doi: 10.13241/j.cnki.pmb.2018.16.036

柳氮磺胺吡啶联合丽珠肠乐治疗溃疡性结肠炎的疗效及对患者炎症反应的影响*

陈 爽[1] 张 艳[1] 陈 亮[2] 沈鹏臻[1] 尹 红[1]

（1 自贡市第四人民医院消化内科 四川 自贡 643000;2 自贡市第一人民医院儿科 四川 自贡 643000）

摘要 目的：观察丽珠肠乐联合柳氮磺胺吡啶治疗溃疡性结肠炎的疗效及对患者炎症反应的影响。**方法：**选取我院2014年6月-2017年6月期间收治的溃疡性结肠炎患者120例，根据数表法将患者分为观察组(n=60)和对照组(n=60)。对照组采用柳氮磺胺吡啶治疗，观察组在对照组的基础上增加丽珠肠乐治疗。连续治疗8周后观察两组患者的临床疗效以及结肠炎症状改善程度，并对两组患者治疗前后的血清炎症因子水平进行检测对比，同时观察两组患者不良反应发生情况。**结果：**观察组临床治疗的总有效率为93.33%(56/60)，高于对照组的80.00%(48/60)(*P<0.05*)。治疗后两组患者Sutherland指数评分、肠道菌群评分、肠镜评分均低于治疗前，且观察组低于对照组(*P<0.05*)。治疗后两组患者CRP、IL-6、TNF-α水平均低于治疗前，且观察组低于对照组(*P<0.05*)。观察组不良反应发生率为13.33%(8/60)，与对照组的8.33%(5/60)比较差异无统计学意义(*P>0.05*)。**结论：**柳氮磺胺吡啶联合丽珠肠乐治疗溃疡性结肠炎的临床疗效显著，能够改善患者的临床症状，降低患者体内的炎症因子水平，且无严重不良反应发生，临床应用价值高，值得进一步推广应用。

关键词：丽珠肠乐；柳氮磺胺吡啶；溃疡性结肠炎；临床疗效；炎症因子

中图分类号：R574.62 **文献标识码：**A **文章编号：**1673-6273(2018)16-3162-05

Effect of Sulfasalazine Combined with Li Zhu Chang Le in Treatment of Ulcerative Colitis*

CHEN Shuang[1], ZHANG Yan[1], CHEN Liang[2], SHEN Peng-zhen[1], YIN Hong[1]

(1 Department of Gastroenterology, Zigong Fourth People's Hospital, Zigong, Sichuan, 643000, China;

2 Department of Pediatrics, Zigong First People's Hospital, Zigong, Sichuan, 643000, China)

ABSTRACT Objective: To observe the effect of sulfasalazine combined with Li Zhu Chang Le in the treatment of ulcerative colitis and its influence on the inflammatory reaction. **Methods:** A total of 120 patients with ulcerative colitis, who were treated in Zigong Fourth People's Hospital from June 2014 to June 2017 were selected and randomly divided into observation group (n=60) and control group (n=60). The control group was treated with sulfasalazine, and the observation group were treated with Li Zhu Chang Le on the basis of the control group's therapy. After 8 weeks of continuous treatment, the clinical efficacy of the two groups and the improvement of the symptoms of colitis were observed, and the levels of serum inflammatory factors before and after treatment were compared between the two groups, at the same time, the incidence of adverse reactions in the two groups was observed. **Results:** The total effective rate(93.33%) of clinical treatment of the observation group was higher than that (80.00%) of the control group (*P<0.05*). The scores of Sutherland index, intestinal flora and enteroscopy after treatment were lower than those before treatment, and the indexes of the observation group were lower than those of the control group (*P<0.05*). The levels of CRP, IL-6 and TNF-α of the two groups after treatment were lower than those before treatment, and the indexes of the observation group were lower than those of the control group (*P<0.05*). The incidence of adverse reactions in the observation group and the control group was 13.33% (8/60) and 8.33% (5/60), respectively, in which, there was no significant difference between the two groups (*P>0.05*). **Conclusion:** The clinical curative effect of Salazonazine combined with Li Zhu Chang Le in the treatment of ulcerative colitis is better, without serious adverse reaction and with high value of clinical application, which is worthy of further popularization and application.

Key words: Li Zhu Chang Le; Sulfasalazine; Ulcerative colitis; Clinical efficacy; Serum inflammatory factors

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

Article ID: 1673-6273(2018)16-3162-05

前言

溃疡性结肠炎是一种发生在乙状结肠和直肠的黏膜或黏膜下层的炎性病变，根据流行病学观察显示该病在临床上有较高的发病率，且出现在各年龄段人群中[1,2]。该病临床表现有腹泻、便血、恶心、呕吐、腹痛以及体重减轻等消化道症状，病程较

* 基金项目：四川省自然科学基金项目(2015FZ0457)

作者简介：陈爽(1981-)，女，硕士，主治医师，从事溃疡性结肠炎防治方面的研究，E-mail: oqbbbd@163.com

(收稿日期：2018-02-05 接受日期：2018-02-28)

长、易反复发作，给患者的生活质量带来了极大的影响[3-5]。目前，对于溃疡性结肠炎的发病原因尚未明确，临床较为认可的观点显示该病的发生与环境、遗传、免疫功能异常、肠道菌群失调等因素有关[6-8]。目前，药物治疗是溃疡性结肠炎的主要治疗方式，其中包括抗菌药、糖皮质激素、免疫抑制剂等，其中磺胺类抗菌药如柳氮磺胺吡啶是临床治疗溃疡性结肠炎的常规治疗药物，有较好的抗炎抗菌作用，在临床上应用广泛[9-11]。但是此类药物治疗后虽然症状缓解明显，但仍有部分患者难以获得较好的疗效。微生态制剂如丽珠肠乐可调节患者肠道的通透性、调整肠道菌群的平衡状态、增强肠道黏膜的屏障功能，从而进一步改善患者结肠的局部炎症反应[12]。为此，本研究以我院近期收治的溃疡性结肠炎患者为研究对象，采用丽珠肠乐联合柳氮磺胺吡啶进行治疗观察，收效良好，现作如下报道。

1 资料与方法

1.1 一般资料

选取我院 2014 年 6 月 12017 年 6 月间收治的 120 例溃疡性结肠炎患者，纳入标准：(1)均符合中华医学会分会制定的溃疡性结肠炎的相关诊断标准[13]，经结肠镜镜检、肠黏膜活检确诊为溃疡性结肠炎；(2)病态分期均为活动期者；(3)本研究治疗药物无严重过敏反应者；(4) 患者知情同意并签署知情同意书。排除标准：(1)伴有严重心肝肾功能不全者；(2)并发肠道的其他病变者；(3)入组前服用类似治疗药物者。根据数表法将患者分为观察组(n=60)和对照组(n=60)。两组患者的基础资料比较差异无统计学意义($P>0.05$)，详见表 1。本研究经医院伦理委员会批准同意。

表 1 两组患者一般资料比较

Table 1 Comparison of general data between two groups

Groups	n	Gender		Age (year)	Course of disease (week)	Lesion site			Degree of disease		
		Male	Female			Whole colon	Sigmoid colon	Rectum	Light	Moderate	Severe
Observation group	60	34	26	39.35± 12.78	7.89± 2.03	23	19	18	19	32	9
Control group	60	31	29	42.71± 13.56	8.12± 2.28	26	20	14	21	35	4
t/x^2	-	0.302		1.397	0.584	0.709			2.157		
P	-	0.583		0.165	0.561	0.701			0.340		

1.2 治疗方法

对照组给予柳氮磺胺吡啶治疗，采用柳氮磺吡啶肠溶片（上海福达制药有限公司，国药准字：H31020840，规格：0.25 g）进行口服给药治疗，给药方式为 3 片 / 次，4 次 /d，4 周为 1 个疗程。观察组患者在对照组的基础上增加双歧杆菌活菌胶囊（丽珠集团丽珠制药厂，商品名：丽珠肠乐，国药准字：S10960040，规格：0.35 g）口服治疗，给药方式为 1 粒 / 次，2 次 /d，于早晚服用，4 周为 1 个疗程。两组患者均服药 2 个疗程后观察疗效。

1.3 评价方法

评价两组患者治疗后临床疗效，疗效判断标准[14]如下：治愈：患者临床症状全部消失，肠镜检查、粪便检查显示患者结肠炎症消失；显效：患者临床症状基本消失，临床各项症状评分有明显下降；有效：患者临床症状有一定改善，各症状评分均较治疗前降低 1 级；无效：患者临床症状无好转。总有效率 = 治愈率 + 显效率 + 有效率。采用 Sutherland 指数评分对两组患者治疗前后的腹泻频率、肠黏膜状态、直肠出血等疾病活动情况进行评分比较，该评分表满分 12 分，得分越高表明患者症状越严重。采用肠道菌群评分对两组患者治疗前后的肠道菌群状态进行评分比较，该量表满分为 5 分，得分越高表明患者的菌群失调越严重。采用肠镜评分对两组患者的肠黏膜状态进行评分比较，该量表满分为 4 分，得分越高表明患者的肠黏膜症状越严重。于治疗前后检测两组患者的炎症因子指标水平，采集患者空腹静脉血 3 mL，采用 TGL-16 型高速离心机进行离心，3000 r/min，10 min，分离得到血清后采用酶联免疫吸附试验检测患者的 C 反应蛋白（C reactive protein，CRP）、白介素 -6（Interleukin-6，IL-6）、肿瘤坏死因子 -α（Tumor necrosis factor-α，TNF-α）水平，试剂盒购置于上海雅培生物科技工程有限公司，严格按照说明书操作规程进行。观察治疗期间不良反应发生情况。

1.4 统计学方法

采用 SPSS 19.0 进行数据处理与分析，计量资料用($\bar{x}\pm s$)表示，采用 t 检验，计数资料用率表示，采取 x^2 检验，检验标准设置为 α=0.05。

2 结果

2.1 两组患者临床疗效比较

观察组临床治疗的总有效率为 93.33%(56/60)，显著高于对照组的 80.00%(48/60)($P<0.05$)，见表 2。

2.2 两组患者 Sutherland 指数评分、肠道菌群评分、肠镜评分比较

治疗前两组患者 Sutherland 指数评分、肠道菌群评分、肠镜评分比较无差异($P>0.05$)，治疗后两组患者 Sutherland 指数评分、肠道菌群评分、肠镜评分均低于治疗前，且观察组低于对照组($P<0.05$)，见表 3。

2.3 两组患者血清炎症因子水平比较

治疗前两组患者 CRP、IL-6、TNF-α 水平比较无差异（$P>0.05$），治疗后两组患者 CRP、IL-6、TNF-α 水平均低于治疗前，

且观察组低于对照组（*P<0.05*），见表 4。

表 2 两组患者临床疗效比较[n(%)]

Table 2 Comparison of clinical efficacy between two groups[n(%)]

Groups	n	Cure	Effective	Good	Invalid	Total effective rate
Observation group	60	23(38.33)	18(30.00)	15(25.00)	4(6.67)	56(93.33)
Control group	60	19(31.67)	16(26.67)	13(21.67)	12(20.00)	48(80.00)
x^2						4.615
P						0.032

表 3 两组患者 Sutherland 指数、肠道菌群、肠镜评分比较（分，$\bar{x}\pm s$）

Table 3 Comparison of Sutherland index, intestinal flora, and enteroscopy score between two groups (scores, $\bar{x}\pm s$)

Groups	n	Sutherlandindex		Intestinal flora		Enteroscopy score	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	60	8.09± 1.98	3.38± 0.49*	3.17± 0.36	1.73± 0.45*	3.09± 0.58	1.19± 0.38*
Control group	60	7.86± 1.85	4.74± 0.65*	3.25± 0.39	2.52± 0.59*	3.16± 0.65	1.77± 0.46*
t	-	0.657	12.942	1.167	8.247	0.622	7.530
P	-	0.512	0.000	0.245	0.000	0.535	0.000

Note: compared with before treatment, **P<0.05*.

表 4 两组患者血清炎症因子水平比较（$\bar{x}\pm s$）

Table 4 Comparison of serum levels of inflammatory factors between two groups($\bar{x}\pm s$)

Groups	n	CRP(mg/L)		IL-6(ng/L)		TNF-α(μg/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	60	14.11± 4.26	5.70± 1.87*	333.29± 35.92	218.98± 16.67*	3.87± 0.88	2.90± 0.60*
Control group	60	13.41± 3.89	8.11± 2.12*	340.12± 30.12	259.31± 22.08*	3.79± 0.81	3.35± 0.69*
t	-	0.940	6.603	1.129	11.292	0.518	3.812
P	-	0.349	0.000	0.261	0.000	0.605	0.000

Note: compared with before treatment, **P<0.05*.

2.4 两组患者不良反应发生率比较

观察组不良反应发生率为 13.33%（8/60），与对照组的 8.33%（5/60）比较差异无统计学意义（*P>0.05*），见表 5。

表 5 两组患者不良反应发生率比较[n(%)]

Table 5 Comparison of incidence of adverse reactions between two groups[n(%)]

Groups	n	Nausea and vomiting	Rash	Dysuria	Diarrhea	Total incidence
Observation group	60	2(3.33)	3(5.00)	2(3.33)	1(1.67)	8(13.33)
Control group	60	2(3.33)	1(1.67)	2(3.33)	0(0.00)	5(8.33)
x^2						0.776
P						0.378

3 讨论

溃疡性结肠炎作为一种非特异性的炎性疾病，临床表现为肠道黏膜的持续性高炎症状态，对患者的肠腔黏膜有严重的损伤[15,16]。由于溃疡性结肠炎的发病原因较多，病情影响因素较为复杂，使得该病的临床治疗难度增大[17,18]。目前，常用的抗菌药物仅仅通过对症治疗来缓解患者的炎症症状，对于溃疡性结肠炎难以达到根治的目的，使得患者在药物治疗后仍然存在复发的可能[19-21]。因此，对症治疗方式仍然有提高的空间。近些年，相关研究人员对于溃疡性结肠炎的发病原因、发病机制的不断深入研究，发现肠道菌群的组成及比例在溃疡性结肠炎的病情发生及进展过程中发挥重要作用，当患者的肠道菌群紊乱时，在

肠道有害细菌的作用下肠道内的食物残渣异常发酵,产生有害物质对患者肠腔及黏膜造成损伤,出现腹痛、腹泻、便血等症状,导致溃疡性结肠炎的发生甚至加重病情[22-24]。因此,通过对患者肠道菌群失调的治疗,可进一步提高溃疡性结肠炎的治疗效果。微生态制剂是治疗肠道菌群失调的常用药物,临床应用显示对肠道菌群比例的调节和维持肠道菌群的稳态有很好的疗效[25,26],这对溃疡性结肠炎的治疗提供了新的思路。

观察组临床治疗的总有效率为 93.33%(56/60),显著高于对照组的 80.00%(48/60)(*P<0.05*),说明采用丽珠肠乐联合柳氮磺胺吡啶治疗溃疡性结肠炎疗效优于柳氮磺胺吡啶单独治疗,此外,治疗后两组患者 Sutherland 指数评分、肠道菌群评分、肠镜评分均低于治疗前,且观察组低于对照组(*P<0.05*),这是因为丽珠肠乐是双歧杆菌活菌胶囊,患者服用后在肠道处可产生乳酸、乙酸,降低肠道病灶处的 pH 值,抑制有害细菌的大量繁殖,并增加肠道益生菌的比例,调整肠道菌群比例,改善患者的肠道菌群失调症状[27]。并且,该药的应用还可与厌氧菌结合在肠黏膜表面形成生物屏障,阻止致病菌的侵袭,从而缓解患者结肠炎症状[28]。也有研究显示[29],丽珠肠乐与柳氮磺胺吡啶合用的疗效增强是因为丽珠肠乐通过调节肠道菌群比例,增加益生菌的比例,促进肠腔内柳氮磺胺吡啶分解成活性代谢物 5-氨基水杨酸,而 5- 氨基水杨酸是发挥药效的活性物质,因此进一步提高疗效。在两组患者炎症因子水平比较中,治疗后两组患者 CRP、IL-6、TNF-α 水平均低于治疗前,且观察组低于对照组(*P<0.05*),表明丽珠肠乐联合柳氮磺胺吡啶治疗能够进一步降低患者的血清炎症因子水平,CRP、IL-6、TNF-α 均为机体内典型的炎症反应因子,其水平的升高表明患者的炎症反应越严重,丽珠肠乐通过对肠道菌群比例的调节,增强益生菌含量,提高肠道的屏障功能和免疫功能,从而降低患者的炎症反应,使得 CRP、IL-6、TNF-α 水平降低[30]。本次研究亦表明观察组不良反应发生率为 13.33%(8/60),与对照组的 8.33%(5/60)比较差异无统计学意义(*P>0.05*),表明丽珠肠乐和柳氮磺胺吡啶的合用安全性良好,未增加不良反应发生率。

综上所述,与柳氮磺胺吡啶单独治疗相比,柳氮磺胺吡啶与丽珠肠乐联用治疗溃疡性结肠炎的疗效更为显著,对患者的症状缓解更为彻底,降低 CRP、IL-6、TNF-α 水平,且不产生用药安全性问题,可为溃疡性结肠炎的治疗提供新的思路。

参 考 文 献(References)

[1] Rubio CA, DE Petris G, Puppa G. Gut-associated Lymphoid Tissue (GALT) Carcinoma in Ulcerative Colitis[J]. Anticancer Res, 2018, 38 (2): 919-921

[2] Laserna-Mendieta EJ, Clooney AG, Carretero-Gomez JF, et al. Determinants of Reduced Genetic Capacity for Butyrate Synthesis by the Gut Microbiome in Crohn's Disease and Ulcerative Colitis [J]. J Crohns Colitis, 2018, 12(2): 204-216

[3] Kawakita H, Katsumata K, Osaka Y, et al. Surgical Case of Ulcerative Colitis Accompanied with Rectal Cancer Combined with Transanal Minimally Invasive Surgery [J]. Gan To Kagaku Ryoho, 2018, 45(1): 130-132

[4] Huguet M, Pereira B, Goutte M, et al. Systematic Review With Meta-Analysis: Anti-TNF Therapy in Refractory Pouchitis and Crohn's Disease-Like Complications of the Pouch After Ileal Pouch-Anal Anastomosis Following Colectomy forUlcerative Colitis [J]. Inflamm Bowel Dis, 2018, 24(2): 261-268

[5] Duh E, Fine S. Human herpesvirus-8 positive iatrogenic Kaposi's sarcoma in the setting of refractory?ulcerative colitis[J]. World J Clin Cases, 2017, 5(12): 423-427

[6] Scott FI, Shah Y, Lasch K, et al. Assessing the Optimal Position for Vedolizumab in the Treatment of Ulcerative Colitis: A Simu lation Model[J]. Inflamm Bowel Dis, 2018, 24(2): 286-295

[7] 易蕊,常娟,刘晓艳,等.TNF-α、IL-6 及 IL-8 在不同程度溃疡性结肠炎患者血清中的表达及意义[J].现代生物医学进展, 2015, 15(14): 2641-2644
Yi Rui, Chang Juan, Liu Xiao-yan, et al. Expressions and Significance of TNF-α, IL-6 and IL-8 in Patients with Ulcerative Colitis at Different Degrees[J]. Progress in Modern Biomedicine, 2015, 15(14): 2641-2644

[8] Goyal S, Rampal R, Kedia S, et al. Urinary potassium is a potential biomarker of disease activity in Ulcerative colitis and displays in vitro immunotolerant role[J]. Sci Rep, 2017, 7(1):18068

[9] Scaioli E, Sartini A, Liverani E, et al. Sulfasalazine in Prevention of Pouchitis After Proctocolectomy with Ileal Pouch-Anal Anastomosis forUlcerative Colitis[J]. Dig Dis Sci, 2017, 62(4): 1016-1024

[10] Yoshino T, Sono M, Yazumi S. Usefulness of sulfasalazine for patients with refractory-ulcerative colits[J]. BMJ Open Gastroenterol, 2016, 3(1): e000103

[11] Seishima R, Okabayashi K, Nagano O, et al. Sulfasalazine, a therapeutic agent for ulcerative colitis, inhibits the growth of CD44v9 (+) cancer stem cells in ulcerative colitis-related cancer [J]. Clin Res Hepatol Gastroenterol, 2016, 40(4): 487-493

[12] 刘大鹏. 柳氮磺胺吡啶联用丽珠肠乐对溃疡性结肠炎结肠组织中防御素的表达的影响和意义 [J]. 中国美容医学, 2012, 21(z2): 102-103
Liu Da-peng. The Impact of Sulfasalazine combined with Lizhuchangle on β Defensin-2 Expression in Colonic Tissue of Ulcerative Colitis[J]. Chinese Journal of Aesthetic Medicine, 2012, 21 (z2): 102-103

[13] 中华中医药学会脾胃病分会. 溃疡性结肠炎中医诊疗共识(2009)[J].中国中西医结合杂志, 2010, 30(5): 527-532
Branch of Gastroiaatestinal Diseases, China Association of Chinese Medicine. Consensus on Chinese Medical Diagnosis and Treatment of Ulcerative Colitis (2009)[J]. Chinese Journal of integrated traditional Chinese and Western Medicine, 2010, 30(5): 527-532

[14] 段志英,李凤春,何丽,等.柳氮磺胺吡啶联合美常安或丽珠肠乐治疗溃疡性结肠炎的临床观察 [J]. 中国医药导报, 2015, 12(25): 137-140
Duan Zhi-ying, Li Feng-chun, He Li, et al.Clinical observation of Sulfasalazine combined with Medilac-S or Bifido-biogen in the treatment of ulcerative colitis[J]. China Medical Herald, 2015, 12(25): 137-140

[15] Shen ZH, Zhu CX, Quan YS, et al. Relationship between intestinal microbiota and ulcerative colitis: Mechanisms and clinical application of probiotics and fecal microbiota transplantation [J]. World J Gastroenterol, 2018, 24(1): 5-14

[16] Buc M. Crohns disease and ulcerative colitis- current view on genetic determination, immunopathogenesis and biologic therapy [J]. Epidemiol Mikrobiol Imunol, 2017, 66(4): 189-197

[17] Baker DM, Lee MJ, Jones GL, et al. The Informational Needs and Preferences of Patients Considering Surgery for Ulcerative Colitis: Results of a Qualitative Study [J]. Inflamm Bowel Dis, 2017, 24(1): 179-190

[18] Salih A, Widbom L, Hultdin J, et al. Smoking is associated with risk for developing inflammatory bowel disease including late onsetulcerative colitis: a prospective study [J]. Scand J Gastroenterol, 2018, 53(2): 173-178

[19] Finotti A, Gasparello J, Lampronti I, et al. PCR detection of segmented filamentous bacteria in the terminal ileum of patients with?ulcerative colitis [J]. BMJ Open Gastroenterol, 2017, 4 (1): e000172

[20] Simadibrata M, Halimkesuma CC, Suwita BM. Efficacy of Curcumin as Adjuvant Therapy to Induce or Maintain Remission in Ulcerative ColitisPatients: an Evidence-based Clinical Review [J]. Acta Med Indones, 2017, 49(4): 363-368

[21] Tsai HH. Editorial: tofacitinib and biologics for moderate-to-severe ulcerative colitis-what is best in class?[J]. Aliment Pharmacol Ther, 2018, 47(4): 539-540

[22] Bonovas S, Lytras T, Nikolopoulos G, et al. Editorial: tofacitinib and biologics for moderate-to-severe ulcerative colitis-what is best in class? Authors' reply [J]. Aliment Pharmacol Ther, 2018, 47 (4): 540-541

[23] Fujita K, Mizumoto Y, Moriyoshi K, et al. Acute onset of ulcerative colitis during chemoradiotherapy for anaplastic lymphoma kinase-positive lung adenocarcinoma [J]. Respirol Case Rep, 2017, 6 (2): e00288

[24] Bálint A, Farkas K, Szepes Z, et al. How disease extent can be included in the endoscopic activity index of ulcerative colitis: the panMayo score, a promising scoring system [J]. BMC Gastroenterol, 2018, 18(1): 7

[25] Addis MF, Bronzo V, Puggioni GM, et al. Relationship between milk cathelicidin abundance and microbiologic culture in clinical mastitis [J]. J Dairy Sci, 2017, 100(4): 2944-2953

[26] Daş T, Sargan A, Yağmur G, et al. Viral Pneumonias in Forensic Autopsies: Evaluation and Classification of Histopathologic Changes With Microbiologic Correlation[J]. Am J Forensic Med Pathol, 2016, 37(4): 255-263

[27] Doi AM, Pignatari AC, Edmond MB, et al. Epidemiology and Microbiologic Characterization of Nosocomial Candidemia from a Brazilian National Surveillance Program [J]. PLoS One, 2016, 11(1): e0146909

[28] 王赛,周国华.氨基水杨酸类联合微生态制剂对溃疡性结肠炎的维持治疗进展[J].实用药物与临床, 2015, 18(4): 463-465, 466
Wang Sai, Zhou Guo-hua. Progress on maintenance treatment for ulcerative colitis by aminosalicylic acids combined with probiotics[J]. Practical Pharmacy and Clinical Remedies, 2015, 18(4): 463-465, 466

[29] Martínez González J, Busto Bea V, Mesonero Gismero F, et al. Rescue therapy with sulfasalazine prior to immunosuppressive or biological agents in ulcerative colitis poorly controlled with mesalazine[J]. Gastroenterol Hepatol, 2013, 36(1): 7-10

[30] 谭琰,邹开芳,钱伟,等.溃疡性结肠炎患者 TLR9 表达变化的研究[J].华中科技大学学报(医学版), 2014, 43(5): 520-527
Tan Yan, Zou Kai-fang, Qian Wei, et al. Expression of Toll-like Receptor 9 in Patients with Ulcerative Colitis [J]. Acta Medicinae Universitatis Scientiae et Technologiae Huazhong, 2014, 43 (5): 520-527

(上接第 3169 页)

[10] Sayyadi M, Shaiegan M, Nikougoftar ZM, et al. Platelet Transfusion Outcome and Flow Cytometric Monocyte Phagocytic Assay (FMPA) [J]. Arch Iran Med, 2016, 19(6): 426-429

[11] Ratcliffe N, Dunbar NM, Brown CI. Enhancing platelet transfusion safety: not a one-size-fits-all approach [J]. Transfusion, 2016, 56(6): 1483-1484

[12] Julmy F, Ammann RA, Mansouri TB, et al. Effects of high-yield thrombocytapheresis on the quality of platelet products [J]. Transfusion, 2008, 48(3): 442-450

[13] Pothapregada S, Kamalakannan B, Thulasingam M. Role of platelet transfusion in children with bleeding in dengue fever [J]. J Vector Borne Dis, 2015, 52(4): 304-308

[14] Takamatsu Y, Jimi S, Sato T, et al. Thrombocytopenia in association with splenomegaly during granulocyte-colony-stimulating factor treatment in mice is not caused by hypersplenism and is resolved spontaneously[J]. Transfusion, 2007, 47(1): 41-49

[15] Slichter SJ, Davis K, Enright H, et al. Factors affecting posttransfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients [J]. Blood, 2005, 105(10): 4106-4114