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益气宁心汤联合贝那普利治疗慢性心衰患者的临床疗效及对血清 GDF-15、sST2、APN 的影响

郑建津 刘雪瑜 郭露薇 蔡炳烨 戴小霞

(厦门大学附属成功医院(解放军第一七四医院) 福建 厦门 363001)

摘要 目的:研究益气宁心汤联合贝那普利治疗慢性心衰患者的临床疗效及对血清生长分化因子-15(GDF-15)、可溶性 ST2 蛋白(sST2)、脂联素(APN)的影响。**方法:**收集 2014 年 3 月至 2015 年 3 月我院收治的 80 例慢性心衰患者,按抽签法分为实验组和对照组,每组 40 例。两组均给予常规基础对症治疗,对照组在此基础上加用贝那普利治疗,每次 10 mg,每天 1 次,实验组在对照组的基础上加用益气宁心汤治疗,每天 1 剂,于早晚服用,两组治疗疗程均为 2 周。观察和比较两组的临床疗效及治疗前后心功能左心室舒张末径(LVEDD)、左心室收缩末期径(LVESD)、左室射血分数(LVEF)、GDF-15、sST2、APN 水平、急性生理学与慢性健康状况评分(APACHE-II)、肺部感染评分(CPIS)的变化。**结果:**治疗后,实验组总有效率显著高于对照组[92.50%(37/40) vs 72.50%(29/40)]($P<0.05$);LVEDD、LVESD 显著低于对照组[(53.56±6.24)mm vs (57.40±6.72)mm, (41.26±4.95)mm vs (46.28±4.86)mm] ($P<0.05$),LVEF 显著高于对照组 [(57.91±5.93)% vs (50.27±5.90)%] ($P<0.05$); 血清 GDF-15、sST2、APN 水平显著低于对照组 [(820.81±73.14)ng/L vs (1192.86±93.62)ng/L, (4.28±1.02)ng/mL vs (20.69±3.48)ng/mL, (13.47±2.18)mg/L vs (16.05±3.63)mg/L] ($P<0.05$); APACHE-II、CPIS 评分显著低于对照组 [(13.90±3.28)分 vs (20.37±4.97)分, (3.24±0.92)分 vs (5.38±1.01)分] ($P<0.05$)。 **结论:**益气宁心汤联合贝那普利治疗慢性心力衰竭能显著提高其临床疗效,改善心功能,可能与其有效降低血清 GDF-15、sST2、APN 的水平有关。

关键词:益气宁心汤;贝那普利;慢性心衰;心功能;生长分化因子-15;可溶性 ST2 蛋白;脂联素

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Curative Efficacy of Yiqi Ningxin Decoction Combined with Benazepril in the Treatment of Chronic Heart Failure and Effects on the Serum GDF-15, sST2, APN Levels

ZHENG Jian-jin, LIU Xue-yu, GUO Lu-wei, CAI Bing-ye, DAI Xiao-xia

(Affiliated Hospital of Xiamen University (first and 74 Hospital of PLA), Xiamen, Fujian, 363001, China)

ABSTRACT Objective: To study the curative efficacy of Yiqi Ningxin Decoction combined with benazepril in the treatment of chronic heart failure and effects on the serum growth differentiation factor -15 (GDF-15), soluble ST2 protein (sST2), adiponectin (APN) levels. **Methods:** 80 cases of patients with chronic heart failure who were treated from March 2014 to March 2015 in our hospital were selected as research objects and divided into the control group and the experimental group according to the draw method, 40 cases in each group. Both groups were given routine basic symptomatic treatment. The control group was additionally treated by benazepril, 10mg every time, 1 time a day, while the experimental group was treated with Yiqi Ningxin Decoction on the basis of control group, 1 dose per day, once morning and evening. Both groups were treated for 2 weeks. Then the curative effect, changes of left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left ventricular ejection fraction (LVEF), DF-15, sST2, APN levels, acute physiology and chronic health evaluation scores (APACHE-II), pulmonary infection score before and after treatment were compared between two groups. **Results:** The total effective rate of experimental group was significantly higher than that of the control group [92.50%(37/40) vs 72.50%(29/40)] ($P<0.05$); the LVEDD, LVESD were significantly lower than the those of the control group [(53.56±6.24)mm vs (57.40±6.72)mm, (41.26±4.95)mm vs (46.28±4.86)mm] ($P<0.05$), the LVEF was significantly higher than that of the control group [(57.91±5.93)% vs (50.27±5.90)%] ($P<0.05$); the serum GDF-15, sST2 APN levels were significantly lower than those of the control group [(820.81±73.14)ng/L vs (1192.86±93.62)ng/L, (4.28±1.02)ng/mL vs (20.69±3.48)ng/mL, (13.47±2.18)mg/L vs (16.05±3.63)mg/L] ($P<0.05$); APACHE-II, CPIS score were significantly lower than those of the control group [(13.90±3.28)score vs (20.37±4.97)score, (3.24±0.92)score vs (5.38±1.01)score] ($P<0.05$). **Conclusion:** Yiqi Ningxin Decoction combined with benazepril could enhance the clinical efficacy of chronic heart failure, it could improve the heart function, which might be ralted to the reduction of serum GDF-15, sST2, APN levels.

作者简介:郑建津(1978-9),女,本科,药师,研究方向:药学,

电话:13391567523, E-mail: tianyubing01@163.com

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前言

慢性心力衰竭是临床上常见的心血管疾病,具有较高的发病率和死亡率。临床研究表明^[1-3]心力衰竭主要是由已存在的心功能疾病、血流动力学超负、炎症等发展而来,会导致人体的心肌结构发生变化,对心功能造成影响,甚至导致患者死亡。慢性心力衰竭的临床表现为乏力、呼吸急促、困难,心跳加速、肺部啰音、胸腔积液。改善患者的心功能、缓解心室结构重建,提高心肌细胞代谢是治疗的关键^[3]。

贝那普利是血管紧张素转换酶抑制药,虽其起效作用慢,但不影响吸收率,且作用时间较长能够有效改善心力衰竭患者临床症状及心功能指标^[4]。益气宁心汤由多种中药材制成,能够改善临床症状,清除氧自由基。目前,临床上对二者联合用药的报道较少。因此,本研究主要探讨了益气宁心汤联合贝那普利对慢性心衰患者的临床疗效及其可能机制。

1 资料与方法

1.1 一般资料

收集 2014 年 3 月至 2015 年 3 月我院收治的 80 例慢性心衰患者,均符合慢性心力衰竭诊断标准^[5]:乏力、呼吸急促、困难,心跳加速、肺部啰音、胸腔积液。纳入肝、肾功能正常患者;配合研究患者;血糖、尿常规正常者;排除患有急性心肌梗死;患有自身免疫性疾病;患有恶性肿瘤患者;患有精神疾病。本研究家属及患者均签署知情同意书,且经医院伦理委员会许可,按抽签法分组。对照组 23 例男,17 例女,年龄 50~80 岁,平均(63.29±5.03)岁,心功能分级:10 例Ⅱ级;19 例Ⅲ级;11 例Ⅳ级。原发病:18 例冠心病;12 例高血压;10 例心肌病;实验组 25 例男,15 例女,年龄 52~80 岁,平均(64.06±5.18)岁,心功能分级:11 例Ⅱ级;19 例Ⅲ级;10 例Ⅳ级。原发病:20 例冠心病;12 例高血压;8 例心肌病。两组性别等一般临床特征比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组患者入院后均给予常规基础对症治疗,包括营养支持、吸氧、强心、利尿、纠正电解质紊乱。对照组患者采用贝那普

利(规格:5 mg;生产厂家:北京诺华制药有限公司;批号:20131210)10 mg 进行治疗,每天 1 次。实验组在基础治疗上,采用益气宁心汤联合贝那普利治疗,贝那普利同对照组,益气宁心汤:28 g 生黄茂,28 g 白参,15 g 麦冬,10 g 丹参,8 g 五味子,25 g 茯苓,10 g 白术,8 g 桂枝,28 g 猪苓,15 g 泽泻,5 g 佛手,5 g 木香,15 g 葶苈子,25 g 大枣。加入水煎煮后服用,每天 1 剂,于早晚服用。两组治疗疗程均为 2 周。

1.3 观察指标

观察两组患者临床疗效,心功能指标左心室舒张末径(LVEDD)、左心室收缩末期内径(LVESD)、左室射血分数(LVEF)的变化,血清生长分化因子-15(GDF-15)、可溶性 ST2 蛋白(sST2)、脂联素(APN)水平的变化,急性生理学及慢性健康状况评分(APACHE-II)、肺部感染评分(CPIS)评分。

1.3.1 APACHE-II、CPIS 评分 APACHE-II 评分:记录两组患者治疗前后的生理指标,采用 APACHE-II 评分进行评估。CPIS 评分:记录两组患者治疗前后生理体征,如体温、痰液量、血气情况等,采用 CPIS 评分进行评估。

1.3.2 指标检测 采用彩色多普勒超声仪对两组患者治疗后心功能 LVEDD、LVESD、LVEF 进行检测。于治疗前后采取静脉血,离心分离血清,采用酶联免疫吸附法对 GDF-15、sST2、APN 进行检测,试剂盒来自美国 ADR 公司。

1.3.3 临床疗效观察 临床症状完全消失,心功能改善Ⅱ级为显效;临床症状有所改善,心功能改善Ⅰ级为有效^[6]。临床症状及心功能无变化为无效。

1.4 统计学分析

选择 SPSS18.0 行数据统计,计量资料用($\bar{x} \pm s$)表示,组间比较用 t 检验,计数资料用[(例)%]表示,组间比较用 χ^2 检验比较, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效对比

实验组总有效率为 92.50%,显著高于对照组 72.50%($P<0.05$),见表 1。

表 1 两组临床疗效对比[(n)%]

Table 1 Comparison of the therapeutic effect between two groups[(n)%]

Groups	Effective	Valid	Invalid	Total effective rate
Experimental group(n=40)	30(75.00)	7(17.50)	3(7.50)	37(92.50)*
Control group(n=40)	24(60.00)	5(12.50)	11(27.50)	29(72.50)

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

2.2 两组治疗前后心功能对比

两组治疗前 LVEDD、LVESD、LVEF 比较差异无统计学意义($P>0.05$),治疗后,两组 LVEDD、LVESD、LVEF 均有所改善,且实验组改善程度更显著($P<0.05$),见表 2。

2.3 两组治疗前后血清 GDF-15、sST2、APN 水平的比较

两组治疗前血清 GDF-15、sST2、APN 水平比较差异无统计学意义($P>0.05$);治疗后,两组血清 GDF-15、sST2、APN 水平均显著降低,且实验组降低程度更显著($P<0.05$),见表 3。

表 2 两组心功能的对比($\bar{x} \pm s$)Table 2 Comparison of the heart function between two groups($\bar{x} \pm s$)

Groups		LVEDD(mm)	LVESD(mm)	LVEF(%)
Experimental group(n=40)	Before treatment	60.27± 8.03	47.93± 5.87	41.26± 4.32
	After treatment	53.56± 6.24* [#]	41.26± 4.95* [#]	57.91± 5.93* [#]
Control group(n=40)	Before treatment	59.64± 8.20	48.80± 5.60	42.18± 4.29
	After treatment	57.40± 6.72*	46.28± 4.86*	50.27± 5.90*

Note: Compared with those before treatment, * $P<0.05$; Compared with the control group, [#] $P<0.05$.

表 3 两组治疗前后血清 GDF-15、sST2、APN 水平对比($\bar{x} \pm s$)Table 3 Comparison of the serum GDF-15, sST2, APN levels before and after treatment two groups($\bar{x} \pm s$)

Groups		GDF-15(ng/L)	sST2(ng/mL)	APN(mg/L)
Experimental group(n=40)	Before treatment	1989.27± 187.36	293.45± 30.86	20.38± 4.05
	After treatment	820.81± 73.14* [#]	4.28± 1.02* [#]	13.47± 2.18* [#]
Control group(n=40)	Before treatment	1987.36± 185.97	291.86± 29.75	19.90± 4.38
	After treatment	1192.86± 93.62*	20.69± 3.48*	16.05± 3.63*

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

2.4 两组治疗前后 APACHE- II、CPIS 评分的比较

两组治疗前后益气宁心汤联合贝那普利治疗慢性心力衰

竭能显著提高其临床疗效,改善心功能,可能与其有效降低血清 GDF-15、sST2、APN 的水平有关。见表 4。

表 4 两组 APACHE- II、CPIS 评分对比($\bar{x} \pm s$, 分)Table 4 Comparison of the APACHE- II, CPIS score of two groups($\bar{x} \pm s$, scores)

Groups		APACHE- II	CPIS
Experimental group(n=40)	Before treatment	27.03± 6.49	7.03± 1.34
	After treatment	13.90± 3.28* [#]	3.24± 0.92* [#]
Control group(n=40)	Before treatment	27.38± 6.42	7.10± 1.32
	After treatment	20.37± 4.97*	5.38± 1.01*

Note: Compared with those before treatment, * $P<0.05$. Compared with the control group, * $P<0.05$; vs the control group, [#] $P<0.05$.

3 讨论

患者心力衰竭后,心肌收缩力会出现下降,导致心排量不能满足患者机体代谢的需要,器官及组织无法得到需要的血液灌注^[7]。研究表明^[8]心肌重构是致使心力衰竭发生的重要机制,临床上可见患者心室形状改变。心肌重构会加剧心肌损伤,导致患者的心功能出现进一步的恶化。改善患者的心肌能量代谢,能够促进保护心肌细胞的内部结构,能够提高患者的心肌收缩功能和舒张功能,从而达到缓解心衰的目的^[9]。贝那普利具有降低患者降低醛固酮水平的作用,能够缓解心肌重塑,从而改善患者的心功能^[10]。本研究结果显示:采用贝那普利治疗后,患者的心功能指标 LVEDD、LVESD、LVEF 均有所改善,说明贝那普利能够优化心肌细胞代谢,可达到充足的血流灌注,从而缓解心室结构重塑的目的。

在中医中,心力衰竭属于“心悸、胸痹”的范畴,主要是由于久病不愈、阳气衰弱所致,且常伴有气血瘀滞、水肿现象^[11]。中医认为^[12],活血化瘀、温阳补气、利水行气为治疗之契机。益气宁心汤由多种中药材制成,其中生黄芪、茯苓皮具有补中益气、利水的功效;白参、麦冬可补气生津;红花、牛膝具有活血通经、

祛瘀止痛的功效;五味子可调节心血管系统,改善血液循环;白术、桂枝可燥湿利水、补气益气;泽漆、葶苈子可行水消痰;佛手可补血益气;木香可行气止痛;甘草可调和诸药^[13-14]。且药理学研究表明^[15]人参能够清除氧自由基,减轻对心肌细胞的损伤,具有显著的强心作用,可保护心功能。诸药合制,可增加心脏的血流灌注,使心肌供血充足,恢复心功能正常运作,同时还可减少心肌耗氧量,提高心肌摄氧能力^[16]。本研究显示,采用联合益气宁心汤治疗的患者 LVEDD、LVESD、LVEF 及治疗疗效显著优于采用单一贝那普利治疗的患者,说明中西医结合较单纯西医治疗具有显著性的优势,可恢复心功能,提高治疗疗效。且本研究通过 APACHE- II、CPIS 评分对两组患者的体温、痰液量、血气情况及相关生理指标评估,发现采用联合益气宁心汤治疗的患者临床症状及体征的改善情况更佳,说明中西医结合对患者的临床症状改善情况更显著。

基础研究显示^[17]sST2、APN 与心力衰竭发展具有密切的关系。sST2 是一种心肌蛋白,具有敏感性及特异性,参与众多的病理生理过程,可反映心室功能紊乱程度,在全身炎症反应和变态反应性疾病中发挥着非常重要的作用^[18]。APN 水平会随着 NYHA 分级的增加而升高,高 APN 水平是心力衰竭患者死亡

的危险因子^[9]。在本研究中,采用联合益气宁心汤治疗的患者sST2、APN水平显著低于采用单一贝那普利治疗的患者,说明了益气宁心汤能够纠正心肌细胞的代谢,改善心功能,抑制sST2、APN的分泌。GDF-15是一种应激反应蛋白,可检测患者的死亡风险以及预后^[21]。国外研究显示^[20]心力衰竭患者的血清GDF-15水平显著高于正常人,GDF-15水平能够反映心力衰竭患者的病情以及心室重构程度^[22]。本研究显示采用联合益气宁心汤治疗的患者GDF-15水平显著低于采用单一贝那普利治疗的患,说明益气宁心汤能够抑制心室重构,保护心肌细胞^[23]。

综上所述,益气宁心汤联合贝那普利治疗慢性心衰患者的临床疗效及对血清生长分化因子-15(GDF-15)、可溶性ST2蛋白(sST2)、脂联素(APN)的影响。

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