

doi: 10.13241/j.cnki.pmb.2017.15.031

参苓白术辅助治疗对老年溃疡性结肠炎伴脓血便患者临床疗效及免疫功能的影响*

赵春林 王 飞 肖 兰 刘 姝 冯 燕

(攀枝花学院附属医院 攀枝花市中西医结合医院 消化内科 四川 攀枝花 617000)

摘要 目的:探讨参苓白术辅助治疗对老年溃疡性结肠炎伴脓血便患者临床疗效及免疫功能的影响。**方法:**选取于我院进行治疗的老年溃疡性结肠炎伴脓血便患者 50 例,随机分为实验组与对照组,每组 25 例。对照组患者给予柳氮磺吡啶结肠溶胶囊进行治疗,实验组患者在对照组的基础上联合使用参苓白术丸进行治疗,两组患者均治疗 3 个月,比较两组患者治疗前后血清白介素-2 (IL-2)、 γ -干扰素 (IFN- γ) 及白介素-10 (IL-10) 水平,并评价两组患者的临床疗效。**结果:**与治疗前相比,两组患者治疗后的血清 IL-2、IFN- γ 水平均显著降低,IL-10 明显升高;与对照组相比,实验组患者血清 IL-2、IFN- γ 水平较低,IL-10 水平更高 ($P < 0.05$);且与对照组相比,实验组患者的临床总有效率较高 ($P < 0.05$)。**结论:**参苓白术散能有效改善老年溃疡性结肠炎伴脓血便患者的免疫功能并提高其临床疗效。

关键词:参苓白术;老年溃疡性结肠炎;免疫功能;临床疗效

中图分类号:R574.62 文献标识码:A 文章编号:1673-6273(2017)15-2920-03

Influence of Adjunctive Therapy with Shenling Baizhu Powder on the Immune Function and Clinical Effect of Elderly Patients with Colitis Gravis and Bloody Purulent Stool*

ZHAO Chun-lin, WANG Fei, XIAO Lan, LIU Shu, FENG Yan

(Department of Gastroenterology, Panzhihua Hospital of traditional Chinese and Western medicine (Affiliated Hospital of Panzhihua University), Panzhihua, Sichuan, 617000, China)

ABSTRACT Objective: To investigate the influence of shenling baizhu powder on the immune function and clinical effect of elderly patients with colitis gravis and bloody purulent stool. **Methods:** 50 elderly patients with colitis gravis and bloody purulent stool who were treated in our hospital were selected and randomly divided into the experimental group and control group with 25 cases in each group, patients in the control group were treated with sulfasalazine colonosoluble capsules, patients in the experimental group were treated on the base of the control group with shenling baizhu powder, patients in both groups of were treated for 3 months, the serum interleukin 2 (IL-2), γ -interferon (IFN- γ) and interleukin 10 (IL-10) levels of both groups were compared before and after treatment, and the clinical efficacy of the two groups of patients were evaluated. **Results:** Compared with before treatment, the serum IL-2, IFN- γ , IL-10 levels of both groups were obviously decreased after treatment; compared with the control group, the serum IL-2, IFN- γ and IL-10 levels of experimental group were significantly lower ($P < 0.05$); and compared with the control group, the total clinical effective rate of experimental group was higher ($P < 0.05$). **Conclusion:** Shenling baizhu powder could effectively improve the immune function and clinical effect of elderly patients with colitis gravis and bloody purulent stool.

Key words: Shenling baizhu powder; Elderly patients with colitis gravis; Immune function; Clinical efficacy

Chinese Library Classification (CLC): R574.62 **Document code:** A

Article ID: 1673-6273(2017)15-2920-03

前言

溃疡性结肠炎 (ulcerative colitis, UC) 亦称溃结, 是消化内科的常见疑难疾病之一, 是一种慢性非特异性炎症, 主要累及直肠、结肠粘膜及粘膜下端等部位^[1], 临床表现主要为腹泻、便秘、便血等^[2]。疾病初期的临床症状较轻, 粪便表面仅有黏液改变, 随着病情的加重, 便次逐渐增多, 可达 10~30 次/天, 粪便呈

糊状软, 因结肠黏膜局部缺血及溶解纤维蛋白活力增加而常混有脓血及黏液^[3,4]。目前研究表明免疫功能异常、感染、过敏反应、情绪变化及遗传得均可诱导该病的发生^[5], 临床治疗老年溃疡性结肠炎伴脓血便的临床效果欠佳^[6]。我国医学认为该病为本虚标实之证, 标实为湿热蕴肠, 损伤肠络, 而本虚为脾虚湿盛, 运化失健所致。参苓白术丸为中成药的一种, 具有益气健脾、渗湿止泻等功效^[7]。因此, 本研究通过分析参苓白术辅助治

* 基金项目: 四川省卫生厅科研基金项目 (130212)

作者简介: 赵春林 (1974-), 男, 本科, 主治医师, 研究方向: 慢性胰腺炎中西医结合治疗, 电话: 18782201296

(收稿日期: 2016-10-23 接受日期: 2016-11-19)

疗对老年溃疡性结肠炎伴脓血便患者血清 TH1 水平的影响,旨在探讨参苓白术辅助治疗老年溃疡性结肠炎伴脓血便患者的临床疗效和价值。

1 资料与方法

1.1 临床资料

选取 2015 年 11 月~2016 年 5 月期间在我院就医的老年溃疡性结肠炎伴脓血便患者 50 例,男性 34 例,女性 16 例,年龄 48~78 岁,平均年龄(63.54 ± 7.67)岁。对所有患者应用随机数字表进行分组,抽到双号的分配为对照组,抽到单号的分配为实验组。实验组患者 25 例,男性 18 例,女性 7 例,年龄 50~78 岁,平均年龄(67.67 ± 7.45)岁;对照组患者 25 例,男性 16 例,女性 9 例,年龄 49~77 岁,平均年龄(66.48 ± 7.38)岁。纳入符合溃疡性结肠炎的诊断标准;溃疡性结肠炎伴有脓血者;自愿参加本次实验,并积极配合医嘱进行治疗。排除有严重肠梗阻、败血症及大出血等严重的并发症者;合并严重肠穿孔与结肠癌者;合并严重肝肾功能不全及造血功能不全者;哺乳及妊娠者;对研究中使用的药物过敏。两组患者在性别组成、年龄分布等一般情况下无显著差异($P > 0.05$)。本次实验由我院伦理协会批准同意,患者了解本次实验后签署知情同意书。

1.2 治疗方法

两组患者均给予戒烟、戒酒,避免食用虾、蟹、花生、牛奶及奶制品等不耐受的食物并忌食辣椒,忌冰冻、生冷食物等一系常规治疗。对照组:在常规的治疗基础上给予柳氮磺吡啶结肠溶胶囊(潮州市强基制药厂 国药准字 H20051173),用法用量:初始每天 1-2g(4-8 粒),逐渐增至每天 3-4g(12-16 粒),饭前口

服。实验组:在对照组治疗的基础上联合参苓白术丸(雷允上药业有限公司 国药准字 Z32020599),用法用量:6g/次,每天服用三次,饭后口服。30 天为一疗程,两组患者均治疗三个疗程。

1.3 观察指标及方法

所有患者于治疗前及治疗结束后 1 天清晨抽取空腹血 3 mL,送于我院的化验科进行检查。其中,血清白介素 2(IL-2)、白介素 10(IL-10)及 γ -干扰素均使用 ELASA 法进行检验,检验所用仪器为 FX-6MG 酶联免疫光谱分析仪,采用浙江爱康生物科技有限公司生产的试剂盒。结肠粘膜采用电子结肠镜进行检测。所有检测方法严格按照说明书进行操作。

1.4 疗效判定标准

治愈:临床症状消失,或基本消失,复查肠镜粘膜恢复正常或者原病灶形成瘢痕组织;有效:临床症状明显改善,复查肠镜病变粘膜有一定程度的恢复;无效:临床症状加重或者无明显改善,复查肠镜病变粘膜加重。

1.5 统计学分析

所有计量数据均录入 SPSS19.0 统计软件进行分析,血清 IL-2、IFN- γ 、IL-10 水平均采用 t 进行检测,两组患者临床疗效采用卡方进行检测,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血清 IL-2、IFN- γ 水平的比较

与治疗前相比,两组患者治疗后的血清 IL-2、IFN- γ 水平均显著降低($P < 0.05$);与对照组相比,实验组患者血清 IL-2、IFN- γ 水平明显较低($P < 0.05$)。见表 1。

表 1 两组患者治疗前后血清 IL-2、IFN- γ 水平比较($\bar{x} \pm s$)

Table 1 Comparison of the serum IL-2 and IFN- γ levels before and after treatment between two groups($\bar{x} \pm s$)

Groups		IL-2(pg / mL)	IFN- γ (pg / mL)
Experimental group(n=25)	Before treatment	32.65 $\pm$ 3.29	22.64 $\pm$ 2.27
	After treatment	22.56 $\pm$ 2.26**	12.64 $\pm$ 1.31**
Control group(n=25)	Before treatment	32.62 $\pm$ 3.28	23.45 $\pm$ 2.41
	After treatment	29.53 $\pm$ 3.04*	20.45 $\pm$ 2.11*

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

2.2 两组患者治疗前后血清 IL-10 水平的比较

与治疗前相比,两组患者治疗后的血清 IL-10 水平均降低

($P < 0.05$);与对照组比较,实验组患者血清 IL-10 水平较低($P < 0.05$)。见表 2。

表 2 两组治疗前后患者血清 IL10 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum IL10 level before and after treatment between two groups($\bar{x} \pm s$)

Groups		IL10(pg/mL)
Experimental group(n=25)	Before treatment	8.63 $\pm$ 0.87
	After treatment	11.68 $\pm$ 1.11**
Control group(n=25)	Before treatment	8.42 $\pm$ 0.85
	After treatment	10.22 $\pm$ 1.11*

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

2.3 两组患者临床疗效的比较

与对照组相比,实验组患者的临床总有效率明显较高,差异有统计学意义($P < 0.05$)。见表 3。

3 讨论

溃疡性结肠炎(UC)是一种以溃疡形成和结肠黏膜的慢性

表 3 两组患者的临床治疗比较

Table 3 Comparison of the clinical efficacy between two groups

Groups	Cure (n)	Effective (n)	Invalid (n)	Improvement rate
Experimental group (n=25)	14	9	2	92%
Control group(n=25)	9	11	5	80%

Note: Compared with the control group, ^aP<0.05.

炎症为病理特征的慢性炎症性肠道疾病^[9]。黏液蛋白的改变是 UC 发病过程中的重要病理变化,其使肠黏膜的屏障作用遭到破坏,导致食物、肠道共生菌群等较难进入肠黏膜,引发一系列炎症变化与抗原特异性免疫反应,炎症细胞大量释放炎症介质及相关细胞因子,从而引起炎症病变与组织破坏,削减了肠黏膜的正常防御功能^[9]。在中医学中,本病属“泄泻”“便血”等范畴,中医认为其与外感六淫,饮食、七情内伤,过劳以及脏腑功能降低所致的脾、胃、肝、肾及大肠的功能失调有关;脾虚腹泻,吸收营养物质发生障碍,导致全身机能受不良影响而低下;脾失健运,脾不升清,中气下陷,升降、血行阻滞,淤滞肠络,致大肠调节与运动功能失调。参苓白术散主要由白术、人参、茯苓、薏苡仁、白扁豆等中药组成,其健脾益气功效显著;药理学研究表明^[10],本方能使机体的免疫功能恢复,对局部炎症的炎性细胞、趋化物、炎性介质的释放具有抑制作用,从而使肠黏膜的炎性反应降低。

有研究显示^[11]免疫机制在 UC 的发生发展过程中的作用十分重要,大量活化的淋巴细胞尤其是 T 细胞在 UC 病变部位活跃,其所分泌表达的各种细胞因子具有十分强力的致炎活性,引起病变加重。T 辅助细胞具有两种亚群,即功能不同的 Th1 与 Th2 细胞亚群;Th1 细胞主司细胞免疫,以表达 IL-2 和 IFN- γ 为主,而 Th2 细胞主司体液免疫,以表达 IL-10 与 IL-4 为主^[12]。通常情况下,两个亚群之间相互调节、拮抗,维持动态平衡,来调节机体的免疫功能,而一旦这种平衡被打破,机体就会出现相应疾病。Th 细胞对炎症性肠病的机制具有重要作用^[13]。相关研究显示^[14]UC 患者体内存在着 Th1 细胞功能的增强与 Th2 细胞功能的减弱。IL-2 是一种多生物学活性的细胞因子,有丝分裂原或抗原刺激以及 IL-1 的诱导能够使 Th1 细胞产生 IL-2,IL-2 通过与 T 细胞、单核细胞、B 细胞表面的受体相结合来发挥作用,能够对 T 细胞的活化与增殖进行促进,增强其杀伤作用,使自然杀伤细胞的活性得到提高,对 B 细胞分泌 Ig 进行促进,诱导产生 LAK 细胞,其水平反映了 Th1 细胞的功能。IFN- γ 作为 Th1 细胞的主要合成产物,可以增强 Th1 细胞的活性,对 Th2 细胞的增生产生抑制作用^[15,16]。本研究结果显示与对照组比较,实验组患者治疗后血清 IL-2、IFN- γ 明显较低,说明参苓白术散辅助治疗能够改善免疫功能。

Th2 细胞、单核细胞以及 B 细胞是白介素 -10 的主要来源场所,具有对炎症反应与促炎因子的释放进行抑制的生物学功能^[17]。IL-10 结合单核巨噬细胞上的高亲和受体后,能对其合成粒细胞集落刺激因子与 IL-1、IL-8、IL-6、IL-12、TNF- α 的能力进行抑制,通过对自然杀伤细胞与中性粒细胞的正面作用来间接对促炎性细胞因子进行抑制,还可以使 TNF 表面受体的表达减弱同时对其释放功能产生抑制作用^[18]。此外,IL-10 还能下调 IL-2 与 IFN- γ ,帮助纠正 Th 细胞亚群被破坏的动态平衡^[19]。在 UC 中,IL-10 利用旁观者抑制机制,对肠道黏膜的免疫性病

理损伤进行抑制,控制炎症反应,其水平可反映 UC 的炎症程度^[20]。本研究结果显示相比于对照组,实验组患者治疗后的 IL-10 水平较高(P<0.05),表明参苓白术散辅助治疗能够有效改善 UC 患者的炎症反应。此外,与对照组比较,实验组患者治疗后好转率较高,证明参苓白术散辅助治疗能够有效提高 UC 的临床疗效。

综上所述,参苓白术散能有效恢复 T 辅助细胞亚群平衡,使炎症与免疫功能得到改善,临床疗效提高。

参考文献(References)

- [1] Long Z, Guan L. Clinical Observation on 72 Cases of Shenling Baizhu Powder in Treatment of Ulcerative Colitis [J]. Journal of Liaoning University of Traditional Chinese Medicine, 2014, 10(4): 19-27
- [2] Chen X, Zhong R, Zhang J. Clinical Observation of Triple Therapy Combined with Shenling Baizhu Powder in Treatment of Chronic Erosive Gastritis [J]. Journal of New Chinese Medicine, 2014, 12(5): 39-48
- [3] Leng D, Chen S, Neonatology D O. Analysis of Effect of Pediatric Knead Ridge combined with Shenling Baizhu Granules in the Treatment of Neonatal Diarrhea [J]. Guangming Journal of Chinese Medicine, 2016, 5(8): 115-126
- [4] Yamamoto-Furusho JK, Sarmiento Aguilar A. Frequency, Clinical Features and Factors Associated with Pouchitis after Proctocolectomy with Ileo-Pouch-Anal Anastomosis in Patients with Ulcerative Colitis: A Latin-American Country Retrospective-Cohort Study[J]. Dig Surg, 2015, 32(6): 489-495
- [5] Shao K F, Xiao P. Effects of Modified Shenling Baizhu San on Immune Function and Toxicity Reaction of Advanced Gastric Cancer Patients in Chemotherapy [J]. Guiding Journal of Traditional Chinese Medicine & Pharmacy, 2016, 6(2): 33-42
- [6] Pan G, Yingming X U. Clinical study of probiotics combined with Shenlingbaizhu powder in the treatment of intestinal flora imbalance of patients with imbalance liver cirrhosis[J]. Journal of Bethune Medical Science, 2016, 12(3): 145-149
- [7] Wakelkamp I M M J, Gerding M N, Meer J W C V D, et al. Both Th1- and Th2-derived cytokines in serum are elevated in Graves' ophthalmopathy [J]. Clinical & Experimental Immunology, 2000, 121 (3): 453-457
- [8] Jacob S E, Nassiri M, Kerdel F A, et al. Simultaneous measurement of multiple Th1 and Th2 serum cytokines in psoriasis and correlation with disease severity [J]. Mediators of Inflammation, 2003, 12 (5): 309-313
- [9] Inagaki A, Ishida T, Ishii T, et al. Clinical significance of serum Th1-, Th2- and regulatory T cells-associated cytokines in adult T-cell leukemia/lymphoma: High interleukin-5 and -10 levels are significant unfavorable prognostic factors [J]. International Journal of Cancer, 2006, 118(12): 3054-3061

(下转第 2906 页)

- Hemoglobin Level in Rheumatoid Arthritis Patients with Diabetes[J]. Progress in Modern Biomedicine, 2016, 16(4): 723-726
- [7] Wei Meng, Xie Qing-yun, Wang Ying, et al. Correlation between Levels of Lipid Profile and Disease Activity in Rheumatoid Arthritis[J]. Progress in Modern Biomedicine, 2016, 16(1): 103-105
- [8] Kurimoto R, Shono K, Onoda M, et al. MYC/BCL2 Double-hit Lymphoma in a Patient with Rheumatoid Arthritis Associated with Methotrexate Treatment[J]. Intern Med, 2016, 55(16): 2271-2275
- [9] Bonnefoy F, Daoui A, Valmary-Degano S, et al. Apoptotic cell infusion treats ongoing collagen-induced arthritis, even in the presence of methotrexate, and is synergic with anti-TNF therapy [J]. Arthritis Res Ther, 2016, 18(1): 184
- [10] Huang Bei, Wang Qing-tong, Liu Kang-kang, et al. Relationship between TNF- α signaling pathway and the function of CD4⁺T cell subsets in rheumatoid arthritis[J]. Chinese Pharmacological Bulletin, 2013, 29(7): 900-903
- [11] Charles-Schoeman C, Lee YY, Shahbazian A, et al. Improvement in HDL Function in Early Rheumatoid Arthritis Patients Treated with Methotrexate Monotherapy or Combination Therapy in the TEAR Trial[J]. Arthritis Rheumatol, 2016, 16(9): 72-75
- [12] Wu Yan-mei, Peng Shou-chun, Shen Jian, et al. Clinical value analysis of serum protein fingerprint in patients with rheumatoid arthritis associated interstitial lung disease[J]. Chinese Journal of Immunology, 2015, 8(2): 236-239
- [13] Elshafie AI, Elkhalfia AD, Elbagir S, et al. Active Rheumatoid Arthritis in Central Africa: A Comparative Study Between Sudan and Sweden[J]. J Rheumatol, 2016, 16(2): 28-31
- [14] Yao Y, Ding C-Z, Fang Y, et al. Combination of MTX and LEF attenuates inflammatory bone erosion by down-regulation of receptor activator of NF- κ B ligand and interleukin-17 in type II collagen-induced arthritis rats [J]. Rheumatology international, 2013, 33 (7): 1845-1853
- [15] Curtis JR, Beukelman T, Onofrei, et al. Elevated liver enzyme tests among patients with rheumatoid arthritis or psoriatic arthritis treated with methotrexate and/or leflunomide [J]. Annals of the Rheumatic Diseases, 2010, 69(1): 43-47
- [16] Bird P, Griffiths H, Tymms K, et al. The SMILE study-safety of methotrexate in combination with leflunomide in rheumatoid arthritis [J]. The Journal of rheumatology, 2013, 40(3): 228-235
- [17] DeCastroAlcantara AC, Leite CAC, Leite ACRM, et al. A longterm prospective real-life experience with leflunomide in juvenile idiopathic arthritis[J]. The Journal of rheumatology, 2014, 41(2): 338-344
- [18] Manders SH, Kievit W, Jansen TL, et al. Effectiveness of Tumor Necrosis Factor Inhibitors in Combination with Various csDMARD in the Treatment of Rheumatoid Arthritis: Data from the DREAM Registry[J]. J Rheumatol, 2016, 7(15): 68-72
- [19] Garg NK, Singh B, Tyagi RK, et al. Effective transdermal delivery of methotrexate through nanostructured lipid carriers in an experimentally induced arthritis model [J]. Colloids Surf B Biointerfaces, 2016, 147(9): 17-24
- [20] Rutanen J, Kononoff A, Arstila L, et al. Five cases of interstitial lung disease after leflunomide was combined with methotrexate therapy[J]. Scandinavian journal of rheumatology, 2014, 43(3): 254-258
-
- (上接第 2922 页)
- [10] Phenekos C, Vryonidou A, Gritzapis A D, et al. Th1 and Th2 Serum Cytokine Profiles Characterize Patients with Hashimoto Thyroiditis (Th1) and Graves Disease (Th2)[J]. Neuroimmunomodulation, 2004, 25(8): 56-79
- [11] Jianke L I, Wang C, Furong L I, et al. Detection of serum Th1,Th2 and Th17 related cytokines in the patients with leprosy [J]. China Journal of Leprosy & Skin Diseases, 2016, 19(22): 351-364
- [12] Malik TA. Inflammatory Bowel Disease: Historical Perspective, Epidemiology, and Risk Factors [J]. Surg Clin North Am, 2015, 95(6): 1105-1122
- [13] Yu B, Chen D F, Wang R Q, et al. Intravenous Esomeprazole for Prevention of Peptic Ulcer Rebleeding: A Randomized Trial in Chinese Patients[J]. Advances in Therapy, 2015, 32(11): 1160-1176
- [14] Morgan XC, Kabakchiev B, Waldron L, et al. Associations between host gene expression, the mucosal microbiome, and clinical outcome in the pelvic pouch of patients with inflammatory bowel disease[J]. Genome Biol, 2015, 8(16): 67
- [15] Ghavidel A. Ulcerative colitis associated with aplastic anemia; a case report[J]. Middle East J Dig Dis, 2013, 5(4): 230-234
- [16] He Y, Chen Z, Liu X, et al. Influence of trace elements mixture on bacterial diversity and fermentation characteristics of liquid diet fermented with probiotics under air-tight condition[J]. PLoS One, 2014, 9(12): e114218
- [17] Yamada A, Arakaki R, Saito M, et al. Role of regulatory T cell in the pathogenesis of inflammatory bowel disease [J]. World J Gastroenterol, 2016, 22(7): 2195-2205
- [18] Pedersen J, Coskun M, Soendergaard C, et al. Inflammatory pathways of importance for management of inflammatory bowel disease [J]. World J Gastroenterol, 2014, 20(1): 64-77
- [19] Yao CK, Muir JG, Gibson PR. Review article: insights into colonic protein fermentation, its modulation and potential health implications [J]. Aliment Pharmacol Ther, 2016, 43(2): 181-196
- [20] Klotz C, Barret M, Dhooge M, et al. Management of diagnosis and treatment in ulcerative colitis[J]. Presse Med, 2015, 44(2): 144-149