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复方丹参滴丸联合曲美他嗪对冠心病合并高脂血症患者血液流变学及血脂的影响 *

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摘要 目的:探讨复方丹参滴丸联合曲美他嗪治疗冠心病合并高脂血症患者的效果。**方法:**选取 2016 年 1 月-2017 年 12 月我院收治的冠心病合并高脂血症患者 81 例,按照治疗方法的不同分为观察组、对照组,分别 41 例、40 例。对照组实施常规联合曲美他嗪进行治疗,观察组在对照组的基础上联合应用复方丹参滴丸进行治疗。比较两组临床疗效、治疗前后血脂、血液流变学相关指标、不良反应的发生情况。**结果:**观察组总有效率显著高于对照组($P<0.05$)。两组治疗前血清 HDL-C、TC、LDL-C、TG 水平间差异不显著($P>0.05$);观察组治疗后血清 TC、LDL-C、TG 水平均显著比对照组低($P<0.05$),血清 HDL-C 水平显著比对照组高($P<0.05$)。两组治疗前 PV、WBC 比较差异不显著($P>0.05$);两组治疗后 PV、WBC 均显著降低($P<0.05$),且观察组以上指标下降更明显($P<0.05$)。两组患者在治疗期间都没发生严重的不良反应。**结论:**与单用曲美他嗪治疗相比,复方丹参滴丸联合曲美他嗪治疗冠心病合并高脂血症效果更优,可明显改善患者血脂水平和血液流变学,且安全性较高。

关键词:冠心病;高脂血症;复方丹参滴丸;曲美他嗪;血液流变学

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Effects of Compound Danshen Dripping Pills and Trimetazidine on the Hemorheology and Blood Lipid of Patients with Coronary Heart Disease Complicated with Hyperlipidemia*

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ABSTRACT Objective: To explore the effects of Compound Danshen Dripping Pills and Trimetazidine on the hemorheology and blood lipid of patients with coronary heart disease complicated with hyperlipidemia. **Methods:** 18 cases of patients with coronary heart disease complicated with hyperlipidemia in our hospital from January 2016 to December 2017 were selected and divided into the control group($n=40$) and the observation group($n=41$) by the treatment methods. The control group was treated with trimetazidine on the basis of routine treatment, and the observation group was treated with compound Danshen dripping pills on the basis of control group. The clinical curative effect, changes of blood lipid levels and hemorheology-related parameters before and after treatment and incidence of adverse reactions were compared between two groups. **Results:** The total effective rate of observation group (82.93%) was significantly higher than that of the control group (72.50%) ($P<0.05$). There was no significant difference in the levels of serum TG, TC, LDL-C and HDL-C levels between the two groups before treatment ($P>0.05$). After treatment, the serum TG, TC, and LDL-C levels of observation group were significantly lower than those in the control group ($P<0.05$), and the serum HDL-C level was significantly higher in the observation group than that of the control group ($P<0.05$). There was no significant difference in the WBC and PV between the two groups before treatment ($P>0.05$). After treatment, the WBC and PV in both groups were significantly decreased ($P<0.05$), which decreased more significantly in the observation group ($P<0.05$). No serious adverse reactions was found in both groups of patients during the treatment. The blood routine, urine routine, and liver and kidney function of two groups were normal before and after treatment. **Conclusions:** Compared with Trimetazidine alone, Compound Danshen Dripping Pills combined with Trimetazidine had significant curative effect on patients with coronary heart disease complicated with hyperlipidemia, it can significantly improve blood lipids and hemorheology with high safety.

Key words: Coronary heart disease; Hyperlipidemia; Compound Danshen Dripping Pills; Trimetazidine; Blood rheology

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前言

冠心病是一种由冠状动脉器质性狭窄或阻塞引起心肌缺血缺氧或心肌梗死的心脏病,冠状动脉狭窄或阻塞多是脂肪物质沿血管内壁堆积所致,在其发展到一定程度即会限制流入心肌的血流,而心脏供氧不足则会引发心绞痛^[1,2]。冠心病早期症状最典型的是心绞痛,严重时会引发心肌梗死甚至猝死,严重威胁患者的身心健康和生命安全^[3,4]。

临床上对于冠心病的治疗主要包括药物治疗、血运重建治疗。其中,药物治疗是所有治疗的基础,规范药物治疗可有效改善患者临床症状、降低死亡率和发生再缺血事件^[5-7]。中药在冠

心病的治疗中也越来越受到医界的重视,复方丹参滴丸是一种中药制剂,常用作冠心病治疗^[8],本研究旨在探讨联用复方丹参滴丸、曲美他嗪对冠心病合并高脂血症的效果,现报道如下。

1 资料与方法

1.1 一般资料

选取 2016 年 1 月~2017 年 12 月我院收治的 81 例冠心病合并高脂血症患者,按治疗方法分成观察组、对照组,分别 41 例、40 例。两组基线资料差异不显著($P>0.05$),见表 1。我院伦理委员会已审批本研究。

表 1 两组基线资料比较($n, \bar{x} \pm s$)

Table 1 The general information of two groups ($n, \bar{x} \pm s$)

Groups	Gender	Age	Disease course	Complication [n(%)]	
	Male/female	(years)	(years)	Hypertension	Diabetes mellitus
Control group(n=40)	21/19	57.426.45	3.370.85	15(37.50)	14(35.00)
Observation group(n=41)	22/19	56.876.66	3.420.76	16(39.02)	15(36.59)

1.2 纳入及排除标准

纳入标准:①符合冠心病诊断标准^[9];②符合高脂血症诊断标准^[10];③年龄<75岁;④无相关药物禁忌症;⑤依从性较高,能够遵医嘱并配合研究;⑥资料齐全;⑦已签知情同意书。排除标准:①合并先天性心脏病、恶性心律失常者;②因甲状腺功能、肾功能等因素造成的血脂异常者;③合并脑血管疾病、肝、肾功能异常者;④合并免疫系统、内分泌系统及凝血功能障碍者;⑤合并精神疾病、严重感染者。

1.3 治疗方法

两组患者均给予常规治疗,常规药物包括硝酸酯类、他汀类及阿司匹林等。对照组在此基础上联合使用盐酸曲美他嗪片(生产厂家:施维雅(天津)制药有限公司,规格:20 mg×30 s,国药准字:H20055465)治疗,在三餐时口服,1片/次,每天3次。观察组患者在以上基础上用复方丹参滴丸(天士力制药集团股份有限公司,国药准字:Z10950111,规格:27 mg×180 s)治疗,口服或含服,每次10丸,每天3次。两组疗程12周。

1.4 观察指标

(1)临床疗效^[11]:显效,心电图基本正常/恢复正常,症状基本消失/心绞痛发作次数减少超过80%;有效,心电图ST段

回升超过0.05 mV,但未达正常水平,T波倒置变浅超过25%/T波由倒置变直立,心绞痛发作次数减少50%到80%;无效,心电图ST段下移无改变/ST段下移减少小于0.05 mV,症状无改善。总有效率=(显效例数+有效例数)/总例数×100%。(2)血脂水平:于治疗前后进行血液采集,检查前禁食水12 h,次日清晨取患者空腹静脉血5 mL,置于抗凝试管例静置30 min(25℃),3000 r/min离心15 min后取血清。使用酶联免疫吸附法检测甘油三酯(triglyceride, TG)、低密度脂蛋白(LDL-C)、总胆固醇(total cholesterol, TC)、高密度脂蛋白(HDL-C)。(3)血液流变学相关指标:于患者治疗前后使用全自动血流变仪检测全血黏度(WBV)、血浆黏度(PV)。(4)观察两组不良反应情况。

1.5 统计学分析

用SPSS 20.0,计量资料、计数资料分别用($\bar{x} \pm s$)、[例(%)]表示,用t检验、 χ^2 检验, $P<0.05$ 表示差异显著。

2 结果

2.1 两组患者临床疗效的比较

治疗后,观察组的临床疗效总有效率(82.93%)显著高于对照组(72.50%)($P<0.05$),见表2。

表 2 两组患者临床疗效的比较[例(%)]

Table 2 Comparison of the clinical efficacy between two groups[n(%)]

Group	Excellent	Effective	Ineffective	Total effective rate
Control group(n=40)	13(32.50)	16(40.00)	11(27.50)	31(72.50)
Observation group(n=41)	21(51.22)	13(31.71)	7(17.07)	34(82.93)*

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

2.2 两组患者治疗前后血脂水平的比较

治疗前,两组TG、TC、LDL-C、HDL-C水平比较差异无统计学意义($P>0.05$);治疗后,观察组TG、TC、LDL-C水平明显比对照组低($P<0.05$),HDL-C水平明显比对照组高($P<0.05$)。见表3。

2.3 两组患者治疗前后血液流变学相关指标的比较

治疗前,两组WBC、PV比较差异无统计学意义($P>0.05$);治疗后,两组WBC、PV均较治疗前显著降低($P<0.05$),且观察组下降更明显($P<0.05$)。见表4。

表 3 两组患者治疗前后血脂水平比较($\bar{x} \pm s$, mmol/L)Table 3 Comparison of the blood lipid levels between two groups before and after treatment ($\bar{x} \pm s$, mmol/L)

Indicators	Control group(n=40)		Observation group(n=41)	
	Before treatment	After treatment	Before treatment	After treatment
TG	2.91± 0.46	1.96± 0.32	2.89± 0.53	1.41± 0.33*
TC	7.52± 2.15	5.72± 1.25	7.57± 2.09	4.38± 1.02*
LDL-C	3.91± 0.63	3.04± 0.42	3.87± 0.57	2.43± 0.42*
HDL-C	1.23± 0.25	1.41± 0.34	1.25± 0.27	1.59± 0.37*

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

表 4 两组患者治疗前后血液流变学相关指标的比较($\bar{x} \pm s$, mPas)Table 4 Comparison of the indicators of hemorheology between two groups before and after treatment($\bar{x} \pm s$, mPas)

Indicators	Control group(n=40)		Observation group(n=41)	
	Before treatment	After treatment	Before treatment	After treatment
WBC	4.88± 0.53	4.15± 0.42*	4.93± 0.57	3.54± 0.41* [#]
PV	2.64± 0.32	2.04± 0.35*	2.66± 0.36	1.43± 0.27* [#]

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

2.4 两组不良反应发生情况的比较

两组治疗期间均未出现严重的不良反应,治疗前后血常规、尿常规及肝肾功能均正常。

3 讨论

冠心病是临床常见的心血管疾病,主要与动脉粥样硬化病变引起血管硬化、输氧能力下降,心脏细胞的供氧量不足、代谢异常,导致心脏收缩能力减弱有关^[12],临床治疗以药物治疗为基础,常用药物包括调脂药、钙通道阻断剂、抗血栓药物等^[13]。冠心病在中医中属“胸痹、心痛”范畴,发病机制是脉络痹阻、血瘀、痰瘀、胸阳不振等,治疗以行气通络止痛、益气活血化瘀为主要原则^[14]。长期高脂血症会促进动脉粥样硬化的发生、发展,并导致血管内皮功能障碍进一步加重,若不合理治疗会使患者病情进行性加重^[15],有研究显示良好的血脂控制有助于冠心病合并高脂血症患者的冠状动脉粥样斑块的消退或减轻^[16]。中医认为高脂血症属“胸痹、血瘀、痰浊”范畴,由阴阳寒热失调、气机逆乱导致心脉痹阻、气虚血行无力^[17]。

曲美他嗪属于抗心绞痛心血管药物,能保护细胞在缺氧或缺血的情况下的能量代谢、维持细胞内环境稳态^[18]。大量研究显示曲美他嗪可增加冠脉血流储备、延迟运动诱发的缺血,能够显著降低心绞痛发作的频率及硝酸甘油的消耗量^[19]。本研究中对照组患者在常规用药的基础上使用曲美他嗪,结果显示患者并未出现严重的不良反应,且治疗总有效率达 72.5%,说明曲美他嗪的使用是安全有效的,这可能与曲美他嗪可通过有助于完善线粒体能量代谢来直接改善心肌功能、提高心脏代谢能力、改善微循环的作用有关。

复方丹参滴丸是通过现代药学技术研制成的中药滴丸制剂,在治疗心绞痛方面的疗效显著^[20]。本研究结果显示观察组的临床疗效总有效率显著比对照组高,说明观察组病情改善情况比对照组优,提示联合用药效果明显,且两组治疗期间均未出现严重的不良反应,说明单用和联合用药的治疗方法是安全

的。复方丹参滴丸含有冰片、三七、丹参等,冰片具有开窍醒神、明目退翳的功效,三七、丹参具有散瘀止血、活血祛瘀的功能,诸药合用可发挥活血化瘀、理气止痛的作用,最终会扩张心血管、增加心血供、改善心绞痛的功效^[21]。现代药理学研究表明复方丹参滴丸中含有的人参皂苷 Rb1、右旋龙脑等物质具有良好的钙通道阻滞作用,还能够增加血小板细胞膜的流动性、降低血小板细胞微黏度及 FIB 水平,从而改善患者血液流变学^[22,23]。本研究结果显示,观察组治疗后血清 LDL-C、TC、TG 水平均显著低于对照组, HDL-C 水平显著比对照组高, WBC、PV 下降程度亦比对照组明显,说明复方丹参滴丸能够改善冠心病合并高脂血症患者的血脂、血流异常。

综上所述,与单用曲美他嗪治疗相比,联合应用复方丹参滴丸与曲美他嗪在治疗冠心病合并高脂血症患者的效果中更佳,可明显改善患者血脂水平和血液流变学,且安全性较高。

参考文献(References)

- [1] Navarboggan A M, Peterson E D, D'Agostino R B, et al. Hyperlipidemia in Early Adulthood Increases Long-Term Risk of Coronary Heart Disease. CLINICAL PERSPECTIVE [J]. South China Journal of Cardiology, 2015, 131(1): 64-64
- [2] Hayward R A. Letter by Hayward Regarding Article, "Hyperlipidemia in Early Adulthood Increases Long-Term Risk of Coronary Heart Disease"[J]. Circulation, 2015, 132(16): e202
- [3] Maneerat Y, Prasongsukarn K, Benjathummarak S, et al. Intersected genes in hyperlipidemia and coronary bypass patients: Feasible biomarkers for coronary heart disease [J]. Atherosclerosis, 2016, 252: e183-e184
- [4] Jain S, Baghel P S, Jain N, et al. Clinical correlation of serum homocysteine level with lipid profile in coronary artery disease patients[J]. Atherosclerosis Supplements, 2015, 4(32): 5444-5451
- [5] Chen S, Redfors B, Liu Y, et al. TCT-825 Outcomes of Patients with and Without Hyperlipidemia Undergoing Revascularization for Left Main Coronary Artery Disease: Analysis from the EXCEL Trial[J].

- Journal of the American College of Cardiology, 2017, 70(18): B335
- [6] Tishko V V, Sokolov A A, Belskih A N, et al. Impact of double filtration plasmapheresis on adhesion molecules levels in patients with stable coronary heart disease after coronary stenting [J]. Atherosclerosis Supplements, 2017, 30: 92
- [7] Martin S S, Michos E D. Mapping Hyperlipidemia in Young Adulthood to Coronary Risk: Importance of Cumulative Exposure and How to Stay Young[J]. Circulation, 2015, 131(5): 445-447
- [8] Puneekar R S, Fox K, Richhariya A, et al. Trends in real-world treatment modifications among high-cardiovascular disease risk patients with hyperlipidemia [J]. Journal of the American College of Cardiology, 2016, 67(13): 1923-1923
- [9] Navar B A M, Peterson E D, sr D R, et al. Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease[J]. Circulation, 2015, 131(5): 451-458
- [10] Lanza G A. Angina Pectoris and Myocardial Ischemia in the Absence of Obstructive Coronary Artery Disease: Role of Diagnostic Tests[J]. Current Cardiology Reports, 2016, 18(2): 1-9
- [11] Simpson L O. Angina, ischemic heart disease and blood viscosity[J]. BMJ, 2015, 339: 464
- [12] Chen C H, Lin C L, Kao C H. Association between gastroesophageal reflux disease and coronary heart disease: A nationwide population-based analysis[J]. Medicine, 2016, 95(27): e4089
- [13] Krychtiuk K A, Kastl S P, Pfaffenberger S, et al. Association of Small Dense LDL Serum Levels and Circulating Monocyte Subsets in Stable Coronary Artery Disease[J]. Plos One, 2015, 10(4): e0123367
- [14] Luo J, Song W, Yang G, et al. Compound Danshen (Salvia miltiorrhiza) dripping pill for coronary heart disease: an overview of systematic reviews[J]. American Journal of Chinese Medicine, 2015, 43(01): 1550002
- [15] Yao Y, Feng Y, Lin W. Systematic review and meta-analysis of randomized controlled trials comparing compound danshen dripping pills and isosorbide dinitrate in treating angina pectoris [J]. International Journal of Cardiology, 2015, 182: 46-47
- [16] Guo J, Yong Y, Aa J, et al. Compound danshen dripping pills modulate the perturbed energy metabolism in a rat model of acute myocardial ischemia[J]. Scientific Reports, 2016, 6: 37919
- [17] Liu H H, Xiong G X, Zhang L P. Therapeutic effect of the compound Danshen dripping pill combined with laser acupoint irradiation on early diabetic retinopathy [J]. Laser Physics Letters, 2017, 14 (6): 065602
- [18] Rehberger-Likozar A, Šebestjen M. Influence of trimetazidine and ranolazine on endothelial function in patients with ischemic heart disease[J]. Coronary Artery Disease, 2015, 26(8): 651
- [19] Zhao Y, Peng L, Luo Y, et al. Trimetazidine improves exercise tolerance in patients with ischemic heart disease[J]. Herz, 2015, 41(6): 1-9
- [20] Zhou W, Yuan W F, Chen C, et al. Study on material base and action mechanism of compound Danshen dripping pills for treatment of atherosclerosis based on modularity analysis[J]. Journal of Ethnopharmacology, 2016, 193: 36-44
- [21] Lu B, Wu X. The Protective Effect of Compound Danshen Dripping Pills on Oxidative Stress after Retinal Ischemia/Reperfusion Injury in Rats[J]. Chinese Medicine, 2015, 6(2): 90-96
- [22] Jia C, Han S, Wei L, et al. Protective effect of compound Danshen (Salvia miltiorrhiza) dripping pills alone and in combination with carbamazepine on kainic acid-induced temporal lobe epilepsy and cognitive impairment in rats[J]. Pharmaceutical Biology, 2018, 56(1): 217
- [23] Zhu Y, Zeng Y, He C, et al. Effects of a Cardiotonic Medicine, Danshen Pills, on Cognitive Ability and Expression of PSD-95 in a Vascular Dementia Rat Model[J]. Neurophysiology, 2016, 48(4): 264-269

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- [17] Qiu, YS, Liao GJ, Jiang NN. REG3A overexpression suppresses gastric cancer cell invasion, proliferation and promotes apoptosis through PI3K/Akt signaling pathway [J]. International Journal of Molecular Medicine, 2018, 3520
- [18] Buckles TC, Ziemba BP, Masson GR, et al. Single-Molecule Study Reveals How Receptor and Ras Synergistically Activate PI3K α and PIP3 Signaling[J]. Biophysical Journal, 2017, 113(11): 2396
- [19] Akinleye A, Avvaru P, Furqan M, et al. Phosphatidylinositol 3-kinase (PI3K) inhibitors as cancer therapeutics [J]. Journal of Hematology & Oncology, 2013, 6(1): 88-104
- [20] Am J U, Gong W J, Su Y, et al. Imperatorin shows selective antitumor effects in SGC-7901 human gastric adenocarcinoma cells by inducing apoptosis, cell cycle arrest and targeting PI3K/ Akt/m-TOR signalling pathway [J]. Journal of the Balkan Union of Oncology, 2017, 22(6): 1471
- [21] Zeng F, Zhao H, Liao J. Androgen interacts with exercise through the mTOR pathway to skeletal muscle hypertrophy [J]. Biology of Sport, 2017, 34(4): 313-321
- [22] Shi YF, Yu DJ, Jiang CY, et al. TRAF6 regulates proliferation of stromal cells in the transition and peripheral zones of benign prostatic hyperplasia via Akt/mTOR signaling[J]. Prostate, 2018, 78(3)
- [23] Shi J, Wang L, Zou C, et al. Tumor microenvironment promotes prostate cancer cell dissemination via the Akt/mTOR pathway[J]. Oncotarget, 2018[Epub ahead of print]
- [24] Zhu L, Ning N, Li Y, et al. Bistractylolide Modulates PI3K-Akt-GSK3 β -Dependent Pathways to Protect against Glutamate-Induced Cell Damage in PC12 and SH-SY5Y Cells [J]. Evidence Based Complementary and Alternative Medicine, 2017, 2017(4): 1291458
- [25] Liu L, Zhou XM, Yang FF, et al. TRIM22 confers poor prognosis and promotes epithelial mesenchymal transition through regulation of AKT/ GSK3 β / β -catenin signaling in non-small cell lung cancer[J]. Oncotarget, 2017, 8(37): 62069-62080
- [26] Zhong ZF, Yu HB, Wang CM, et al. Furanodiene Induces Extrinsic and Intrinsic Apoptosis in Doxorubicin-Resistant MCF-7 Breast Cancer Cells via NF- κ B-Independent Mechanism [J]. Front Pharmacol, 2017, 8: 648