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美沙拉秦对缓解期溃疡性结肠炎患者血清炎症因子的影响

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摘要 目的:探讨美沙拉秦对缓解期溃疡性结肠炎(UC)患者血清炎性因子水平的影响。**方法:**收集 2013 年 5 月至 2016 年 5 月于我院治疗的缓解期 UC 患者 153 例,随机分为观察组 75 例及对照组 78 例。对照组患者给予常规治疗,观察组在对照组的基础上加用美沙拉秦治疗。观察比较两组治疗前后的血清白细胞介素 -6(IL-6)、白细胞介素 -8(IL-8)、白细胞介素 -17(IL-17)、肿瘤坏死因子 -α(TNF-α)水平、疾病活动指数(DAI)评分、临床疗效、病情复发和不良反应的发生情况。**结果:**治疗后,观察组治疗总有效率为 96.0%,明显高于对照组的 62.8% (P<0.05);观察组的血清 IL-6、IL-8、IL-17 及 TNF-α 水平均较治疗前明显降低,且显著低于对照组(P＜0.05);两组的 DAI 评分均有明显改善,但观察组的改善幅度明显大于对照组(P＜0.05);观察组患者的复发率(2.6%)显著低于对照组(21.8%)(P＜0.05),两组不良反应发生率比较差异无统计学意义(P＞0.05)。**结论:**美沙拉秦治疗缓解期溃疡性结肠炎的临床疗效显著,可显著抑制患者的炎症反应,同时可改善患者的临床症状,降低复发率,且安全性高。

关键词:溃疡性结肠炎;缓解期;美沙拉秦;炎性因子;疗效

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Effect of Mesalazine on the Serum Inflammatory Factors of Patients with Ulcerative Colitis in Remission

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ABSTRACT Objective: To investigate the effect of mesalazine on the serum inflammatory factors of patients with ulcerative colitis in remission. **Methods:** 153 patients with ulcerative colitis in remission admitted into our hospital were divided into the control group and the observation group. 78 cases in the control group were treated with conventional treatment, and 75 cases in the observation group were treated with mesalazine based on the control group. The serum inflammatory factors including IL-6, IL-8, IL-17, TNF-α, DAI score, clinical efficacy, relapse and adverse reaction in both groups were observed and compared. **Results:** After treatment, the clinical effective rate of observation group was 96.0%, which was much higher than that of the control group (62.8%, P＜0.05). The serum levels of IL-6, IL-8, IL-17, TNF-α of both group were markedly lower than those before treatment, which were much lower in the observation group than those of the control group (P＜0.05). The DAI score in both groups showed obvious improvement, and the DAI score of observation group was much better than that of the control group (P＜0.05). In addition, the incidence of relapse was 2.6% in the observation group, which was significantly lower than that of the control group (21.8%, P＜0.05), and there was no significant difference in the incidence of adverse reactions between the two groups (P＞0.05). **Conclusion:** Mesalazine had a great capability of treating patients with ulcerative colitis in remission by inhibiting the serum levels of inflammatory factors, improving the clinical symptoms and decreasing incidence of relapse with high safety.

Key words: Ulcerative colitis; Remission; Mesalazine; Inflammatory factors; Clinical efficacy

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前言

消化性结肠炎(ulcerative colitis,UC)是临床上常见的消化内科疾病,主要为直肠或结肠发病所表现出的一种慢性非特异性炎性疾病,临床表现为腹泻、腹痛、脓液脓血便等,部分患者还存在眼睛、关节损害等肠外表现[1,2]。该病的发病机制比较复杂,目前尚未完全清楚,可能与遗传、肠道菌群失衡以及免疫力等因素相关[3,4]。近年来,UC 的发病率逐年攀升,且病情容易反复,对患者的身心健康及经济负担带来严重影响[5]。目前,对于 UC 的治疗,临床上常采用药物治疗及手术治疗的方式,而缓解期患者通常选择药物治疗[6]。本研究拟探讨美沙拉秦对缓解期溃疡性结肠炎患者血清炎性因子的影响。现作如下报道。

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1 资料与方法

1.1 病例资料

收集 2013 年 5 月至 2016 年 5 月在盘锦市中心医院接受治疗的 153 例缓解期溃疡性结肠炎患者，均符合中华医学会消化病学分会制作的《炎症性肠病诊断与治疗的共识意见》中诊断标准[7]。入选标准：① 处于缓解期的 UC 患者；② 常规粪便以及霉菌的生物培养无致病性；③ 入院前 1 个月内未接受其他治疗。排除标准：① 属爆发型 UC 者；② 属缺血性肠炎、感染性结肠炎或放射性肠炎等其他肠道疾病者；③ 合并消化道肿瘤、肠梗阻及中毒性结肠扩张等疾患者；④ 对本次治疗药物有过敏反应者。将患者随机分为对照组(78 例)和观察组(75 例)，其中对照组，男性患者 40 例，女性患者 38 例，年龄 24～60 岁，平均(42.1± 6.3)岁，平均病程(14.6± 4.1)个月；观察组，男性患者 39 例，女性患者 36 例，年龄 24～62 岁，平均(42.4± 6.1)岁，平均病程(15.0± 4.2)个月。两组一般资料比较差异均无明显统计学意义，具有可比性(P>0.05)。

1.2 治疗方法

对照组予以患者常规治疗，如严格指导患者饮食，改善营养，调节酸碱平衡及水电解质紊乱，适时进行有氧运动等。观察组在对照组的基础上给予患者美沙拉秦(安徽东盛制药有限公司，国药准字 H20020211)，口服，4 次 /d，0.5 g/ 次。所有患者均维持 4 周的治疗。

1.3 观察指标

(1)炎性因子测定：分别于治疗前和治疗 4 周后的晨间空腹抽取患者静脉血 3～5 mL，离心，取上清。采用酶联免疫吸附法(ELISA)测定白细胞介素 -6(IL-6)、白细胞介素 -8(IL-8)、白细胞介素 -17(IL-17)、肿瘤坏死因子 -α(TNF-α)。试剂盒有上海酶联生物科技有限公司提供。(2)采用疾病活动指数(Disease activity index，DAI) 评分系统结合患者的大便粘稠度以及大便出血情况、体重下降百分率评价患者治疗前后的症状情况。评价标准：体重下降百分率＞15%， 记 4 分；10%＜体重下降百分率≤ 15%，记 3 分；5%＜体重下降百分率≤ 10%，记 2 分；1%＜体重下降百分率≤ 5%，记 1 分；体重不变，记 0 分。腹泻和(或)明显出血，记 4 分；大便松散和(或)隐血阳性，记 2 分；大便正常，记 0 分。DAI 评分 =(体重下降率 + 大便粘稠度 + 出血情况)评分 /3。(3)记录药物治疗期间，两组病情复发和不良反应的发生情况。

1.4 疗效评价标准

显效：临床症状全部消失，肠粘膜炎症基本褪去，患者的状态良好；有效：临床症状大幅度缓解，肠粘膜炎症病变降低量大于 50%，患者的不适症状有所缓解；无效：临床症状及体征均未缓解甚至加重，肠粘膜炎症无变化甚至加重，患者状态较差，且不适症状有加重迹象[8]。

1.5 统计学分析

用 SPSS18.0 处理数据，计量资料以($\bar{x}\pm s$)表示，组间比较采用 t 检验，计数资料以(%)表示，行 x^2 检验，以 P＜0.05 表示差异具有统计学意义。

2 结果

2.1 两组治疗有效率的比较

观察组临床总有效率为 96.0%，显著高于对照组(62.8%，P<0.05)，见表 1。

表 1 两组临床疗效比较[例(%)]

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

Groups	n	Remarkable effect	Improvement	Invalid	Total effective
Control group	78	29(37.2)	20(25.6)	29(37.2)	49(62.8)
Observation group	75	49(65.3)	23(30.7)	3(4.0)	41(96.0)①

Note: Compared with the control group, ① P＜0.05.

2.2 两组治疗前后血清炎性因子水平的比较

治疗前，两组血清 IL-6、IL-8、IL-17 及 TNF-α 水平比较差异无明显统计学意义(P＞0.05)。治疗后，两组的血清 IL-6、IL-8、IL-17 及 TNF-α 水平均较治疗前显著降低，且观察组以上指标显著低于对照组(P＜0.05)。见表 2。

2.3 两组治疗前后 DAI 评分的比较

治疗前，两组的 DAI 评分比较差异无统计学意义 (P＞0.05)。治疗后，两组的 DAI 评分均较治疗前明显改善，且观察组的改善幅度明显大于对照组(P＜0.05)。见表 3。

表 2 两组治疗前后血清炎性因子水平比较(ng/L，$\bar{x}\pm s$)

Table 2 Comparison of levels of serum inflammatory factors between the two groups before and after treatment (ng/L, $\bar{x}\pm s$)

Groups	Time	IL-6	IL-8	IL-17	TNF-α
Control group (n=78)	Before treatment	125.92± 18.81	191.87± 24.18	456.86± 80.11	103.07± 15.20
	After treatment	119.47± 17.58	185.81± 23.58	400.89± 72.09	97.37± 14.13
Observation group (n=75)	Before treatment	126.55± 17.62	188.95± 25.74	460.92± 72.11	101.91± 14.22
	After treatment	101.82.± 14.33①	156.51± 21.46①	316.70± 52.08①	79.29± 12.18①

Note: Compared with the control group, ① P＜0.05.

表 3 两组治疗前后 DAI 评分比较($\bar{x}\pm s$)

Table 3 Comparison of the DAI score between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	DAI score	
		Before treatment	After treatment
Control group	78	5.13± 1.72	4.26± 1.26[a]
Observation group	75	5.10± 1.75	3.49± 1.04[a b]

Note: Compared with those before treatment, [a] P＜0.05; Compared with those of control group, [b] P＜0.05.

2.4 两组病情复发及不良反应发生情况的比较

治疗期间,对照组患者有 17 例患者病情出现复发(复发率为 21.8%),无不良反应发生,而观察组患者仅有 2 例患者出现病情复发的现象(复发率为 2.6%),有 2 例患者出现不良反应,其中 1 例出现头晕,1 例出现恶心呕吐(发生率为 2.6%)。观察组复发率显著低于对照组(P＜0.05),而两组不良反应发生率比较差异并无统计学意义(P＞0.05)。

3 讨论

UC 是一种临床上常见的非特异性炎症性肠病, 其发病不受年龄、性别等因素影响,临床上常见于中、青年人群[9]。晚期 UC 往往易反复发作、迁延不愈,且极易合并其他并发症,给患者的生活质量和身心健康造成了严重影响[10]。因此,缓解期的强化治疗对于提高患者治愈率和改善预后有重要的意义。目前,对缓解期 UC 患者,临床上通常采用保守治疗,通过控制饮食、改善营养、适量运动等措施纠正患者的非健康生活习惯,而达到维持治疗的目的[11]。然而,保守维持治疗的效果并不理想,病情病程长,反复发作,往往会给患者的精神和治疗信心造成过多负面影响,并且反复治疗也容易给患者的家庭带来诸多经济困难[12]。美沙拉秦是 5- 氨基水杨酸类药物,在阻滞结肠粘膜对白三烯的释放,降低中性粒细胞、血管内皮细胞、巨噬细胞等多种可刺激白细胞介素分泌及释放的细胞因子水平,以及清除自由基、活性氧等方面效果明显,同时还可有效缓解炎性递质对肠道黏膜的损伤[13-15]。

本研究探讨了美沙拉秦对缓解期溃疡性结肠炎的临床疗效及其对患者血清炎性因子的影响。研究表明美沙拉秦不仅可长期维持治疗效果,并且特殊制作的控释制剂材料可较好地保护药物有效成分免受小肠的吸收, 从而可准确达到病变部位,达到提升疗效的目的[16]。本研究结果显示美沙拉秦联合治疗的患者临床治疗有效率 (96.0%) 显著高于接受常规治疗的患者(62.8%), 提示在保守维持治疗的基础上加用美沙拉秦可显著提升 UC 的临床疗效。研究表明 UC 的发病与抗炎细胞因子和促炎细胞因子间的动态平衡受损有密切关系,患者机体产生的包括 IL-6、IL-8 在内的炎性细胞因子会对机体组织造成损伤[17],而 IL-17 以及 TNF-α 作为机体重要的促炎因子,参与并作用了 UC 病理损伤及病情发展的整个过程,可诱导肠粘膜的炎性反应[18]。另外,UC 患者血浆及肠粘膜中 TNF-α 含量明显高于健康人群,并且在活动期的水平会明显高于非活动期[19,20]。本研究结果显示美沙拉秦联合治疗的患者血清 IL-6、IL-8、IL-17 及 TNF-α 均较治疗前明显改善,且显著低于对照组,提示美沙拉秦治疗 UC,可明显抑制患者体内的炎症反应,从而进一步改善患者的临床症状。两组的 DAI 评分均有明显改善,但美沙拉秦联合治疗的患者的改善幅度明显大于接受常规治疗的患者,说明常规维持治疗也可一定程度改善患者的症状,但美沙拉秦的治疗效果更为显著。此外,观察组患者的复发率(2.6%)显著低于对照组(21.8%),两组不良反应发生率比较无统计学差异,提示美沙拉秦对缓解期的 UC 患者具有明显的维持治疗作用,安全性好,可有效巩固临床疗效,从而有助于患者病情的恢复。

综上所述,美沙拉秦治疗缓解期溃疡性结肠炎的临床疗效显著,可显著抑制患者的炎症反应,同时可改善患者的临床症状,降低复发率,且安全性高。

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