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温阳益气汤对阳虚血瘀证慢性心力衰竭患者血清 sST2 及 GDF-15 的影响 *

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摘要 目的:探讨温阳益气汤对阳虚血瘀证慢性心力衰竭患者血清可溶性 ST2(sST2)及血清生长分化因子 15(GDF-15)的影响。**方法:**以 2019.2-2020.5 于我院就诊的慢性心力衰竭患者 133 例为研究对象,随机平均分为对照组(常规西医治疗)和观察组(在对照组的基础上给予温阳益气汤治疗)。观察并记录两组患者治疗效果和不良反应,心脏彩超仪器检测心功能指标(SV、CO、LVEF、LVED),ELISA 法检测血清 sST2 及 GDF-15 的表达水平,生活质量评分量表评价患者生活质量。**结果:**(1)观察组总有效率显著高于对照组($P<0.05$);(2)治疗后两组以上指标均较治疗前显著增加($P<0.05$),且治疗后观察组 SV、CO、LVEF 均较对照组显著增加($P<0.05$),而 LVED 无显著变化($P>0.05$);(3)治疗后两组患者 sST2、GDF-15 均较治疗前显著降低($P<0.05$),且观察组以上指标均较对照组显著降低($P<0.05$);(4)治疗前两组患者社会领域、身軀领域、情绪领域、经济领域得分差异无统计学意义($P>0.05$),治疗后两组患者社会领域、身軀领域、情绪领域、经济领域得分均较治疗前显著增加,且治疗后观察组以上评分也显著高于对照组($P<0.05$)。**结论:**温阳益气汤能使 sST2、GDF-15 表达降低,改善患者心功能和生活质量,疗效佳,具有一定临床参考意义。

关键词:温阳益气汤;阳虚血瘀证;慢性心力衰竭;sST2;GDF-15

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Effect of Wenyang Yiqi Decoction on Serum ST2 and GDF-15 in Patients with Chronic Heart Failure of Yang Deficiency and Blood Stasis Syndrome*

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ABSTRACT Objective: To explore the effect of Wenyang Yiqi Decoction on serum soluble ST2 (sst2) and serum growth differentiation factor 15 (GDF-15) in patients with chronic heart failure of Yang deficiency and blood stasis syndrome. **Methods:** 133 patients with chronic heart failure treated in our hospital from February 2019 to May 2020 were taken as the research object, and randomly divided into a control group (conventional Western medicine treatment) and an observation group (on the basis of the control group given to Wenyang Yiqi Decoction). The treatment effects and adverse reactions of the two groups of patients were observed and recorded, Cardiac ultrasound equipment is used to detect cardiac function indicators (SV, CO, LVEF, LVED), Cardiac color Doppler ultrasound instrument detects cardiac function indexes (SV, CO, LVEF, LVED), ELISA method was used to detect the expression levels of serum sST2 and GDF-15, and the quality of life score scale was used to evaluates the quality of life of patients. **Results:** (1) The total effective rate of the observation group was significantly higher than that of the control group ($P<0.05$); (2) After treatment, more than two groups of indicators were significantly increased ($P<0.05$), and after treatment, the observation group SV, CO, LVEF were significantly lower than the control group($P<0.05$), but there is no significant change in LVED ($P>0.05$); (3) After treatment, sST2 and GDF-15 in both groups were significantly lower than before treatment($P<0.05$), and the above indicators in the observation group were significantly lower than those in the control group ($P<0.05$); (4) There was no statistically significant difference in scores in the social, physical, emotional, and economic fields between the two groups before treatment ($P>0.05$), after treatment, the scores of the social, physical, emotional, and economic fields of the two groups of patients increased significantly compared with those before treatment, and the scores above the observation group after treatment were also significantly higher than those of the control group ($P<0.05$). **Conclusion:** Wenyangyiqi decoction can reduce the expression of ST2 and GDF-15, improve the heart function and quality of life of patients, and has good curative

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effect, which has certain clinical reference significance.

Key words: Wenyangyiqi Decoction; Yang deficiency and blood stasis syndrome; Chronic heart failure; sST2; GDF-15

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前言

慢性心力衰竭是指心脏收缩和舒张功能障碍导致的心脏射血受限,是心内科常见的疾病之一,随着人口老龄化的加重,慢性心力衰竭的发病率越来越高,逐渐成为威胁患者生命健康的主要疾病之一^[1-2]。慢性心力衰竭主要临床症状包括气促、乏力、运动耐力降低和体液潴留导致的水肿等,作为心脏器质性疾病引起的严重并发症,是临床心血管疾病致死的主要原因,据统计慢性心力衰竭患者5年病死率与癌症相当,不仅严重影响患者的生活质量,而且加重了患者的经济负担^[3,4]。慢性心衰的治疗方式主要包括强心、利尿、扩血管等,但是随着疾病的进展,部分患者会出现电解质紊乱和耐药现象,导致药物的应用受限,延误患者的治疗^[5,6]。随着中医的不断发展,中医辨证论治认为心衰的主要病因为心肾阳虚,气血淤滞,治疗上宜温心肾之阳,行心肾之气,在改善患者症状、维持心功能、提高生活质

量、减少再住院率等方面具有一定的优势^[7,8]。目前研究发现sST2及GDF-15作为继BNP之后新的生物标记物,对心衰的诊断、危险分层和预后评估有一定的价值^[9]。基于此,本研究探讨温阳益气汤对阳虚血瘀证慢性心力衰竭患者的疗效及其对血清sST2及GDF-15的影响,报道如下。

1 资料与方法

1.1 一般资料

选取2019年2月至2020年5月于我院就诊的慢性心力衰竭患者133例,按照随机数字表法分为观察组(66例)与对照组(67例),两组患者性别、年龄、病程等一般资料差异无统计学意义($P>0.05$),见表1。本研究经我院伦理委员会批准,患者同意签署知情同意书。冠心病(Coronary heart disease, CHD),心脏瓣膜病(Valvular heart disease, VHD),心肌病(Cardiomyopathy, CO),肺源性心脏病(Pulmonary heart disease, PHD)。

表1 两组患者一般资料

Table 1 General data of the two groups of patients

Groups	Gender		Age (years)	Duration of disease (month)	Cardiac function grading			Basic diseases			
	male	female			II	III	IV	CHD	VHD	CO	PHD
Observation group	32	34	59.25±8.12	8.45±2.27	5	32	29	26	10	10	20
Control group	30	37	60.94±7.63	8.10±2.01	7	28	32	28	9	13	17

1.2 纳入与排除标准

纳入标准:(1)符合慢性心力衰竭衰竭的西医诊断标准^[10];(2)符合心衰的中医诊断标准,且中医辨证候为阳虚血瘀证^[11];(3)患者同意签署知情同意书。

排除标准:(1)严重肝肾功能损伤;(2)患者合并严重室性心律失常、急性心肌梗死、心源性休克等;(3)有相关药物过敏史者;(4)近期为进行药物治疗;(5)合并有精神病或不愿或无法合作者。

1.3 研究方法

对照组患者均给予ACEI、利尿剂、洋地黄等药物治疗,同时辅以低流量吸氧,控制盐摄入量,保持休息,调节饮食。观察组患者在西医常规治疗基础上,给予温阳益气汤治疗,温阳益气汤构成:益母草30g,桃仁、红花、川芎及五味子各10g,附子6g,人参、当归、茯苓、桂枝及白术各15g,黄芪20g。将所有药物与水混合沸水熬至200mL,于每日早晚口服。患者均治疗6个疗程,1个疗程15天,疗程之间间隔3天。

1.4 观察指标

1.4.1 疗效判定 对患者治疗疗程结束后进行疗效评价,慢性心力衰竭的疗效标准评定^[10],分为:(1)恶化:NYHA分级降低,患者的症状、体征恶化;(2)无效:NYHA分级改善不足1级,症

状及体征无明显改善;(3)有效:NYHA分级提高1-2级,症状及体征明显改善,但活动后仍有发生;(4)显效:NYHA分级提高2级及以上,症状及体征完全改善;治疗总有效率=(显效+有效)/总例数。

1.4.2 心功能指标 观察两组患者治疗前和治疗后心功能各指标。每分钟搏出量(SV)、心输出量(CO)、左室舒张末期内径(LVED)、左心室射血分数(LEVF)水平变化情况采用心脏彩超仪器为飞利浦IE33全数字化多普勒超声诊断仪,由专业超声科医生进行评估。

1.4.3 两组患者sST2及GDF-15比较 分别与治疗前和疗程结束后当天抽取患者外周静脉血5mL,用3000r/min的速度离心10分钟,静置取上清备用。用ELISA法检测血清sST2及GDF-15的表达水平,试剂盒由试剂盒由德国罗氏公司提供,所有操作严格按照说明书执行。

1.4.4 生活质量评分^[12] 生活质量评分采用明尼苏达生活质量问卷评价两组患者治疗前及治疗结束当天的生活质量评分,应用逆向转换法计算,各领域及综合分的转换分数最高为100分,转换分换算的基本公式:转换分=(该领域可能的最高得分-原始分)/该领域可能的最高得分×100,分数越高表示生活质量越差。

1.4.5 不良反应 观察两组患者呕吐、头晕等不良反应的发生情况

1.5 统计学方法

数据处理采用 SPSS19.0 统计软件,计数资料以率[n(%)]的形式表示,计数资料用秩和检验或者 χ^2 检验;计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,比较采用 t 检验, $P < 0.05$ 为有统计学

2 结果

2.1 两组患者疗效比较

观察组总有效率显著高于对照组($P < 0.05$),见表 2。

表 2 两组患者疗效比较

Table 2 Comparison of curative effect between the two groups

Groups	Deterioration	Invalid	Effective	Excellent	Total effective rate(%)
Observation group	2	5	32	27	89.39*
Control group	7	10	28	22	74.63

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

2.2 两组患者心功能指标比较

治疗前两组患者 SV、CO、LVED、LVEF 差异无统计学意义($P > 0.05$),治疗后两组以上指标均较治疗前显著增加($P < 0.$

05),且治疗后观察组 SV、CO、LVEF 均较对照组显著增加($P < 0.05$),而 LVED 无显著变化($P > 0.05$),见表 3。

表 3 两组患者心功能指标比较

Table 3 Comparison of cardiac function indexes between the two groups

Groups	SV(mL)		CO(L/min)		LVED(mm)		LVEF(%)	
	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	40.56 $\pm$ 6.34	49.19 $\pm$ 5.69**	3.29 $\pm$ 0.18	4.02 $\pm$ 0.26**	68.94 $\pm$ 6.05	66.87 $\pm$ 5.12*	39.13 $\pm$ 6.14	47.95 $\pm$ 7.83**
Control group	41.04 $\pm$ 7.84	57.45 $\pm$ 5.27*	3.30 $\pm$ 0.12	4.31 $\pm$ 0.18*	69.13 $\pm$ 7.27	65.57 $\pm$ 7.94*	40.20 $\pm$ 5.68	54.95 $\pm$ 9.34*

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

2.3 两组患者 sST2 及 GDF-15 比较

治疗前两组患者 sST2、GDF-15 相比差异均无统计学意义($P > 0.05$);治疗后两组患者 sST2、GDF-15 均较治疗前显著降

低($P < 0.05$),且观察组以上指标均较对照组显著降低($P < 0.05$),见表 4。

表 4 两组患者 sST2 及 GDF-15 比较

Table 4 Comparison of SST2 and GDF-15 between the two groups

Groups	GDF-15(ng/L)		sST2(ng/mL)	
	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	1893.28 $\pm$ 268.90	834.17 $\pm$ 128.30**	284.95 $\pm$ 36.37	86.42 $\pm$ 21.57**
Control group	1956.13 $\pm$ 215.63	1478.31 $\pm$ 116.83*	291.52 $\pm$ 31.94	142.58 $\pm$ 35.25*

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

2.4 生活质量评分

治疗前两组患者社会领域、身躯领域、情绪领域、经济领域得分差异无统计学意义($P > 0.05$),治疗后两组患者社会领域、身躯领域、情绪领域、经济领域得分均较治疗前显著增加,且治疗后观察组以上评分也显著高于对照组($P < 0.05$),见表 5。

3 讨论

慢性心力衰竭是心室充盈和射血障碍引起的临床综合征,主要临床特征为神经内分泌激活、心室功能不全和外周血流分布异常,目前研究发现慢性心力衰竭主要的发病机制为冠心

病、心肌病等导致心脏结构改变,造成心脏充盈和射血能力下降,进一步导致血液淤积于心脏和器官灌注不足,从而导致呼吸困难、水肿乏力等临床症状^[13,14]。慢性心力衰竭的主要治疗方案为增强心脏射血能力、利尿消肿和扩张外周血管等,但是对于重症患者和顽固性心衰患者的疗效欠佳,且存在治疗周期较长,易反复发作等问题^[15]。传统医学认为慢性心力衰竭属于“心悸、喘症、水肿”范畴,其病因之本为心肾阳虚,治疗时宜温阳宣气、活血化痰、利水消肿等。温阳宣气汤由益母草、桃仁、红花、川芎、五味子、附子、人参、当归、茯苓、桂枝等多味中药构成,具有活血化痰、利水温阳的作用,与慢性心力衰竭病机符合,病理一致,适合运用于慢性心力衰竭的治疗中^[16-18]。

表 5 两组患者生活质量评分

Table 5 Quality of life scores of patients in the two groups

Groups	Social fields		Body field		Emotional field		Areas of the economy	
	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	52.17± 7.85	68.34± 7.14 ^{*#}	50.45± 7.84	71.67± 5.94 ^{*#}	53.37± 6.89	78.67± 6.05 ^{*#}	45.76± 8.57	66.81± 6.15 ^{*#}
Control group	53.27± 5.63	60.13± 6.83 [*]	51.73± 5.94	62.45± 6.18 [*]	54.16± 7.15	67.12± 6.38 [*]	47.25± 6.04	54.10± 7.28 [*]

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

SV、CO、LVEF 均为反应心脏功能的超声检查结果,其中 LVEF 与心肌的收缩能力有关,临床上主要用 LVEF 反应心功能^[19]。本研究结果显示观察组总有效率显著高于对照组($P < 0.05$);治疗后 SV、CO、LVEF 等指标水平均显著高于治疗前,且观察组显著高于对照组($P < 0.05$)。表明在西医治疗的基础上联合应用温阳益气汤治疗慢性心力衰竭的临床疗效更佳,并能使 SV、CO、LVEF 提高。温阳益气汤由多味中药组成,川芎、当归、茯苓、附子等诸药联合作用具有温阳益气的作用,在此基础上辅以活血化瘀利水治疗慢性心力衰竭,加用附子温阳,泽泻、冬瓜皮、大腹皮利水,当归、川芎活血化瘀^[20,21]。2019 年的一项临床研究也发现观察组较对照组具有较高的治疗有效率,宜气汤能够抑制慢性心力衰竭患者心室重构,进而提高患者生活质量,且不良反应少,具有一定的临床价值^[22]。

sST2 是白细胞介素 1 受体家族成员之一,主要与白细胞介素 33 结合,当心肌成纤维细胞或者心肌细胞压力负荷和容量负荷增加时,其表达明显增加^[23]。GDF-15 是以一种应激反应蛋白,被发现当机体出现肿瘤、心肌缺血、类风湿性关节炎等时,该蛋白的表达水平将会升高,能够促进大多数肿瘤细胞凋亡,同时还具有保护细胞,促进生长的作用^[24]。研究表明,sST2 是心脏功能的标志物之一,心室功能障碍和心肌重构现象发生则表明 IL-33/ST2L 信号通路的心肌保护作用被阻断,sST2 含量显著上升,而 GDF-15 是与心肌重塑相关的心血管保护因子,可抑制细胞凋亡^[25,26]。进一步研究发现治疗后两组患者 sST2、GDF-15 均减小,观察组小于对照组($P < 0.05$)。表明温阳益气汤能降低慢性心力衰竭患者 sST2、GDF-15 的表达。郑建津等人通过研究中西医结合方法治疗慢性心衰的临床疗效及对 GDF-15、sST2、脂联素(APN)的影响,该治疗方法能够降低患者 sST2、GDF-15 的表达,有效治疗慢性心衰^[27]。与本文结果类似,为本研究结果提供了证据支持。

现代药理学研究发现当归中的阿魏酸不仅具有一定扩张血管、增强心脏功能,并且在抑制心脏重构、改善心肌缺血方面有重要作用,附子具有较好的扩张血管、抗心律失常作用,对于改善心脏功能具有积极作用^[28,29]。联合诸药共同发挥改善心脏重构、扩张外周血管、减轻心脏负荷的作用,并使患者 sST2、GDF-15 表达水平降低,从而达到治疗慢性心力衰竭的目的。进一步对两组患者生活质量进行评价发现,治疗后治疗前两组患者社会领域、身躯领域、情绪领域、经济领域得分均增加,观察组大于对照组($P < 0.05$)。表明经温阳益气汤治疗后,两组患者生活质量明显提高。苗娟娟^[30]等人通过分析临床疗效、生活质量评分以及治疗前后心功能各项指标,也发现观察组高于对照组,且治疗期间均未出现明显不良反应,与本文结果一致。表明

温阳益气汤治疗慢性心力衰竭的安全性较高,适合运用于临床,值得进一步推广。

综上,在西医治疗的基础上联合应用温阳益气汤治疗慢性心力衰竭的临床疗效更佳,使 sST2、GDF-15 表达降低,改善患者心功能和生活质量,具有一定的临床应用价值。

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