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枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠治疗溃疡性结肠炎的临床疗效*

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摘要 目的:探讨枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠治疗溃疡性结肠炎的临床疗效。**方法:**选取2014年5月~2018年6月淮安市淮阴医院诊治的溃疡性结肠炎患者120例,根据患者入院先后顺序分为两组,对照组在常规治疗的基础上给予枯草杆菌二联活菌肠溶胶囊,观察组在对照组的基础上给予康复新液保留灌肠。比较两组患者的治疗总有效率、治疗前后血清白介素-8(IL-8)、白介素-6(IL-6)和肿瘤坏死因子-α(TNF-α)水平、血小板(PLT)和血酶原时间(PT)、纤维蛋白原(FIB)水平的变化及不良反应的发生情况。**结果:**治疗后,观察组总有效率为95.00%,对照组为83.33%,观察组显著高于对照组(*P*<0.05)。两组患者治疗后血清IL-8、IL-6、TNF-α水平及PLT、FIB均较治疗前显著下降,且观察组以上指标均显著低于对照组(*P*<0.05),而两组治疗后PT水平均较治疗前显著升高,且观察组显著高于对照组(*P*<0.05)。两组不良反应发生率相比无统计学差异(*P*>0.05)。**结论:**枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠治疗可显著降低溃疡性结肠炎患者的炎性因子水平,改善凝血功能,提高临床治疗效果,且安全性较高。

关键词:枯草杆菌二联活菌肠溶胶囊;康复新液灌肠;溃疡性结肠炎;疗效

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Clinical Effect of *Bacillus Subtilis* and *Enterococcus Faecium* Enteric Capsule Combined with Kangfuxin Solution Enema in the Treatment of Ulcerative Colitis*

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ABSTRACT Objective: To explore the clinical effect of *bacillus subtilis* and *enterococcus faecium* enteric capsule combined with Kangfuxin solution enema in the treatment of ulcerative colitis. **Methods:** 120 cases of ulcerative colitis were selected in the huaiyin hospital of huai 'an city from May 2014 to June 2018, and they were divided into two groups according to the sequence of admission. The control group was given the *bacillus subtilis* and *enterococcus faecium* enteric capsule on the basis of conventional treatment, and the observation group was given the Kangfuxin solution enema on the basis of control group. The total effective rate, changes of serum IL-8, IL-6, TNF-α, PLT, PT and FIB levels before and after treatment and the incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of observation group and control group were 95.00% and 83.33%, which was significantly higher in the observation group than that of the control group (*P*<0.05). After treatment, the levels of serum IL-8, IL-6, TNF-α, PLT and FIB were significantly decreased in both groups compared with before treatment (*P*<0.05). The above indexes in the observation group were significantly lower in the observation group than those in the control group (*P*<0.05). After treatment, the PT levels in both groups were significantly higher than before treatment, which was significantly higher in the observation group than that of the control group (*P*<0.05). There was no statistical difference in the incidence of adverse reactions between the two groups (*P*>0.05). **Conclusion:** *Bacillus subtilis* and *enterococcus faecium* enteric capsule combined with Kangfuxin solution enema can significantly reduce the level of inflammatory factors, improve the coagulation function and clinical treatment effect in the patients with ulcerative colitis, and it had high security.

Key words: *Bacillus subtilis* and *enterococcus faecium* enteric capsule; Kangfuxin solution enema; Ulcerative colitis; Clinical effect

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引言

溃疡性结肠炎是一种不明原因的非特异性炎性反应性肠病，是消化系统常见的疾病之一，临床表现为反复腹痛、腹泻、粘液脓血便等，病变部位主要为大肠黏膜及黏膜下层[1-3]。该病好发于 20~40 岁青年人群，病程较长，且容易反复，严重者可继发胃穿孔、出血、中毒性巨结肠、结肠息肉，甚至胃肠癌的发生，给患者带来巨大的心理压力并影响其生活质量[4,5]。溃疡性结肠炎的发病机制尚不明确，有研究显示[6,7]溃疡性结肠炎的发生可能与肠道菌群的失调密切相关。也有研究表明[8,9]，各种细胞因子作用于结肠黏膜，促炎因子和抗炎因子失衡引发局部炎症反应是其基本的病理过程，这些细胞因子的参与程度和数量与疾病的进展及预后关系密切。另有研究认为人体中血小板数量与凝血机能对溃疡性结肠炎病情的评估具有重要价值[10,11]。

目前，临床对于溃疡性结肠炎的治疗主要采用糖皮质激素、益生菌、免疫制剂等，旨在改善患者的临床症状、促进溃疡愈合、减少复发并提高患者的生活质量[12-14]。灌肠给药的方式药物可直接作用于病变部位，作用时间长，临床效果更好[15,16]。因此，本研究主要探讨了枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠对溃疡性结肠炎的治疗效果，结果报道如下。

1 资料与方法

1.1 病例资料

选取我院诊治的溃疡性结肠炎患者 120 例，研究时间段为 2014 年 5 月 ~2018 年 6 月，所有患者均符合溃疡性结肠炎的诊断标准。纳入标准：① 经结肠镜及组织学检查确诊；② 年龄 18~65 岁；③ 病变部位主要为直肠、乙状结肠；④ 病情为轻型和重型。排除标准：① 感染性肠炎者；② 重度溃疡性结肠炎者；③ 合并重要器官功能障碍者；④ 合并全身系统性炎症者。根据患者入院先后顺序分为两组，对照组 60 例，男 31 例，女 29 例；年龄 25~60 岁，平均 45.32± 3.25 岁；病程 10~40 个月，平均 31.25± 5.27 个月；病变程度：轻度 37 例，中度 23 例。观察组 60 例，男 32 例，女 28 例；年龄 28~63 岁，平均 47.01± 3.58 岁；病程 11~42 个月，平均 33.11± 5.52 个月；病变程度：轻度 36 例，中度 24 例。两组一般资料比较无统计学差异（*P>0.05*），具有可比性。

1.2 治疗方法

对照组在常规治疗的基础上口服枯草杆菌二联活菌肠溶胶囊（北京韩美药品有限公司，国药准字 S20030087，250 mg/粒），2 粒 / 次，3 次 /d。观察组在对照组的基础上进行康复新液（昆明赛诺制药有限公司，国药准字 Z53020054，50 mL; 100 mL）保留灌肠，取 50 mL 康复新液于 100 mL 生理盐水中稀释，并加热至 37℃，患者取膝胸位，臀部抬高，将灌肠管置入肛门 10~15 cm 处，液面距离肛门不超过 30cm，缓慢灌注药液，拔出肛管后保留药液 20~30 min，每天灌肠 1 次。两组均治疗 8 周。

1.3 观察指标

① 临床治疗效果：完全缓解：症状完全消失，结直肠镜显示黏膜大致正常，2 个月无复发；有效：症状基本消失，结直肠镜显示有轻度炎症或者假息肉；无效：症状无改善或加重，结直肠镜显示黏膜没有好转。总有效率 = 完全缓解率 + 有效率。② 治疗前后炎性因子水平，分别于治疗前后抽取两组患者的空腹静脉血 10 mL，离心后取上清液待测。采用酶联免疫吸附法测定 IL-8、IL-6 和 TNF-α 水平，试剂盒均由上海酶联生物科技有限公司生产。③ 治疗前后凝血相关指标的水平，分别于治疗前后采用 XT-20001 型血细胞分析仪和 CA-1500 全自动凝血分析仪（均由希森美康医用电子上海有限公司生产）分别测定 PLT 和 PT、FIB 水平。④ 不良反应的发生情况。

1.4 统计学方法

采用 SPSS 20.0 进行数据分析，计量资料用 $\bar{x}\pm s$ 表示，组间比较行 t 检验；计数资料采用例和百分率表示，组间比较行 x^2 检验，以 *P<0.05* 表示差异有统计学意义。

2 结果

2.1 两组临床总有效率的比较

治疗后，观察组总有效率为 95%，显著高于对照组（83.33%，*P<0.05*），见表 1。

表 1 两组患者总有效率比较[例(%)]

Table 1 Comparison of the total effective rate between the two groups[n(%)]

Groups	n	Complete remission	Effective	Invalid	Total effective rate
Control Group	60	45(75.00)	12(20.00)	3(5.00)	57(95.00)
Observation group	60	33(55.00)	17(28.33)	10(16.67)	50(83.33)
x^2	-				4.227
P	-				0.040

2.2 两组治疗前后炎性因子水平的比较

两组患者治疗前血清 IL-8、IL-6 和 TNF-α 水平相比差异无统计学意义（*P>0.05*）。治疗后，两组血清 IL-8、IL-6 和 TNF-α 水平均较治疗前显著下降，且观察组以上指标均显著低于对照组（*P<0.05*），见表 2。

2.3 两组治疗前后凝血指标的比较

治疗前，两组患者 PLT、PT 和 FIB 水平比较无统计学差异（*P>0.05*），观察组治疗后 PLT 和 FIB 水平均较治疗前显著下降，且显著低于对照组（*P<0.05*），而 PT 水平较治疗前显著升高，且显著高于对照组（*P<0.05*），见表 3。

2.4 两组不良反应发生情况的比较

对照组患者发生白细胞轻度下降、恶心呕吐各 1 例，观察组患者发生轻度头晕、恶心呕吐各 1 例，发生肛门刺激症状 2 例。两组不良反应的发生情况比较无统计学差异（*P>0.05*），均经

对症处理后恢复正常,两组均无严重不良反应发生。

表 2 两组患者治疗前后血清炎性因子水平比较($\bar{x}\pm s$)

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

Groups	n	IL-8		IL-6		TNF-α	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control Group	60	1.32± 0.33	0.95± 0.28*	180.32± 41.28	115.56± 32.47*	255.32± 64.13	188.27± 52.15*
Observation group	60	1.28± 0.27	0.82± 0.25*	182.54± 42.12	78.65± 20.13*	258.64± 65.87	152.34± 41.22*
t	-	0.727	2.683	-0.292	7.484	-2.80	4.187
P	-	0.469	0.008	0.771	＜0.001	0.780	＜0.001

Note: Compared with before treatment, *$P<0.05$.

表 3 两组患者治疗前后凝血指标比较($\bar{x}\pm s$)

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

Groups	n	PLT(× 10^9/L)		FIB(g/L)		PT(s)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	60	220.32± 54.23	210.68± 50.33	3.44± 0.84	3.35± 0.64	9.12± 2.33	10.01± 2.98
Observation group	60	228.98± 56.37	187.56± 48.64*	3.52± 0.87	2.58± 0.51*	9.32± 2.45	13.25± 3.54*
t	-	-0.858	2.559	-0.512	7.288	-0.458	5.424
P	-	0.393	0.012	0.610	＜0.001	0.648	＜0.001

Note: Compared with before treatment,*$P<0.05$.

3 讨论

溃疡性结肠炎患者是大肠癌的高危人群,其发病率逐年升高,约为 4%左右,多见于男性[17,18],其发病主要与炎症因子失衡和免疫异常有关。另外,溃疡性结肠炎患者由于血液成分、血液流变学的改变和感染等因素并发血栓,加重肠黏膜的糜烂。康复新液的主要成分有多种肽类和多元醇,具有去腐生肌和通利血脉的功效[19]。枯草杆菌二联活菌肠溶胶囊可与肠道黏膜上皮细胞紧密结合,并促进粘液的分泌,在肠道黏膜上形成一层保护膜,还可通过抑制细菌的黏附和定植拮抗致病菌,提高肠黏膜保护作用。益生菌还可抑制炎性因子的释放,进一步促进溃疡的愈合[20-22]。

在正常生理状态下,机体肠道中的各种炎性因子处于动态平衡。当这个平衡被打破后,会出现各种肠道疾病[23,24]。在溃疡性结肠炎患者中,单核巨噬细胞分泌并释放的白介素和肿瘤坏死因子失衡引发链式反应, 最终导致肠黏膜结构破坏。IL-8、IL-6 和 TNF-α 是介导炎症过程的细胞因子。有研究显示[25]溃疡性结肠炎患者的血清和肠黏膜中的 TNF-α、IL-8 和 IL-6 水平显著升高,提示其参与了溃疡性结肠炎的进展过程[25]。本研究中,观察组患者治疗后血清 IL-8、IL-6 和 TNF-α 水平均较治疗前显著下降,且均明显低于对照组,表明枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠可显著降低患者的炎性反应过程。这是由于康复新液可提高患者的免疫功能,抑制肠道炎症,提高免疫细胞和血清溶菌酶的活性,降低 NO 水平,从而促进机体抗炎和促炎反应的平衡[26,27]。

PLT 参与了止血和血栓形成的过程,溃疡性结肠炎患者的静脉中存在形成血栓的血小板聚集物,PLT 水平持续升高可增加微小血栓发生的风险并加重溃疡[28,29]。FIB 水平升高和 PT 的缩短均提示患者处于高凝状态,不利于患者的愈合[30]。本研究显示观察组治疗后 PLT 和 FIB 水平均较治疗前显著下降,而 PT 水平显著升高,提示枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠可显著改善患者的高凝状态, 可能与康复新液具有通利血脉的功效,可改善患者肠道黏膜表面的血流灌注,从而促进溃疡的愈合有关。本研究结果还显示观察总有效率显著高于对照组,说明两种药物联合应用可提高临床疗效,这可能与康复新液可促进毛细血管再生和肉芽组织的生长, 促进肠道坏死组织的脱落从而促进溃疡面的再生的修复有关。另外,康复新液灌肠给药可提高药物的利用度、延长药物作用时间,从而提高临床效果。两组均仅有少数患者发生轻度头晕、恶心呕吐和肛门刺激症状,均经对症处理后明显改善,提示其安全性均较高[31]。

综上所述,枯草杆菌二联活菌肠溶胶囊联合康复新液灌肠治疗可显著降低溃疡性结肠炎患者的炎性因子水平,改善凝血功能,提高临床治疗效果,且安全性较高。

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