

doi: 10.13241/j.cnki.pmb.2019.23.034

银杏蜜环口服溶液联合尼可地尔对冠心病患者血清 HsCRP、HCY、IMA、LP-PLA2 水平的影响*

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摘要 目的:研究银杏蜜环口服溶液联合尼可地尔对冠心病患者血清超敏 C 反应蛋白(High-sensitivity C-reactive protein, HsCRP)、同型半胱氨酸 (Homocysteine, HCY)、缺血修饰白蛋白 (Ischemia Modified Albumin, IMA) 和脂蛋白相关磷脂酶 A2 (Lipoprotein-related phospholipase A2, Lp-PLA2) 水平的影响。**方法:**选择 2016 年 11 月~2018 年 11 月在我院全科医学科、急诊科收治的 80 例冠心病患者,根据就诊顺序,用抽签法随机分为两组,每组 40 例患者。对照组口服尼可地尔治疗,观察组采取银杏蜜环口服溶液联合尼可地尔治疗,两组均持续治疗 2 周。比较两组治疗前后的血清 HsCRP、HCY、IMA、LP-PLA2 水平,左室舒张末径(left ventricular end-diastolic diameter, LVEDD)、心输出量(cardiac output, CO)和左室射血分数(left ventricular ejection fraction, LVEF)等心功能指标的变化。**结果:**治疗后,观察组的总有效率为 92.50%(37/40),明显高于对照组[75.00%(30/40)]($P<0.05$);两组治疗后的血清 HsCRP、HCY、IMA、LP-PLA2 水平均较治疗前明显降低($P<0.05$),且观察组以上指标均明显低于对照组($P<0.05$);两组治疗后的 LVEDD 均较治疗前明显降低,而 CO 和 LVEF 均较治疗前明显升高(P 均 <0.05),且观察组治疗后的 LVEDD 与对照组相比明显降低,而 CO 和 LVEF 显著升高($P<0.05$)。**结论:**银杏蜜环口服溶液联合尼可地尔治疗冠心病的疗效明显优于单独口服尼可地尔治疗,其机制可能与降低血清 HsCRP、HCY、IMA、LP-PLA2 水平相关。

关键词:银杏蜜环口服溶液;尼可地尔;冠心病

中图分类号:R541.4 文献标识码:A 文章编号:1673-6273(2019)23-4545-04

Effect of Ginkgo Leaf Extract and Armillariella Mellea Powders Oral Solution Combined with Nicorandil on the Serum Levels of HsCRP, HCY, IMA and LP-PLA2 in Patients with Coronary Heart Disease*

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ABSTRACT Objective: To investigate the effect of Ginkgo Leaf Extract and Armillariella Mellea Powders Oral Solution combined with nicorandil on the serum levels of high-sensitivity C-reactive protein (HsCRP), homocysteine (HCY), ischemia-modified albumin (IMA) and lipoprotein-related phospholipase A2 (Lp-PLA2) levels in patients with coronary heart disease. **Methods:** Eighty patients with coronary heart disease admitted to our department of general medicine and emergency department from November 2016 to November 2018 were randomly divided into two groups according to the order of treatment, with 40 patients in each group. The control group was treated with nicorandil, and the observation group was treated with ginkgo melamine oral solution combined with nicorandil. Both groups continued treatment for 2 weeks. Serum HsCRP, HCY, IMA, LP-PLA2 levels, left ventricular end-diastolic diameter (LVEDD), cardiac output (CO), and left ventricular ejection fraction were compared between the two groups. Left ventricular ejection fraction (LVEF) changes in cardiac function indicators. **Results:** After treatment, the total effective rate of observation group was 92.50% (37/40), which was significantly higher than that of the control group [75.00% (30/40)] ($P<0.05$). The levels of serum HsCRP, HCY, IMA and LP-PLA2 in both groups were significantly lower than those before treatment ($P<0.05$), and the above indicators in the observation group were significantly lower than the control group ($P<0.05$). The LVEDD of the two groups was significantly lower than that before treatment, and CO and LVEF were significantly higher than those before treatment ($P<0.05$), and the LVEDD after treatment in the observation group was significantly lower than that of the control group, while CO and LVEF were significantly increased ($P<0.05$). **Conclusion:** The

* 基金项目:陕西省自然科学基金基础研究计划-青年人才项目(2014JQ2-8050)

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(收稿日期:2019-03-06 接受日期:2019-03-30)

efficacy of ginkgo biloba oral solution combined with nicorandil was significantly better than that of nicorandil alone in the treatment of coronary heart disease. The mechanism may be related to the reduction of serum HsCRP, HCY, IMA and LP-PLA2 levels.

Key words: Ginkgo Leaf Extract and Armillariella Mellea Powders Oral Solution; Nicorandil; Coronary heart disease

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

Article ID: 1673-6273(2019)23-4545-04

前言

冠心病患者常见于老年群体,主要是由于患者心肌细胞结构受损,引起心血管硬化堵塞、心脏收缩力减弱,使心功能显著降低,导致相关临床症状出现^[1-3]。目前,临床上常以改善微循环、扩冠、降血脂和预防血栓等治疗为主,但是单纯采用西药仅能减轻冠心病患者的症状表现或预防危险情况的发生,尚无法达到根治的目的^[4-6]。

近年来,随着中医药治疗心内科疾病的疗效日益被认可,中西药结合治疗冠心病得到广泛应用^[7]。银杏密环口服溶液是由天麻蜜环菌以及银杏叶提取物等制成的一种复方口服制剂,味甜,微苦,具有增加冠状动脉血流量、活血化瘀、抑制血小板聚集、扩张冠状动脉、抗血栓形成和改善微循环等功能,可以用于治疗心绞痛、冠心病以及缺血性脑出血疾病。本研究主要探讨了银杏密环口服溶液与尼可地尔联用治疗冠心病的临床疗效,并分析其可能的作用机制。

1 资料与方法

1.1 一般资料

选择2016年11月~2018年11月在我院全科医学科、急诊科诊治的80例冠心病患者为研究对象,符合诊断标准^[8],尚能有效控制合并的高血压和糖尿病等基础病,均知情同意。排除标准:肥厚型及限制型心肌、心包疾病者;内分泌、免疫和造血系统障碍者;严重的心律失常者;器质性心脏疾病者;酒精或药物依赖者。根据就诊顺序,用抽签法随机分为两组。观察组40例,男23例,女17例;年龄45~82岁,平均(63.74±5.39)岁;病程(4.32±1.19)年。对照组40例,男24例,女16例;年龄44~82岁,平均(62.45±6.31)岁;病程(4.49±1.26)年。两组的

基线资料对比无统计学差异($P>0.05$),具有可比性。

1.2 治疗方法

两组均在控制饮食、降脂、抗凝等治疗基础上采用本研究疗法。对照组:口服尼可地尔(批号:国药准字H13023941,生产厂家:邯郸市冀南制药公司,规格:5 mg)治疗,每次5 mg,每天3次。观察组:加服银杏蜜环口服溶液(批号:国药准字H20013079,生产厂家:天银制药公司,规格:10 mL)治疗,每次10 mL,每天3次。两组均连续治疗2周。

1.3 观察指标

疗效标准:分为显效,有效和无效。①显效:心电图结果显示缺血现象消失,临床症状改善;②有效:心电图结果表明缺血现象缓解,临床症状缓解;③无效:心电图显示缺血现象未改善,临床症状未缓解。

于治疗前后采集3 mL外周血,用酶联免疫吸附法检测血清超敏C反应蛋白(HsCRP)、同型半胱氨酸(HCY)、缺血修饰白蛋白(IMA)和脂蛋白相关磷脂酶A2(Lp-PLA2)的水平。

于治疗前后用贝尔斯BLS-X8彩色超声多普勒诊断仪测定左室舒张末径(LVEDD)、心输出量(CO)和左室射血分数(LVEF)。

1.4 统计学分析

采用SPSS17.0对数据进行统计学分析,计量数据以 $\bar{x} \pm s$ 表示,组间比较行t检验,组间率的比较用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效的对比

治疗后观察组的总有效率为92.50%,显著高于对照组75.00%($P<0.05$),见表1。

表1 两组临床疗效对比[例(%)]

Table 1 Comparison of the clinical effect between two groups[n(%)]

Groups	n	Effective	Valid	Invalid	The total effect rate
Observation group	40	16 (40.00)	14 (35.00)	10 (25.00)	75.00
Control group	40	21 (52.50)	16 (40.00)	3 (7.50)	92.50*

Note: Compared with the control group, * $P<0.05$.

2.2 两组治疗前后血清 HsCRP、HCY、IMA、LP-PLA2 水平的对比

两组治疗后的血清 HsCRP、HCY、IMA、LP-PLA2 水平均较治疗前明显降低($P<0.05$),且观察组以上指标均显著低于对照组($P<0.05$),见表2。

2.3 两组治疗前后 LVEDD、CO 和 LVEF 对比

两组治疗后的 LVEDD 较治疗前明显降低,CO 和 LVEF 较治疗前明显升高(P 均 <0.05),且观察组以上指标的改善更明显($P<0.05$),见表3。

2.4 两组不良反应发生情况的比较

观察组发生恶心1例,耳鸣1例,便秘2例;对照组发生恶心2例,耳鸣1例,便秘1例。两组不良反应发生情况相比无明显差异($P>0.05$)。

3 讨论

冠心病的发作往往与情绪激动、季节改变、饱食、体力活动增加、大量饮酒及吸烟等相关,患者发病时常表现为呼吸急促、胸闷气短和头晕恶心等症状,主要的病理改变为冠状动脉内的斑块出血、破裂和血栓形成。如急性发作或者未及时治疗能引

表 2 两组治疗前后的血清 HsCRP、HCY、IMA、LP-PLA2 水平的对比($\bar{x}\pm s$)Table 2 Comparison of the serum HsCRP, HCY, IMA and LP-PLA2 levels before and after treatment between two groups($\bar{x}\pm s$)

Groups	n		HsCRP(mg/L)	HCY(μ mol/L)	IMA(μ g/L)	LP-PLA2(U/L)
Observation group	40	Before treatment	8.73 $\pm$ 1.16	19.32 $\pm$ 2.48	43.29 $\pm$ 4.26	493.62 $\pm$ 49.57
		After treatment	3.25 $\pm$ 0.97 [#]	16.21 $\pm$ 1.75 [#]	26.78 $\pm$ 3.15 [#]	463.26 $\pm$ 42.63 [#]
Control group	40	Before treatment	8.75 $\pm$ 1.24	19.46 $\pm$ 2.17	43.97 $\pm$ 5.23	494.23 $\pm$ 48.29
		After treatment	1.64 $\pm$ 0.58 ^{*#}	12.48 $\pm$ 1.35 ^{*#}	20.63 $\pm$ 2.95 ^{*#}	431.78 $\pm$ 41.25 ^{*#}

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

表 3 两组治疗前后的 LVEDD、CO 和 LVEF 对比($\bar{x}\pm s$)Table 3 Comparison of the LVEDD, CO and LVEF before and after treatment between two groups($\bar{x}\pm s$)

Groups	n		LVEDD (cm)	CO (L/min)	LVEF (%)
Observation group	40	Before treatment	5.92 $\pm$ 0.73	2.75 $\pm$ 0.43	37.64 $\pm$ 2.95
		After treatment	4.63 $\pm$ 0.82 [#]	4.23 $\pm$ 0.56 [#]	44.39 $\pm$ 3.52 [#]
Control group	40	Before treatment	5.93 $\pm$ 0.84	2.77 $\pm$ 0.52	38.14 $\pm$ 2.63
		After treatment	3.71 $\pm$ 0.54 ^{*#}	5.17 $\pm$ 0.63 ^{*#}	50.23 $\pm$ 4.17 ^{*#}

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

发心肌急性缺血甚至坏死,病情严重时患者可能会在短时间内发生心源性猝死^[8-12]。该种疾病在中老年人群尤为常见,主要的诱因是冠状动脉粥样硬化病变,加上多数患者作息时间和饮食习惯不规律,往往伴有高脂血症^[13-15]。尼可地尔对钾通道具有较高的选择性,可以针对性地对冠脉血管发挥效果,明显扩张冠状动脉,增加心肌供氧量以及冠脉血流量,从而能较大幅度地降低心绞痛的发作风险^[16-19]。但是单独用药只能改善冠心病部分的症状体征,治疗效果较差,会使患者的住院时间延长,为患者造成沉重的心理和经济负担^[20]。

银杏蜜环口服溶液具有活血止痛的效果,可以有效治疗心绞痛、冠状动脉性心脏病以及高脂血症等疾病。该药的药理作用包括:① 拮抗血小板活化因子,使血液的流变性得到改善;② 清除氧自由基,有效抗氧化;③ 降低血脂,对动脉粥样硬化的发生进行预防;④ 保护机体的心脑血管^[21]。本研究发现,观察组的总有效率明显高于对照组,表明银杏蜜环口服溶液联合尼可地尔对冠心病的疗效相比单独用药疗效更佳。其原因是二者联用可以有效的通脉止痛、活血化瘀、防微血栓形成以及抗氧化应激等作用。

当机体的内皮功能失调后,血清 Hcy 水平会明显升高,大大降低血管内皮依赖性的舒张功能,并且可以与低密度脂蛋白发生相互的作用,对脂质的代谢造成抑制,使得胆固醇在细胞内出现大量的堆积^[22,23]。有研究显示高 Hcy 血症是引起缺血性脑血管病的重要危险因素^[24]。HsCRP 是预测心血管事件发生危险性的一种强有效因子^[25]。研究发现,HsCRP 水平与脑梗死患者神经功能缺损程度以及梗死面积相关^[26]。LP-PLA2 可以将血小板活化因子进行有效的水解,而血小板活化因子是一种炎性因子,因此认为 LP-PLA2 可以抑制炎症反应,甚至可以通过降低动脉粥样硬化斑块局部发生的炎症反应,而发挥抑制动脉粥样硬化形成的效果^[27,28]。LP-PLA2 还可以通过对氧化低密度脂蛋白分子中氧化修饰的磷脂进行水解,而生产大量的氧化型游离脂肪酸以及溶血磷脂酰胆碱,而氧化型游离脂肪酸以及溶血磷脂酰胆碱均为比较强烈的致炎因子,可以促进细胞因子以及

细胞黏附分子的生成,诱导单核细胞进一步分化成泡沫细胞和巨噬细胞,进而引发动脉粥样硬化斑块的形成。IMA 是一种较为灵敏的缺血性生物标志物,有助于早期发现和诊断脑血管疾病^[29,30]。两组治疗后的血清 HsCRP、HCY、IMA、LP-PLA2 水平平均明显降低,且观察组更低,提示银杏蜜环口服溶液联合尼可地尔可以通过降低血清 HsCRP、HCY、IMA、LP-PLA2 水平,从而减缓病情。

综上所述,银杏蜜环口服溶液联合尼可地尔治疗冠心病的疗效明显优于单独口服尼可地尔的疗效,其机制可能与降低血清 HsCRP、HCY、IMA、LP-PLA2 水平相关。

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