

Progress of Traditional Chinese Medicine Combined with Probiotics in Treating Ulcerative Colitis

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Abstract: In recent years, intestinal microecology has been proved to be related to ulcerative colitis. Probiotics can regulate intestinal microflora. Ecology has the characteristics of definite curative effect and high safety, and modern research has also confirmed that traditional Chinese medicine has its unique advantages in treating ulcerative colitis. Therefore, this paper summarizes the research progress of traditional Chinese medicine combined with probiotics in the treatment of ulcerative colitis in order to provide reference for clinical treatment and research.

Keywords: Ulcerative colitis; Chinese medicine; Probiotics; Intestinal microecology

1. Introduction

Ulcerative colitis is a chronic non-specific intestinal inflammatory disease whose etiology is not completely clear, and characterized by continuous and diffuse inflammatory changes of colorectal mucosa. It is characterized by "abdominal pain, diarrhea, mucus pus and bloody stool" [1], with repeated disease migration, poor prognosis and even cancer risk, which affects the quality of life of patients and brings double burdens to patients physically, mentally and economically. Nowadays, the etiology of ulcerative colitis is attributed to immune factors, and a large number of modern experimental studies have confirmed that the change of the structure and diversity of intestinal flora is the key factor of intestinal abnormal immune and inflammatory response. In terms of treatment, western medicine mainly treats with aminosalicic acid and glucocorticoids, but in terms of the long-term control degree of the disease, the effect is not good, the condition is easy to recur, the side effects are serious, the economic burden is heavy, and the quality of life of patients is seriously affected. It is found that probiotics can effectively improve the intestinal barrier of patients with ulcerative colitis and correct the unbalanced intestinal flora. As a green, convenient and economical treatment method, Chinese medicine has been confirmed by experimental research in recent years. Therefore, the application of probiotics combined with traditional Chinese medicine in the treatment of ulcerative colitis has the advantages of high clinical efficacy, less adverse reactions, high acceptance and lower cost than western medicine. This paper reviews the research progress of traditional Chinese medicine combined with probiotics in the treatment of UC in order to provide reference for clinical treatment and research.

2. Relationship between probiotics and ulcerative colitis

The health of intestinal environment is maintained by intestinal flora, immune system, intestinal vascular barrier and intestinal cells. The interaction between intestinal flora and intestinal barrier balances the intestinal environment, thus participating in human metabolism and immunity in an orderly manner, and ultimately affecting human metabolism and immunity. If the organism is affected by various factors, the imbalance of intestinal flora will be caused, and the balance between beneficial and harmful intestinal flora will be broken; Or destroy the intestinal barrier to facilitate harmful bacteria to invade the barrier itself, which will eventually trigger abnormal immune response in the intestine, thus producing inflammatory bowel disease. Existing studies have confirmed that inflammatory bowel disease is characterized by imbalance of microbial flora [2]. Among them, the dysfunction of intestinal epithelial barrier caused by imbalance of intestinal flora in UC patients is mainly due to the significant decrease of beneficial flora in the intestine, and the obvious increase of harmful flora leads to the immune response

of intestinal mucosa [3]. Therefore, intestinal flora imbalance plays an important role in the production and development of UC [4]. Probiotics, as living microorganisms [5], which are beneficial to the health of the host when ingested in sufficient amount, are mainly composed of various kinds of intestinal probiotics, such as yeast, bifidobacteria, lactobacillus, etc. After entering the intestine, they can colonize the intestinal mucosa and compete with pathogenic microorganisms to inhibit the growth of pathogenic microorganisms, so they have the functions of correcting the unbalanced flora environment in the intestine and enhancing the intestinal barrier and immunity. Existing experimental studies have confirmed that probiotics can regulate the composition of intestinal microflora [6] by inhibiting the growth of pathogenic bacteria, increasing beneficial metabolites in the intestine through fermentation and promoting the growth of beneficial bacteria in the intestine, so as to improve the intestinal environment of patients with inflammatory bowel disease. Studies have also shown that probiotics can improve the intestinal barrier function by regulating anti-inflammatory factors and inflammatory cytokines [7], or prevent pathogens from inducing protective immune response through immunity and modifying intestinal-associated lymphoid cells, and alleviate the function of intestinal tract disorder by enhancing local immune response [8]. Therefore, probiotics can regulate the gut microbiota through different mechanisms, improve intestinal barrier function, and thus improve the symptoms of inflammatory bowel diseases such as ulcerative colitis. In addition, Ren Yue and others considered that probiotics can significantly improve the induced remission rate in inducing UC in active period compared with placebo group, and it is safe and available [9]. Therefore, the scientific and safety of probiotics in the treatment of ulcerative colitis have reliable theoretical basis.

3. Correlation between intestinal flora and TCM theory

Intestinal microecology is mainly concerned about the influence of intestinal flora on human body. Huang Kun [10] summarized the relevant research literature of intestinal flora and concluded that intestinal flora may participate in the progress of many human diseases such as liver diseases, pancreatitis, cardiovascular diseases, gastrointestinal diseases, metabolic system diseases, etc, and may play an important role in it by participating in metabolism, which shows the importance of intestinal flora to human body. At present, it is believed that the influence of intestinal flora on human health is mainly related to the balance between beneficial bacteria and pathogenic bacteria. The balance between colonies affects the nutrition, immunity and growth of the host. In the long evolution process, a balanced and dynamic physiological combination has been formed with the host, and it can dynamically adjust itself within the physiological range according to the different stages and environments of the host, so as to maintain the balance between the intestinal microecology and the host itself. This dynamic balance is different from that of traditional Chinese medicine [11]. If various factors cause the number of intestinal colonies to be abnormal or the original ecological balance is destroyed after location transfer, the human body will become ill [12]. Therefore, the mutual balance of intestinal flora in human body is the condition to maintain the healthy intestinal microecology, and it forms a unified organic whole with the host. Balanced healthy intestinal flora and its metabolites meet the needs of the host's growth and metabolism, and the intestinal flora also depends on the host's support, and they are interdependent and interactive [13]. The dynamic balance of intestinal flora is one of the important conditions for the host body to reach the secret state of yin and yang in equilibrium, especially the balanced relationship between beneficial flora and pathogenic flora can make the host body reach the ideal state of yin and yang in equilibrium, and the unity between intestinal flora and the host and the external environment of the host accords with the understanding of holistic view of traditional Chinese medicine. In addition, some scholars have suggested that intestinal microecology is related to physique. Chinese medicine believes that physique has the characteristics of heredity, diversity, unity of form and spirit, group convergence, relative stability, dynamic variability and acquired adjustability. Modern medical research also believes that intestinal flora is influenced by genes [14]. At the same time, there are differences in the abundance and diversity of intestinal flora among people with different growth stages, diets, living habits, mental and psychological states and environments [15], and the abundance and diversity of intestinal flora of people with the same physique are close to the same [16], which are in line with the understanding of intestinal microenvironment in modern medicine, and provide ideas for syndrome differentiation and treatment of traditional Chinese medicine, which is convenient to start with the cause.

4. Modern research progress of probiotics in the treatment of UD

Du Xiaodong [17] compared the number of intestinal flora and intestinal mucosal barrier index of 50 patients who took oral probiotics before and after 8 weeks of treatment, and confirmed that the number

of beneficial bacteria *Bifidobacterium* and *Lactobacillus* in the intestine increased significantly after taking oral probiotics ($P < 0.05$), the number of *Escherichia coli* decreased significantly ($P < 0.05$), and the levels of serum ET, D- lactic acid and PCT decreased significantly ($P < 0.05$), which confirmed that oral probiotics can correct the unbalanced intestinal flora and effectively repair and improve the intestinal barrier function of UC patients. Wang Zhuo [12] and others divided 224 patients into 7 groups and gave them different treatment schemes. The study confirmed that the effective rate of oral probiotics group was significantly higher than that of the control group without oral probiotics, and confirmed that oral probiotics could effectively improve the clinical symptoms of UC patients. The study confirmed that probiotics could increase the number of beneficial bacteria in the intestine, regulate the levels of serum D- lactic acid and endotoxin lipopolysaccharide, affect the permeability of intestinal mucosa, and thus improve the intestinal mucosal barrier function. Zhu Yu [18] and others confirmed through experiments that *Lactobacillus casei-Dioscorea opposita* fermentation compound starter can significantly inhibit the expression of inflammatory factors such as IL-8 and TNF- α and MPO activity in intestinal tissue, regulate the protein expression, intestinal flora distribution and fatty acid metabolism, and effectively improve the colon tissue injury in UC model mice. Yan Bo [19] divided 104 patients with ulcerative colitis into two groups, and they were given conventional treatment and conventional treatment combined with probiotic treatment respectively. The results confirmed that the treatment rate after probiotic auxiliary intervention was higher than that of the control group ($P < 0.05$), and significantly improved macrophage activity, enhanced intestinal barrier function, hindered the growth of pathogenic microorganisms and promoted excretion. Chen Gang [20] and others confirmed through research that the infiltration of inflammatory cells in colonic submucosa of experimental rats in the probiotic group in the three experimental groups was reduced, and mucosal congestion and edema were obviously alleviated, and thus it was speculated that probiotics realized their anti-inflammatory and immunomodulatory functions by regulating the balance of Th1/Th2 cytokines. Wang [21] and other experiments confirmed that *Saccharomyces boulardii* can reduce the levels of TNF- α and IL-6, balance the intestinal flora and reduce the canceration of ulcerative colitis in mice. Chen Yanqin [22] administered probiotics orally to three out of seven groups of mice. The results confirmed that the experimental group intervened by probiotics could effectively reduce the intestinal inflammation and ulcer course of mice and protect the intestinal mucosa. And a large number of experimental studies have confirmed that FMT can balance intestinal flora and promote the healing of intestinal mucosa, improve the symptoms of UC patients [23]. Fang [24] and other experimental studies have confirmed that fecal transplantation can improve the intestinal flora diversity of recurrent active ulcerative colitis, increase the number of *Bacteroides* in the intestine, and have high safety.

5. Research progress of treating UD with traditional Chinese medicine

Feng [25] treated 41 UC patients in each group for 8 weeks, respectively. The results confirmed that adding *Pinellia Heart-Draining Decoction* could significantly increase the number of probiotics in the intestine, regulate the expression of inflammatory immune cytokines and improve the symptoms of patients. Wen [26] treated UC patients with *Jianchang Yuyang San* for 8 weeks. It was concluded that *Jianchang Yuyang San* can regulate intestinal probiotics to adjust the influence of Th1/Th2 cytokines, regulate immune and inflammatory reactions, and reduce intestinal mucosal inflammatory reactions in UC patients, and its curative effect is better than mesalazine enteric-coated tablets ($P < 0.05$). Chen [27] and others confirmed the curative effect of *Shen Ling Baizhu San* combined with western medicine on chronic recurrent UC through clinical trials. By observing the level of inflammatory factors in patients' serum before and after treatment, they thought that its mechanism might be related to regulating $\beta 2AR/\beta$ -arrestin2/NF- κ B signaling pathway and the expression of inflammatory cytokines downstream. In addition, Liu [28] and others confirmed that *Shen Ling Baizhu San* can inhibit the colon injury and the expression of inflammatory factors in UC mouse model, which may be related to inhibiting the expression of NLRP3 inflammatory body signal pathway related proteins and related inflammatory factors. Liu [29] confirmed that the addition of *Jianpi Zhixie decoction* to the treatment of western medicine can make patients get higher clinical benefits, and at the same time significantly reduce the adverse reaction rate ($P < 0.05$). Cao [30] confirmed through animal experiments that *Peony Decoction* can correct the unbalanced intestinal flora and reduce the inflammatory reaction in the intestine of mice, thus achieving the ideal effect of treating UC. Xu [31] confirmed through clinical trials that the combination of *Peony Decoction* and *Important Formula for Painful Diarrhea* can significantly improve the total effective rate of patients ($P < 0.05$) and significantly reduce the adverse reaction rate ($P < 0.05$). Zhang [32] treated 49 patients with UC in acute stage with oral mesalazine enteric-coated tablets and *Pulsatilla Decoction* combined enema respectively. The results confirmed that the clinical benefits of patients in the Chinese medicine treatment group were significantly higher than those in the western medicine group,

and the improvement of inflammatory indexes in the Chinese medicine treatment group was significantly better than that in the treatment group. Yang ^[33] treated 64 UC patients in the control group with ornidazole and sodium chloride injection, and the experimental group was treated with Yiqi Yukui Decoction on the basis of the control group. The results confirmed that the combined experimental group could correct the number of beneficial and pathogenic bacteria in the intestine, increase the number of bifidobacteria and lactobacillus in the intestine, and improve the hypercoagulability in the intestine of patients. The benefit of patients in the Chinese medicine group was significantly higher than that in the western medicine treatment group only. Pan ^[34] confirmed through research that Four Spirits Pill can reduce the heavy inflammatory factors in rats' serum by interfering with ZEB1 signal, and significantly inhibit the intestinal inflammatory activity of UC rats, thus reducing cell apoptosis, improving the pathological condition of colon tissue, protecting colon and achieving therapeutic effect on UC rats. Qin ^[35] treated 42 patients with active UC with Fufang Qingdai Decoction enema, and compared the symptoms, inflammatory indexes, mucosal endoscopic and pathological changes and adverse reactions before and after treatment. The results confirmed that the infiltration of inflammatory cells in the mucosa of the focus was significantly improved after treatment, and the symptoms, endoscopic scores and histopathological scores were significantly improved compared with before treatment, which could significantly inhibit the inflammatory activities of active UC and improve the quality of life of patients. Du ^[36] concluded through clinical trials that the application of Mume Pill combined with mesalazine in the treatment of ulcerative colitis can significantly improve the clinical outcome of patients. Benefit degree, significantly improve the symptoms of patients, improve the clinical efficacy, and can significantly improve the immune function of patients, the effect is better than that of mesalazine alone ($P < 0.05$). Lu ^[37] and others confirmed through network pharmacology, that is, animal experiments that Qinbai Decoction may inhibit its inflammatory reaction by affecting the expression of NF- κ B p65/TNF- α pathway and the expression of related anti-inflammatory factor IL-10, thus alleviating the mucosal damage of UC mice and achieving the purpose of relieving and treating ulcerative inflammation. Wang ^[38] and other researchers found that Qingchang Wenzhong prescription could enhance the intestinal barrier and protect the intestinal epithelium by up-regulating the expression of cytoplasmic transcription factor AhR, thus reversing the pathological progress of UC.

6. Research progress of probiotics combined with traditional Chinese medicine in the treatment of UD

Zhou Cheng ^[39] divided patients with mild and severe ulcerative colitis into three groups, and treated them with mesalazine, probiotics combined with Pulsatilla Decoction and probiotics combined with mesalazine for 6 weeks respectively. Through endoscopic evaluation, it was confirmed that Traditional Chinese medicine combined with probiotics had the best effect on improving intestinal mucosal injury in UC patients ($P < 0.05$). Li ^[40] treated 18 UC patients in each group with oral mesalazine, oral Chaishao Liu jun granules and probiotics sprayed under colonoscopy for 12 weeks. The study confirmed that the latter could obviously correct the disordered intestinal flora, reduce the bacterial count of enterococcus and enterococcus, increase the bacterial count of Bifidobacterium and Lactobacillus, and inhibit the expression of inflammatory factors such as NLRP-6, reduce the inflammatory reaction and maintain the intestinal homeostasis, thus achieving effectiveness. Chen ^[41] and others treated 60 patients with mild to moderate UC with mesalazine and Fufang Qingdai granules combined with probiotics for one month and followed up for one year. The results confirmed that Fufang Qingdai granules combined with probiotics could significantly reduce the number of pathogenic bacteria and increase the number of probiotics. The difference between the two groups was statistically significant ($P < 0.05$). The results of follow-up colonoscopy confirmed that the recurrence rate of Fufang Qingdai granules combined with probiotics was low, and the difference between the two groups was statistically significant ($P < 0.05$). Based on the preliminary experimental research of its research group, it is believed that Fufang Qingdai granules may achieve anti-inflammatory and analgesic effects by affecting the expression of pathway-related inflammatory factors such as NF- κ B, so as to play a therapeutic role in UC. Jiang ^[42] divided 62 patients with mild to moderate UC into two groups, and treated them with sulfasalazine enteric-coated tablets and Huadu Yuchang recipe combined with probiotics for 6 months respectively. The changes of flora, curative effect and recurrence rate of the two groups were statistically significant ($P < 0.05$). Traditional Chinese medicine combined with probiotics can significantly correct the imbalance of intestinal flora, improve patients' symptoms and reduce the recurrence rate. Ma ^[43] treated 82 UC patients in each group with probiotics, among which the study group was treated with Quyu Shengxin recipe. Results The curative effect of the study group was significantly better than that of the control group, and the scores of TCM syndromes and the reduction of serum TNF- α levels were significantly better than those of the control group, with statistical differences ($P < 0.01$). It was considered that CD4 and CD8

were significantly higher after treatment. The change of it may be related to the fact that its compound preparation can enhance the production of immune factors and improve immune function. Zhao^[44] and others treated 63 UC patients in each group with oral Huangqin Decoction Granules and probiotics on the basis of the former for 8 weeks. The results showed that the indexes of inflammatory factors such as IL-6, TNF- α and disease activity index were significantly improved before and after treatment. Combined with the results of colonoscopy observation, it was confirmed that probiotics combined with Huangqin Decoction Granules could effectively improve the clinical curative effect of UC, and the curative effect of probiotics treatment group was better than that of control group ($P < 0.05$). Wang Zhuo^[45] and others confirmed through clinical research that Gegen Qinlian decoction combined with probiotics is significantly superior to probiotics combined with western medicine mesalazine in the treatment of UC, which can significantly improve the benefit of UC patients, mainly in improving the symptoms of patients, reducing the level of inflammation and promoting the repair of intestinal mucosa.

7. Summary

To sum up, the existing literature proves that the curative effect of traditional Chinese medicine combined with probiotics in the treatment of ulcerative colitis is better than that of western medicine or traditional Chinese medicine alone. The existing clinical experiments prove that it can significantly improve the clinical benefit index of patients with ulcerative colitis, obviously improve the symptoms of patients and improve the total effective rate. And the experimental research proves that the treatment scheme of probiotics combined with ulcerative colitis is also effective in reducing the level of intestinal inflammation, repairing the intestinal barrier and slowing down the progress of the disease. Traditional Chinese medicine combined with probiotics has more green, safe and economical advantages than western medicine in terms of drug traceability, economic evaluation, recurrence rate and side effects of drugs. Especially in terms of patients' benefit, it has obvious advantages in improving symptoms, recurrence rate and side effects, so it is worthy of clinical reference and promotion.

With the continuous exploration of the relationship between traditional Chinese medicine and intestinal microecology, the application of probiotics or traditional Chinese medicine in the treatment of ulcerative colitis has been proved to be effective through animal or clinical experiments, which is worthy of clinical reference and promotion. Moreover, the combination of traditional Chinese medicine and probiotics in the treatment of ulcerative colitis is an effective scheme based on the grasp of the holistic view of traditional Chinese medicine and the theory of yin and yang, combined with the scientific experimental research results. As the saying goes, "healthy qi exists in the body, and evil cannot be dried, and its qi will be deficient when combined with evil." Traditional Chinese medicine corrects the biased constitution of UC patients by applying traditional Chinese medicine based on syndrome differentiation, and at the same time, it can expel evil qi or replenish the healthy qi of the defective human body to strengthen the body resistance and eliminate evil spirits, and improve the symptoms of patients. By using probiotics to help the "healthy qi" in the intestinal microecology, the unbalanced intestinal flora can be corrected, and the damaged intestinal mucosa can be repaired and improved, so that the body can reach a state of balance between yin and yang. However, at present, there are few related researches on the treatment of UC with traditional Chinese medicine combined with probiotics. In the future, large-scale clinical research should be carried out to explore the relationship between traditional Chinese medicine and intestinal flora, and the relationship between traditional Chinese medicine syndrome types and intestinal flora, so as to treat patients with ulcerative colitis with different syndromes more pertinently, and to overcome the practical problems of ulcerative colitis with traditional Chinese medicine and probiotics from the perspective of intestinal flora, providing more reliable basis for clinical promotion.

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