合治疗对 2 型糖尿病(T2DM)合并冠心病(CHD)患者血糖、血脂及血管内皮功能的影响。**方法:**将 120 例 T2DM 合并 CHD 患者上随机分为研究组与对照组各 60 例,在原饮食、运动疗法及降压、降糖治疗方案不变的条件下,对照组加用阿托伐他汀钙片治疗,研究组加用阿托伐他汀钙片与降脂通脉胶囊治疗。检测和比较两组治疗前后总胆固醇(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)、空腹血糖(FBG)、餐后 2h 血糖(2hPBG)、一氧化氮(NO)及内皮素(CE)-1 水平的变化。**结果:**两组治疗后 FBG、2hPBG 水平均较治疗前明显下降($P<0.05$),而组间比较差异无统计学意义($P>0.05$)。两组治疗后 TG、TC、LDL-C 水平均较治疗前明显下降($P<0.05$),HDL-C 水平均较治疗前明显升高($P<0.05$),且研究组 TG、TC、LDL-C 水平显著低于对照组($P<0.05$),HDL-C 水平显著高于对照组($P<0.05$)。两组治疗后血清 NO 水平均较治疗前明显升高($P<0.05$),血清 CE 水平均较治疗前明显下降($P<0.05$),且研究组血清 NO 水平明显高于对照组($P<0.05$),血清 CE 水平明显低于对照组($P<0.05$)。两组治疗过程中均未见明显不良反应。**结论:**降脂通脉胶囊联合阿托伐他汀可显著改善 T2DM 合并 CHD 患者的血脂和血管内皮功能,但不会进一步降低血糖。

关键词:降脂通脉胶囊;阿托伐他汀钙片;2 型糖尿病;冠心病

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Effects of Integrated Traditional Chinese and Western Medicine on the Blood glucose, Blood Lipid and Vascular Endothelial Function of Patients with T2DM Complicated with Coronary Heart Disease*

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ABSTRACT Objective: To explore the effects of integrated traditional Chinese and Western Medicine on the blood glucose, blood lipid and vascular endothelial function of patients with T2DM complicated with coronary heart disease(CHD). **Methods:** 120 cases of patients with T2DM combined with CHD were randomly divided into the study group and the control group with 60 cases in each group. In the original diet, exercise therapy and antihypertensive treatment, hypoglycemic treatment under the same conditions, the control group was treated with Atorvastatin Calcium Tablets treatment, and the study group was treated with Atorvastatin Calcium Tablets and Jiangzhi Tongmai Capsule. The changes of total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), 2h postprandial blood glucose (2hPG) and nitric oxide (NO) and endothelin (CE) -1 levels were measured and compared between two groups before and after treatment. **Results:** The FBG and 2hPG levels of both groups were dramatically reduced after treatment compared with those before treatment ($P<0.05$), while no statistically significant difference was found between two groups ($P>0.05$). The TG, TC and LDL-C levels of both groups after treatment were dramatically reduced compared with that before treatment($P<0.05$), while the HDL-C levels were remarkably increased compared with that before treatment ($P<0.05$). Additionally, the levels of TG, TC and LDL-C in study group were remarkably reduced compared with those in the control group($P<0.05$), while the level of HDL-C in study group was remarkably enhanced compared with that of the control group($P<0.05$). The serum NO levels of both groups after treatment were dramatically increased compared with those before treatment ($P<0.05$), the serum CE levels after treatment were dramatically reduced compared with those before treatment ($P<0.05$), and level of serum NO in

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study group was remarkably increased compared with that in the control group ($P<0.05$), the level of serum CE in study group was remarkably reduced compared with that in the control group ($P<0.05$). The patients in both groups showed no significant adverse reactions during treatment. **Conclusions:** Jiangzhi Tongmai Capsule combined with atorvastatin can significantly improve the blood lipid and vascular endothelial function of patients with T2DM complicated with CHD, which no further reduce the blood glucose.

Key words: Jiangzhi Tongmai Capsule; Atorvastatin; Type 2 diabetes mellitus; Coronary heart disease

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前言

动脉粥样硬化性心血管疾病是糖尿病 (diabetes mellitus, DM)主要的并发症及死因,据统计死于该并发症的 DM 患者可达 70%~80%^[1,2]。DM 脂代谢紊乱是冠状动脉血管病变的重要因素,2 型糖尿病(type 2 diabetes mellitus, T2DM)患者中存在血脂代谢异常的比例达 40.5%~50%^[3,4]。国外研究显示对 T2DM 合并血脂紊乱的患者,通过纠正异常血脂阻止或延缓动脉粥样硬化,可将心血管疾病的发生几率降低 31%^[5,6]。他汀类药物的主要作用是调脂,此外亦具有抗炎、保护血管内皮的作用,然而即使是最积极的低密度脂蛋白胆固醇 (low density lipoprotein-cholesterol, LDL-C) 西医治疗也仅能使 40%的心血管事件得到防控^[7]。研究表明具有化痰祛湿、活血化瘀的作用的降脂通脉胶囊在调节血脂、稳定动脉粥样硬化斑块方面亦具有较好的作用^[8,9]。本研究采用降脂通脉胶囊联合阿托伐他汀钙治

疗 T2DM 合并冠心病(coronary heart disease, CHD),探讨其对患者血糖、血脂及血管内皮功能的影响,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 6 月至 2016 年 6 月我院收治的 120 例 T2DM 合并 CHD 患者,纳入标准:①符合 1999 年世界卫生组织(World Health Organization, WHO)通过的 T2DM 诊断标准^[10]及 CHD 诊断标准^[11];②年满 18 周岁;③无严重肝、肾、造血系统等原发性疾病;④对治疗方案知情同意,并具有良好的依从性。排除标准:⑤过敏体质;⑥近 6 个月内有严重创伤、心脑血管事件、重大手术史;⑦近 2 周内使用过对血脂代谢有影响的药物;⑧孕妇及哺乳期妇女。将所有患者随机分为研究组与对照组,每组各 60 例,两组患者的一般资料比较差异无统计学意义($P>0.05$),具有可比性,见表 1。

表 1 两组患者的一般临床资料比较

Table 1 Comparison of the general and clinical data between two groups

Groups	Amount	Gender	Age	BMI	Course of disease	(SBP)/mmHg	(DBP)/mmHg
Study group	60	37/23	49.60± 11.16	23.70± 1.24	7.39± 2.76	131.19± 12.10	82.27± 6.14
Control group	60	39/21	51.47± 12.71	24.07± 1.35	7.36± 2.09	132.31± 10.98	82.46± 7.54
P	-	0.540	0.393	0.120	0.946	0.596	0.880

1.2 治疗方法

两组原饮食、运动疗法及降压、降糖治疗方案不变,对照组加用阿托伐他汀钙片 (立普妥)(辉瑞制药有限公司, 国药准字 H20051408),每晚睡前口服 20 mg,连用 4 周;研究组加用阿托伐他汀钙片与降脂通脉胶囊 (云南优克制药公司, 国药准字 Z20026429),阿托伐他汀钙片用法及用量同对照组,降脂通脉胶囊每次 3 粒,每天 3 次,连用 4 周。两组均停用其它降脂、抗凝、扩张血管的药物。

1.3 观察指标

治疗前后空腹 12 h 后抽取静脉血 3 mL,离心取上层血清, -20 °C 冷藏待检。采用 HITACHI7020 型全自动生化分析仪测定总胆固醇(total cholesterol, TC)、甘油三酯(triglycerides, TG)、低密度脂蛋白胆固醇(LDL-C)及高密度脂蛋白胆固醇(high density lipoprotein-cholesterol, HDL-C),采用化学发光法测定空腹血糖(fasting blood glucose, FBG),馒头餐糖耐量试验后再抽血检测餐后 2 h 血糖(2 h postprandial blood sugar, 2 h PBG),采用硝酸还原酶法测定一氧化氮(nitric oxide, NO),采用放射免疫法测定内皮素(cholesterol ester, CE)-1。

1.4 统计学方法

使用 SPSS19.0 统计学软件对所有数据进行分析处理,计

量资料以 $\bar{x} \pm s$ 表示,组间比较使用 t 检验,计数资料以 % 表示,组间比较使用 χ^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组治疗前后血糖水平的比较

两组治疗后 FBG、2hPBG 水平均较治疗前明显下降 ($P<0.05$),且组间比较差异无统计学意义($P>0.05$),见表 2。

2.2 两组治疗前后血脂水平的比较

两组治疗后 TG、TC、LDL-C 水平均较治疗前明显下降 ($P<0.05$),HDL-C 水平均较治疗前明显升高 ($P<0.05$),且研究组 TG、TC、LDL-C 水平显著低于对照组 ($P<0.05$),HDL-C 水平显著高于对照组 ($P<0.05$),见表 3。

2.3 两组治疗前后血清 NO、CE 水平的比较

两组治疗后血清 NO 水平均较治疗前明显升高 ($P<0.05$),血清 CE 水平均较治疗前明显下降 ($P<0.05$),且研究组血清 NO 水平明显高于对照组 ($P<0.05$),血清 CE 水平明显低于对照组 ($P<0.05$),见表 4。

2.4 两组不良反应发生情况的比较

研究组与对照组均未见明显不良反应,且均完成治疗,疗程结束后检查血常规和肝功能均未见明显异常。

表 2 两组治疗前后血糖水平的比较(mmol/L)

Table 2 Comparison of the blood glucose level between the two groups before and after treatment (mmol/L)

Groups	Amount	FBG		2hPG	
		Before treatment	After treatment	Before treatment	After treatment
Study group	60	13.59± 0.77	9.47± 0.85*	13.43± 2.28	9.24± 1.85*
Control group	60	13.66± 0.94	9.45± 0.93*	14.36± 2.25	9.37± 1.31*
P	--	0.656	0.902	0.051	0.657

Note: compared with the same group before treatment, *P<0.05.

表 3 两组治疗前后血脂水平的比较(mmol/L)

Table 3 Comparison of the blood lipid levels between the two groups before and after treatment (mmol/L)

Groups	Amount	TG		TC		LDL-C		HDL-C	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	60	3.59± 0.57	1.42± 0.66*	6.43± 1.28	3.54± 1.90*	4.75± 1.93	2.70± 0.84*	1.39± 0.51	1.99± 0.76*
Control group	60	3.66± 0.85	2.85± 0.71*	6.36± 1.25	5.37± 2.09*	4.83± 1.44	3.07± 0.65*	1.36± 0.74	1.71± 0.83*
P	--	0.597	0.000	0.762	0.000	0.797	0.008	0.796	0.010

Note: compared with the same group before treatment, *P<0.05.

表 4 两组治疗前后血清 NO、ET 水平的比较(pg/L)

Table 4 Comparison of the serum NO, CE levels between the two groups before and after treatment (pg/L)

Groups	Amount	NO		CE-1	
		Before treatment	After treatment	Before treatment	After treatment
Study group	60	72.27± 8.11	94.60± 10.16*	62.09± 5.37	50.99± 7.14*
Control group	60	72.46± 9.09	86.47± 9.71*	62.18± 6.69	55.28± 8.38*
P	--	0.904	0.000	0.935	0.003

Note: compared with the same group before treatment, *P<0.05.

3 讨论

T2DM 脂代谢紊乱对动脉粥样硬化性心血管疾病的发生有重要影响,接近半数的 T2DM 患者 TG、TC 及 HDL-C 超出正常范围,而 LDL-C 正常或过高^[12,13]。研究显示 HDL-C 下降 10 mg/dL、LDL-C 上升 10 mg/dL 可分别使 CHD 的患病风险提高 22%、12%^[14]。血 TG 与冠心病的发生和死亡密切相关,且独立于 HDL-C 和 LDL-C 的变化^[15]。因此,调脂治疗是 T2DM 伴 CHD 患者治疗过程中的重要环节。阿托伐他汀钙是目前临床用于降脂治疗主要的他汀类药物,主要是可通过竞争性抑制 HMG- CoA 还原酶活性而使肝细胞 LDL 受体的表达上调,使更多的 LDL 被受体结合而被清除,减少肝细胞对脂蛋白的合成,从而促进紊乱的血脂恢复正常^[16,17]。

中医学将 CHD 归于 "胸痹"、"真心痛" 范畴,多为本虚标实,以气虚、阳虚为本,气滞、瘀血、痰浊、寒凝为标;而合并血脂异常的 CHD 患者多为虚实夹杂,脾肾亏虚为本,瘀血痰浊其标^[18,19]。降脂通脉胶囊是由姜黄、决明子、三七、泽泻、铁线草组成的中药调脂药物,具有化痰祛湿、活血化瘀的作用^[20,21]。现代药理研究证明三七总皂苷有着突出的扩血管、降血液黏度、改善微循环及调脂的作用^[22,23];决明子可降低血 TC、TG 水平,并可抑制血管内皮细胞增生^[24,25];姜黄油和姜黄素可抗 LDL 氧化,可阻止或延缓动脉粥样硬化形成^[26];泽泻可降低 TC、TG 水

平,升 HDL-C 水平,并可提高纤溶酶活性,抗血小板聚集,抗主动脉内膜粥样斑块生成^[27];铁线草可减轻炎症反应,减轻由脂质过氧化物所致的血管内皮损伤。本研究结果显示两组治疗后 TG、TC、LDL-C、HDL-C 水平均明显改善,但经过联合治疗的研究组改善幅度更明显,说明阿托伐他汀钙的降脂效果是疗效确切,而与降脂通脉胶囊联合后可进一步起到良好的调节血脂作用。冀茂昌^[28]采用阿托伐他汀联合灯盏细辛注射液治疗 T2DM 伴 CHD 患者的血脂异常亦获得良好效果,提示中西医调脂药结合使用的价值高。

血管内皮细胞损伤是动脉粥样硬化的始动因素^[29]。内皮细胞功能障碍是 DM 患者早期动脉硬化症的重要病理特征^[30]。NO 和 E 是由内皮细胞分泌的血管舒缩因子,NO 具有保护血管的作用,可使血管平滑肌松弛,能扩张血管以增加器官的血流量;CE 可损伤血管内皮细胞,可加剧血管平滑肌的收缩,导致组织缺血缺氧。二者相互拮抗,在维持正常的血管舒缩方面有重要作用。研究表明高血糖可促进血管内皮的氧化应激,促使血管舒张及收缩因子分泌紊乱,打破 NO 和 CE-1 的平衡状态,引起血管痉挛,破坏内皮细胞的血氧供给,促使炎症及血栓的形成,从而引发内皮细胞损伤^[31]。阿托伐他汀钙由于可激活内源性 NO 合成酶,促进内皮细胞合成 NO,所以除了调脂作用外,还具有修复血管内皮细胞损伤作用。对照组治疗后 NO、CE 水平明显改善,而研究组加用降脂通脉胶囊后进一步改善,说

明降脂通脉胶囊在提高 NO 水平,降低 CE 水平,纠正 NO 与 CE 的失衡,改善血管内皮功能等诸多方面具有积极作用,其中的原因可能与降脂通脉胶囊含有多种活性成分有关。两组的血糖比较无统计学意义,说明在原有降糖方案的基础上,加用阿托伐他汀及降脂通脉胶囊不会进一步降低血糖。

综上,降脂通脉胶囊联合阿托伐他汀可显著改善 T2DM 合并 CHD 患者的血脂和血管内皮功能,但不影响机体的血糖水平。

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