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益气温阳活血利水法治疗心肾综合征的疗效及对患者心肾功能及血浆脑钠肽、肾素、血管紧张素、醛固酮水平的影响*

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摘要 目的:探讨益气温阳活血利水法治疗心肾综合征的临床疗效及对患者心肾功能及血浆脑钠肽(BNP)、肾素(PRA)、血管紧张素Ⅱ(AngⅡ)、醛固酮(ALD)水平的影响。**方法:**研究对象为本院2017年3月~2018年9月收治的124例心肾综合征患者,采用随机数字表将其分成观察组与对照组,每组62例。两组患者均给予常规西医对症治疗,观察组同时给予中医益气温阳活血利水法治疗,两组均连续治疗3周后进行疗效评价。比较两组治疗前后心肾功能、血浆BNP、PRA、AngⅡ、ALD水平的变化情况。**结果:**治疗后,观察组总有效率为,显著高于对照组($P<0.01$);两组左心射血分数(LVEF)、表皮生长因子受体(eGFR)均较治疗前明显上升,SCr、BUN、血浆CysC、BNP、PRA、AngⅡ、ALD水平均较治疗前明显降低($P<0.01$),且观察组LVEF、eGFR明显高于对照组,SCr、BUN、血浆CysC、BNP、PRA、AngⅡ、ALD水平显著低于对照组($P<0.01$);观察组LVESD、LVEDD与治疗前比较明显降低($P<0.01$),而对照组治疗前后LVESD、LVEDD无明显变化($P>0.05$)。**结论:**益气温阳活血利水法治疗心肾综合征的临床疗效显著优于单用常规西医对症治疗,其可有效改善患者的心肾功能,降低患者的血浆BNP、PRA、AngⅡ、ALD水平。

关键词:益气温阳活血利水;心肾综合征;心肾功能;血浆肾素系统

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Effect of Yiqiwenyang - huoxuelishui Therapy on the Heart and Renal Function as Well as the Plasma BNP, PRA, AngⅡ, ALD Levels of Patients with Cardiorenal Syndrome*

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ABSTRACT Objective: To investigate the effect of Yiqiwenyang-huoxuelishui therapy on the heart and renal function as well as the plasma brain natriuretic peptide (BNP), renin (PRA), angiotensinⅡ (AngⅡ), aldosterone (ALD) levels of patients with cardiorenal syndrome. **Methods:** The subjects of this study were selected from 124 cases of patients with cardiorenal syndrome admitted in our hospital from March 2017 to September 2018. They were divided into the observation group and the control group based on a random number table, 62 cases in each group. Both groups were treated with conventional western medicine, and the observation group was additionally given Yiqiwenyang - huoxuelishui therapy. The clinical efficacy was evaluated for both groups at 3 weeks after treatment. The heart and renal function, changes of plasma BNP, PRA, AngⅡ, ALD levels before and after treatment were compared between the two groups. **Results:** After treatment, the total effective rate of the observation group was 0, which was significantly higher than that of the control group ($P<0.01$). Two groups of left heart ejection fraction (LVEF), epidermal growth factor receptor (eGFR) was a significant increase in the, SCr, BUN, serum CysC, BNP, PRA, AngⅡ, ALD levels were significantly lower than before treatment ($P<0.01$), and LVEF and eGFR observation group was obviously higher than that of control group, SCr, BUN, serum CysC, BNP, PRA, AngⅡ, ALD were significantly lower than control group ($P<0.01$); LVESD and LVEDD in the observation group were significantly lower than before treatment ($P<0.01$), while LVESD and LVEDD in the control group were not significantly changed before and after treatment ($P>0.05$). **Conclusion:** Yi Yang qi and temperature, water treatment was more effective in the treatment of cardiorenal syndrome than the conventional western medicine alone, it can effectively improve the heart function, reduce the blood plasma BNP, PRA, AngⅡ, ALD levels.

Key words: Yiqiwenyang - huoxuelishui therapy; Cardiorenal syndrome; Heart and renal function; Renin - angiotensin system

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前言

心肾综合征是心脏或肾脏发生急、慢性功能障碍后诱发另一脏器出现功能障碍,二者互为因果,并形成恶性循环,最终引发心、肾功能共同损害^[1,2]。由于心脏与肾脏损害之间形成恶性循环后可加速多器官功能障碍或衰竭,因此患者的病死率较高^[3,4]。临床治疗心肾综合征时旨在保护肾脏,改善心功能,同时积极处理并发症,但目前尚缺乏确切的治疗方案,西药对其治疗主要采取的是对症支持治疗,但仅能短期缓解症状,长期使用易引发一系列不良反应,加重机体损害^[5,6]。中医认为心肾综合征属本虚标实之证,本虚为心肾阳衰、心肾不交,标实为血瘀、水饮内停^[7,8]。针对心肾综合征的发病机制,本研究采取了中医益气温阳活血利水法治疗心肾综合征患者并取得了较好的疗效。现将结果报道如下。

1 资料与方法

1.1 一般资料

选择本院 2017 年 3 月~2018 年 9 月收治的 124 例心肾综合征患者,依据就诊顺序对患者做编号,并按随机数字表分为观察组(n=62 例)与对照组(n=62 例)。观察组男 28 例,女 34 例;年龄 46~88 岁,平均(66.4±8.5)岁;病程 4~23 年,平均(11.5±5.7)年;心功能分级:II 级 29 例,III 级 26 例,IV 级 7 例;原发病:冠心病 30 例,高血压性心脏病 22 例,瓣膜性心脏病 5 例,风湿性心脏病 3 例,扩张型心肌病 1 例,肺源性心脏病 1 例。对照组男 30 例,女 32 例;年龄 45~87 岁,平均(64.9±9.3)岁;病程 4~21 年,平均(10.8±5.2)年;心功能分级:II 级 27 例,III 级 31 例,IV 级 4 例;原发病:冠心病 33 例,高血压性心脏病 21 例,瓣膜性心脏病 4 例,风湿性心脏病 2 例,扩张型心肌病 2 例。两组一般临床资料比较差异无统计学意义($P>0.05$),具有可比性。

1.2 诊断标准

符合 2008 年威尼斯会议《急性透析质量改善计划共识会议报告》中有关心肾综合征的诊断标准^[9]。中医辨证为阳虚血瘀证:主症为胸闷、胸痛;次症为心悸、气短、浮肿、畏寒肢冷、口唇青紫、舌质胖、脉细涩或结代。符合主症≥1 项,次症≥1 项,结合舌脉,可确诊。

1.3 纳入与排除标准

纳入标准:(1)符合以上临床诊断及辨证标准;(2)年龄 45~90 岁;(3)心功能分级 II~IV 级;(4)自愿签署知情同意书;(5)研究通过医院伦理委员会批准。排除标准:(1)合并脑卒中、主

动脉瓣狭窄、肺栓塞、严重出血倾向、严重感染;(2)合并严重肝脏疾病、心包血液病、自身免疫性疾病、全身系统疾病;(3)合并严重呼吸困难疾病,如上消化道出血、慢性阻塞性肺疾病并肺性脑病等;(4)伴孤立肾的单侧肾动脉狭窄或双侧肾动脉狭窄;(5)合并精神异常或神经系统疾病;(6)妊娠或哺乳期妇女;(7)过敏体质,对研究药物过敏。

1.4 治疗方法

对照组给予包括利尿剂、血管紧张素转化酶抑制剂(ACEI)、洋地黄类药物、β 受体阻滞剂、纠正贫血、纠正水电解质紊乱、纠正酸碱失衡等在内的常规西药治疗,对合并高血压、糖尿病、高脂血症等基础疾病者,给予相应对症治疗。观察组同时给予中医益气温阳活血利水法治疗,方药组成:黄芪 60 g,党参、鹿衔草、鸡骨草各 30 g,川芎、丹参各 15 g,山萸肉、淫羊藿、茯苓、白术、泽兰、砂仁(后下)各 10 g,大黄 6 g,随证加减。血瘀甚者加红花 6 g;水湿甚、肢体浮肿甚者加通草 5 g、车前子 30 g。每日 1 剂,水煎至 180 mL 后,分早晚服用,连续治疗 8 周。

1.5 疗效评定

显效:胸闷、胸痛、心悸、气短等症状基本消失,水肿基本消退,尿量显著增多,各项指标检查趋于正常,心功能改善至少 2 级;有效:症状有所缓解,水肿大部分消退,尿量增多,各项指标检查明显好转,心功能改善 1 级;无效:症状、水肿、尿量、实验室检查、心功能等均无明显改善或加重。以显效及有效为总有效。

1.6 观察指标

(1)心功能:治疗前后采用超声心动仪测定患者的左室射血分数(LVEF)、左心室收缩末内径(LVESD)、左心室舒张末内径(LVEDD),采用酶联免疫吸附试验(ELISA)检测血浆脑钠肽(BNP)水平。(2)肾功能:采用生化分析仪测定患者的血肌酐(SCr)、尿素氮(BUN)、胱抑素 C(CysC)水平,肾动态显像法测定患者的肾小球滤过率(eGFR)。(3)肾素系统:采用放免法测定患者的血浆肾素活性(PRA)、血管紧张素 II(Ang II)、醛固酮(ALD)水平。

1.7 统计学分析

采取 SPSS20.0 软件处理数据,计数资料采用 χ^2 检验,计量资料采用 t 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

观察组经 8 周治疗后总有效率为 90.32%(56/62),相对于对照组[67.74%(42/62)]显著升高($P<0.01$),见表 1。

表 1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between two groups[n(%)]

Groups	n	Excellent	Effective	Invalid	Total effective rate
Observation group	62	41	15	6	56(90.32)
Control group	62	28	14	20	42(67.74)
P					0.002

2.2 两组治疗前后心功能的比较

两组经 8 周治疗后 LVEF 均较治疗前明显上升,而血浆

BNP 水平明显降低($P<0.01$), 观察组 LVEF、血浆 BNP 水平较 LVEDD 与治疗前比较明显降低 ($P<0.01$), 而对照组治疗前后
对照组改善更明显 ($P<0.01$), 观察组经 8 周治疗后 LVESD、LVESD、LVEDD 水平无明显变化($P>0.05$), 见表 2。

表 2 两组治疗前后心功能指标的比较($\bar{x} \pm s$)Table 2 Comparison of the cardiac function indexes between two groups before and after treatment($\bar{x} \pm s$)

Groups	Time	LVEF(%)	LVESD(mm)	LVEDD(mm)	BNP(ng/L)
Observation group (n=62)	Before treatment	42.04 $\pm$ 3.13	35.12 $\pm$ 1.34	49.56 $\pm$ 2.28	435.56 $\pm$ 75.24
	After treatment	49.92 $\pm$ 2.98**	32.25 $\pm$ 1.25**	45.27 $\pm$ 2.53**	246.12 $\pm$ 86.78**
Control group (n=62)	Before treatment	42.58 $\pm$ 3.28	34.87 $\pm$ 1.58	49.12 $\pm$ 2.06	429.62 $\pm$ 90.21
	After treatment	46.78 $\pm$ 3.07 [#]	34.59 $\pm$ 1.44	48.67 $\pm$ 2.32	348.62 $\pm$ 76.24 [#]

Note: compared with this group before treatment, * $P<0.01$; compared with control group after treatment, [#] $P<0.01$.

2.3 两组治疗前后肾功能的比较

两组经 8 周治疗后 SCr、BUN、CysC 水平均较治疗前明显

降低, 而 eGFR 明显升高($P<0.01$), 且观察组各项肾功能指标较
对照组改善更为显著($P<0.01$), 见表 3。

表 3 两组治疗前后肾功能的比较($\bar{x} \pm s$)Table 3 Comparison of the renal function indexes between two groups before and after treatment($\bar{x} \pm s$)

Groups	Time	SCr(μ mol/L)	BUN(mmol/L)	CysC(mg/L)	eGFR(mL/min)
Observation group (n=62)	Before treatment	233.52 $\pm$ 36.89	26.45 $\pm$ 5.23	1.30 $\pm$ 0.22	59.78 $\pm$ 5.99
	After treatment	142.36 $\pm$ 22.49**	6.52 $\pm$ 1.76**	0.85 $\pm$ 0.16**	77.46 $\pm$ 6.82**
Control group (n=62)	Before treatment	229.18 $\pm$ 42.34	26.03 $\pm$ 4.97	1.28 $\pm$ 0.25	60.12 $\pm$ 6.02
	After treatment	168.90 $\pm$ 27.78*	12.67 $\pm$ 2.67*	1.15 $\pm$ 0.14*	71.67 $\pm$ 7.14*

Note: compared with this group before treatment, * $P<0.01$; compared with control group after treatment, [#] $P<0.01$.

2.4 两组治疗前后肾素系统相关指标比较

两组经 8 周治疗后血浆 PRA、Ang II、ALD 水平均较治疗

前明显下降($P<0.01$), 且观察组治疗后血浆 PRA、Ang II、ALD
水平明显低于对照组($P<0.01$), 见表 4。

表 4 两组治疗前后肾素系统相关指标比较($\bar{x} \pm s$, ng/L)Table 4 Comparison of the renin system related indexes between two groups before and after treatment($\bar{x} \pm s$, ng/L)

Groups	Time	PRA	Ang II	ALD
Observation group (n=62)	Before treatment	4.31 $\pm$ 0.56	265.36 $\pm$ 56.46	614.56 $\pm$ 76.57
	After treatment	1.24 $\pm$ 0.39**	66.78 $\pm$ 35.82**	156.24 $\pm$ 36.56**
Control group (n=62)	Before treatment	4.28 $\pm$ 0.62	258.35 $\pm$ 51.08	605.68 $\pm$ 72.45
	After treatment	3.14 $\pm$ 0.45*	112.34 $\pm$ 42.35*	255.82 $\pm$ 68.22*

Note: compared with this group before treatment, * $P<0.01$; compared with control group after treatment, [#] $P<0.01$.

3 讨论

心肾综合征的发病机制目前尚不明确, 一般认为与肾素 - 血管紧张素 - 醛固酮系统(RASS 系统)活化、血流动力学变化以及细胞因子失调等相关^[11,12]。目前, 临床对其治疗尚缺乏标准的治疗方案, 仍以经验用药为主, 如给予利尿、强心、营养心肌、降压等, 避免病情持续恶化^[12,13]。正性肌力药、利尿剂、ACEI、 β 受体阻滞剂等为常用的治疗心肾综合征的药物, 尽管其能短期缓解症状, 但也存在明显的药物不良反应, 导致临床使用受到限制^[14,15]。例如, 利尿剂的大量使用可引起水电解质失衡, 诱发低血压, 使肾损害加重; 正性肌力药物长期使用可使病死率增加; ACEI 可使肾小球滤过率下降, 急性心衰情况下可加重肾损害^[16,17]。近年来, 中医辨证论治法开始广泛应用于心肾综合征的治疗^[18,20]。张晶等^[21]对心肾综合征心肾阳虚证患者采取益气温阳

活血利水方辅助治疗后总有效率达 83.33%, 显著高于对照组, 且治疗后 LVEF、SCr 显著改善, 不良反应发生率则显著低于对照组。杨雪卿等^[22]对络风内动辨证心肾综合征患者采取络风宁 2 号治疗后血浆脂蛋白相关磷脂酶 A2(Lp-PLA2)、超敏 C 反应蛋白(hs-CRP)水平明显下降, 心肌营养素 1(CT-1)水平明显升高, 且这 3 项指标改善效果显著优于单用西药治疗组。

中医无心肾综合征, 可归于中医“胸痹”、“水肿”、“喘促”等范畴^[23-25]。心肾同属少阴, 心肾综合征属少阴的阴阳失调, 全身气血不畅, 机能衰竭, 温煦无力, 水气不利, 水停为饮^[26-28]。又因阳气衰虚, 无法推动血液运行, 可致血瘀、水饮停聚。可见, 心肾阳虚、水饮内停、气滞血瘀为心肾综合征的基本病机。其中, 本虚为心肾阳虚, 标实为血瘀、水饮^[29]。根据该病的病因病机, 本研究采取了益气温阳活血利水法进行治疗, 该中医疗法中包含了心衰的四大基本治疗法则, 即益气、温阳、活血、利水。益气

温阳有助于增强各项机体功能,活血化瘀能促使血流阻滞状态得以改善,并增强利尿效果,减少利尿剂抵抗与使用利尿剂引起的副作用,改善心肾功能^[30]。《类证治裁》记载:"肾为气之根……,肾主纳气";《素问》中记载:"肾者水脏,主津液"。肾主纳气、主水,肾脏功能失调可致气喘声微、尿少水肿;脾主运化水湿,脾脏功能失调可致运化水湿无力,致使水湿内停。本研究采用的益气温阳活血利水中药汤剂方由多味中药组成,方内以黄芪、党参共为君药,具有健脾益气、消肿利水之功效;以山萸肉、淫羊藿、鹿衔草共为臣药,均为滋补肾阳之品,具有温肾助阳、行水化气之功效;川芎、丹参活血祛瘀,白术、党参、砂仁、茯苓、泽兰、鸡骨草均归脾经,具有健脾利湿、行水活血之功效,上述诸药共为佐药。此外,方中添加大黄,旨在利用其泻下作用,促使肌酐、尿素随尿液排出体外,同时抑制肾代偿性肥大,促使高代谢状态得以缓解^[31]。全方标本兼治,诸药共用可奏益气温阳、活血利水的功效,可使患者的心肾功能得以改善。本研究结果显示在西药治疗基础上联合益气温阳活血利水法治疗后总有效率达 90.32%,与单用西药治疗(67.74%)相比显著升高。另外,西药治疗基础上联合益气温阳活血利水法治疗后的肾功能及肾功能指标改善效果也显著优于单用西药治疗。由此可见,与常规西药治疗相比,联合给予益气温阳活血利水法中药治疗心肾综合征能有效提高临床治疗效果。

心肾综合征患者的 RSSA 系统处于亢进状态中,其原因主要包括以下几点:血钠浓度降低,使得远曲小管 Na⁺ 随之减少,致密斑细胞在受到刺激后可大量分泌出肾素;入球小动脉压下降,使得肾血流量降低,刺激了致密斑细胞,牵张感受器可被牵拉,引发球旁细胞大量分泌肾素。本研究结果显示:西药治疗基础上联合益气温阳活血利水法治疗的患者血浆 PRA、Ang II、ALD 水平显著降低,且均明显低于单用西药治疗后,表明益气温阳活血利水法能抑制心肾综合征患者的血浆 PRA、Ang II、ALD 分泌及释放,这可能是益气温阳活血利水法能显著改善心肾综合征患者的心肾功能的机理之一。

综上所述,在常规西药治疗基础上联合益气温阳活血利水法中药汤剂治疗心肾综合征能有效缓解胸闷、胸痛、心悸、气短等临床症状,提高心功能分级,促进肾功能指标改善,从而提高临床有效率,此外,患者的血浆 BNP、PRA、Ang II、ALD 水平均有明显降低,这可能是益气温阳活血利水法的作用机制之一,其确切的作用机制仍有待进一步研究。

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