

Effects of the Treatment of Dong Medicine Five-Flavour Anti-Diarrhoea Soup Combined with Melalazine on Serum Complement C3, C4, Interleukin-23 and Interleukin-17 in Patients with Ulcerative Colitis

XIAO CHENG*, C. BO, LI MEILING AND LI ZHI

Department of Gastroenterology, The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang, Guizhou 550003, China

Cheng *et al.*: Effects of the Treatment of Dong Medicine Five-Flavor Anti-Diarrhea Soup

To investigate the clinical effect of the treatment of dong medicine five-flavor anti-diarrhea soup combined with melalazine on the chronic recurrence type (spleen deficiency and dampness accumulation type) ulcerative colitis. A total of 60 patients conforming to the diagnostic criteria of traditional Chinese and Western medicine in the anorectal department and gastroenterology department of the First Affiliated Hospital, Guizhou University of Traditional Chinese Medicine from September 2019 to December 2020 were randomly selected and grouped. Patients in the treatment group took dong medicine five-flavor anti-diarrhea soup combined with melalazine enteric tablets (30 patients). Patients in the control group received oral melalazine intestinal-soluble tablets (30 patients). Changes in the traditional Chinese medical syndrome scores, Baron endoscopic scores, Mayo scores, serum complement C3 and C4, serum interleukin-23 and interleukin-17 were recorded before and after 8 w of treatment in the treatment and control groups, and total traditional Chinese medicine symptoms were observed and recorded. The treatment group was better than the control group in improving the total points of traditional Chinese medical symptoms, Mayo and Baron scores and reducing complement C3 and C4 and serum interleukin-23 and interleukin-17 levels, which were demonstrated as statistically significant ($p < 0.05$). The treatment effects of dong medicine five-flavor anti-diarrhea soup combined with melalazin on the chronic recurrence type (spleen deficiency and dampness accumulation type) ulcerative colitis of the treatment group are better that of the control group regarding the Mayo scores, Baron endoscopic scores, remission of various symptoms of traditional Chinese medicine, reduction of serum complement and C3, C4, interleukin-23 and interleukin-17 levels.

Key words: Colitis gravis, ulcerative colitis, Baron endoscopic score, Mayo score, serum complement

Colitis gravis (Ulcerative Colitis, (UC)) is an inflammatory bowel disease with complicated and unclear etiology. Its main manifestations include mucinous blood stool, abdominal pain, diarrhea and tenesmus and its main lesion site is the mucosa and submucosa of the colorectal rectum^[1]. In recent years, the incidence of UC patients has increased sharply and it is gradually developing into a worldwide disease development trend, which seriously threatens people's quality of life. However, the current disease mechanism of UC remains unknown and it is found that the family is likely to be related to the genetics, environment, stress, immune dysfunction, bacterial and viral infection, and dysregulated inflammatory response^[2]. Relying on the humoral immunity of immunoglobulin and complement is inseparable from complement C3 and complement C4 in the development of UC^[3]. The T helper 17 (Th17) inflammatory pathway mediated by Interleukin (IL)-23/IL-17 inflammatory axis is one

of the therapeutic ways of UC and studied by many scholars^[4-6]. At present, melalazine is often used as a common agent in the clinical treatment of UC, but long-term salicylic acid preparation may also be required after treatment remission and it has clear efficacy to inhibit inflammatory factors to achieve its therapeutic goal^[7]. However, there are also adverse reactions and many side effects caused by oral drugs^[8-10]. Other treatments have large clinical use limitations. The valuable experience and treatment effect accumulated in the dong folk treatment are effectively reflected, which can make it clear that the five flavors of dong medicine have the clinical effect of invigorating the spleen and benefiting dampness, promoting blood circulation and stopping diarrhea. The aim of this study is to explore the comparison of melalazine gut-soluble tablets with dong medicine based on serum complement C3 and C4, serum IL-23 and IL-17 to investigate the effectiveness and safety of using dong medicine five-flavor anti-

*Address for correspondence

E-mail: gyxc163@163.com

diarrhea soup combined with melalazine Enteric Coated Tablet (ECT) to treat the spleen deficiency and dampness accumulation type colitis gravis. This study is expected to provide a new treatment idea and scheme for the clinical treatment of chronic recurrent colitis gravis and play the role of dong medicine in the treasure house of medicine with Chinese ethnic characteristics.

MATERIALS AND METHODS

General information:

The clinical cases collected in this study were derived from the anorectal department and gastroenterology department of the First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine (TCM) from July 2019 to July 2020. 60 UC patients diagnosed with chronic recurrent type. The patients were divided into treatment group and control group, and were expressed according to random numbers.

Diagnostic and dialectical criteria:

Referring to the consensus opinions on the diagnosis and treatment of inflammatory bowel disease (Beijing, 2018)^[11], formulated by the inflammatory enteropathy group of the digestive diseases branch of the Chinese medical association. Referring to the colitis gravis TCM diagnosis and treatment expert consensus opinion (2017)^[12].

This topic mainly studies the evidence of spleen deficiency and dampness, the clinical symptoms include diarrhea and loose stool, mixed with undigested food; mucus pus and blood stool, more white and red, or white freezing and abdominal distension. Secondary disease include food intake; limb drowsiness; abdominal pain; fatigue; tongue vein; tongue light red, teeth, thin white greasy and pulse is thin or smooth. Syndrome diagnosis include 2 main diseases and 2 secondary diseases, referring to the tongue vein, can be used for the diagnosis.

This disease can be diagnosed by meeting the above TCM diagnostic criteria and Western medicine diagnostic criteria.

Inclusion criteria: Patients aged 18 y to 65 y with diagnostic criteria for chronic recurrence of Western medicine colitis gravis; patients with colitis gravis with TCM spleen deficiency and dampness; patients with no unconscious disorders and mental disorders; patients with good compliance and signed informed consent; patients reviewed and approved by the hospital medical ethics committee.

Exclusion criteria: Patients with complications such as intestinal obstruction, colorectal cancer or intestinal perforation; patients belonging to the primary hairstyle or burst UC; patients allergic to the treatment processes; patients with severe heart, liver, renal impairment; pregnancy or pre-pregnancy and lactation patients; patients who cannot follow various reasons; patients with aspirin and other anticoagulation drugs in the past 1 mo; patients with diseases that may cause changes in IL-17 (or) IL-23 content, such as rheumatoid arthritis, encephalitis, systemic lupus erythematosus; patients with hypertension, diabetes and patients participating in other clinical studies.

Treatment method:

Control group: Oral melalazine ECT (0.5 g×40 tablets/box produced by the German Losan Pharma GmbH company, batch number: H20171358), taking method-1 g three times per day.

Treatment group: On the basis of the control group, adding oral TCM dong medicine five-flavor anti-diarrhea soup. The components of the dong medicine five-flavor anti-diarrhea soup include Daemhnysem 20 g, Nagswang 15 g, Shang Shengzhu 15 g, Kaokdid 10 g and Meixzaolgo 10 g.

Efficacy: Invigorating the spleen and improving dampness, promoting blood circulation and stopping diarrhea.

Taking method: Bags of TCM are made in the decocting pharmacy of our hospital. 1 dose is two bags, 1 bag is 120 ml and one dose is divided twice a day for 8 w, with bland diet no tobacco and alcohol.

Efficacy evaluation criteria:

Evaluation criteria of TCM efficacy: The efficacy evaluation criteria of TCM symptoms refer to the efficacy evaluation criteria in the guidelines for clinical research of chronic non-specific colitis gravis^[13] in the guidelines for clinical research of new TCM drugs (Trial).

Integral points for imaging of the subintestinal mucosa: Baron endoscopic grading criteria. The records were recorded once before and after treatment. Level 1 includes no spontaneous or contact bleeding and vascular texture; level 2 includes rough and abnormal mucosa; level 3 includes mucosal contact bleeding; level 4 includes severe contact or spontaneous bleeding and level 5 includes obvious ulcer formation with spontaneous bleeding.

Comparison of Mayo scores: Referring to the modified

Mayo scoring system in the consensus opinions on the diagnosis and treatment of inflammatory bowel disease. No single item evaluation >1 point; mild activity period 3-5 points; moderate activity period 6-10 points and severe activity period 11-12 points.

Detection of clinical indicators: The index levels of serum complement C3 and C4 were recorded before and after 8 w of treatment in UC patients. It was detected by immunospecific turbidity assay and subjected to comparative evaluation. Complement C3, C4 determination kit (Mike Biological Company, Inc.) and biochemical instrument 008AS-Hitachi. IL-17 and IL-23 (enzyme-linked immunosorbent assay) in serum were detected and compared.

Statistical analysis:

All the collected data were analyzed using the Statistical Package for the Social Sciences (SPSS) 25.0 software. The rank-sum test, t-test and Chi-square (χ^2) test were used to obtain the corresponding conclusions. Results are expressed as mean \pm standard deviation ($\bar{x}\pm s$). The above tests were statistically significant if $p<0.01$. Statistics are available if $p<0.05$.

RESULTS AND DISCUSSION

The total integral reduction of TCM symptoms was better than the control group ($p<0.05$). This implies that the total integral of TCM syndrome decreased significantly for the patients treated with dong medicine five-flavor anti-diarrhea soup combined with melalazine compared with that of the patients with oral melalazine ECT alone, as shown in Table 1.

The improvement in the treatment group was better than that in the control group in the Mayo score comparison

($p<0.05$). This implies that the Mayo scores received a significant decrease for the patients treated with dong medicine five-flavor anti-diarrhea soup combined with melalazine compared with that of the patients with oral melalazine ECT alone, as shown in Table 2.

The improvement in the treatment group was better than the Baron scores in control patients ($p<0.05$). This implies that the Baron scores was significantly decreased for the patients treated with dong medicine five-flavor anti-diarrhea soup combined with melalazine compared with that of the patients with oral melalazine ECT alone, as shown in Table 3.

The reduction in serum complement C3 and C4 treatment groups was better than that in the control group ($p<0.05$). Therefore, it is considered that the difference between serum complement C3 and C4 between treatment group and control group is significant. This implies that the serum complement C3 and C4 were significantly decreased for the patients treated with dong medicine five-flavor anti-diarrhea soup combined with melalazine compared with that of the patients with oral melalazine ECT alone, as shown in Table 4.

The patient sera serum IL-17 and IL-23 reduction in the treatment group is better than the control group ($p<0.05$). Serum IL-17 and IL-23 were considered significantly in the treatment group compared with that of the control group, implying a significant decrease regarding the serum IL-17 and IL-23 for the patients treated with dong medicine five-flavor anti-diarrhea soup combined with melalazine compared with that of the patients with oral melalazine ECT alone, as shown in Table 5.

TABLE 1: TOTAL INTEGRATION OF TCM

Group	Case numbers	$\bar{x}\pm s$	Z	p
Treatment group	30	7.46 \pm 4.09	-3.019	0.003
Control group	30	9.80 \pm 4.07		

TABLE 2: MAYO SCORE OF THE TWO GROUPS

Group	Case numbers	$\bar{x}\pm s$	Z	p
Treatment group	30	3.10 \pm 1.422	-2.025	0.043
Control group	30	3.80 \pm 0.805		

TABLE 3: BARON SCORE OF THE TWO GROUPS

Group	Case numbers	$\bar{x}\pm s$	Z	p
Treatment group	30	1.2 \pm 1.13	-2.439	0.018
Control group	30	1.93 \pm 1.2		

TABLE 4: DISTRIBUTION OF SERUM COMPLEMENT C3 AND C4 AFTER TREATMENT IN THE TWO GROUPS (g/l)

Groups	Case numbers	$\bar{x} \pm s$ in the treatment group	$\bar{x} \pm s$ in the control group	P
Treatment group	30	1.041 \pm 0.11	1.136 \pm 0.19	0.018
Control group	30	0.28 \pm 0.08	0.33 \pm 0.09	0.023

TABLE 5: COMPARISON OF TWO SERUM IL-17 AND IL-23 (pg/ml)

Groups	Case numbers	$\bar{x} \pm s$ in the treatment group	$\bar{x} \pm s$ in the control group	P
Treatment group	30	122.96 \pm 23.32	138.56 \pm 28.37	0.033
Control group	30	348.80 \pm 46.28	381.70 \pm 50.63	0.024

In recent years, colitis gravis with the specific pathogenesis is multifactorial, which may be related to diet, psychology, genetics, immunity, infection, etc. At present, the treatment of UC in China, especially in ethnic minorities in China, needs to be further developed and applied. On the basis of fully carrying forward the medical resources of ethnic minority areas and combining with the local scientific and advanced ethnic minority drug treatment, it can develop into an effective method and treatment measures for treating UC that complement each other, which can be improved quickly and more scientifically. Compared with the treatment of Western medicine that is easy to relapse or even caused by many side effects, Chinese traditional medicine has significant advantages in the reduction of curative effect and recurrence rate. Dong medicine is a great part of Chinese medicine with national characteristics, with the basic theoretical thought of "heaven, earth, gas, water and human", and dong medicine is worth further development and promotion. The dong medicine five-flavor anti-diarrhea soup has the effect of invigorating the spleen and promoting dampness, promoting blood circulation and stopping diarrhea. It is selected on the basis of dong folk collection and combined with clinical observation. Related animal basic experiments validated that dong medicine five-flavor anti-diarrhea soup could mitigate the inflammatory response in the UC rat model, and played an exact and good role in the rat experiments of colitis gravis^[14,15]. Emerging disciplines such as ethnic native pharmacology, ethnic native botology, anthropology can make the research more reasonable and scientific. In particular, Qiandongnan region has the medication technology and practical experience with the traditional characteristics of ethnic minorities. Dong medicine five-flavor anti-diarrhea soup is made of Daemhnysem, Nagswang,

Meixzaolgo, Kaokdid and Shang Shengzhu. The main medicine in the prescription is the Daemhnysem with Shang Shengzhu, Kaokdid, Meixzaolgo and Nagswang as adjuvants. Daemhnysem is smooth and astringent, which is recorded in "hemostasis and treating dysentery" in "Fujian folk herbal medicine". Pharmacological activity has immunomodulatory effect and is used in the prescription to play its role of convergence and stopping diarrhea. Kaokdid belongs to the lung, spleen, liver meridians and its medicinal taste is cold and bitter with the effect of spleen and antidiarrhea, detoxification and dampness. In "King Kong surrenders everything" it has "silver powder for detoxification, anti-heat dysentery" records. The pharmacological activity has antibacterial, anti-inflammatory and other effects, which can better play its role of convergence and stop diarrhea. Nagswang is cold and bitter, which has been confirmed in the antibacterial effect study of modern pharmacology and plays a role in clearing heat and detoxification in this prescription. Meixzaolgo has been validated in modern pharmacological studies of anti-inflammatory, antibacterial and improved immunity. Its efficacy has been recorded as early as the addendum of materia medica, which can lead the medicine to the target in the whole prescription. Shang Shengzhu has recorded in "Fujian folk herbal medicine". Research shows that it has anti-inflammatory, antibacterial and detoxification effects because the whole grass contains various chemical components called raw catechin acid, which can play the effect of removing blood stasis and hemostasis in the whole prescription. The above five drugs were used together on the basis of modern pharmacological research. The valuable experience accumulated in the folk treatment of the dong nationality and the treatment effect are effective, which can clarify the clinical effect of this prescription of invigorating

the spleen and benefiting dampness, promoting blood circulation and stopping diarrhea. Clinical use in the treatment of UC is active and effective with cheap price and high safety, which can be accepted by ordinary people.

This study investigated the clinical effect of the treatment of dong medicine five-flavor anti-diarrhea soup combined with melalazine on the chronic recurrence type (spleen deficiency and dampness accumulation type) UC. The research result showed positive curative effects with significantly reduced clinical indicators and improved the symptoms and signs as well as low price, few side effects, high safety. Dong medicine five-flavor anti-diarrhea soup has reached the purpose of treating UC by regulating serum complement C3, C4 and IL-23/IL-17 levels combined with melalazine.

Conflict of interests:

The authors declared no conflict of interests.

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