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银杏叶滴丸联合瑞舒伐他汀对老年冠心病患者的临床效果*

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摘要 目的:研究银杏叶滴丸联合瑞舒伐他汀对老年冠心病患者的临床效果。**方法:**选择2017年8月~2019年12月于我院的75例老年冠心病患者,将其随机分为两组。对照组口服瑞舒伐他汀,观察组联合口服银杏叶滴丸联合瑞舒伐他汀。比较两组的左室舒张末径(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);血清白细胞介素-2(Interleukin-2, IL-2)、P选择素、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)水平。**结果:**观察组的有效率95.49%,明显高于对照组71.05%($P<0.05$);治疗后,两组的纤维蛋白原、全血高切黏度、红细胞聚集指数、全血低切黏度、最大血小板聚集率和血浆黏度、LVEDD、血清IL-2、P选择素、TNF- α 水平明显降低($P<0.05$),且观察组明显低于对照组,CO以及LVEF明显升高($P<0.05$),且观察组上述指标的变化均优于对照组($P<0.05$)。**结论:**银杏叶滴丸联合瑞舒伐他汀能有效抑制老年冠心病患者体内的炎症反应程度,改善血液流变学,恢复患者的心功能,值得推广。

关键词:银杏叶滴丸;瑞舒伐他汀;老年冠心病;血液流变学;心功能

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Clinical Effect of Ginkgo Biloba Dropping Pills Combined with Rosuvastatin on Elderly Patients with Coronary Heart Disease*

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ABSTRACT Objective: To investigate the effect of Ginkgo biloba dropping pills combined with rosuvastatin on elderly patients with coronary heart disease. **Methods:** Selected 75 cases of elderly patients coronary heart disease with coronary heart disease who were treated in our hospital from August 2017 to December 2019, divided into two groups randomly. The control group was treated with rosuvastatin, and the observation group was treated with ginkgo leaf drop pills combined with rosuvastatin. LVEDD, CO, LVEF, serum levels of IL-2, P-selectin and TNF- α were compared between the two groups. **Results:** The effective rate of the observation group was 95.49 %, which was significantly higher than 71.05 % of the control group ($P<0.05$). After treatment, the two groups had significant levels of fibrinogen, whole blood high shear viscosity, red blood cell aggregation index, whole blood low shear viscosity, maximum platelet aggregation rate, plasma viscosity, LVEDD, serum IL-2, P-selectin, and TNF- α levels Decrease ($P<0.05$), and the observation group was significantly lower than the control group, CO and LVEF were significantly increased ($P<0.05$), and the changes in the above indicators of the observation group were better than those of the control group ($P<0.05$). **Conclusion:** Ginkgo biloba dripping pills combined with rosuvastatin can effectively inhibit the inflammatory reaction in elderly patients with coronary heart disease, improve hemorheology, and restore the heart function of patients.

Key words: Ginkgo Biloba Dropping Pills; Rosuvastatin; Senile Coronary Heart Disease; Hemorheology; Cardiac Function

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前言

冠心病是因为脂质代谢异常而导致机体的动脉内膜发生

脂类物质堆积,从而形成动脉粥样病变,且引起一系列临床症状的发生^[1-3]。目前的疗法包括手术治疗、心脏介入治疗和药物治疗,改善冠心病患者的心肌缺氧、缺血症状,有效控制使动脉

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粥样硬化的危险因素,改善缺血缺氧所引起的心律失常以及心脏机械功能障碍,进而促使冠心病患者的心脏灌注情况保持良好的状态^[4,5]。单纯采用钙拮抗剂、 β -受体阻滞剂、抗血小板药物、硝酸酯类药物、抗凝药物等西药仅能减轻冠心病患者的症状表现,无法根治^[6,7]。他汀类药物是治疗冠心病患者的一线药物,能明显降低低密度脂蛋白水平,但单用的效果不佳^[8]。银杏叶滴丸具有通络和活血化瘀的效果,主治瘀血阻络而导致的心痛、胸痹和半身不遂等。但尚未见将其与瑞舒伐他汀联用的报道。本研究创新性地分析了银杏叶滴丸联合瑞舒伐他汀对老年冠心病患者的效果。

1 资料与方法

1.1 一般资料

选择2017年8月~2019年12月我院诊治的老年冠心病患者75例,随机分为两组。观察组37例,男21例,女16例;年龄60~89岁,平均 (67.34 ± 2.29) 岁;病程1~13年,平均 (5.97 ± 0.46) 年;其中,急性冠脉综合征17例,慢性稳定性冠脉病20例;NYHA II级患者19例,NYHA III级患者15例,NYHA IV级患者3例。对照组38例,男22例,女16例;年龄60~89岁,平均 (68.13 ± 1.75) 岁;病程1~13年,平均 (5.73 ± 0.54) 年;其中,急性冠脉综合征18例,慢性稳定性冠脉病20例;NYHA II级患者20例,NYHA III级患者15例,NYHA IV级患者3例。两组的基线资料具有可比性($P>0.05$)。

纳入标准:(1)均符合冠心病的诊断标准^[9];(2)年龄60~89岁;(3)均知情同意。排除标准:(1)合并甲状腺疾病、呼吸系统疾病、恶性肿瘤、循环系统疾病、感染性疾病、栓塞性疾病、自身免疫性疾病的患者;(2)合并出血性病变的患者;(3)合并原

发性心肌病、主动脉瓣膜病的患者;(4)对银杏叶滴丸和瑞舒伐他汀过敏的患者;(5)合并房室传导阻滞。

1.2 治疗方法

两组均积极控制血糖、血压、血脂,有心绞痛发作的患者可以含服硝酸甘油片0.5 mg。对照组口服瑞舒伐他汀,每次10 mg,1次/d;观察组联合口服银杏叶滴丸,每次5丸,每天3次。共治疗两周。

1.3 观察指标

疗效标准^[9]:① 显效:静息状态下缺血性现象基本消失,胸闷和心悸症状基本得到缓解;② 有效:静息状态下缺血性现象有所改善,症状基本明显缓解;③ 无效:静息状态下缺血性现象基本未改变,症状无改变。

治疗前后,采取贝克曼库尔特AU5800全自动生化仪检测冠心病患者的纤维蛋白原、全血高切黏度、红细胞聚集指数、全血低切黏度、最大血小板聚集率和血浆黏度;且检测两组的LVEDD、CO和LVEF;冠心病患者均空腹采集3 mL上肢静脉血,用ELISA法检测血清IL-2、P选择素、TNF- α 水平,试剂盒均购自上海晶抗生物公司。

1.4 统计学分析

采用SPSS 21.0,计量资料以 $\bar{x} \pm s$ 表示,对比用t检验,计数资料用%表示,对比用 χ^2 检验, $P<0.05$ 有统计学意义。

2 结果

2.1 两组疗效对比

观察组的总有效率[95.49%(35/37)],明显高于对照组[71.05%(27/38)],两组对比有差异($P<0.05$),见表1。

表1 两组疗效对比[例(%)]

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

Groups	n	Effective	Valid	Invalid	The total effect rate
Control group	38	16(42.10)	11(28.95)	11(28.95)	27(71.05)
Observation group	37	21(56.76)	14(37.84)	2(5.41)	35(94.59)*

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

2.2 两组血液流变学相关指标对比

治疗后,两组的纤维蛋白原、全血高切黏度、红细胞聚集指数、全血低切黏度、最大血小板聚集率和血浆黏度明显降低

($P<0.05$),且观察组的纤维蛋白原、全血高切黏度、红细胞聚集指数、全血低切黏度、最大血小板聚集率和血浆黏度明显低于对照组($P<0.05$),见表2。

表2 两组血液流变学相关指标对比($\bar{x} \pm s$)

Table 2 Comparison of Hemorheology related indexes between the two groups ($\bar{x} \pm s$)

Group	Fibrinogen (g/L)	Whole blood high shear viscosity (mPaos)	Erythrocyte aggregation index	Whole blood low shear viscosity (mPaos)	Maximum platelet aggregation rate (%)	Plasma viscosity (mPaos)
Control group (n=38)						
Before treatment	4.79 $\pm$ 0.63	5.99 $\pm$ 1.38	5.09 $\pm$ 0.63	8.25 $\pm$ 0.76	74.42 $\pm$ 11.15	4.04 $\pm$ 0.67
After treatment	3.62 $\pm$ 0.45 [#]	4.72 $\pm$ 1.05 [#]	4.39 $\pm$ 0.57 [#]	6.73 $\pm$ 0.52 [#]	63.39 $\pm$ 11.82 [#]	2.59 $\pm$ 0.41 [#]
Observation group(n=37)						
Before treatment	4.78 $\pm$ 0.65	5.97 $\pm$ 1.26	5.04 $\pm$ 0.65	8.24 $\pm$ 0.79	75.54 $\pm$ 12.37	4.05 $\pm$ 0.63
After treatment	3.23 $\pm$ 0.34 ^{**}	3.22 $\pm$ 0.75 ^{**}	3.02 $\pm$ 0.31 ^{**}	5.25 $\pm$ 0.34 ^{**}	57.26 $\pm$ 10.31 ^{**}	2.05 $\pm$ 0.17 ^{**}

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

2.3 两组 LVEDD、CO 以及 LVEF 对比 高($P<0.05$),且观察组的 LVEDD 明显更低,CO 和 LVEF 明显治疗后,两组的 LVEDD 明显降低,CO 以及 LVEF 明显升高($P<0.05$),见表 3。

表 3 两组 LVEDD、CO 以及 LVEF 对比($\bar{x} \pm s$)
Table 3 LVEDd, CO and LVEF were compared between the two groups ($\bar{x} \pm s$)

Groups		LVEDD(cm)	CO(L/min)	LVEF(%)
Control group (n=38)	Before treatment	5.92± 0.67	2.79± 0.45	37.24± 2.65
	After treatment	4.63± 0.54 [#]	4.22± 0.47 [#]	44.13± 3.34 [#]
Observation group (n=37)	Before treatment	5.93± 0.68	2.78± 0.50	38.13± 2.78
	After treatment	3.72± 0.46 ^{*#}	5.16± 0.68 ^{*#}	50.29± 4.57 ^{*#}

2.4 两组血清 IL-2、P 选择素、TNF-α 水平对比 ($P<0.05$), 且观察组的血清 IL-2、P 选择素、TNF-α 水平明显低于对照组($P<0.05$),见表 4。

表 4 两组血清 IL-2、P 选择素、TNF-α 水平对比($\bar{x} \pm s$)
Table 4 Comparison of serum IL-2, P-selectin and TNF - α levels between the two groups ($\bar{x} \pm s$)

Groups		IL-2 (ng/mL)	P-selectin (ng/L)	TNF- α (ng/mL)
Control group (n=38)	Before treatment	6.17± 1.34	42.29± 10.17	2.59± 0.43
	After treatment	4.27± 1.03 [#]	35.27± 5.46 [#]	1.93± 0.24 [#]
Observation group (n=37)	Before treatment	6.19± 1.58	41.96± 11.38	2.57± 0.46
	After treatment	3.19± 0.54 ^{*#}	24.17± 3.59 ^{*#}	1.64± 0.13 ^{*#}

3 讨论

研究发现,冠心病患者主要表现为心悸、胸闷、乏力及胸痛等,严重者可能会出现心力衰竭以及心肌梗死等症状^[10-13],严重威胁患者的生命^[14]。冠心病与高血压、不良生活方式和糖尿病等相关^[15-17],因此在中老年人群尤为常见^[18-20]。目前,临床上常用手术治疗、心脏介入治疗和药物治疗,以改善患者的心肌缺氧、缺血症状,达到治疗的目的^[21,22]。

祖国传统医学将冠心病归属于“心悸”、“胸痹”、“真心痛”以及“怔忡”等病证的范畴。多由饮食不节、老年体虚、寒邪内侵、情志失调等造成心脉痹阻,不通则痛,因而老年冠心病患者在治疗上主要是通脉止痛、活血化瘀,即增加冠脉血流量、扩张冠状动脉和改善心肌营养。银杏叶滴丸的成分主要包括银杏内酯以及黄酮素等,其中,银杏内酯具有比较强的抗氧化作用,能调节机体内的微循环状态,使血液的黏稠度降低;黄酮素作为一种强效的血小板激活因子抑制剂,能有效抗血栓形成、改善微循环、抑制血小板聚集、清理氧自由基以及降低血小板表面活性。药理研究表明,银杏叶提取物具有清除自由基、抗氧化、改变血液流变性、降脂、保护心脑血管和预防动脉粥样硬化等多种的药理活性^[23]。治疗后,观察组的纤维蛋白原、全血高切黏度、红细胞聚集指数、全血低切黏度、最大血小板聚集率和血浆黏度明显低于对照组;与唐勇等^[24]的研究结果相一致,该学者探究银杏叶滴丸对老年冠脉动脉硬化心脏病(冠心病)患者血小板聚集性及心脏功能的影响,对照组给予阿司匹林与氯吡格雷行双联抗血小板治疗,研究组在对照组基础上口服银杏叶滴丸治疗,治疗后两组血小板聚集性、凝血功能状况及心脏功能相关指标水平均明显改善,且治疗后研究组血小板聚集率显著

低于对照组。本研究结果表明银杏叶滴丸联合瑞舒伐他汀能显著改善老年冠心病患者的血液流变学。治疗后, 观察组的 LVEDD 明显降低,CO 和 LVEF 明显升高,与周红霞^[25]的研究类似,该学者探讨银杏叶滴丸联合非洛地平治疗冠心病心绞痛的有效性与安全性,对照组,口服非洛地平缓释片,治疗组在对照组的基础上口服银杏叶滴丸,治疗后,两组 LVEF 和舒张期冠状动脉血流峰值速度显著升高,LVEDD 显著降低,且治疗组患者这些指标治疗后水平明显优于对照组。表明银杏叶滴丸联合瑞舒伐他汀在改善老年冠心病患者心功能方面具有更加显著的优势,有助于提升疾病的整体治疗效果。其原因为,银杏叶滴丸可以抑制机体内心肌缺血再灌注过程中自由基的生成,明显降低心肌肌球蛋白的释放量,有效促进心肌功能的恢复。

血清 P 选择素作为一种炎症标志物,主要存在于机体的内皮细胞以及血小板中,一旦血小板激活或内皮细胞受到损伤,都能导致血清 P 选择素水平的升高,从而进一步促进血栓的形成以及血小板聚集^[26,27]。临床上常常选择血清 P 选择素含量来判断心肌缺血和心肌梗死患者的稳定状态以及病情严重程度^[28]。在动脉粥样硬化的发生过程中,患者机体内的巨噬细胞和中性粒细胞能促使 TNF-α 的生成,如果冠状动脉受到损伤,就会使 TNF-α 的分泌量进一步增加,血清 TNF-α 水平的升高还能诱导白细胞介素的生成,两者均能介导免疫炎症反应,使粥样斑块形成的速度加快^[29,30]。本研究治疗后,观察组的血清 IL-2、P 选择素、TNF-α 水平明显低于对照组,王荣等^[31]在单硝酸异山梨的基础上联用银杏叶滴丸,患者的血清 IL-2、TNF-α 水平明显降低。与本研究结果相一致。表明银杏叶滴丸联合瑞舒伐他汀能明显降低冠心病患者的炎症因子含量,减轻炎症反应程度,缓解心肌损伤。本研究为老年冠心病的治疗提供了新的治

疗方法与思路,但也存在一定的不足,样本量少,结果可能存在一定的偏倚,也没有探究银杏叶滴丸治疗冠心病的具体机制,后续研究还需要在动物实验中探究其作用机制。

综上所述,银杏叶滴丸联合瑞舒伐他汀能有效抑制老年冠心病患者体内的炎症反应程度,改善血液流变学,恢复患者的心功能,值得推广。

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血管细胞粘附分子表达,有效促进嗜酸粒细胞迁移和聚集^[9]。本研究 ECRSwNP 患者 EP1 mRNA 与 IL-5、IL-13 mRNA 的表达存在正相关。EP1 表达增加与 ECRSwNP 中表现出的 Th2 极化有关,进一步表明 EP1 受体可能通过趋化和活化嗜酸粒细胞等炎症细胞合成 IL-5、IL-13 等炎症因子,促进鼻息肉组织炎症的发生和发展。

CRSwNP 对患者的生活质量和社会经济造成沉重的负担,传统药物疗效不能使患者满意。目前针对 PGE2 的非甾体抗炎药或 COX-2 阻断剂由于前列腺素的广泛抑制而导致多种不良反应。后期应用 EP1 受体特异性拮抗剂或激动剂进行体内和体外实验,深入研究 EP 受体在 ECRSwNP 炎症机制中的具体作用,有望作为一种新的有前途的靶点药物被研发。

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