Journal of Hainan Medical University

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Effect of retention enema by caulis sargentodoxae enema combined with oral drugs on the immune inflammatory response and intestinal flora of UC patients

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ARTICLE INFO

Article history:
Received 28 Aug 2017
Received in revised form 3 Sep 2017
Accepted 9 Sep 2017
Available online 14 Sep 2017

Keywords:
Ulcerative colitis
Caulis sargentodoxae enema
Immune response
Inflammatory response
Intestinal flora

ABSTRACT

Objective: To study the effect of retention enema by caulis sargentodoxae enema combined with oral drugs on the immune inflammatory response and intestinal flora of UC patients. **Methods:** A total of 128 UC patients who received treatment in the hospital between January 2013 and April 2017 were collected and divided into control group and observation group by random number table. Control group received conventional oral drug therapy, and the observation group received retention enema by caulis sargentodoxae enema combined with oral drug therapy. Before treatment and after 4 weeks of treatment, the differences in the levels of immunoglobulin and inflammatory response indexes in serum as well as intestinal flora levels in mucosa lesion tissue were compared between the two groups. **Results:** The differences in levels of immunoglobulin and inflammatory response indexes in serum as well as intestinal flora levels in mucosa lesion tissue were not statistically significant between the two groups of patients before treatment. After 4 weeks of treatment, IgA, IgG, IgM and IL-4 contents in serum as well as bifidobacterium and lactobacillus levels in mucosa lesion tissue of observation group were higher than those of control group while ESR, CRP, IL-6 and TNF-α contents as well as E. coli level in mucosa lesion tissue were lower than those of control group. **Conclusion:** Retention enema by caulis sargentodoxae enema combined with oral drugs can effectively optimize the immune inflammatory state and balance the intestinal flora distribution in patients with UC.

1. Introduction

Ulcerative colitis (UC) belongs to the nonspecific intestinal inflammatory disease, the lesions are mostly confined to the mucosa and submucosa of rectum and sigmoid colon, and current clinical treatment is given priority to salazosulfapyridine salicylic acid preparation, which inhibits the colonic mucosa from releasing leukotriene and oxygen free radicals, inhibits mast cells from releasing inflammatory mediators and so on to exert therapeutic effect[1,2]. Many cases have shown that UC illness can appear repeatedly after salazosulfapyridine salicylic acid preparation treatment, some patients still have serious colon ulcer, and many scholars recommend adding traditional Chinese medicine enema in the overall therapy in order to expand UC treatment effect through the cooperation of Chinese and western medicine, and the combination of oral and external therapy[3,4]. In the study, retention enema by caulis sargentodoxae enema was introduced to the treatment of patients with UC on the basis of oral medication, and its effects were elaborated from immune status, inflammation and intestinal flora distribution, now reported as follows.

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Fund Project: Science and Technology Plan Project of Jiangsu Province No: SBE2015720130.

2. Information and methods

2.1 Case information

A total of 128 UC patients who received treatment in the hospital between January 2013 and April 2017 were collected, and patients' families signed informed consent. The enrolled patients were divided into control group and observation group by random number table, 64 cases in each group. Control group included 34 men and 30 women, they were 21-48 years old, and the course of disease was 0.6-5 years; observation group included 32 men and 32 women, they were 23-47 years old, and the course of disease was 1-6 years. There was no statistically significant difference in the distribution of gender, age and course of disease between the two groups ($P>0.05$), the subsequent study data were comparable, and the study was approved by the hospital ethics committee.

Inclusion criteria: (1) combined with typical clinical manifestations of UC such as diarrhea and feces with mucus pus blood; (2) diagnosed with UC by colonoscopy and biopsy; (3) cooperating with the whole treatment and examination, without dropping out and with complete clinical data.

Exclusion criteria: (1) combined with other autoimmune diseases; (2) combined with infectious diseases of other tissue organs; (3) combined with severe heart, liver and kidney insufficiency.

2.2 Therapy

Control group of patients received clinical routine oral drug treatment for UC, including mesalazine (Sunflower Group Jiamusi Luling Pharmaceutical Co., Ltd., approved by H19980148) 1.0 g, 3 times/d, for 4 weeks of treatment.

Observation group received retention enema by caulis sargentodoxae enema (approved by Suzhou Z04001867) combined with oral drug therapy, which was as follows: caulis sargentodoxae enema (containing caulis sargentodoxae, senecio, dandelion, hedyotis diffusa, cordate houttuynia, etc.) 100 mL for retention enema, 1 time/d, for 4 weeks of treatment.

2.3 Observation indexes

Before treatment and after 4 weeks of treatment, 5.0 mL fasting cubital venous blood was obtained from two groups of patients, treated with low molecular heparin sodium, and centrifuged at low speed to get the supernatant liquid, which was cryopreserved for test. Rate nephelometry was used to detect serum immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) levels. ELISA was used to determine the levels of inflammatory markers in serum, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-4 (IL-4), interleukin-6 (IL-6), and tumor necrosis factor α (TNF-α). Colonoscope was used to get the mucous tissue from intestinal lesion for bacteriological examination, and the levels of bifidobacteria, lactobacillus and Escherichia coli were determined.

2.4 Statistical methods

Immunoglobulin, inflammatory response indexes and intestinal flora belonged to measurement data and were in terms of (Mean ± SD) and comparison was by t test. $P<0.05$ was the standard of statistical significance in differences in obtained statistics.

3. Results

3.1 Immunoglobulin

Comparison of serum immunoglobulin IgA, IgG and IgM contents between two groups of patients before and after treatment was as follows: before treatment, the differences in serum IgA, IgG and IgM contents were not significant between the two groups of patients ($P>0.05$). After 4 weeks of treatment, serum IgA, IgG and IgM contents of both groups were higher than those before treatment ($P<0.05$), and serum IgA, IgG and IgM contents of observation group were higher than those of control group ($P<0.05$), shown in Table 1.

Table 1.

Comparison of serum immunoglobulin contents between two groups of patients before and after treatment (g/L).

Groups	n	Time	IgA	IgG	IgM
Control group	64	Before treatment	1.95±0.27	11.73±1.93	0.75±0.08
		After 4 weeks of treatment	2.11±0.24*	12.51±1.62*	0.87±0.09*
Observation group	64	Before treatment	1.96±0.26	11.68±1.89	0.76±0.09
		After 4 weeks of treatment	2.75±0.35*#	14.37±1.82*#	0.98±0.13*#

Note: compared with same group before treatment, $^{*}P<0.05$; compared with control group after 4 weeks of treatment, $^{\#}P<0.05$.

3.2 Inflammatory response indexes

Comparison of serum inflammatory response indexes ESR (mm/h), CRP (mg/L), IL-4 (pg/mL), IL-6 (pg/mL) and TNF-α (pg/mL) levels between two groups of patients before and after treatment was as follows: before treatment, the differences in serum ESR, CRP, IL-4, IL-6 and TNF-α levels were not significant between the two groups of patients ($P>0.05$). After 4 weeks of treatment, serum ESR, CRP, IL-6 and TNF-α contents of both groups were lower than those before treatment while IL-4 contents were higher than those before treatment ($P<0.05$), and serum ESR, CRP, IL-6 and TNF-α contents of observation group were lower than those of control group while IL-4 content was higher than that of control group ($P<0.05$), shown in Table 2.

3.3 Intestinal flora

Comparison of bifidobacterium, lactobacillus and E. coli levels in diseased intestinal mucosa tissue between two groups of patients before and after treatment was as follows: before treatment, the differences in bifidobacterium, lactobacillus and E. coli levels in mucosa lesion tissue were not significant between the two groups of patients ($P>0.05$). After 4 weeks of treatment, bifidobacterium and lactobacillus levels in mucosa lesion tissue of both groups were higher than those before treatment while E. coli levels were lower than those before treatment ($P<0.05$), and bifidobacterium and lactobacillus levels in mucosa lesion tissue of observation group were higher than those of control group while E. coli level was lower than that of control group ($P<0.05$), shown in Table 3.

4. Discussion

Mesalazine, as the active ingredient of SASP treatment of UC, has become the mainstream drug for treatment of the disease, which dose-dependently inhibits prostaglandin synthesis in colonic mucosa, inhibits neutrophil lipoxygenase activity and so on[5-7]. However, with the increase of the application dose, the probability of gastrointestinal discomfort increases in patients, and some patients still have recurrence of intestinal inflammation in the large dose. Retention enema with TCM is the effective method for clinical treatment of a variety of pelvic and colorectal inflammatory diseases, traditional Chinese medicine directly contacts with local diseased tissue by methods such as osmosis, and can effectively exert the therapeutic effect of drugs, it belongs to external therapy, but its role is similar to that of oral administration[8,9]. Caulis sargentodoxae enema is made up of caulis sargentodoxae, senecio, dandelion, hedyotis diffusa, cordate houttuynia and other Chinese patent drugs, caulis sargentodoxae and hedyotis diffusa detoxify and remove stasis, dandelion, cordate houttuynia and senecio clear away heat and toxic materials as well as eliminate dampness and check dysentery, and many studies have confirmed that retention enema by caulis sargentodoxae enema has been successfully applied in the treatment of patients with chronic pelvic inflammatory disease[10]. In this study, retention enema by caulis sargentodoxae enema was used as adjuvant therapy for patients with UC, and the role of oral western medicine combined with external TCM treatment in optimizing the disease of UC patients was discussed.

Immunological factors are recognized as one of the causes of UC, and intestinal mucosal immunity relies mainly on the immunoglobulin secreted on mucosal surface and in enteric cavity, which is the first line of defense to maintain the steady state of intestinal mucosa[11,12]. In the case of pathogen invasion and intestinal mucosal injury, IgA expression decreases and causes the intestinal flora disorder, and the expression of IgA further decreases with the aggravation of flora disorder, and the two form a vicious cycle[13,14]. IgM and IgG also play an important role in the immune protection of the body, and the decline of their expression means that the body's self-defensive ability decreases[15]. In the study, differences in serum immunoglobulin contents were compared between two groups of patients, and it was found that compared

Table 2.

Comparison of serum inflammatory response index levels between two groups of patients before and after treatment.

Groups	n	Time	ESR	CRP	IL-4	IL-6	TNF-α
Control group	64	Before treatment	31.27±4.89	25.38±3.41	9.73±1.62	62.82±7.95	11.84±1.93
		After 4 weeks of treatment	22.09±2.64*	13.26±1.75*	15.68±2.15*	31.75±4.36*	7.56±0.84*
Observation group	64	Before treatment	31.18±4.76	25.27±3.39	9.69±1.58	61.75±7.83	11.79±1.85
		After 4 weeks of treatment	15.37±2.18*#	7.09±0.85*#	27.94±3.52*#	17.08±2.51*#	4.11±0.57*#

Note: compared with same group before treatment, *$P<0.05$; compared with control group after 4 weeks of treatment, #$P<0.05$.

Table 3.

Comparison of intestinal flora levels in mucosa lesion tissue between two groups of patients before and after treatment (Lg10 n/g).

Groups	n	Time	Bifidobacterium	Lactobacillus	E. coli
Control group	64	Before treatment	6.34±0.72	7.16±0.85	9.82±1.17
		After 4 weeks of treatment	7.19±0.77*	7.85±0.83*	8.53±0.96*
Observation group	64	Before treatment	6.31±0.75	7.18±0.89	9.86±1.21
		After 4 weeks of treatment	8.76±0.96*#	8.27±0.91*#	7.29±0.83*#

Note: compared with same group before treatment, *$P<0.05$; compared with control group after 4 weeks of treatment, #$P<0.05$.

with those before treatment, serum IgA, IgG and IgM contents of both groups of patients increased after treatment, indicating that both therapies can enhance the immunity of the patients with UC to different extent; further compared with those of control group, serum IgA, IgG and IgM contents of observation group were higher after treatment, confirming that retention enema by caulis sargentodoxae enema combined with oral drugs could be more effective to enhance the body's immune function.

Intestinal local and systemic inflammatory reaction is one of the most typical clinical signs of UC, a large amount of pro-inflammatory factors are released in local intestinal mucosa and intensify intestinal internal environment disturbance, meanwhile anti-inflammatory factors are excessively consumed and at low levels, and the body is in a pro-inflammatory/anti-inflammatory imbalance state [16-17]. ESR is a reliable indicator for the degree of inflammation of the body, and the higher its level, the more serious the inflammatory response in the body. CRP, IL-6 and TNF-α are the factors with strong pro-inflammatory action, which can be abnormally highly expressed in serum at the early stage of UC; IL-4 has anti-inflammatory properties and is continuously at low levels in the course of UC, and it is a sign of decreased anti-inflammatory capacity of the body[18-20]. In this study, differences in the serum levels of inflammation indexes were compared between the two groups of patients, and it was found that compared with those before treatment, serum ESR, CRP, IL-6 and TNF-α levels decreased while IL-4 levels increased, showing that both therapies can ease the pro-inflammatory/anti-inflammatory imbalance; further compared with those of control group, serum ESR, CRP, IL-6 and TNF-α levels of observation group were lower while IL-4 level was higher after treatment, confirming that retention enema by caulis sargentodoxae enema combined with oral drugs can effectively inhibit the systemic inflammatory response and increase the anti-inflammatory ability in patients with UC.

The imbalance of intestinal flora is an important precipitating factor in the process of UC immunological injury, and UC is worse as the flora imbalance intensifies[21,22]. Bifidobacterium and lactobacillus are the dominant bacterial community in normal human, and equivalent to conditioned pathogen E. coli roughly in the number, conditional pathogens are massively produced when dominant bacterial community decrease, and they cause intestinal infectious diseases, further guide the changes in intestinal microenvironment and autoimmunity, and gradually lead to progress in UC[23,24]. In this study, intestinal flora number distribution was compared between the two groups of patients, and it was found that compared with those before treatment, bifidobacterium and lactobacillus levels in diseased intestinal mucosa tissue of both groups of patients increased while E. coli levels decreased, showing that both therapies can balance the intestinal flora distribution to different degree; further compared with those of control group, bifidobacterium and lactobacillus levels in diseased intestinal mucosa tissue of observation group were higher while E. coli level was lower after treatment, confirming that retention enema by caulis sargentodoxae enema combined with oral drugs can effectively reverse the intestinal flora imbalance, and this is also the one of the important mechanisms for it to treat UC.

It is thus clear that at the same time of routine oral salazosulfapyridine salicylic acid preparation, retention enema by caulis sargentodoxae enema can further optimize the patient's immune status and inhibit the systemic inflammatory response, the specific mechanism is directly related to its effect on reversing intestinal flora imbalance, and the therapy is worthy of popularization and application in clinical practice in the future.

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