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· 临床研究 ·

参苓白术散与美沙拉嗪对溃疡性结肠炎患者血清 IL-17、IL-23 及 TNF- α 水平的影响 *辛 群^{1,2} 孙 擎² 葛现才² 张 勤² 齐元福³

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摘要 目的:探讨参苓白术散联合美沙拉嗪治疗脾胃气虚型溃疡性结肠炎的疗效及对血清细胞因子水平的影响。**方法:**按照随机数字表法将 2013 年 1 月至 2014 年 1 月我院收治的脾胃气虚型溃疡性结肠炎患者分为两组, 对照组给予美沙拉嗪口服治疗, 观察组在对照组基础上予参苓白术散口服治疗, 比较两组患者的临床疗效及血清细胞因子的水平变化。**结果:**观察组患者治疗的总有效率优于对照组, 差异有统计学意义($P < 0.05$); 治疗后, 两组患者 Sutherland DAI 评分均获得改善, 且观察组优于对照组, 差异具有统计学意义($P < 0.05$); 两组患者的 IL-17、IL-23 及 TNF- α 水平均显著降低, 且观察组低于对照组, 差异具有统计学意义($P < 0.05$)。**结论:**参苓白术散联合美沙拉嗪对脾胃气虚型溃疡性结肠炎具有良好的临床疗效, 能够改善患者血清细胞因子的水平。

关键词:参苓白术散; 美沙拉嗪; 溃疡性结肠炎; 细胞因子

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Effects of Shenlingbaizhu Powder and Mesalazine on the IL-17, IL-23 and TNF- α of Patients with Ulcerative Colitis*XIN Qun^{1,2}, SUN Qing², GE Xian-cai², ZHANG Qin², QI Yuan-fu³

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ABSTRACT Objective: To explore the effects of Shenlingbaizhu powder combined with mesalazine on the treatment of ulcerative colitis and its influence on levels of cytokines. **Methods:** The patients with ulcerative colitis who were treated in our hospital from January 2013 to 2014 were selected and randomly divided into the observation group and the control group. The patients in the observation group were treated by shenlingbaizhu powder combined with mesalazine, while the patients in the control group were treated with the mesalazine. Then the levels of cytokines in serum of patients were detected and compared between the two groups. **Results:** The total effective rate of observation group was better than that of the control group with statistically significant difference ($P < 0.05$); After the treatment, the Sutherland DAI score of patients in the two groups improved, and the observation group was better than that of the control group with statistically significant difference ($P < 0.01$); The expression levels of IL-17, IL-23 and TNF- α reduced and the observation group was lower than those of the control group with statistically significant differences ($P < 0.01$). **Conclusion:** The effect of Shenlingbaizhu powder combined with mesalazine on the treatment of ulcerative colitis could be better with the improvement of the cytokines levels.

Key words: Shenling baizhu powder; Mesalazine; Ulcerative colitis; Cell infactors

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前言

溃疡性结肠炎(ulcerative colitis, UC)作为结直肠慢性非特异性炎症性疾病,临床表现为黏液脓血便、腹痛腹泻等,易反复发作,严重影响患者的身体健康和生活质量^[1-3]。脾胃气虚型溃疡性结肠炎是中医辨证分型中较为常见的疾病,其发病率逐渐

上升且趋向年轻化^[4]。目前临床常用美沙拉嗪治疗脾胃气虚型溃疡性结肠炎,但治疗后的不良反应较多,患者多出现不同程度的头痛、恶心呕吐等症状^[5,6]。参苓白术散含有多种常见的中药成分,具有健脾调中,益气升提的功效^[7]。本研究采用参苓白术散联合美沙拉嗪治疗脾胃气虚型溃疡性结肠炎,并以美沙拉嗪治疗的患者为对照比较两组的临床疗效以及血清细胞因子

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的变化情况,为临床治疗提供参考。

1 资料与方法

1.1 临床资料

选取 2013 年 1 月~2014 年 1 月我院收治的脾胃气虚型溃疡性结肠炎患者 75 例为研究对象,按照随机数字表法分为观察组(37 例)和对照组(38 例)。观察组包括男 22 例,女 15 例;年龄 19~63 岁,平均(39.5±8.2)岁;病程为 4 个月~7 年,平均(9.1±2.7)月。对照组包括男 17 例,女 21 例;年龄 18~65 岁,平均(40.8±7.6)岁;病程为 5 个月~8 年,平均(9.6±3.1)月。两组患者的基线资料无显著性差异($P>0.05$),具有可比性。

1.2 纳入及排除标准

纳入标准:①西医诊断标准参照《中国炎症性肠病诊断治疗规范的共识意见》;②中医辨证标准参照《中药新药临床研究指导原则》;③无缺血性肠炎、感染性结肠炎、结直肠癌患者、克罗恩病及放射性肠炎等疾病的患者;④符合医学伦理学要求;⑤患者及家属知情同意,并签署知情同意书。排除标准:①孕产妇、哺乳期妇女;②有心功能不全者;③有肝、肾功能障碍者;④近 1 个月内通过激素及免疫抑制剂治疗的患者;⑤合并有其他严重的系统性疾病者;⑥有过敏史者;⑦合并有其他严重的并发症如肠梗阻、肠穿孔等;⑧近 2 个月内有参加其他临床药物试验的患者。

1.3 治疗方法

对照组予以口服美沙拉嗪(国药准字:H19980148,葵花药业集团佳木斯鹿灵制药有限公司提供)治疗,1.0g/次,4 次/d。观察组在对照组的基础上给予参苓白术散(国药准字:Z11020947,北京同仁堂制药有限公司提供)口服治疗,6.0 g/次,3 次/d。两组疗程均为 8 周,服药期间患者禁食其它不易消化的食物以及辛辣、刺激性食物。

1.4 评价指标

①临床疗效评价标准参照《对炎症性肠病诊断治疗规范的建议》:显效:临床症状消失,大便次数 ≤ 2 次/d,且高倍镜下无红、白细胞;有效:临床症状基本消失,大小便次数 2~4 次/d,大便成形,高倍镜下红、白细胞少于 10 个;无效:治疗后临床症状无缓解,大便常规检查无任何改变。②于治疗前后评价两组的 Sutherland DAI 评分,分 4 个等级:症状缓解、轻度活动、中度活动以及重度活动;③血清细胞因子检测:采用酶联免疫吸附测定法(ELISA)分别检测两组 IL-17、IL-23、TNF- α ,具体操作:在治疗前后分别抽取两组患者的外周静脉血,通过肝素抗凝后以 2000 r/min 离心后于 -75℃ 下保存,并参照说明书进行检测,试

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1.5 统计处理

采用 SPSS19.0 软件进行统计分析,计量资料用($\bar{x} \pm s$)表示,两独立样本比较采用 t 检验,计数资料采用率表示,用秩和检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患者的临床疗效比较

观察组显效 27 例(75.00%)、有效 6 例(16.67%),无效 3 例(8.33%),对照组显效 17 例(45.95%),有效 13 例(35.13%),无效 7 例(18.92%),两组的临床疗效比较,差异有统计学意义($P<0.05$),观察组的临床疗效优于对照组。见表 1。

表 1 两组的临床疗效[n(%)]

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

Group	Case	Excellent	Effective	Invalid
Observation	37	27(75.00)	6(16.67)	3(8.33)
Control	38	17(45.95)	13(35.13)	7(18.92)

Note: compared between two groups, $Z=-2.155$, $P=0.031$.

2.2 两组患者治疗前后的 Sutherland DAI 评分情况

治疗前两组 Sutherland DAI 评分差异无统计学意义($P>0.05$),治疗后两组的 Sutherland DAI 评分均小于治疗前,差异有统计学意义($P<0.05$),观察组治疗后的 Sutherland DAI 评分小于对照组,差异有统计学意义($P<0.01$)。见表 2。

表 2 治疗前后两组的 Sutherland DAI 评分($\bar{x} \pm s$)

Table 2 Comparison of the Sutherland DAI score of patients between the two groups($\bar{x} \pm s$)

Group	Case	Before treatment	After treatment
Observation	37	7.96±1.25	3.93±0.98*
Control	38	8.12±1.07	4.87±1.14*
t		1.632	3.706
P		0.561	0.039

Note: compared with before, $P<0.01$.

2.3 两组治疗前后血清细胞因子水平比较

两组治疗后的 IL-17、IL-23、TNF- α 水平较治疗前降低,差异有统计学意义($P<0.01$),治疗前两组的 IL-17、IL-23、TNF- α 水平比较差异无统计学意义($P>0.05$),治疗后观察组的 IL-17、IL-23、TNF- α 水平小于对照组,差异有统计学意义($P<0.05$)。见表 3。

表 3 两组治疗前后血清细胞因子水平($\bar{x} \pm s$)

Table 3 Levels of inflammatory factors in the serum of patients in the two groups($\bar{x} \pm s$)

Group	Indicators	Before treatment	After treatment	t	P
Observation	IL-17(pg/mL)	465.8±93.3	221.3±97.5 [△]	21.632	0.000
	IL-23(pg/mL)	902.5±65.0	328.9±57.1 [△]	26.085	0.000
	TNF- α (ng/mL)	57.6±11.2	12.8±12.0 [△]	18.817	0.000
Control	IL-17(pg/mL)	469.8±93.4	305.8±89.2	19.653	0.000
	IL-23(pg/mL)	890.6±63.7	461.7±59.8	24.136	0.000
	TNF- α (ng/mL)	56.8±10.6	21.2±11.3	20.005	0.000

Note: compared with control group, $^{\Delta}P<0.05$.

3 讨论

溃疡性结肠炎又称慢性非特异性溃疡性结肠炎,其发病的原因及机制到目前为止尚无明确的定论,可能是因为免疫、遗传和感染等因素共同作用,从而引起肠道黏膜的免疫系统出现异常的反应而最终导致的炎症反应所致^[8-10]。随着人们饮食结构和生活习惯的不断改变,溃疡性结肠炎的发病率呈逐步上升趋势^[11]。溃疡性结肠炎患者主要有腹泻、腹痛、黏液脓血便以及里急后重等,同时可伴有不同程度的肠外表现如结节性红斑、口腔溃疡等临床症状,其病理改变主要以弥漫性炎症性反应为主^[12-14]。目前临床对于溃疡性结肠炎的治疗原则是:控制病情的发作,缓解病情的同时减少并发症等的发生^[15]。美沙拉嗪作为新型的5-氨基水杨酸控制剂,它具有抑制免疫功能的作用,因此常用作溃疡性结肠炎的治疗,但是研究显示免疫抑制剂的长期使用会给患者带来不同程度的不良反应如恶心、呕吐等^[16]。

从中医角度看,溃疡性结肠炎发病的原因多是因为外感六淫疫毒,内伤饮食七情,从而使脾胃受损,升降失调,清浊相混,迫于大肠,酿生湿热,阻滞气血,血败肉腐,壅滞成脓,内溃成疡,以脾胃虚弱为本,湿热蕴结为标,因而在中医学上将溃疡性结肠炎纳入“泄泻”、“五更泄”的范畴,认为该病主要发生于脾胃,脾虚失运、湿邪内生、清浊不分,因而导致泄泻,故将“泄泻”、“五更泄”与脾胃功能虚弱认定为有一定的联系,因此溃疡性结肠炎患者在中医上又可称为脾胃气虚型溃疡性结肠炎^[17]。参苓白术散因为具有健脾调中,益气升提的功效,对于虚劳、内伤、气虚以及阳虚的慢性腹泻的患者,通过益气健脾、补中固卫就可以达到其功效^[18]。参苓白术散首次出现是在《太平惠民和剂局方》^[19]:其中提到人参甘温,主入脾经,擅补脾胃之气;白术甘温而性燥,既可以益气补虚,又能健脾燥湿;茯苓甘淡,为利水渗湿、健脾助运之要药;淮山药甘平,为平补脾胃之品;莲子肉甘平而涩,长于补脾厚肠胃,涩肠止泻,健脾开胃;扁豆甘平补中,健脾化湿;薏苡仁甘淡微寒,健脾利湿;砂仁辛温芳香,化湿醒脾,行气和胃;桔梗宣开肺气,通利水道;炙甘草益气和中,调和诸药;大枣补益脾胃。研究显示该药也具有抗菌镇痛、止泻等作用,并且能够有效的抑制肠黏膜的损伤,增强机体清除自由基和抗氧化的能力,以及调节紊乱的免疫功能等^[20]。

本研究采用中药参苓白术散联合美沙拉嗪治疗脾胃气虚型溃疡性结肠炎,并以美沙拉嗪治疗的患者为对照比较两组的临床疗效及对患者血清细胞因子的影响。结果显示,观察组患者的临床疗效显著优于对照组($P<0.05$),说明中药参苓白术散联合美沙拉嗪治疗脾胃气虚型溃疡性结肠炎具有抗炎镇痛的作用,这与既往研究结果一致^[15]。此外,治疗后两组患者的Sutherland DAI评分均低于治疗前($P<0.05$),说明参苓白术散、美沙拉嗪均能有效改善患者的病情。观察组治疗后的Sutherland DAI评分小于对照组($P<0.05$),原因可能是美沙拉嗪通过抑制炎症介质白三烯及前列腺素的合成,从而控制肠壁炎症反应^[16,17]。

血清细胞因子IL-17、IL-23以及TNF- α 作为炎症介质介导了结肠黏膜的病理损伤,IL-23扩增了Th17细胞并且使其存活,同时分泌IL-17。IL-17具有募集和激活嗜中性粒细胞功能的作用^[18],可在自身免疫性疾病中发挥免疫学效应。而TNF- α

作为巨噬细胞或者是单核细胞活化后产生的细胞因子,参与多种病理生理过程,如细胞免疫、炎症性反应等。因此,在脾胃气虚型溃疡性结肠炎患者中血清细胞因子各水平会存在不同程度的升高^[19]。本研究中,治疗后两组患者的IL-17、IL-23、TNF- α 水平较治疗前降低($P<0.05$),说明参苓白术散、美沙拉嗪能够有效抑制促炎因子的表达,降低血清细胞因子水平,最终抑制肠壁炎症,缓解肠黏膜损伤。我们还发现,治疗后观察组IL-17、IL-23、TNF- α 水平低于对照组,说明参苓白术散联合美沙拉嗪用于脾胃气虚型溃疡性结肠炎的效果较好,这与有关研究结果一致^[20]。

综上所述,参苓白术散联合美沙拉嗪可以有效缓解脾胃气虚型溃疡性结肠炎患者的病情,同时降低血清各细胞因子的水平以达到抑制炎症性反应的效果,临床有重要的参考价值。

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