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四君子汤治疗功能性消化不良的临床疗效分析

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摘要 目的:分析四君子汤治疗功能性消化不良的疗效及对患者生活质量的影响。**方法:**以2013年1月至2015年12月西安高新医院诊治的132例功能性消化不良患者为研究对象,将其根据就诊顺序分为观察组和对照组,每组66例,对照组给予奥美拉唑肠溶片和多潘立酮片治疗,观察组在对照组的基础之上给予四君子汤加减治疗。比较两组的临床疗效,血清胃动素(MTL)、胃泌素(GAS)、5-羟色胺(5-HT)及血管活性肠肽(VIP)水平以及生活质量评分。**结果:**治疗后,观察组的总有效率为93.94%,显著高于对照组的78.79%($P<0.05$)。治疗后,两组的中医症状积分均较治疗前显著降低($P<0.05$),且观察组显著低于对照组($P<0.05$)。观察组治疗后的MTL、GAS水平、生理功能(PF)、社会功能(SP)、生理职能(RP)、情感职能(RE)、躯体疼痛(BP)、活力(VT)、精神健康(MH)和总体健康(GH)评分均较治疗前显著升高($P<0.05$),且明显高于对照组($P<0.05$),5-HT及VIP较治疗前显著降低($P<0.05$),且低于对照组($P<0.05$)。**结论:**四君子汤加减治疗功能性消化不良的临床疗效显著,并可有效提高患者的生活质量,可能与其调节血清MTL、GAS、5-HT、VIP水平有关。

关键词:功能性消化不良;四君子汤;生活质量;血清胃动素(MTL);胃泌素(GAS);5-羟色胺(5-HT);血管活性肠肽(VIP)

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Analysis of the Clinical Effect of Si Jun Zi Decoction on the Functional Dyspepsia

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ABSTRACT Objective: To investigate the curative effect of Si Jun Zi decoction on patients with functional dyspepsia. **Methods:** 132 cases of patients with functional dyspepsia in our hospital from January 2013 to December 2015 were divided into the observation group and control group, 66 cases in each group. Patients in the control group were treated with omeprazole enteric-coated capsules and domperidone tablets, patients in the observation group were treated with Si Jun Zi Tang on the base of control group therapy. The curative effect, levels of Motilin(MTL), gastrin(GAS), 5-hydroxy-tryptamine(5-HT) and vasoactive intestinal peptide(VIP) and quality of life were compared between two groups. **Results:** After treatment, the curative effect of observation group (93.94%) was significantly higher than that of the control group(78.79%)($P<0.05$). The levels of MTL, GAS and quality of life scores(physiological function (PF), social function (SP), physiological function (RP), functions of emotion (RE), body pain (BP), energy(VT), mental health(MH) and general health(GH)) of observation group were significantly higher than those of the control group ($P<0.05$), and the levels of 5-HT and VIP of observation group were significantly lower than those of the control group($P<0.05$). **Conclusion:** Si Jun Zi Tang could effectively improve the curative effect, and quality of life of patients with functional dyspepsia, and this might be related to the change of levels of MTL,GAS, 5-HT and VIP.

Key words: Functional dyspepsia; Si Jun Zi decoction; Living quality; Serological marker

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前言

功能性消化不良又称消化不良,是消化科门诊的常见疾病。在我国,消化不良患者约占普通内科门诊的10%^[1]。根据其

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临床表现为不同又可分为餐后不适综合征和上腹痛综合征,均具有慢性、持续性、反复性发作的特点,严重影响患者的生活质量^[2]。西医治疗主要以改善胃肠动力、抑制胃酸分泌、抗幽门螺旋杆菌感染以及抗抑郁焦虑等对症治疗为主,但目前尚未得到满意疗效^[3]。功能性消化不良属祖国医学的“痞满”、“嘈杂”、“噎气”、“胃脘痛”等范畴,中医辨证分型有脾虚气滞型、脾胃湿热型、脾胃虚寒型、肝胃不和型及寒热错杂型五类,中医治疗以健脾益气、理气和胃为原则^[4]。四君子汤为祖国医学中益气健脾名方^[5]。本研究拟分析四君子汤治疗脾虚气滞型功能性消化

不良的疗效及对患者生活质量的影响。

1 资料与方法

1.1 一般资料

以 2013 年 1 月至 2015 年 12 月西安高新医院诊治的 132 例功能性消化不良患者为研究对象,所有患者西医诊断符合功能性消化不良 2006 年罗马 III 标准,中医诊断符合 2006 年中华中医药学会脾胃病分会制定的《中医消化病诊疗指南》中脾虚气滞型功能性消化不良的相关诊断标准。所有患者均知情同意本研究且可获得随访,年龄 18-75 岁,就诊前两周末服用过其他药物,排除合并严重心、肝、肾等器官功能障碍及其他系统疾病患者,排除对治疗药物过敏者,排除妊娠及哺乳期妇女。将 132 例患者根据就诊顺序分为观察组和对照组,每组 66 例,其中观察组男 23 例,女 43 例,年龄 19-73 岁,平均年龄(49.83 12.35)岁,病后才能 0.5-10 年,平均病程(5.82 5.99)年,上腹痛综合征 31 例,餐后不适综合征 35 例;对照组男 24 例,女 42 例,年龄 18-73 岁,平均年龄(50.23 12.05)岁,病后才能 0.5-10 年,平均病程(5.90 6.03)年,上腹痛综合征 30 例,餐后不适综合征 36 例。两组一般资料比较,差异无统计学意义($P > 0.05$),具有可比性。

1.2 治疗方法

对照组:给予奥美拉唑肠溶片(生产厂家:太极集团重庆涪陵制药厂有限公司,国药准字 H20093560,批号:1405044,规格:20 mg)和多潘立酮片(生产厂家:西安杨森制药有限公司,国药准字 H10910003,批号:141215,规格:10 mg),用法用量:奥美拉唑肠溶片:口服,每天 1 次,每次 1 片;多潘立酮:口服,每日 3 次,每次 1 片,持续用药 4 周。观察组:在对照组额的基础上给予四君子汤加减,组方:党参、茯苓、白术、甘草各 10 g。腹痛明显者加延胡索 15 g、香附 15 g;反酸烧心者加乌贼骨 20 g,积食停滞者加麦芽 20g。每日 1 剂,水煎,早晚两次服用,持续用药 4 周。

1.3 观察指标

(1)临床疗效:参照《中药新药临床指导原则》中的中药新药

治疗痞满的临床研究指导原则评价两组患者治疗前后胃脘或脘腹胀满、胃脘痛、嗳气呃逆、恶心呕吐等 15 项症状评分,每个症状 0、1、2、3 分四个等级,0 分表示无症状,3 分表示症状最严重,累积所有症状积分为最终中医症状积分,最高 45 分。痊愈:症状、体征基本消失或完全消失,中医症状积分减少 95%及以上,显效:症状、体征明显改善,中医症状积分减少 70%-94%,有效:症状、体征有好转,中医症状积分减少 30%-69%,无效:症状、体征无明显改善或加重,中医症状积分减少小于 30%。总有效率=(痊愈+显效+有效)/总例数 $\times 100\%$ 。 (2)血清学指标:治疗前及治疗后分别采集患者空腹外周静脉血 5 mL,分离血清,采用面联免疫吸附法检测患者血清胃动素(MTL)、胃泌素(GAS)、5-羟色胺(5-HT)及血管活性肠肽(VIP)水平,试剂盒均购自上海沪锋生物科技有限公司,检测采用长春光机医疗仪器有限公司生产的全自动酶标仪。 (3)生活质量:治疗前后的生活质量改善情况采用 SF-36 生活质量评估量表评估患者,量表共包括生理功能(PF)、社会功能(SP)、生理职能(RP)、情感职能(RE)、躯体疼痛(BP)、活力(VT)、精神健康(MH)和总体健康(GH) 8 个维度,每个维度的最终计算分值为 0-100 分,分值越高表示健康状况越好。 (4)不良反应:观察两组治疗期间有无腹泻、头晕、皮疹等与用药相关的不良反应发生。

1.4 统计学分析

采用 SPSS17.0 进行统计分析,计数资料(治疗有效率)以%表示,采用卡方检验,计量资料(血清学指标水平、生活质量评分)以均值 $\pm$ 标准差表示,采用 t 检验,以 $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

观察组的总有效率为 93.94%,显著高于对照组的 78.79% ($P < 0.05$)。治疗前,观察组和对照组的中医症状积分比较差异无统计学意义($P > 0.05$);治疗后,观察组和对照组的中医症状积分均较治疗前显著降低 ($P < 0.05$),且观察组显著低于对照组 ($P < 0.05$),见表 1。

表 1 两组临床疗效的比较(例,%)

Table 1 Comparison of the clinical effect between two groups(n,%)

Groups	Cases	Recovery	Excellent	Effective	Invalid	Overall response rate(%)	TCM symptom score(Scores)	
							Before treatment	After treatment
Observation group	66	10	16	36	4	93.94 ^a	22.75 $\pm$ 1.02	7.99 $\pm$ 0.69 ^a
Control group	66	6	18	28	14	78.79	23.06 $\pm$ 1.13	13.65 $\pm$ 1.01 ^b

Note: Compared with control group, ^a $P < 0.05$; Compared with before treatment, ^b $P < 0.05$.

2.2 两组治疗前后血清学指标水平比较

治疗前,观察组和对照组的 MTL、GAS、5-HT 及 VIP 水平比较差异无统计学意义($P > 0.05$);治疗后,观察组的 MTL、GAS 水平均较治疗前显著升高($P < 0.05$),5-HT 及 VIP 较治疗前显著降低($P < 0.05$),对照组的 MTL 水平较治疗前显著升高($P < 0.05$),5-HT 较治疗前显著降低($P < 0.05$),观察组的 MTL、GAS 水平显著高于对照组 ($P < 0.05$),5-HT 及 VIP 水平显著低于对照组 ($P < 0.05$),见表 2。

2.3 两组治疗前后生活质量评分比较

治疗前,观察组和对照组的的生活质量评分量表中维度评分(PF、SF、RP、RE、BP、VT、MH、GH) 比较差异无统计学意义($P > 0.05$);治疗后,观察组的 PF、SF、RP、RE、BP、VT、MH、GH 评分均较治疗前显著升高 ($P < 0.05$),对照组的 SF、RP、RE、BP、VT、GH 评分均较治疗前显著升高 ($P < 0.05$),且观察组的 PF、SF、RP、RE、BP、VT、MH、GH 评分均显著高于对照组($P < 0.05$),见表 3。

表 2 两组治疗前后血清学指标水平比较

Table 2 Comparison of the serological index level between two groups before and after treatment

Groups	Cases		MTL(pg/mL)	GAS(pg/mL)	5-HT(ng/mL)	VIP(pg/mL)
Observation group	66	before treatment	229.17 78.32	23.69 15.18	116.25 31.66	27.99 3.65
		after treatment	281.36 91.28 [°]	28.85 15.71 ^{°°}	90.12 30.90 [°]	19.94 4.02 ^{°°}
Control group	66	before treatment	229.26 80.16	23.56 14.62	116.55 32.68	27.73 3.65
		after treatment	241.32 87.78 [°]	24.12 16.93	102.53 31.19 [°]	24.72 3.89

Note: Compared with control group, [°] P<0.05; Compared with before treatment, ^{°°} P<0.05.

表 3 两组治疗前后生活质量评分比较

Table 3 Comparison of the scores of quality of life between two groups before and after treatment

Groups	Cases		PF	SF	RP	RE	BP	VT	MH	GH
Observation group	66	Before treatment	97.60±	65.06±	70.77±	80.91±	65.33±	60.55±	63.07±	47.96±
			5.68	7.92	9.51	8.02	11.85	11.03	8.01	13.06
		After treatment	98.98±	81.45±	83.02±	96.65±	78.88±	79.08±	69.96±	58.83±
			4.02	9.91 ^{°°}	9.03 [°]	8.66 ^{°°}	13.02 ^{°°}	11.33 ^{°°}	8.61 ^{°°}	11.71 ^{°°}
Control group	66	Before treatment	97.35±	64.95±	70.65±	80.21±	65.32±	60.97±	62.96±	47.99±
			6.50	8.02	9.66	8.32	12.29	11.70	8.33	13.90
		After treatment	97.23±	75.23±	75.56±	85.02±	73.78±	68.99±	63.77±	52.20±
			6.89	7.89 [°]	9.87 [°]	8.06 [°]	12.90 [°]	11.59 [°]	8.42	12.69 [°]

Note: Compared with control group, [°] P<0.05; Compared with before treatment, ^{°°} P<0.05.

3 讨论

功能性消化不良是消化系统常见疾病,临床表现以食欲不振、上腹痛、早饱、暖气、恶心、呕吐等为主^[67]。目前临床对于功能性消化不良的具体发病机制目前尚未确定,但可能与胃肠动力障碍、胃底容受性受损、内脏高敏感、胃肠道激素、自主神经系统功能异常、幽门螺旋杆菌感染以及社会心理因素有关^[89]。因病因机制不明确,因此西医治疗以控制症状为主,如改善胃肠动力、抑制胃酸分泌、保护胃黏膜等,但均未获得理想疗效^[10]。功能性消化不良属祖国医学的"痞满"、"嘈杂"、"暖气"、"胃脘痛"等范畴,祖国医学认为其病因病机可能与外邪入侵,食滞内停,痰湿中阻或情志失畅致使胃气下降、脾虚肝郁、中焦气滞,升降功能失调等有关,而脾胃虚弱为关键,中医治疗主要为辨证施治,调节脾胃功能^[11,12]。

四君子汤由《伤寒论》中"理中丸"发展而来,出自《太平惠民和剂局方》,全方由人参、茯苓、白术和甘草四位中药组成,方中君药人参具有补元气,健脾养胃的功效,臣药白术味甘苦,性温,可补气健脾,燥湿利水,佐药茯苓味甘淡,性平,可利水渗湿,健脾化痰,使药甘草味甘,性平,可益气滋养,通阳复脉,全方诸药调和,益气健脾,为祖国传统医学补益脾胃之名方^[13]。因该病症在祖国医学中辩证分型较多,因此临床常以四君子汤为基础辩证加减。现代药理研究从和分析生物学及细胞学水平证实,四君子汤对脾虚症胃肠消化功能具有显著影响,具有增加平滑肌张力,收缩胃平滑肌,促进胃肠蠕动,保护胃黏膜的作用^[14]。吕林^[15]等研究证实,四君子汤可显著改善功能性消化不良餐后不适综合征患者胃中液体食物分布,促进胃排空,从而发挥健脾促胃动力作用。

近年来,中西药联合治疗功能性消化不良越来越广泛。贺会刚^[16]等研究显示中医药联合治疗功能性消化不良的临床疗

效与单用西药相比差异显著。本研究中,治疗后,观察组的总有效率显著高于对照组的,生活质量评分均优于对照组,提示四君子汤可显著协同提高西药治疗功能性消化不良的临床疗效,改善患者的临床症状,提高生活质量,原因可能为西药可及时缓解患者的临床症状,而中药通过整体调节机体阴阳平衡,标本兼治,同时还可降低西药的不良反应,进而提高生活质量^[17]。

胃动素(MTL)、胃泌素(GAS)、5-羟色胺(5-HT)及血管活性肠肽(VIP)为临床评价胃肠功能的常用生化指标。MTL由Mo细胞分泌,受肠道神经系统和胃肠激素的调节,主要生理功能为兴奋胃平滑肌,触发胃肠消化间期Ⅲ期运动,GAS由G细胞分泌,主要刺激壁细胞分泌盐酸,也有刺激胰液和胆汁的分泌及胃蛋白酶原分泌等作用,胃肠功能受损患者的MTL和GAS的表达量降低^[18]。5-HT由近端胃粘膜分泌,参与调节胃肠运动,并与胃肠敏感性有关,VIP是一种碱性肽,胃肠道含量最高,参与消化系统的多种生理过程,如松弛消化道括约肌、抑制胃容受舒张性反射、减慢胃排空等,存在胃肠功能障碍的患者体内的5-HT和VIP表达量均显著高于正常个人^[19]。本研究结果显示观察组的MTL、GAS水平均较治疗前显著升高,且高于对照组,5-HT及VIP较治疗前显著降低,且低于对照组,对照组的MTL水平较治疗前显著升高,5-HT较治疗前显著降低,提示与单用西药相比,四君子汤联合西药可显著改善患者MTL、GAS、5-HT及VIP水平的表达。这些结果表明四君子汤协同增加西药治疗功能性消化不良的临床疗效的机制可能与改善胃肠动力及运动,调节胃肠敏感性及容受性有关^[20]。

综上所述,四君子汤加减治疗功能性消化不良的临床疗效显著,并可有效提高患者的生活质量,可能与其调节血清MTL、GAS、5-HT、VIP水平有关。

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