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益心康泰胶囊联合倍他乐克治疗冠心病心绞痛效果 及对临床症状、机体细胞因子的影响*

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摘要 目的:探讨益心康泰胶囊联合倍他乐克治疗冠心病心绞痛效果及对临床症状、机体细胞因子的影响。**方法:**选取 2020 年 10 月到 2023 年 10 月收治的 80 例冠心病心绞痛患者,分为观察组、对照组,各 40 例。对照组采取倍他乐克治疗,观察组采取益心康泰胶囊联合倍他乐克治疗,对比两组患者治疗前后心绞痛发作次数、持续时间及中医证候积分变化,中性粒细胞明胶酶相关载脂蛋白(NGAL)、心肌营养素 1(CT-1)、白细胞介素-18(IL-18)、白三烯 B4(LTB4)、组织内转化生长因子 β 结合蛋白(LTBP-2)相关机体细胞因子变化,血流变学指标变化,最后采取明尼苏达心力衰竭生活质量问卷(MLHFQ)评价两组患者生存质量。**结果:**治疗后:两组患者临床症状有所改善,且观察组较对照组改善幅度大($P<0.05$);患者机体细胞因子水平降低,且观察组较对照组低($P<0.05$);两组患者血小板聚集率、血浆黏度、全血低切、全血高切水平降低,且观察组低于对照组($P<0.05$);两组患者 MLHFQ 评分升高,且观察组高于对照组($P<0.05$)。**结论:**对冠心病心绞痛患者使用益心康泰胶囊联合倍他乐克进行治疗,可减少心绞痛发作次数,缩短心绞痛持续时间,减轻患者临床症状,同时可改善患者机体细胞因子表达水平,降低血液黏度,提升患者生存质量。

关键词:益心康泰胶囊;倍他乐克;冠心病;心绞痛;临床症状;细胞因子;生存质量

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The Effect of Yixin Kangtai Capsule Combined with Betaloc in the Treatment of Coronary Heart Disease Angina Pectoris and Its Impact on Clinical Symptoms and Body Cytokines*

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ABSTRACT Objective: To explore the therapeutic effect of Yixin Kangtai Capsules combined with Betaloc in the treatment of coronary heart disease angina pectoris, as well as its impact on clinical symptoms and body cytokines. **Methods:** 80 CAD angina patients admitted from October 2020 to October 2023 were selected and divided into observation group and control group, 40 patients each. The Matched group received treatment with Betaloc, while the observation group received treatment with Yixin Kangtai Capsules combined with Betaloc. The number and duration of angina attacks, changes in traditional Chinese medicine syndrome scores, neutrophil gelatinase associated lipoprotein (NGAL), cardiotrophin-1 (CT-1), and interleukin-18 (IL-18) were compared between the two groups of patients before and Post-treatment Leukotriene B4 (LTB4), tissue transforming growth factor β Transforming growth factors within the organization β The changes in cytokines and hemorheological indicators related to the binding protein (LTBP-2) were evaluated, and the quality of life of the two groups of patients was evaluated using the Minnesota Heart Failure Quality of Life Questionnaire (MLHFQ). **Results:** Post-treatment: The clinical symptoms of the two groups improved, and the observation group improved greatly compared with the matched group ($P<0.05$); Post-treatment, The cytokine levels were reduced in both groups, and the observation group was lower than the matched group ($P<0.05$); Post-treatment, platelet aggregation rate, plasma viscosity, whole blood low shear, and whole blood high shear levels were significantly reduced in both groups of patients, and the observation group was lower than the matched group ($P<0.05$); Post-treatment, the MLHFQ scores of the two groups of patients increased, and the observation group was higher than the matched group ($P<0.05$). **Conclusion:** For patients with coronary heart disease and angina pectoris, Yixin Kangtai capsule combined with betalk can reduce the number of angina attacks, shorten the duration of angina pectoris, reduce the clinical symptoms of patients, improve the cytokine

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expression level of patients, reduce blood viscosity, and improve the quality of life of patients.

Key words: Yixin Kangtai Capsules; Betaloc; Coronary heart disease; Angina pectoris; Clinical symptoms; Cytokines; Quality of Life
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前言

冠心病心绞痛是由于冠状动脉痉挛或狭窄引起的心肌缺血,引发的发作性胸痛,其中包括稳定型心绞痛及不稳定型心绞痛两种类型,如不及时治疗,有发展为急性心肌梗死的高度风险,严重时危及生命^[1]。当前临床上针对冠心病多以抗血小板药物、他汀类及 β 受体阻滞剂等药物进行治疗,但长期口服不良反应发生率增加,同时对心绞痛症状的改善效果有限^[2]。倍他乐克,即酒石酸美托洛尔片,属于 β 受体阻滞剂,能够选助阻断 β_1 受体,可预防左心室重构,延缓心力衰竭和心绞痛的进展^[3]。研究显示美托洛尔作为冠心病心绞痛的二级预防类药物,可改善心绞痛发作次数,但长期服用可能导致心动过缓,引起心悸等不适症状^[4]。中医学认为冠心病心绞痛为"胸痹"范畴,血瘀为标实,心气血亏为本虚,属虚实夹杂之证,需以活血为主。益心康泰胶囊为临床上常用的中成药,具有清附降浊、祛瘀通络之效^[5]。据报道联合益心康泰胶囊可改善不稳定型心绞痛症状,改善心肌缺血,减轻炎症反应^[6]。因此,本研究探讨冠心病心绞痛患者使用益心康泰胶囊联合倍他乐克治疗,其对临床症状、机体细胞因子影响。

1 资料与方法

1.1 一般资料

选取2020年10月到2023年10月收治80例冠心病心绞痛患者,分为观察组、对照组,各40例。本研究经我院伦理委员会批准。

1.2 纳排标准

纳入标准:年龄 ≥ 18 岁;符合冠心病诊断标准^[7],但冠脉病变未达到冠脉介入或搭桥标准,且合并心绞痛症状;对本研究所用药物无过敏;对本研究知情并签署同意书。

排除标准:合并恶性肿瘤者;合并肝肾功能严重障碍者;合并缓慢型心律失常者;合并免疫功能疾病者;合并精神类疾病或认知功能障碍不能配合研究者。

1.3 方法

两组患者均参照《美国和欧洲稳定性冠心病诊治指南》^[8]进行规范化治疗,包括利尿剂、阿司匹林、他汀类药物,并合理饮食,控制诱因等。

对照组:口服倍他乐克,即酒石酸美托洛尔片(阿斯利康制药;H32025391;25 mg \times 20 s),2次/d,25 mg/次。

观察组:以对照组为基础,加用口服益心康泰胶囊(青海益欣药业;Z20025113;0.5 g \times 20 s),每日3次,每次1 g。两组患者均连续服药1个月后对比其临床疗效。

1.4 观察指标

(1)记录心绞痛发作次数及持续时间,计算1 d之内平均心绞痛发作次数与持续时间,并评价中医证候积分^[9],其中包括不寐、自汗、腰膝酸软、畏寒肢冷、疲倦乏力、心悸、气短、胸闷、

胸痛9项症状进行评分,每项0~3分,总分为0~27分,分数越高代表症状越严重。

(2)抽取患者5 mL空腹静脉血,离心后取上层清液检测中性粒细胞明胶酶相关载脂蛋白(NGAL)、心肌营养素1(CT-1)、白细胞介素-18(IL-18)、白三烯B4(LTB4)、组织内转化生长因子 β 结合蛋白(LTBP-2)表达水平,酶标仪DG5033A。

(3)分别在治疗前后采用全自动血流变仪测定两组患者血流变学指标,其中包括血小板聚集率、血浆黏度、全血低切、全血高切。

(4)治疗前后应用MLHFQ评分评价两组患者生活质量,该量表共21条目,分为身体领域、情绪领域、其他领域,各条目0~5分,总分为0~105分,分数越低代表患者生存质量越高^[10]。

1.5 统计学方法

采取SPSS 23.0,计数资料以(n/%)表示, χ^2 检验;计量资料用($\bar{x} \pm s$)表示,t检验;以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基线资料

共纳入80例冠心病心绞痛患者,各40例。其中对照组男23例,女17例;年龄为51~78岁,平均(61.21 \pm 3.21)岁;合并基础疾病:高血压20例,糖尿病9例,高血脂11例;心绞痛类型:稳定型心绞痛25例,不稳定型心绞痛15例。观察组男24例,女16例;年龄为50~79岁,平均(61.27 \pm 4.26)岁;合并基础疾病:高血压18例,糖尿病10例,高血脂12例;心绞痛类型:稳定型心绞痛24例,不稳定型心绞痛16例。两组患者一般资料对比无显著差异($P > 0.05$)。

2.2 临床症状对比

治疗后两组患者临床症状有所改善,且观察组较对照组改善幅度大($P < 0.05$),见表1。

2.3 机体细胞因子水平对比

治疗前两组患者NGAL、CT-1、IL-18、LTB4、LTBP-2水平对比无差异($P > 0.05$),治疗后均降低,且观察组与对照组比较有差异($P < 0.05$),见表2。

2.4 血流变学指标对比

治疗后两组患者血流变学指标降低,且观察组较对照组低($P < 0.05$),见表3。

2.5 生存质量对比

治疗后两组患者MLHFQ评分升高,且观察组较对照组高($P < 0.05$),见表4。

3 讨论

冠心病作为一种常见心血管疾病,目前仍是我国居民的首位死亡原因。若不及时治疗心绞痛,病情在不断进展中,心绞痛发作次数也会增多,最终会诱发心肌梗死,造成心脏损害^[11-13]。美托洛尔作对 β_1 受体产生阻断作用,降低心肌耗氧量,减轻心

绞痛症状^[14]。益心康泰胶囊作为中成药制剂,具有益气养阴、活血祛瘀、通经活络等症状,可改善血液粘稠度,缓解心肌缺血症状^[15,16]。因此,本研究针对我院冠心病心绞痛患者采取益心康泰胶囊联合美托洛尔进行治疗,希望能够为临床提供参考意见。

表 1 临床症状对比($\bar{x} \pm s$)
Table 1 Comparison of Clinical Symptoms($\bar{x} \pm s$)

Groups	n	Episodes of angina pectoris (times per day)		Duration of angina pectoris(min)		Traditional Chinese Medicine Syndrome Points(portion)	
		Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment
Observation group	40	2.23± 0.35	0.62± 0.14*	5.83± 1.37	2.26± 0.42*	21.21± 3.37	11.12± 2.12*
Matched group	40	2.11± 0.52	1.25± 0.32*	5.31± 1.36	3.51± 0.37*	21.47± 4.25	15.21± 3.93*
t		0.129	11.408	0.704	14.124	0.303	5.793
P		0.230	<0.001	0.092	<0.001	0.763	<0.001

Note: compared with baseline, *P<0.05, the same below.

表 2 机体细胞因子水平对比($\bar{x} \pm s$)
Table 2 Comparison of cytokine levels in the body($\bar{x} \pm s$)

Groups	n	NGAL(ng/L)		CT-1(pg/mL)		IL-18(ng/L)	
		Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment
Observation group	40	65.11± 4.52	42.62± 3.24*	66.40± 12.09	35.31± 6.43*	10.82± 2.27	4.85± 1.28*
Matched group	40	65.23± 3.35	51.25± 3.32*	66.43± 11.10	47.19± 8.38*	10.83± 2.11	7.48± 1.17*
t	-	0.135	11.766	0.012	7.113	0.027	9.592
P	-	0.893	<0.001	0.991	<0.001	0.972	<0.001

续表 2
Continuation table 2

Groups	n	LTB4(pg/mL)		LTBP-2(mg/L)	
		Baseline	Post-treatment	Baseline	Post-treatment
Observation group	40	134.32± 24.16	108.17± 13.68*	22.45± 3.55	15.65± 2.24*
Matched group	40	134.28± 23.23	116.16± 14.44*	22.36± 4.53	19.15± 3.36*
t	-	0.086	2.540	0.006	5.482
P	-	0.917	0.013	0.995	<0.001

表 3 血流变学指标对比($\bar{x} \pm s$)
Table 3 Comparison of Hemorheological Indicators($\bar{x} \pm s$)

Groups	n	Platelet aggregation rate(%)		Plasma viscosity(mPa·s)		Whole blood low cut (mPa·s)		Whole blood high cut (mPa·s)	
		Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment
Observation group	40	75.67± 10.02	47.65± 4.54*	2.33± 0.45	1.41± 0.14*	26.68± 3.62	14.30± 3.28*	5.75± 1.15	3.38± 0.32*
Matched group	40	75.52± 9.95	61.75± 7.23*	2.35± 0.52	1.86± 0.16*	26.27± 3.75	21.20± 3.05*	5.68± 1.17	4.16± 0.45*
t		0.261	10.446	1.231	8.336	0.776	9.939	0.795	13.551
P		0.794	<0.001	0.220	<0.001	0.439	<0.001	0.427	<0.001

本研究发现,治疗后两组患者临床症状有所改善,且观察组较对照组改善幅度大(P<0.05),与 Shen M 等^[17]、Chen W 等^[18] 研究结果一致。Shen M 等研究显示,美托洛尔对冠心病心绞痛

治疗效果确切,可减少患者心绞痛发作次数,改善血管内皮功能,但总有效率为 82.86%,有较大可提升空间。Chen W 等研究显示,益心康泰胶囊可改善不稳定心绞痛患者的临床症状,降

表4 生存质量对比($\bar{x} \pm s$,分)
Table 4 Comparison of Quality of Life($\bar{x} \pm s$, score)

Groups	n	Physical field		Emotional domain		Other areas		Total score	
		Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment
Observation group	40	23.64± 5.31	32.56± 7.11*	13.56± 3.41	20.36± 4.25*	26.36± 5.32	33.93± 5.13*	63.57± 8.16	86.87± 8.37*
Matched group	40	23.51± 5.46	27.87± 5.13*	13.69± 4.56	17.56± 4.46*	26.26± 6.41	30.01± 4.05*	63.46± 7.12	75.44± 5.66*
t	-	1.482	11.513	1.185	2.874	1.216	8.677	1.265	7.155
P	-	0.143	<0.001	0.240	0.005	0.228	<0.001	0.210	<0.001

低患者不良心血管事件发生率。这是因为益心康泰胶囊含有锁阳、黄芪等有效成分,这些成分协同作用,能够减轻血管狭窄及堵塞情况,促进血液循环,改善心绞痛持续、频发发作情况。另外从中医学角度来看,益心康泰胶囊成分为多种高原藏药,配伍独特,具有通附降浊、化痰通脉、益气行滞之效,与冠心病行交通的虚实夹杂之证的治疗机理相符^[9]。

研究显示冠心病心绞痛发作过程中会出现机体细胞因子水平改变情况^[20]。其中 NGAL 可介导 NF- κ B,作用于心血管疾病炎症反应^[21]。CT-1 为心肌肥厚所产生的一种因子,过度表达会加重心绞痛症状。IL-18 属于炎症因子之一,研究发现,IL-18 能够诱导冠脉平滑肌细胞的迁移和增殖,加重冠心病发生与发展^[22]。LTB4 可促使血管壁黏附,加重冠心病患者血管内皮炎症损伤,破坏斑块稳定性^[23]。LTBP-2 属于细胞外基质蛋白,机体发生弹性纤维凝聚、细胞黏附和內皮损伤后其水平呈现升高状态^[24]。本研究发现,治疗后两组患者机体细胞因子水平降低,观察组与对照组比较有差异($P < 0.05$),证明在倍他乐克基础上增加益心康泰胶囊可改善患者机体炎症反应,可能与改善 NGAL、CT-1、IL-18、LTB4、LTBP-2 水平等机制相关。

冠心病的发生与发展过程中与血流变学具有重要关系,研究显示多数冠心病患者血液黏度高于健康群体,同时血液高黏滞也是冠心病发病的原因之一^[25]。在血液中黏滞因素将会造成人体血液高黏滞,进而导致心血管不良事件的增加。本研究结果显示,治疗后两组患者血小板聚集率、血浆黏度、全血低切、全血高切水平明显降低,且观察组低于对照组($P < 0.05$)。证明在倍他乐克基础上增加益心康泰胶囊可改善患者血液黏度,减轻机体黏滞状态,与王晟等研究结果一致^[26]。分析原因为现代药理学研究表明,益心康泰胶囊可改善体内微循环,扩张动脉血管,同时还可改善氧自由基代谢,降低血液黏度^[27]。

本研究表明,治疗后两组患者 MLHFQ 评分升高,观察组较对照组高($P < 0.05$),证明在倍他乐克基础上增加益心康泰胶囊可提升冠心病心绞痛患者的生存质量。冠心病作为无法根治的慢性疾病,多以药物治疗维持,避免造成严重冠状动脉狭窄,引发心肌梗死,再加上心绞痛症状影响,患者生存质量较差^[28]。而采取益心康泰胶囊联合倍他乐克治疗,可在常规治疗基础上进一步改善患者心绞痛症状,并通过药理成分,进一步改善患者血液高凝状态,缓解患者临床症状的同时,延缓冠心病的发展,提升患者生存质量^[29]。

综上,对冠心病心绞痛患者使用益心康泰胶囊联合倍他乐

克进行治疗,可减少心绞痛发作次数,缩短心绞痛持续时间,减轻患者临床症状,同时可改善患者机体细胞因子表达水平,降低血液黏度,提升患者生存质量。但本研究存在一定不足,如为单中心研究,样本量较小,将在后续加大样本量进一步验证。

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