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## 参苓白术散联合复方谷氨酰胺肠溶胶囊对肠易激综合征患者的肠黏膜屏障功能及 5-HT、IFN- $\gamma$ 、IL-8 水平的影响\*

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**摘要 目的:** 探讨参苓白术散联合复方谷氨酰胺肠溶胶囊对肠易激综合征患者的肠黏膜屏障功能及 5-羟色胺 (5-HT)、 $\gamma$ -干扰素 (IFN- $\gamma$ )、白细胞介素 8 (IL-8) 水平的影响。**方法:** 选取 2017 年 3 月至 2018 年 1 月的 89 例肠易激综合征患者。按照随机数表法分为观察组 (n=46) 和对照组 (n=43), 对照组采用复方谷氨酰胺肠溶胶囊治疗, 观察组采用参苓白术散联合复方谷氨酰胺肠溶胶囊治疗。观察两组治疗疗效, 肠黏膜屏障功能 (DAO、D-乳酸、细菌内毒素), 血清 5-HT、IFN- $\gamma$ 、IL-8 水平, 不良反应发生率。**结果:** 治疗后, 观察组总有效率显著高于对照组 [93.47% vs 72.09%] ( $P < 0.05$ ); 中医症状积分显著低于对照组 [(2.81 $\pm$  0.42) 分 vs (5.79 $\pm$  0.74) 分] ( $P < 0.05$ ); DAO、D-乳酸、细菌内毒素水平均显著低于对照组 [(10.02 $\pm$  1.50) U/L vs (11.85 $\pm$  1.98) U/L, (7.18 $\pm$  1.37) mg/L vs (8.56 $\pm$  1.53) mg/L, (0.60 $\pm$  0.08) pg/mL vs (0.75 $\pm$  0.12) pg/mL] ( $P < 0.05$ ); 血清 5-HT、IFN- $\gamma$ 、IL-8 水平均显著低于对照组 [(351.08 $\pm$  20.93) pg/mL vs (364.12 $\pm$  29.71) pg/mL, (26.95 $\pm$  5.02) pg/mL vs (31.28 $\pm$  6.10) pg/mL, (2.97 $\pm$  0.51) ng/L vs (4.03 $\pm$  0.62) ng/L] ( $P < 0.05$ ); 不良反应总发生率显著低于对照组 [6.52% (3/46) vs 20.93% (9/43)] ( $P < 0.05$ )。**结论:** 参苓白术散联合复方谷氨酰胺肠溶胶囊治疗肠易激综合征患者的临床疗效显著, 可改善临床症状, 改善肠黏膜屏障功能, 及 5-HT、IFN- $\gamma$ 、IL-8 水平, 减轻炎症反应, 安全可靠。

**关键词:** 参苓白术散; 复方谷氨酰胺肠溶胶囊; 肠易激综合征; 肠黏膜屏障功能

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## Effects of Shenling Baizhu Powder Combined with Compound Glutamine on Intestinal Mucosal Barrier Function and Levels of 5-HT, IFN- $\gamma$ and IL-8 in Patients with Irritable Bowel Syndrome\*

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**ABSTRACT Objective:** To explore the effects of shenling baizhu powder and combined with compound glutamine on intestinal mucosal barrier function and levels of 5-hydroxytryptamine (5-HT), interferon- $\gamma$  (IFN- $\gamma$ ) and interleukin-8 (IL-8) in patients with irritable bowel syndrome. **Methods:** 89 Irritable bowel syndrome who received therapy from March 2017 to January 2018 in our hospital were selected as research objects. According to random number table, those patients were divided into the observation group (n=46) and the control group (n=43). The control group was treated with compound glutamine, while the observation group treated with Shenling Baizhu Powder Combined with compound glutamine. Then the therapeutic efficacy, intestinal mucosal barrier function (DAO, D-lactic acid, ET), serum levels of 5-HT, IFN-gamma and IL-8, incidence of adverse reactions of two groups after treatment were compared. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of control group (93.47% vs 72.09%) ( $P < 0.05$ ). The score of self-appraisal of clinic symptoms was significantly lower than that of the control group [(2.81 $\pm$  0.42) scores vs (5.79 $\pm$  0.74) scores] ( $P < 0.05$ ). The levels of DAO, D-lactic acid and ET were significantly lower than those of the control group [(10.02 $\pm$  1.50) U/L vs (11.85 $\pm$  1.98) U/L, (7.18 $\pm$  1.37) mg/L vs (8.56 $\pm$  1.53) mg/L, (0.60 $\pm$  0.08) pg/mL vs (0.75 $\pm$  0.12) pg/mL] ( $P < 0.05$ ). Serum levels of 5-HT, IFN-gamma and IL-8 were significantly lower than those of the control group [(351.08 $\pm$  20.93) pg/mL vs (364.12 $\pm$  29.71) pg/mL, (26.95 $\pm$  5.02) pg/mL vs (31.28 $\pm$  6.10) pg/mL, (2.97 $\pm$  0.51) ng/L vs (4.03 $\pm$  0.62) ng/L] ( $P < 0.05$ ). The total incidence of adverse reactions was significantly lower than that in the control group [6.52% (3/46) vs 20.93% (9/43)] ( $P < 0.05$ ). **Conclusion:** Shenling Baizhu Powder combined with compound glutamine in the treatment of irritable bowel syndrome has a significant clinical effect. It can improve clinical symptoms, restore intestinal mucosal barrier function, and 5-HT, IFN-gamma, IL-8 levels, alleviate inflammation, and it is safe and reliable.

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## 前言

肠易激综合征是临床上常见的胃肠道功能性疾病,临床表现为腹部不适、腹痛腹泻、恶心呕吐、大便性状发生改变,具有起病缓慢、间歇性发作、病程长的特点,给患者的日常生活治疗造成了严重的影响<sup>[1]</sup>。目前对于该病的发病机制尚不明确,但临床认为<sup>[2]</sup>,炎症、胃肠动力异常、精神心理等多种因素与肠易激综合征的发生存在密切的关系。以往临床上多采用止泻类药物及抗胆碱类药物治疗肠易激综合征,虽可有效改善患者的临床症状,但停药后极易复发,无法达到满意的治疗效果<sup>[3]</sup>。复方谷氨酰胺肠溶胶囊是一种新型黏膜保护药,可快速修复组织,阻止肠道损伤所导致的炎症介质升高,保护患者的肠道黏膜<sup>[4]</sup>。参苓白术散是由多种中药材制成的中成药,具有保护胃肠道黏膜、调节胃肠道菌群的作用<sup>[5]</sup>。随着对该病的不断深入研究,5-羟色胺(5-HT)、 $\gamma$ -干扰素(IFN- $\gamma$ )、白细胞介素8(IL-8)被证实存在肠易激综合征中存在一定的联系<sup>[6]</sup>。本文旨在探讨参苓白术散联合复方谷氨酰胺肠溶胶囊对肠易激综合征患者的作用机制及治疗疗效。

## 1 资料与方法

### 1.1 一般资料

收集2017年3月至2018年2月我院的89例患者,均符合罗马III关于IBS诊断标准。纳入标准<sup>[7]</sup>:IBS病情尺度调查表评分 $\geq 75$ 分;近期未采用药物治疗;配合研究者;对本次治疗药物不过敏者;排除标准:妊娠期或哺乳期者;伴有严重器质性疾病;患有恶性肿瘤疾病;患有严重凝血功能障碍;患有精神疾病;同时参与其他研究者。

按照随机数表法将所有患者分为观察组( $n=46$ )和对照组( $n=43$ ),观察组男29例,女15例,年龄20~65岁,平均( $41.82 \pm 6.01$ )岁,病程5~52个月,平均( $30.12 \pm 5.60$ )个月,IBS-SSS评分( $267.30 \pm 9.42$ )分;对照组男26例,女17例,年龄21~65岁,平均( $42.05 \pm 5.58$ )岁,病程6~51个月,平均

( $29.86 \pm 5.78$ )个月,IBS-SSS评分( $268.92 \pm 8.59$ )分。两组以上资料均无显著差异( $P > 0.05$ )。

### 1.2 治疗方法

两组患者均给予活菌制剂改善肠道微环境、止泻等常规治疗,对照组在此基础上,采用复方谷氨酰胺肠溶胶囊肠溶胶囊(生产厂家:地奥集团成都药业股份有限公司)治疗,每次2粒,每天3次,治疗疗程为2周。观察组在对照组的基础上,采用参苓白术散治疗(生产厂家:北京同仁堂股份有限公司同仁堂制药厂,于早晚两次服用,治疗疗程为一个月)。

### 1.3 观察指标

观察两组治疗疗效,肠黏膜屏障功能(DAO、D-乳酸、细菌内毒素),血清5-HT、IFN- $\gamma$ 、IL-8水平,不良反应发生率。

**1.3.1 指标检测** 分别于两组治疗前后采集6ML静脉血,离心分离血清后放置等待检测,血清5-HT、IFN- $\gamma$ 、IL-8水平均采用酶联免疫吸附法检测,试剂盒购置北京中生金域诊断技术有限公司,肠黏膜屏障功能指标(二胺氧化酶(DAO)、D-乳酸和细菌内毒素),采用我科室JY-DLT肠道屏障功能生化指标分析系统分析。

**1.3.2 中医症状积** 分别于两组治疗前后,采用中医症状积分量表对患者的临床症状进行评估,分值越高表明症状越严重。

**1.3.3 疗效评定标准** 治愈:临床症状完全消失,肠功能恢复正常<sup>[8]</sup>。有效:临床症状、肠功能有所改善,中医症状积分减少60~89%;无效:临床症状无变化。

### 1.4 统计学分析

使用SPSS18.0统计软件进行统计,数据均符合正态分布,计量资料以( $\bar{x} \pm s$ )表示,采用t检验,计数资料以[(例)%]表示,用 $\chi^2$ 检验比较,采用 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 两组治疗疗效对比

观察组总有效率为93.47%,显著高于对照组72.09%( $P < 0.05$ ),见表1。

表1 两组治疗疗效情况对比[(例)%]

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

Groups	n	Cure	effective	invalid	Total effective rate(%)
Observation group	46	38(82.60)	15(32.60)	3(6.52)	43(93.47)*
Control group	43	21(48.84)	10(23.26)	12(27.91)	31(72.09)

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

### 2.2 两组治疗前后中医症状积分对比

治疗前,两组中医症状积分均无显著差异( $P > 0.05$ ),治疗后,两组中医症状积分均较治疗前显著降低,两组治疗后具有显著差异( $P < 0.05$ ),见表2。

### 2.3 两组治疗前后肠黏膜屏障功能对比

治疗前,两组DAO、D-乳酸、细菌内毒素水平均无显著

差异( $P > 0.05$ ),治疗后,两组DAO、D-乳酸、细菌内毒素水平均较治疗前显著降低,两组治疗后具有显著差异( $P < 0.05$ ),见表3。

### 2.4 两组治疗前后血清5-HT、IFN- $\gamma$ 、IL-8对比

治疗前,两组血清5-HT、IFN- $\gamma$ 、IL-8水平均无显著差异( $P > 0.05$ ),治疗后,两组血清5-HT、IFN- $\gamma$ 、IL-8水平均较治疗

前显著降低,两组治疗后具有显著差异( $P<0.05$ ),见表4。

表 2 两组治疗前后中医症状积分对比( $\bar{x}\pm s$ ,分)

Table 2 Comparison of self-appraisal of clinic symptoms between the two groups before and after treatment( $\bar{x}\pm s$ , scores)

Groups	n	Self-appraisal of clinic symptoms	
		Before treatment	After treatment
Observation group	45	9.17± 2.06	2.81± 0.42**
Control group	43	10.03± 2.39	5.79± 0.74*

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

表 3 两组治疗前后肠黏膜屏障功能对比( $\bar{x}\pm s$ )

Table 3 Comparison of serum SOD, MDA and NO levels between the two groups before and after treatment( $\bar{x}\pm s$ )

Groups	n	DAO(U/L)		D- lactic acid(mg/L)		ET(pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	45	13.05± 3.16	10.02± 1.50**	10.03± 1.69	7.18± 1.37**	0.92± 0.13	0.60± 0.08**
Control group	43	13.21± 3.09	11.85± 1.98*	10.11± 1.74	8.56± 1.53*	0.95± 0.16	0.75± 0.12*

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

表 4 两组治疗前后 5-HT、IFN- $\gamma$ 、IL-8 水平对比( $\bar{x}\pm s$ )

Table 4 Comparison of serum 5-HT, IFN- $\gamma$  and IL-8 levels between the two groups before and after treatment( $\bar{x}\pm s$ )

Groups	n	5-HT(pg/mL)		IFN- $\gamma$ (pg/mL)		IL-8(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	45	386.54± 51.52	351.08± 20.93**	36.01± 7.16	26.95± 5.02**	7.10± 0.83	2.97± 0.51**
Control group	43	387.05± 51.07	364.12± 29.71*	35.87± 7.03	31.28± 6.10*	7.16± 0.90	4.03± 0.62*

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

### 2.5 两组不良反应发生率对比

观察组不良反应总发生率为 6.52%, 显著低于对照组 20.93% ( $P<0.05$ )。

### 3 讨论

肠易激综合征占胃肠道疾病中 30%~50%, 随着时间的变化及生活节奏、饮食习惯的改变, 肠易激综合征的发生率也越来越多<sup>[9]</sup>。以往有研究认为<sup>[10-12]</sup>, 肠道菌群失调在该病的发生发展过程中存在重要的作用, 且多种致病因素均可导致机体大肠杆菌及其他致病菌数量明显增加, 乳酸杆菌、双歧杆菌等益生菌数量减少, 从而引发一系列肠道临床症状, 破坏患者的肠道粘膜屏障, 使肠粘膜通透性增加, 肠腔细菌等病原体通过肠上皮屏障进入固有层, 激活及紊乱肠道免疫系统。临床研究表明确<sup>[13]</sup>, 肠易激综合征患者的粘膜通透性较正常人显著增加, 在动物的实验中也发现, 腹痛症状的严重程度与肠粘膜通透性的增加有关。谷氨酰胺是人体必需氨基酸, 可提供能源物质给胃结肠粘膜细胞, 修复肠道黏膜, 改善患者的临床症状<sup>[14]</sup>。本研究显示, 两组患者采用谷氨酰胺治疗后临床症状、肠黏膜屏障功能指标(DAO、D- 乳酸、细菌内毒素)水平均较治疗前显著改善。说明了复方谷氨酰胺肠溶胶囊在治疗肠易激综合征具有一定的治疗疗效。

中医认为<sup>[15]</sup>, 肠易激综合征属于“泄泻、腹痛”等范畴, 肝脾不调, 肝郁气滞、脾失健运为发病机制, 加之情志异常, 致使

肝气郁滞, 横逆犯脾, 气机失调, 水湿内停。临床以补脾胃、益肺气为治疗之契机<sup>[16]</sup>。参苓白术散中的党参具有健脾、补中、润肺、补气的作用<sup>[17]</sup>。白术能够健脾益气, 燥湿利水<sup>[18]</sup>。茯苓可渗湿利水, 健脾和胃, 宁心安神; 炒山药具有健脾补肺、益胃补肾的功效<sup>[19]</sup>。薏苡仁能够健脾止泻, 白扁豆能够健脾化湿; 砂仁具有温脾、止泻、理气的作用<sup>[20]</sup>。诸药合用, 可达到健脾益气、止泻的功效<sup>[21]</sup>。药理学研究表明<sup>[22]</sup>, 甘草可缓解胃肠道痉挛, 减轻腹部临床症状, 恢复且保护胃肠道功能。本研究显示, 采用联合参苓白术散治疗的患者临床症状、肠黏膜屏障功能指标(DAO、D- 乳酸、细菌内毒素)水平、中医症状积分及治疗疗效均显著优于采用单独复方谷氨酰胺肠溶胶囊治疗的患者。说明了两种药物联合治疗可显著改善患者的临床症状, 改善且促进肠黏膜屏障功能恢复, 提高治疗疗效。在本研究治疗期间, 发现采用联合治疗的不良反应总发生率显著低于采用单独复方谷氨酰胺肠溶胶囊治疗的患者。说明了两种药物联合治疗不会增加不良反应情况, 安全有效<sup>[23]</sup>。

基础研究表明<sup>[24]</sup>, 肠易激综合征患者血清 5-HT、IFN- $\gamma$ 、IL-8 水平显著高于正常人。5-HT 为神经递质, 分布在松果体和下丘脑, 可调节胃肠动力和内脏敏感性<sup>[25]</sup>。有研究表明<sup>[26]</sup>, 患者出现肠易激综合征后, 肠道会大量释放 5-HT, 增加患者胃肠动力反应, 发生腹部临床症状。IFN- $\gamma$  属于促炎因子, 通过氧自由基释放, 可促使局部组织变形及坏死<sup>[27]</sup>。IL-8 是一种趋化因子家族的细胞因子, 参与和调节病理过程, 可促进机体炎症

反应<sup>[28,29]</sup>。本研究显示,采用联合参苓白术散治疗的患者血清5-HT、IFN- $\gamma$ 、IL-8水平均显著低于采用单独复方谷氨酰胺肠溶胶囊治疗的患者。说明了两种药物联合治疗可更进一步降低机体炎症反应,控制疾病发展,提高治疗疗效<sup>[30]</sup>。

综上所述,参苓白术散联合复方谷氨酰胺肠溶胶囊治疗肠易激综合征患者的临床疗效显著,可改善临床症状,恢复肠黏膜屏障功能,及5-HT、IFN- $\gamma$ 、IL-8水平,减轻炎症反应,安全可靠。

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