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复方丹参滴丸联合沙库巴曲缬沙坦对老年心肌梗死患者 PCI 术后 炎症反应、心室重塑和心肌灌注的影响 *

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摘要 目的:探讨复方丹参滴丸联合沙库巴曲缬沙坦对老年心肌梗死患者经皮冠状动脉介入术(percutaneous coronary intervention, PCI)术后炎症反应、心室重塑和心肌灌注的影响。**方法:**采用随机数字表法将本院 2017 年 3 月至 2020 年 2 月间收治的行 PCI 治疗的 68 例老年心肌梗死为研究对象,分为对照组(34 例)和观察组(34 例)。两组均行常规药物治疗,在此基础上予以对照组沙库巴曲缬沙坦治疗,予以观察组复方丹参滴丸联合沙库巴曲缬沙坦治疗。比较两组治疗前后血浆中超敏 C 反应蛋白(high-sensitivity creactive protein, hs-CRP)、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、白细胞介素-8(interleukin-8, IL-8)、N 末端脑钠肽前体(N-terminal-pro-brain-natriuretic-peptide, NT-proBNP)、左室舒张末期前后径(left ventricular end-diastolic diamete, LVEDD)、左室射血分数(left ventricular ejection fraction, LVEF)、左室质量指数(left ventricular mass index, LVMI)以及治疗后 TIMI 血流分级。**结果:**两组血浆 hs-CRP、TNF- α 、IL-8 和 NT-proBNP 水平以及 LVEDD 和 LVMI 水平较治疗前明显降低, LVEF 水平明显增加($P<0.05$)。观察组治疗后血浆 hs-CRP、TNF- α 、IL-8 和 NT-proBNP 水平以及 LVEDD 和 LVMI 水平明显低于对照组, LVEF 水平明显高于对照组($P<0.05$)。两组术后 20 min TIMI 血流分级均明显好转,观察组术后 20 min 时 TIMI 血流分级明显优于对照组($P<0.05$)。两组不良反应总发生率比较无明显差异($P>0.05$)。**结论:**复方丹参滴丸联合沙库巴曲缬沙坦能够明显降低老年心肌梗死患者 PCI 术后炎症反应,抑制心室重塑,改善心肌灌注,安全性较高。

关键词:急性心肌梗死; PCI 手术; 复方丹参滴丸; 沙库巴曲缬沙坦; 老年; 炎症因子; 心室重塑; 心肌灌注

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Effects of Compound Danshen Dripping Pills Combined with Sarkubatrovalsartan on Elderly Patients with Myocardial Infarction after PCI*

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ABSTRACT Objective: To investigate the effects of Compound Danshen dripping pills combined with sarkubatrovalsartan on inflammatory response, ventricular remodeling and myocardial perfusion after percutaneous coronary intervention (PCI) in elderly patients with myocardial infarction. **Methods:** A total of 68 elderly patients with myocardial infarction, who were treated with PCI in Aerospace Central Hospital from March 2017 to February 2020, were chosen as research subjects and randomly divided into control group (n=34) and observation group (n=34). The two groups were treated with conventional drug therapy, on the basis of which, the patients in the control group were treated with sakubatravalsartan, and the patients in the observation group were treated with Compound Danshen dripping pills combined with sarkubatrovalsartan. The plasma levels of high-sensitivity Creactive protein (hs CRP), tumor necrosis factor- α (TNF- α), interleukin-8 (IL-8), N-terminal pro brain natriuretic peptide (NT proBNP), left ventricular end-diastolic diamete (LVEDD), left ventricular ejection fraction (LVEF), and left ventricular mass index (LVMI) were compared between the two groups before and after treatment; TIMI blood flow classification and ST segment depression after treatment were analyzed. **Results:** The levels of hs CRP, TNF- α , IL-8, NT-proBNP, LVEDD and LVMI of the two groups were significantly lower than those before treatment, and LVEF levels were significantly increased ($P<0.05$). After treatment, the plasma levels of hs CRP, TNF- α , IL-8, NT-proBNP, LVEDD and LVMI of the observation group were significantly lower than these of the control group, and the LVEF level was significantly higher than that in the control group ($P<0.05$). The TIMI blood flow classification of the two groups was significantly improved 20 min after operation, and the TIMI blood flow classification of the observation group was significantly better than that of the control group ($P<0.05$).

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There was no significant difference in the total incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Compound Danshen dripping pills combined with sakubatrovalsartan can significantly reduce the inflammatory reaction, inhibit ventricular remodeling and improve myocardial perfusion in elderly patients with myocardial infarction.

Key words: Acute myocardial infarction; PCI operation; Compound Danshen dripping pills; Sakubatrovalsartan; Elderly; inflammatory factors; Ventricular remodeling; Myocardial perfusion

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前言

急性心肌梗死是临床常见的以发病急、病情进展快、死亡率高、预后差为主要特点的一种心血管疾病,已经成为引起我国居民死亡的最主要原因之一^[1]。老年人因机体功能衰退,并发病较多,是急性心肌梗死的主要易感人群^[2],PCI是目前治疗急性心肌梗死的重要手段,能够快速恢复患者闭塞血管血流^[3,4],但PCI术中容易引起血管内皮细胞损伤、心功能不全和术后复流术后复流还可能加重患者心肌血流再通后的再灌注损伤,进而诱发心力衰竭^[5,6]。有研究表明,急性心肌梗死患者因肾素-血管紧张素-醛固酮系统(RAAS)过度激活引起心室重构,因此临床多采用血管紧张素转换酶抑制剂类(ACEI)药物、醛固酮拮抗剂类药物抑制该系统过度激活,以达到改善心肌梗死心功能不全患者预后的效果,但仍可见部分急性心肌梗死患者在PCI术后出现心功能恶化^[7,8]。沙库巴曲缬沙坦是一种血管紧张素II受体拮抗剂(ARBs)药物,能够通过阻断血管紧张素II受体阻断RAAS系统,其效果优于ACEI类药^[9]。但西药毒副作用大、且价格较高,难以被广泛接受。复方丹参滴丸已被证实具有抗心肌缺血缺氧、改善心肌再灌注的作用^[10,11],本研究探讨复方丹参滴丸联合沙库巴曲缬沙坦对老年心肌梗死患者PCI术后炎症反应、心室重塑和心肌灌注的影响,报道如下。

1 资料与方法

1.1 一般资料

选取本院2017年3月至2020年2月间收治的行PCI治疗的68例老年心肌梗死患者,分为对照组和观察组,各34例。对照组,男18例、女16例;年龄62~74岁,平均(68.48±4.37)岁;纽约心功能分级(NYHA):II级11例、III级19例、IV级4例;合并基础疾病:糖尿病4例、高血压7例、高脂血症3例。观察组,男17例、女17例;年龄61~74岁,平均(68.85±4.43)岁;NYHA分级:II级9例、III级20例、IV级5例;合并基础疾病:糖尿病5例、高血压9例、高脂血症2例。两组一般资料比较无差异($P>0.05$)。

纳入标准:(1)符合中华医学会心血管分会2001年制定的急性心肌梗死诊断标准^[12];(2)年龄≥60岁;(3)在我院接受PCI手术;(4)患者家属均知情并同意本次研究。

排除标准:(1)合并重要脏器(肝肾等)功能不全者;(2)合并造血功能及免疫功能异常者;(3)合并精神疾病、认知功能低下等可造成沟通障碍者;(4)对本次研究所用药物过敏者。剔除未遵医嘱服药者。

1.2 治疗方法

两组入院后均接受常规治疗,入院当日给予对照组沙库巴

曲缬沙坦钠片(北京诺华制药有限公司;商品名:诺欣妥;批准文号:国药准字J20190001;规格:100 mg/片),100 mg/次,2次/d,连续给药3个月。观察组是在上述对照组治疗基础上给予复方丹参滴丸(天士力制药集团股份有限公司;批准文号:国药准字Z10950111;规格:27 mg/粒)治疗,20粒/次,3次/d,连用3 d后调整为10粒/次,3次/d,连续治疗3个月。

1.3 观察指标

(1)实验室指标:采集所有患者晨起空腹静脉血5 mL,3000 r/min离心5 min后分离血浆,检测血浆中hs-CRP、TNF- α 、IL-8、NT-proBNP。(2)心室重塑指标:分别于治疗前和治疗后采用美国GE公司LOGIQ 晶准E8彩色多普勒超声诊断仪测量患者LVEDD、LVEF、LVMI。(3)心肌灌注指标:分别于术前和术后20 min观察两组TIMI血流分级,0~1级为PCI术后未开通,2~3级为术后再通。(4)不良反应:记录两组治疗期间异常出血、胃肠不适、腹痛等。

1.4 统计学方法

采用SPSS 25.0。计量资料符合正态分布,表示为" $\bar{x}\pm s$ ",比较用t检验;计数资料表示为n(%),比较用 χ^2 检验。 $P<0.05$ 有统计学意义。

2 结果

2.1 两组血浆hs-CRP、TNF- α 、IL-8和NT-proBNP水平比较

两组血浆hs-CRP、TNF- α 、IL-8和NT-proBNP水平治疗前均无差异($P>0.05$)。经治疗,两组上述指标水平均明显降低($P<0.05$),且观察组较对照组更低($P<0.05$),见表1。

2.2 两组LVEDD、LVEF和LVMI水平比较

两组治疗前LVEDD、LVEF和LVMI水平比较无差异($P>0.05$)。经过治疗,两组LVEDD和LVMI水平明显下降,观察组的下降幅度较对照组大;LVEF水平明显上升($P<0.05$),观察组的增加幅度较对照组大($P<0.05$),见表2。

2.3 两组TIMI血流分级比较

两组术前TIMI血流分级比较,差异无统计学意义($Z=0.061$, $P>0.05$)。术后20 min时,两组TIMI血流分级均明显好转($P<0.05$)。观察组术后20 min时TIMI血流分级明显优于对照组($Z=2.003$, $P<0.05$),见表3。

2.4 两组不良反应发生情况比较

比较两组不良反应的发生情况可知,对照组(20.59%)略高于观察组(17.65%),但无明显差异($P>0.05$),见表4。

3 讨论

急性心肌梗死是因冠状动脉发生病变引起继发性血供减少,造成严重心肌缺血事件^[13]。老年是急性心肌梗死高发时期,

表 1 两组血浆 hs-CRP、TNF- α 、IL-8 和 NT-proBNP 水平比较($\bar{x}\pm s$)Table 1 Comparison of plasma hs-CRP, TNF- α , IL-8 and NT-proBNP levels between two groups ($\bar{x}\pm s$)

Indicators	Control group(n=34)		Observation group(n=34)	
	Pre-treatment	After treatment	Pre-treatment	After treatment
hs-CRP(mg/L)	7.65 $\pm$ 1.67	5.17 $\pm$ 1.32*	7.82 $\pm$ 1.63	3.29 $\pm$ 1.02**
TNF- α (ng/L)	29.81 $\pm$ 5.36	19.36 $\pm$ 4.59*	30.42 $\pm$ 6.28	12.18 $\pm$ 2.87**
IL-8(ng/mL)	31.59 $\pm$ 4.63	22.43 $\pm$ 3.19*	32.07 $\pm$ 4.81	17.08 $\pm$ 2.79**
NT-proBNP(pg/L)	4 105.74 $\pm$ 459.65	1 364 $\pm$ 318.75*	4 198.65 $\pm$ 510.63	782.59 $\pm$ 204.72**

Note: Compared with Pre-treatment of the same group, * $P<0.05$; compared with the control group at the same time, ** $P<0.05$.

表 2 两组 LVEDD、LVEF 和 LVMI 水平比较($\bar{x}\pm s$)Table 2 Comparison of LVEDD, LVEF and LVMI levels between two groups ($\bar{x}\pm s$)

Indicators	Control group(n=34)		Observation group(n=34)	
	Pre-treatment	After treatment	Pre-treatment	After treatment
LVEDD(mm)	41.02 $\pm$ 2.78	37.46 $\pm$ 2.49*	41.28 $\pm$ 3.15	32.36 $\pm$ 2.75**
LVEF(%)	46.26 $\pm$ 5.46	50.34 $\pm$ 5.18*	46.13 $\pm$ 5.72	55.49 $\pm$ 6.37**
LVMI(g/m ²)	131.18 $\pm$ 10.54	122.63 $\pm$ 10.10*	131.76 $\pm$ 11.43	104.73 $\pm$ 10.85**

表 3 两组术前和术后 20 minTIMI 血流分级比较[例(%)]

Table 3 Comparison of TIMI blood flow grading before and 20 min after operation between two groups [n (%)]

Groups	Time	Level 0	Level 1	Level 2	Level 3
Control group(n=34)	Preoperative	13(38.24)	19(55.88)	2(5.88)	0(0.00)
	20 min postoperatively	3(8.82)	7(20.59)	10(29.41)	14(41.18)
	Z	5.181			
	P	0.000			
Observation group (n=34)	Preoperative	14(41.18)	17(50.00)	3(8.82)	0(0.00)
	20 min postoperatively	0(0.00)	4(11.76)	9(26.47)	21(61.76)
	Z	5.114			
	P	0.000			

表 4 两组不良反应发生情况对比[例(%)]

Table 4 Comparison of side effects between two groups [n (%)]

Groups	Vascular edema	Hyperkalemia	Low blood pressure	Gastrointestinal discomfort	Total incidence(%)
Control group(n=34)	3(8.82)	0(0.00)	4(11.76)	0(0.00)	20.59
Observation group(n=34)	2(5.88)	1(2.94)	2(5.88)	1(2.94)	17.65

患者发病后心功能仍会受到不同程度的影响,随之造成相关心脏并发症和由此引发的死亡较多^[14,15]。PCI 是最常采用的急性心肌梗死治疗方案,能够快速改善心肌血流灌注^[16]。研究表明 PCI 实施过程中可能造成不稳定斑块脱落引起血管微栓栓塞,加之手术创伤引起的血管内膜损伤和炎症反应,可造成心室重塑、术后血管灌注不足,最终引起心力衰竭^[17,18]。临床上还可见部分老年急性心肌梗死患者经 PCI 已经开通梗死血管,但会出现复流,给患者预后造成了严重影响^[19,20]。因此近年来如何有效控制 PCI 术后炎症反应、抑制心室重塑、改善心肌灌注成为临床医生普遍关注的热点和亟待解决的难题。

沙库巴曲缬沙坦是由沙库巴曲和缬沙坦复合而成的一种血管紧张素 II 受体拮抗剂(ARBs)药物,前者能够通过抑制脑啡肽酶发挥排钠利尿和抗血管作用^[21],后者能够抑制 RAAS 系统起到排钠利尿、减少醛固酮释放,进而发挥抑制心肌重塑的作用^[22,23]。Sim 等^[24]研究还发现缬沙坦能够抑制心肌肥厚和纤维化,进而改善心脏病患者的血流动力学和心功能。Batra 等^[25]研究则发现缬沙坦能够抑制血管因子、去甲肾上腺素释放提高前列腺素和缓激肽表达,进而增加肾血流量、抑制醛固酮分泌,发挥降血压和减轻心脏负荷的作用。赵玉君等^[26]研究结果表明沙库巴曲缬沙坦能够明显改善急性心肌梗死患者 PCI 术后心

力衰竭患者心功能,提高运动耐力。

但由于西药具有较多的毒副作用,价格较高,难以被普遍接受,近年来中医药在治疗心肌梗死、心力衰竭等疾病方面的报道逐年增加,其效果和安全也受到较多关注和认可。复方丹参滴丸是由丹参、三七、冰片等组成,其主要有效成分为丹参酮 II A、丹参酚酸 B 和总丹参酮等,杨增强等^[27]研究发现丹参酮 II A 能够提高机体 SOD 活性进而抑制急性心肌梗死复流后内皮损伤和血流再开通后氧化应激造成的血液再灌注损伤。本次研究也发现,在沙库巴曲缬沙坦治疗基础上给予行 PCI 治疗的老年心肌梗死患者加用复方丹参滴丸能够明显降低血浆 hs-CRP、TNF- α 、IL-8 和 NT-proBNP 水平以及 LVEDD 和 LV-MI 水平,提高 LVEF 水平,与耿艳琼等^[28]的研究结果类似,该学者探究经皮冠状动脉介入术后应用复方丹参滴丸辅助治疗急性心肌梗死的疗效观察,结果显示复方丹参滴丸能够明显改善急性心肌梗死患者 PCI 术后心功能,降低患者术后 LVEDD、LVESD,提高 LVEF 和左心室射血量。同时史付力^[29]研究也与本研究类似,发现复方丹参滴丸能够明显降低急性心肌梗死患者 hs-CRP、TNF- α 、IL-8 等炎症因子水平和左室后壁厚度、LVEF、LVMI 等心室重塑指标水平。方芳等^[30]发现给予老年心肌梗死患者长期口服复方丹参滴丸能够明显减少 PCI 术后左室重构发生率。说明复方丹参滴丸具有一定抗氧化和钙拮抗剂的作用,可扩张静脉血管、降低心脏负荷,减少心室充盈和左室舒张末期容量,进而发挥抑制左心室重构和改善心功能的作用。

TIMI 心肌灌注血流分级是用于评价心肌灌注程度的临床常用的方法,能反映出心肌微循环的再灌注程度同时又能客观反映心肌组织的整体和局部功能状态,能够对患者的近期预后做出预测,具有相对较高的临床应用价值^[31]。本研究结果显示术后 20 min 时,两组 TIMI 血流分级均明显好转,且观察组术后 20 min 时 TIMI 血流分级明显优于对照组,与李丹芳^[32]的研究类似,该学者探讨复方丹参滴丸联合阿托伐他汀改善急性心肌梗死经皮冠状动脉介入术(PCI)术后炎症反应和心肌灌注的临床疗效,结果显示观察组 TIMI 血流分级 2~3 级的患者明显多于对照组,术后 90 min ST 段回落百分比 $\geq 70\%$ 的患者明显多于对照组。分析其原因为复方丹参滴丸联合沙库巴曲缬沙坦能够改善老年心肌梗死患者 PCI 术后血液动力学指标,稳定粥样斑块,明显改善即刻的心肌灌注。本研究两组患者不良反应总发生率比较无明显差异,说明老年心肌梗死患者 PCI 术后应用复方丹参滴丸联合沙库巴曲缬沙坦治疗,不会增加患者的不良反应,安全有效。

综上,复方丹参滴丸联合沙库巴曲缬沙坦能够明显降低老年心肌梗死患者 PCI 术后炎症反应,抑制心室重塑,改善心肌灌注,安全性较高。本研究纳入病例数较少,未进行术后长期随访,因此还需要设计大样本前瞻性研究,以便系统探讨复方丹参滴丸在老年心肌梗死患者 PCI 术后炎症反应、心室重塑和心肌灌注的影响并深入探讨其作用机制。

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