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灯盏生脉胶囊联合单硝酸异山梨酯缓释片对老年冠心病心绞痛患者 心功能、血脂及血清 IL-6、CRP 水平的影响*

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摘要 目的:观察单硝酸异山梨酯缓释片联合灯盏生脉胶囊对老年冠心病心绞痛患者血脂、心功能及血清 C 反应蛋白(CRP)、白介素-6(IL-6)水平的影响。**方法:**选择 2018 年 3 月至 2020 年 7 月期间我院收治的 92 例老年冠心病心绞痛患者,采用随机数字表将患者分为两组,分别为对照组 46 例和研究组 46 例。对照组给予单硝酸异山梨酯缓释片治疗,研究组则给予灯盏生脉胶囊联合单硝酸异山梨酯缓释片治疗,疗程均为 3 个月。对比两组临床症状、心电图变化、心功能、血脂及血清 IL-6、CRP 水平,记录两组不良反应发生情况。**结果:**研究组的临床总有效率高于对照组($P<0.05$);研究组的心电图总改善率高于对照组($P<0.05$)。治疗 3 个月后,两组血清低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、总胆固醇(TC)、IL-6、CRP 水平较治疗前降低,且研究组低于对照组($P<0.05$),高密度脂蛋白胆固醇(HDL-C)水平较治疗前升高,且研究组高于对照组($P<0.05$)。治疗 3 个月后,两组左心室收缩末期内径(LVESD)较治疗前降低,且研究组低于对照组($P<0.05$),左心室射血分数(LVEF)、心输出量(CO)较治疗前升高,且研究组高于对照组($P<0.05$)。两组不良反应发生率组间对比无差异($P>0.05$)。治疗 3 个月后,研究组硝酸甘油用量少于对照组,心绞痛发作频率、心绞痛持续时间、心绞痛缓解时间短于对照组($P<0.05$)。**结论:**老年冠心病心绞痛患者在单硝酸异山梨酯缓释片治疗的基础上联合灯盏生脉胶囊治疗,效果显著,可有效改善其心功能、血脂,调节炎症因子水平,安全性较好。

关键词:老年;灯盏生脉胶囊;血脂;冠心病心绞痛;C 反应蛋白;单硝酸异山梨酯缓释片;心功能;白介素-6

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Effects of Dengzhan Shengmai Capsule Combined with Isosorbide Mononitrate on Cardiac Function, Blood Lipid, Serum IL-6 and CRP Levels in Elderly Patients with Coronary Heart Disease and Angina Pectoris*

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ABSTRACT Objective: To observe the effect of isosorbide mononitrate combined with Dengzhan Shengmai Capsule on blood lipid, cardiac function and serum C-reactive protein (CRP) and interleukin-6 (IL-6) levels in elderly patients with coronary heart disease and angina pectoris. **Methods:** 92 elderly patients with coronary heart disease and angina pectoris in our hospital from March 2018 to July 2020 were selected, and they were divided into two groups by drawing lots, 46 cases in the control group and 46 cases in the study group. The control group was treated with isosorbide mononitrate, while the study group was treated with Dengzhan Shengmai capsule combined with isosorbide mononitrate. The course of treatment was 3 months. The clinical symptoms, electrocardiographic effect, cardiac function, blood lipid, serum IL-6 and CRP levels were compared between the two groups, and the incidence of adverse reactions was recorded. **Results:** The total effective rate of the study group was higher than that of the control group ($P<0.05$). The total effective rate of electrocardiographic in the study group was higher than that in the control group ($P<0.05$). After 3 months of treatment, the levels of serum low density lipoprotein cholesterol (LDL-C), triglyceride (TG), total cholesterol (TC), IL-6 and CRP in the two groups were lower than those before treatment, and the level of high density lipoprotein cholesterol (HDL-C) in the study group was higher than that in the control group ($P<0.05$). After 3 months of treatment, the left ventricular end systolic diameter (LVESD) of the two groups was lower than

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that before treatment, and the study group was lower than that of the control group ($P<0.05$), the left ventricular ejection fraction (LVEF) and cardiac output (CO) were higher than those before treatment, and the study group was higher than that of the control group ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). After 3 months of treatment, the dosage of nitroglycerin in the study group was less than that in the control group, the frequency of angina pectoris attack, the duration of angina pectoris and the remission time of angina pectoris in the study group were shorter than those in the control group ($P<0.05$). **Conclusion:** The combination of isosorbide mononitrate sustained-release tablets and Dengzhan Shengmai capsule in the treatment of elderly patients with coronary heart disease and angina pectoris has significant effect, which can effectively improve their cardiac function, blood lipid, regulate the level of inflammatory factors, and has good safety.

Key words: Elderly; Dengzhan Shengmai capsule; Blood lipid; Angina pectoris of coronary heart disease; C-reactive protein; Isosorbide mononitrate sustained release tablets; Cardiac function; Interleukin-6

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前言

冠心病心绞痛是指由于冠状动脉粥样硬化引起的心肌缺氧、缺血,进而导致胸部发作性疼痛或不适^[1]。若未能得到及时治疗,可引起心肌梗死甚至死亡^[2]。目前,临床主要采用硝酸酯类药物、钙拮抗剂、抗凝类药物、抗血小板药物、 β 受体阻滞剂等药物治疗冠心病心绞痛^[3]。单硝酸异山梨酯缓释片是治疗冠心病心绞痛的常用药物,通过松弛血管平滑肌,扩张血管来降低心肌的负荷,进而改善胸闷、胸痛等症状^[4],然而单硝酸异山梨酯缓释片同时也可扩张脑血管,易引起头痛,一定程度上限制疗效提升^[5,6]。灯盏生脉胶囊的主要成分为人参、五味子、灯盏细辛、麦冬,可发挥活血健脑、益气养阴的功效^[7]。本研究选取我院收治的部分老年冠心病心绞痛患者,在单硝酸异山梨酯缓释片基础上辅助灯盏生脉胶囊治疗,观察其治疗效果,以期为临床应用提供指导。

1 资料与方法

1.1 临床资料

选择2018年3月至2020年7月期间我院收治的老年冠心病心绞痛患者92例。诊断标准参考《慢性稳定性心绞痛诊断与治疗指南》^[8]中的相关标准:静息心电图有两个及以上的相邻导联ST段下移 ≥ 0.1 mV,有阵发性胸痛症状。纳入标准:(1)患者及家属均知情同意参加本研究;(2)年龄 ≥ 60 岁;(3)经临床表现、心电图、超声心动图等确诊。排除标准:(1)ST段抬高的急性心肌梗死者;(2)对本次研究用药存在过敏症者;(3)合并严重高血压、肝肾功能异常、糖尿病等疾病者;(4)因其他心脏疾病、神经系统疾病、消化系统疾病所致胸痛者;(5)合并血液系统疾病、恶性肿瘤、自身免疫性疾病者;(6)妊娠或哺乳期妇女;(7)同时参与其他研究者。采用随机数字表法将患者分为研究组46例、对照组46例,研究组女20例,男26例,年龄61~78岁,平均(70.26 \pm 4.23)岁;心绞痛分级:II级10例、III级28例、IV级8例;病程7个月~5年,平均(3.19 \pm 0.61)年;体质指数20~26 kg/m²,平均(23.41 \pm 0.52)kg/m²。对照组女19例,男27例,年龄60~75岁,平均(69.92 \pm 4.64)岁;心绞痛分级:II级8例、III级29例、IV级9例;病程10个月~5年,平均(3.19 \pm 0.51)年;体质指数20~27 kg/m²,平均(23.32 \pm 0.57)kg/m²。两组患者一般资料对比无差异($P>0.05$),具有可比性。

1.2 治疗方法

对照组给予单硝酸异山梨酯缓释片(批准文号:国药准字H19991039,山东鲁南贝特制药有限公司,规格:40 mg/片),口服,40 mg/次,1次/天。研究组给予单硝酸异山梨酯缓释片(用药方案同对照组)联合灯盏生脉胶囊(批准文号:国药准字Z20026439,云南生物谷药业股份有限公司,规格:0.18 g/粒)治疗,口服,2粒/次,3次/d。两组均治疗3个月。

1.3 评价指标

(1)临床疗效^[9]:心绞痛发作频率和持续时间降低80%以上,心电图恢复正常为显效。心绞痛发作频率和持续时间降低50%~80%,心电图ST段回升0.05 mV以上为有效。心电图没有改善,心绞痛发作频率和持续时间降低不到50%为无效。总有效率=显效率+有效率。(2)心电图变化:心电图恢复正常为显效;心电图ST段回升0.05 mV以上为有效;心电图有所改善但为达到上述标准为无效。总改善率=显效率+有效率。(3)心功能:于治疗前、治疗3个月后使用心功能检测仪测定左心室收缩末期径(LVESD)、左心室射血分数(LVEF)、心输出量(CO)。(4)血脂及炎症因子:分别抽取两组治疗前、治疗3个月后次日空腹静脉血4 mL,C反应蛋白(CRP)、白介素-6(IL-6)水平采用酶联免疫吸附试验法检测。血清中低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、高密度脂蛋白胆固醇(HDL-C)、总胆固醇(TC)水平采用全自动生化分析仪检测。(5)安全性评价:观察两组不良反应发生情况,包括肝肾功能异常、晕厥、低血压、心动过缓、头痛等。(6)临床症状:观察两组患者治疗前、治疗3个月后的心绞痛发作频率、心绞痛持续时间、硝酸甘油用量、心绞痛缓解时间。

1.4 统计学方法

采用SPSS25.0进行统计分析,计量资料用($\bar{x} \pm s$)表示,采用t检验,计数资料以率(%)表示,采用 χ^2 检验,以 $\alpha=0.05$ 为检验标准, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组疗效及心电图变化对比

两组临床疗效显示,研究组无效5例,有效26例,显效15例,临床疗效总有效率为89.13%(41/46);对照组无效16例,有效21例,显效9例,临床总有效率为65.22%(30/46);研究组的临床总有效率高高于对照组($\chi^2=7.472, P=0.000$)。两组心电图变

化显示,对照组显效 10 例,有效 22 例,无效 14 例,心电图总改善率为 69.57%(32/46);研究组显效 17 例,有效 25 例,无效 4 例,心电图总改善率为 91.30%(42/46);研究组的心电图总改善率高于对照组($\chi^2=6.825, P=0.000$)。

2.2 两组血脂指标对比

治疗前,两组血脂指标组间比较无差异($P>0.05$),治疗 3 个月后,两组 LDL-C、TG、TC 下降,HDL-C 升高($P<0.05$),治疗 3 个月后,研究组 HDL-C 高于对照组,LDL-C、TG、TC 低于对照组($P<0.05$),详见表 1。

表 1 两组血脂指标对比($\bar{x} \pm s$)

Table 1 Comparison of blood lipid indexes between the two groups($\bar{x} \pm s$)

| Groups | Time | LDL-C(mmol/L) | TG(mmol/L) | HDL-C(mmol/L) | TC(mmol/L) |
|---------------------|--------------------------|---------------|--------------|---------------|--------------|
| Control group(n=46) | Before treatment | 3.81± 0.78 | 2.54± 0.49 | 1.32± 0.29 | 6.35± 0.54 |
| | 3 months after treatment | 2.64± 0.63* | 1.88± 0.37* | 1.71± 0.34* | 4.87± 0.39* |
| Study group(n=46) | Before treatment | 3.78± 0.54 | 2.57± 0.43 | 1.35± 0.37 | 6.39± 0.58 |
| | 3 months after treatment | 1.89± 0.47*# | 1.43± 0.32*# | 1.93± 0.38*# | 3.51± 0.42*# |

Note: compared with before treatment, * $P<0.05$. compared with control group treatment, # $P<0.05$.

2.3 两组血清 IL-6、CRP 对比

治疗前,两组 IL-6、CRP 比较未见差异($P>0.05$),治疗 3 个月后,两组 IL-6、CRP 较治疗前降低($P<0.05$),治疗 3 个月后,研究组 IL-6、CRP 较对照组低($P<0.05$),详见表 2。

表 2 两组血清 IL-6、CRP 对比($\bar{x} \pm s$)

Table 2 Comparison of serum IL-6 and CRP between the two groups($\bar{x} \pm s$)

| Groups | Time | IL-6(pg/mL) | CRP(mg/L) |
|---------------------|--------------------------|----------------|--------------|
| Control group(n=46) | Before treatment | 113.27± 28.54 | 6.24± 0.53 |
| | 3 months after treatment | 82.71± 19.42* | 4.78± 0.42* |
| Study group(n=46) | Before treatment | 112.08± 15.59 | 6.11± 0.42 |
| | 3 months after treatment | 64.34± 12.63*# | 3.14± 0.36*# |

Note: compared with before treatment, * $P<0.05$. compared with control group treatment, # $P<0.05$.

2.4 两组心功能指标对比

治疗前,两组 LVEF、LVESD、CO 比较未见差异($P>0.05$),治疗 3 个月后,两组 LVESD 较治疗前降低,LVEF、CO 较治疗前升高($P<0.05$),治疗 3 个月后,研究组 LVESD 低于对照组,LVEF、CO 高于对照组($P<0.05$),详见表 3。

治疗 3 个月后,两组 LVESD 较治疗前降低,LVEF、CO 较治疗

表 3 两组心功能指标对比($\bar{x} \pm s$)

Table 3 Comparison of cardiac function indexes between the two groups($\bar{x} \pm s$)

| Groups | Time | LVESD(cm) | LVEF(%) | CO(L/min) |
|---------------------|--------------------------|--------------|---------------|--------------|
| Control group(n=46) | Before treatment | 4.31± 0.47 | 43.67± 5.82 | 3.24± 0.38 |
| | 3 months after treatment | 3.48± 0.39* | 49.78± 4.51* | 4.73± 0.41* |
| Study group(n=46) | Before treatment | 4.26± 0.34 | 44.54± 6.23 | 3.19± 0.42 |
| | 3 months after treatment | 3.02± 0.27*# | 56.41± 6.18*# | 5.91± 0.57*# |

Note: compared with before treatment, * $P<0.05$. compared with control group treatment, # $P<0.05$.

2.5 两组临床症状缓解情况对比

治疗前,两组硝酸甘油用量、心绞痛持续时间、心绞痛发作频率、心绞痛缓解时间对比无差异($P>0.05$),治疗 3 个月后,两组硝酸甘油用量减少,心绞痛发作频率、心绞痛缓解时间、心绞痛持续时间缩短($P<0.05$),治疗 3 个月后,研究组硝酸甘油用量少于对照组,心绞痛持续时间、心绞痛发作频率、心绞痛缓解时间短于对照组($P<0.05$),详见表 4。

治疗前,两组硝酸甘油用量、心绞痛持续时间、心绞痛发作频率、心绞痛缓解时间对比无差异($P>0.05$),治疗 3 个月后,两组硝酸甘油用量减少,心绞痛发作频率、心绞痛缓解时间、心绞痛持续时间缩短($P<0.05$),治疗 3 个月后,研究组硝酸甘油用量少于对照组,心绞痛持续时间、心绞痛发作频率、心绞痛缓解时间短于对照组($P<0.05$),详见表 4。

2.6 两组不良反应发生率对比

3 讨论

现有的研究认为冠心病心绞痛的发病机制主要是血脂过高引起的血液黏稠,在凝血、炎症等因素的影响下作用于冠状动脉内膜,形成粥样斑块,导致心脏组织缺血、缺氧,引发心绞痛^[10,11]。冠心病患者中约有 80%伴有心脏痛,随着患者病情恶化,心绞痛症状加重以及用药量的增加,最终可导致心功能不

对照组不良反应发生率为 13.04%,包括肝功能异常心动过缓各 1 例,头痛、低血压各 2 例。研究组不良反应发生率为

表 4 两组临床症状缓解情况对比
Table 4 Comparison of clinical symptom relief between the two groups

| Groups | Time | Angina attack frequency (n/week) | Duration of angina pectoris (min/n) | Angina relief time (min) | Nitroglycerin dosage (mg) |
|---------------------|--------------------------|----------------------------------|-------------------------------------|--------------------------|---------------------------|
| Control group(n=46) | Before treatment | 7.33± 1.58 | 8.95± 1.31 | 8.26± 1.37 | 8.72± 1.33 |
| | 3 months after treatment | 5.02± 1.12* | 6.37± 1.08* | 6.28± 1.29* | 6.07± 1.26* |
| Study group(n=46) | Before treatment | 7.39± 1.13 | 8.89± 1.14 | 8.31± 1.24 | 8.65± 1.27 |
| | 3 months after treatment | 3.83± 0.86*# | 4.35± 0.83 *# | 3.24± 0.82*# | 4.49± 0.83*# |

Note: compared with before treatment, *P<0.05. compared with control group treatment, #P<0.05.

可逆性损伤而导致死亡^[12,13]。治疗冠心病心绞痛最主要的目的在于提高患者冠状动脉供血,恢复心肌供血供氧情况。单硝酸异山梨酯缓释片能有效激活环磷酸鸟苷依赖性蛋白激酶的活性,改善心肌缺血、缺氧程度,缓解心绞痛症状^[14,15]。现临床有关西药治疗冠心病心绞痛的研究已至瓶颈,加上冠心病心绞痛的患病群体以老年为主,老年冠心病心绞痛合并基础疾病多,身体各项机能退化,长期单一用药不良反应较大,有待进一步的疗效提升。在中医学中,冠心病心绞痛发病原因是气阴两虚、血行不畅,中医的治疗认为可用活血、化瘀、通经络来缓解心绞痛^[16]。既往研究报道证实^[17],灯盏生脉胶囊可抑制血小板及红细胞凝聚,减少血浆内皮素大量释放,具有良好的抗心肌缺血作用。

本次研究结果显示,研究组心绞痛症状缓解情况、心功能改善情况均优于对照组,疗效优越。说明灯盏生脉胶囊联合单硝酸异山梨酯缓释片对老年冠心病心绞痛患者有较好的治疗效果,可能与单硝酸异山梨酯缓释片、灯盏生脉胶囊均具有良好的抗心肌缺血作用,可发挥协同增效作用,继而减轻心功能损伤有关。血清炎性因子在冠心病心绞痛的发生过程中发挥重要作用,IL-6 可释放氧自由基,使心肌细胞受损^[18],高浓度的 CRP 既可激活斑块内膜中的补体,破坏内皮细胞功能,又可参与动脉粥样硬化斑块形成^[19]。本研究结果显示灯盏生脉胶囊联合单硝酸异山梨酯缓释片治疗可有效调节炎症细胞因子水平。灯盏生脉胶囊中的有效化学成分咖啡酸酯、灯盏花素、芹菜素等酮类化合物具有清除氧自由基、抑制血小板聚集、抗炎、改善微循环、抗缺血再灌注损伤等作用^[20]。冠心病心绞痛患者中往往伴有明显的血脂异常,而在引发冠心病心绞痛的因素中,高血脂也是最常见和最危险的因素之一,高血脂可升高血液黏稠度,加快动脉粥样硬化进程,引起心脏血管的微循环障碍^[21,22]。因此,血脂的调节效果也常被用作冠心病心绞痛治疗效果的观察指标之一。本次研究结果证实灯盏生脉胶囊联合单硝酸异山梨酯缓释片具有显著的调脂效果。以往的基础实验证实灯盏生脉胶囊中的有效化学成分咖啡酸酯可明显降低小鼠肝脏中 TC 浓度^[23]。不少学者的研究也表明灯盏生脉胶囊可有效降低血液粘稠度,通过多种途径实现抗氧化作用,从而调节 TG 水平^[24,25]。另通过对比两组安全性可知,灯盏生脉胶囊联合单硝酸异山梨酯缓释片不会增加不良反应发生率,属于相对安全的用药方案。

综上所述,老年冠心病心绞痛患者在单硝酸异山梨酯缓释片治疗的基础上联合灯盏生脉胶囊治疗,效果显著,可有效改善其血脂、心功能及炎症刺激,安全有效,但本研究未设置随访观察患者远期预后,且纳入病例数较少,有待扩大样本、增加随访作进一步研究。

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