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## 川芎嗪注射液对冠心病心绞痛患者临床症状及血液流变学的影响

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**摘要 目的:**探讨川芎嗪注射液对冠心病(CHD)心绞痛患者临床症状及血液流变学的影响。**方法:**选择 2014 年 3 月至 2016 年 3 月在我院进行治疗的 CHD 心绞痛患者 60 例,按随机数字表法分为实验组和对照组各 30 例,对照组患者给予常规治疗,实验组患者在常规治疗基础上加用川芎嗪注射液治疗,两组患者均治疗 20 d,比较两组患者临床疗效及治疗前后心绞痛症状、血液流变学指标和血脂指标。**结果:**实验组治疗后的总有效率高于对照组( $P<0.05$ )。两组治疗后心绞痛发作次数、发作时长均减少,且实验组少于对照组( $P<0.05$ )。治疗后,两组的全血黏度、血浆黏度、红细胞聚集指数、纤维蛋白原(Fib)、总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)均低于治疗前,且实验组低于对照组, ( $P<0.05$ )。**结论:**川芎嗪在治疗 CHD 心绞痛方面具有显著的疗效,不仅能够有效改善患者心绞痛症状,还能改善血液流变学异常情况,因此值得临床推广使用。

**关键词:**冠心病;心绞痛;川芎嗪注射液;血液流变学

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## Influence of Ligustrazine Injection on Clinical Symptoms and Hemorheology in Patients With Coronary Heart Disease and Angina Pectoris

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**ABSTRACT Objective:** To explore the influence of ligustrazine injection on clinical symptoms and hemorheology in patients with coronary heart disease (CHD) and angina pectoris. **Methods:** 60 patients with CHD and angina pectoris who were treated in our hospital from March 2014 to March 2016 were selected, and they were divided into study group and control group with 30 cases in each group. The control group were treated conventional treatment, while the study group were treated ligustrazine injection on the basis of routine treatment. Two groups were treated for 20 days, and the clinical efficacy, angina symptoms, hemorheology index and blood lipid index of the two groups were compared before and after treatment. **Results:** The total effective rate of study group was higher than control group after treatment ( $P<0.05$ ). The angina attack frequency and duration in two groups were significantly lowered after treatment, and the study group was significantly lower than that of the control group ( $P<0.05$ ). The levels of whole blood viscosity, plasma viscosity, erythrocyte aggregation index, fibrinogen(Fib), total cholesterol(TC), triglyceride(TG), low density lipoprotein cholesterol(LDL-C) in two groups after treatment were lower than before treatment, and the study group was lower than the control group ( $P<0.05$ ). **Conclusion:** Ligustrazine has significant curative effect in treatment of CHD and angina pectoris, which not only can effectively improve the angina pectoris symptoms, but also improve hemorheology abnormal situation, therefore, it is worth promotion and application in clinic.

**Key words:** Coronary heart disease; Angina pectoris; Ligustrazine injection; Hemorheology

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### 前言

冠心病(coronary heart disease, CHD)是临床上最为常见的心血管疾病之一,常发于中老年人,患者通常存在较为严重的异常脂质代谢情况,使得患者原本光滑的动脉内膜出现脂质沉积,从而在血管内膜上形成黄白色的脂质斑块,斑块导致血管变窄,血流不畅,心肌缺乏充足的营养,患者便出现心肌缺血缺

氧,从而导致心绞痛的发生<sup>[1,2]</sup>。文献显示,脂质代谢紊乱、血液流变学异常等与冠心病心绞痛的发生和发展具有较强的相关性<sup>[3]</sup>。川芎嗪注射液作为临床常用的一种活血化淤类中药注射剂,其有效成分川芎嗪具有较强的降低血黏度、改善血流动力学、扩张冠状动脉及抗凝等作用,可以有效缓解心肌缺血状态,显著降低 CHD 心绞痛患者发病率<sup>[4,5]</sup>。目前,相关研究主要集中在评价川芎嗪注射液对 CHD 心绞痛的临床疗效,缺少对其作用机制的研究。本研究采用川芎嗪注射液治疗 CHD 心绞痛,旨在分析其对患者临床症状及血液流变学的影响,现报道如下。

### 1 资料与方法

#### 1.1 一般资料

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收集 2014 年 3 月至 2016 年 3 月我院收治的 60 例 CHD 心绞痛患者,所有患者均符合世界卫生组织(WHO)与国际心脏病学会和协会对冠心病的诊断标准,即符合《缺血性心脏病的命名及诊断标准》<sup>[6]</sup>,经临床症状及心电图确诊;排除具有免疫系统疾病患者,合并心肌梗死、心脏扩大以及其他脏器严重疾病的患者。按照随机数字表法将患者均分为实验组和对照组,实验组 30 例,男 18 例,女 12 例;年龄 45~80 岁,平均年龄(62.03±5.73)岁;病程 3~10 年,平均病程(5.26±4.12)年;美国纽约心脏病学会(NYHA)分级:I 级 8 例、II 级 15 例、III 级 7 例。对照组 30 例,男 17 例,女 13 例;年龄 43~78 岁,平均年龄(57.97±5.88)岁;病程 5~11 年,平均病程(5.63±6.86)年;NYHA 分级:I 级 9 例、II 级 16 例、III 级 5 例。两组患者的性别构成比、年龄等基线治疗经比较无统计学差异( $P>0.05$ )。

## 1.2 方法

患者均接受健康生活方式的指导,如禁止吸烟,禁止饮酒、日常进食低盐低脂饮食、适当活动、控制自身情绪避免忌情绪过分波动。根据患者个体病情严重程度,适当给予强心利尿降血压等对症处理。其中对照组患者给予阿司匹林(拜耳医药保健有限公司,国药准字 J20080078)100 mg/次/d 和吸氧等常规治疗。实验组在对照组患者的基础上给予川芎嗪注射液(江苏先声药业有限公司,国药准字 H20058845)40 mg/d 进行治疗。均治疗 2 个疗程,每个疗程 10 d。

## 1.3 观察指标

(1)治疗后评估两组患者的疗效<sup>[7]</sup>:① 显效:I、II 级心绞痛

基本消失,心绞痛症状分级下降 2 级,心电图不再异常;② 有效:I 级心绞痛基本消失,心绞痛症状分级下降 1 级,心电图显示 ST 段降低,与治疗前比较回升  $>0.05$  mV,但仍没达到正常水平;无效:患者心绞痛症状没有得到显著的改善,治疗前后心电图表现一致。总有效率=(显效患者+有效患者)/患者总数 $\times 100\%$ 。(2)记录治疗前后心绞痛发作次数及发作时长。(3)两组患者入院 1 d 及治疗 20 d 后,空腹肘静脉取血 5 mL,4℃ 环境下 3000 r/min 离心 10 min 分离出血浆,放 -20℃ 冰箱保存。采用北京普利生仪器有限公司 LBY-N6G 全自动血液流变仪检测全血黏度、血浆黏度、红细胞聚集指数、纤维蛋白原(Fibrinogen, Fib)及红细胞比容(Hematocrit, Hct),利用 Mindray BS-300/BS-330E 全自动生化分析仪对总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)进行检测,并分析各项指标与分组的关系。

## 1.4 统计学方法

采用 SPSS 19.0 统计软件录入数据及统计分析,计量资料采用( $\bar{x} \pm s$ )描述,两独立样本比较采用成组 t 检验,计数资料采用率(%)描述,比较采用卡方检验,检验标准 $\alpha=0.05$ 。

# 2 结果

## 2.1 两组患者临床疗效比较

治疗后实验组总有效率高于对照组( $X^2=11.368, P=0.000$ ),见表 1。

表 1 两组患者临床疗效对比[n(%)]

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

| Groups        | n  | Excellence | Effective | Invalid   | Total effective rate |
|---------------|----|------------|-----------|-----------|----------------------|
| Control group | 30 | 11(36.67)  | 9(30.00)  | 10(33.33) | 20(66.67)            |
| Study group   | 30 | 14(46.67)  | 13(43.33) | 3(10.00)  | 27(90.00)            |

## 2.2 两组治疗前后心绞痛发作次数、发作时长比较

治疗后,两组的心绞痛发作次数、发作时长均较治疗前减

少,且实验组心绞痛发作次数、发作时长少于对照组( $P<0.05$ )。见表 2。

表 2 治疗前后两组心绞痛发作次数、发作时长比较

Table 2 Comparison of angina pectoris attack frequency and duration before and after treatment

| Groups        | n  | Attack frequency(times) |                 | Attack duration(min) |                 |
|---------------|----|-------------------------|-----------------|----------------------|-----------------|
|               |    | Before treatment        | After treatment | Before treatment     | After treatment |
| Control group | 30 | 3.17±1.02               | 2.65±0.96*      | 5.64±1.31            | 4.33±1.12*      |
| Study group   | 30 | 3.21±1.08               | 1.51±0.55**     | 5.57±1.17            | 2.47±0.75**     |
| t             |    | 1.895                   | 9.925           | 2.965                | 6.965           |
| P             |    | 0.206                   | 0.010           | 0.113                | 0.020           |

Note: Compared with before treatment, \* $P<0.05$ ; Compared with study group, \*\* $P<0.05$ .

## 2.3 两组血液流变学指标比较

两组治疗后的全血黏度、血浆黏度、红细胞聚集指数及 Fib 均低于治疗前,且实验组各指标均低于对照组( $P<0.05$ )。见表 3。

## 2.4 两组血脂指标比较

两组治疗后的血浆 TC、TG 及 LDL-C 水平较治疗前降低,且实验组治疗后血浆 TC、TG 及 LDL-C 水平低于对照组( $P<0.05$ )。见表 4。

# 3 讨论

表 3 治疗前后两组各血液流变学指标比较

Table 3 Comparison of hemorheology indexes before and after treatment in the two groups

| Groups        | n  | Whole blood viscosity |                         | Plasma viscosity(mPa·s) |                         | Red cell aggregation index(%) |                         | Fib( g/L )       |                         | Hct( % )         |                 |
|---------------|----|-----------------------|-------------------------|-------------------------|-------------------------|-------------------------------|-------------------------|------------------|-------------------------|------------------|-----------------|
|               |    | (mPa·s)               |                         | s)                      |                         |                               |                         |                  |                         |                  |                 |
|               |    | Before treatment      | After treatment         | Before treatment        | After treatment         | Before treatment              | After treatment         | Before treatment | After treatment         | Before treatment | After treatment |
| Control group | 30 | 5.23±1.22             | 4.63±1.14*              | 1.63±0.64               | 1.55±0.35*              | 4.35±0.35                     | 3.62±0.54*              | 3.57±0.55        | 3.08±0.32*              | 48.12±3.09       | 48.11±3.11      |
| Study group   | 30 | 5.19±1.19             | 3.59±1.11* <sup>#</sup> | 1.61±0.51               | 1.21±0.42* <sup>#</sup> | 4.31±0.36                     | 2.59±0.53* <sup>#</sup> | 3.51±0.33        | 2.11±0.58* <sup>#</sup> | 48.11±3.10       | 47.55±3.07      |
| t             | -  | 0.821                 | 6.937                   | 0.903                   | 5.357                   | 0.891                         | 7.500                   | 1.122            | 14.089                  | 0.722            | 0.805           |
| P             | -  | 0.503                 | 0.009                   | 0.437                   | 0.037                   | 0.110                         | 0.018                   | 0.375            | 0.005                   | 0.573            | 0.613           |

Note: Compared with before treatment, \*P<0.05; Compared with study group, <sup>#</sup>P<0.05.

表 4 治疗前后两组各血脂指标比较

Table 4 Comparison of blood lipid indexes before and after treatment in the two groups

| Groups        | n  | TC( mmol/L )     |                         | TG( mmol/L )     |                         | LDL-C( mmol/L )  |                         | HDL-C( mmol/L )  |                 |
|---------------|----|------------------|-------------------------|------------------|-------------------------|------------------|-------------------------|------------------|-----------------|
|               |    |                  |                         |                  |                         |                  |                         |                  |                 |
|               |    | Before treatment | After treatment         | Before treatment | After treatment         | Before treatment | After treatment         | Before treatment | After treatment |
| Control group | 30 | 6.16±1.06        | 5.72±0.99*              | 1.89±0.87        | 1.69±0.41*              | 3.94±0.71        | 3.17±0.85*              | 1.19±0.26        | 1.28±0.27       |
| Study group   | 30 | 6.13±1.03        | 5.17±0.81* <sup>#</sup> | 1.91±0.92        | 1.41±0.35* <sup>#</sup> | 3.96±0.69        | 2.66±0.51* <sup>#</sup> | 1.20±0.25        | 1.34±0.40       |
| t             | -  | 0.614            | 5.357                   | 1.214            | 0.891                   | 0.715            | 7.113                   | 0.722            | 0.802           |
| P             | -  | 0.701            | 0.037                   | 0.312            | 0.514                   | 0.605            | 0.008                   | 0.597            | 0.534           |

Note: Compared with before treatment, \*P<0.05; Compared with study group, <sup>#</sup>P<0.05.

CHD 作为中老年人常见的心血管疾病,其死亡率和发病率均较高<sup>[8]</sup>。目前在我国,CHD 仍然是心脑血管疾病中对中老年人健康危害最严重的疾病,也是心血管疾病致死的重要原因,并且该病严重时往往需要手术介入,治疗费用较高,常给患者带来沉重经济负担。目前研究已发现<sup>[9]</sup>,CHD 发病原因主要是由于患者体内血脂代谢出现异常,导致冠状动脉发生粥样硬化性狭窄,甚至形成血栓阻塞血管,从而造成心肌的缺血缺氧。心绞痛是 CHD 常见的临床症状,是由于各种因素增加了突发心肌耗氧量,同时有脂质斑块的狭窄冠状动脉无法提供充足的血液供应量所致的心肌暂时性缺血,临床症状表现为胸痛、胸闷、心悸等<sup>[10]</sup>。CHD 的高危因素包括高血压、吸烟、糖尿病、肥胖等,部分研究表明,长期存在以上危险因素,最终会引起血液流变学改变<sup>[11]</sup>。临床试验结果发现<sup>[12]</sup>,当血液流变学改变时,特别是血浆粘度升高,冠状动脉内血流阻力增加,微循环灌注减少,加重心绞痛程度。川芎嗪为伞形科多年生草本植物,具有抑制血小板聚集、扩张小动脉、改善微循环和脑血流的作用。目前,临床上川芎嗪主要用于治疗高血压、CHD、缺血性脑血管疾病等,疗效明显<sup>[13]</sup>。

本研究将川芎嗪用于 CHD 合并心绞痛患者治疗,结果发现其治疗总有效率为 90.00%,而对照组总体有效率仅为 66.67%,提示川芎嗪注射液具有明显改善患者心功能,降低患者心功能分级的作用。本组研究还发现,实验组患者经过治疗后其心绞痛发作次数和持续时间均显著降低,同时实验组明显

低于对照组,提示川芎嗪注射液具有较好的抑制 CHD 患者心绞痛发生和缩短患者心绞痛发作持续时间的作用。CHD 患者心绞痛发作常因患者情绪激动、运动量增加等原因导致心肌耗氧量突然增加,与此同时被脂质斑块占据的管腔变小的冠状动脉不能相应地供给充足的血液,从而导致心肌短暂性缺血,引起心前区疼痛、胸闷等心绞痛症状。川芎嗪通过抑制花生四烯酸 2 的代谢,从而增加血小板或者血浆内腺苷-3',5'-环化一磷酸(cAMP)的浓度,而血小板内 cAMP 生成过多就会阻止脂联素(ADP)的释放,从而阻碍 ADP 介导的血小板活化作用来抑制血小板聚集,同时川芎嗪注射液还可以通过置换血小板膜上的 Ca<sup>2+</sup> 使得血小板膜上正电荷减少,负电荷增加,相同电荷增加之后发生同种电荷排斥效应,从而有效的阻止了血小板的聚集<sup>[14]</sup>。此外,川芎嗪还在一定程度上具有促使已经聚集的血小板发生解聚的作用。同时,川芎嗪还具有对抗肾上腺素和氯化钾引起的动脉收缩效应,从而在患者可能发生心绞痛时,其可通过对抗肾上腺素和氯化钾从而减弱冠脉收缩,使冠状动脉处于舒张状态,从而让冠状动脉的血流不至于显著减少,同时降低动脉的压力和冠状动脉的阻力,进而保证心肌的有效供血,减少心绞痛发生频率和持续时间降低<sup>[15]</sup>。治疗后两组患者全血黏度、血浆黏度、红细胞聚集指数及 Fib 和 TC、TG 及 LDL-C 均低于治疗前,且实验组低于对照组(P<0.05)。说明川芎嗪可针对性的降低血液流变学异常,促进血液内 TG、TC、LDL-C 的代谢转运,从而发挥治疗 CHD 心绞痛的作用。研究显示<sup>[16]</sup>,血

脂异常与血液流变学指标异常与患者动脉粥样硬化密切相关。动脉粥样硬化是由于长期高血脂症对动脉内膜形成功能性的损伤,导致血管内皮细胞表面生物学特性发生改变,黏附因子增加,单核细胞黏附聚集并渗透进入血管内皮细胞间质,形成巨噬细胞,巨噬细胞吞噬低密度脂蛋白从而演变为泡沫细胞,泡沫细胞堆积形成动脉粥样硬化的早期病变,即脂质条纹。由于血浆当中低密度脂蛋白等的持续升高,脂质堆积导致形成脂质核心,而此时巨噬细胞合成细胞因子刺激平滑肌进入到脂质条纹中,从而促使脂质条纹最终演变为粥样斑块。粥样斑块的形成为导致血液循环不畅,流动受阻,出现更多的湍流,进一步损伤血管内壁,从而出现恶性循环。同时,血脂增加以及血小板聚集导致血液黏度增加,从而出现血液流变学改变等<sup>[17,18]</sup>。川芎嗪能够通过增加内皮细胞前列环素,对血管内皮细胞损伤起到治疗作用和保护作用,同时能够抑制血栓素 A2 合成,从而减少血小板聚集,降低血浆粘度,并直接激活纤溶酶原促使聚集血小板解聚,从而对 CHD 心绞痛患者发挥治疗作用<sup>[19,20]</sup>。

综上所述,川芎嗪在治疗 CHD 心绞痛方面具有显著的疗效,其不单对患者心绞痛症状改善具有良好的功效,同时还具有改善血液流变学指标等功能,值得在临床上推广使用。

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