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# Crohn's Disease Treated by Chinese Medicine

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## Abstract

Crohn's disease is an inflammatory bowel disease with variable clinical symptoms, it can affect the whole gastrointestinal tract from the oral cavity to the anus and lead to lower quality of life and greater social and economic loss. Traditional Chinese medicine (TCM) has a long history and is unique characteristic by the theory of overall concept and treatment based on syndrome differentiation, it should be an important part of world medicine. This chapter introduces the research advance of Crohn's disease in TCM, including its name, location, etiology and pathogenesis, syndrome differentiation, therapeutic criteria, treatment methods and other contents. The mechanism of TCM treatment of Crohn's disease remains to be further studied.

**Keywords:** Crohn's disease, Chinese medicine, acupuncture and moxibustion, diagnosis, syndrome differentiation, treatment

## 1. Introduction

Crohn's disease (CD) is an inflammatory disease of the gut, it and ulcerative colitis is called inflammatory bowel disease (IBD). The etiology of CD is unknown that related to genetics, environment, humoral immunity and cellular immunity to some extent. It may be due to the complex interaction between genetic susceptibility, environmental factors, and changes in intestinal microflora, resulting in mucosal immune response abnormalities and impaired epithelial barrier function, giving rise to congenital and adaptive immune response disorders [1, 2].

CD is a proliferative disease that runs through all layers of the intestinal wall and it can occur anywhere in the gastrointestinal tract, the most common being the terminal ileum and colon [2, 3]. CD has various clinical manifestations, mainly characterized by diarrhea, mucous pus and blood stool, accompanied by abdominal pain, tenesmus, fever, anemia, nutritional disorders and other systemic symptoms of varying degrees. It can also be accompanied by joint, skin, eyes, oral mucosa, liver and other extraintestinal lesions, or cause perianal lesions, intestinal obstruction, gastrointestinal bleeding, perforation and other complications [4]. This disease is mainly divided into inflammatory stage, stenosis stage and perforation stage, patients usually develop from inflammation to stenosis or perforation [3]. At present, the global incidence of CD is on the rise, and the onset age is mostly between 20 and 40 years old, with no significant gender difference [5]. CD has prolonged course, repeated attacks, and not easy to cure, which seriously affects the quality of life of patients, and aggravates the social and economic burden. Therefore, it urgently needs to be solved and further studied.

In 2012, the Inflammatory Bowel Disease Group of Gastroenterology Branch of Chinese Medical Association formulated The Consensus Opinion on the Diagnosis and Treatment of Inflammatory Bowel Disease, which standardized the clinical diagnosis and treatment of CD. In recent years, with the increasing incidence of CD, in order to meet clinical needs and better guide the clinical work, the staff of the Inflammatory Bowel Disease Group of Gastroenterology Branch of Chinese Medical Association, finally revised the 2018 edition of The Consensus Opinion on the Diagnosis and Treatment of Inflammatory Bowel Disease after extensive discussions.

As the etiology of CD is unknown, there is no radical cure at present and the side effects of drugs are obvious in some CD patients. However, the advantages of Traditional Chinese medicine (TCM) in CD treatment are gradually emerging. With the in-depths of research on CD, more and more TCM doctors and scholars have summarized the etiology and pathogenesis, TCM classification, syndrome differentiation methods and treatment principles, and summarized the characteristic treatment methods of TCM, providing the diagnosis and treatment ideas and guidance for the understanding and treatment of CD.

## **2. Diagnosis of CD by Western medicine**

The diagnosis of CD depends on a combination of symptoms, endoscopy, radiology, and histopathological findings. Colonoscopy and mucosal biopsy are usually the main methods. A history of smoking, family history, gastrointestinal infection, malnutrition or anemia are all factors that should be taken into account when making a diagnosis [1].

### **2.1 Clinical manifestations**

The clinical presentation of CD depends on the site of pathological changes and the severity of inflammation, which can be divided into four aspects [6]:

(1) Digestive system performance: Spasmodic pain in right lower abdomen or peri-umbilicus, accompanied by borborygmus, aggravation after meals, it can be alleviated after defecation; diarrhea intermittent attacks in early stage, and more persistent in later stage. If the lesions involve the lower colon or rectum, mucinous blood stool and tenesmus may be present. Abdominal mass occurs in the right lower abdomen and around the umbilicus, mostly caused by mesenteric lymph node enlargement, internal fistula or local abscess formation. (2) General performance: Patients with intermittent low or moderate fever, a few show remittent fever, accompanied by toxemia; Nutritional disorders due to anorexia, and chronic diarrhea, including emaciation, anemia, hypoproteinemia, vitamin deficiency, calcium deficiency, osteoporosis, etc. The balance of water, electrolyte, acid and base is disturbed in acute stage. (3) Extraintestinal manifestations: Some patients have iridocyclitis, uveitis, finger pestles, arthritis, erythema nodosum gangrenous pyoderma, oral mucosal ulcer, chronic hepatitis, small bile duct peripheral inflammation, sclerosing cholangitis and so on. Amyloidosis or thromboembolic disease can be seen occasionally. (4) Perianal manifestations: Fistulas, fissures, abscesses, and stenosis around the anus or rectum [7]. It even affects the organs outside the gut.

### **2.2 Endoscopic examination and diagnosis**

Colonoscopy is the most sensitive method in the diagnosis of CD, which can improve the accuracy of clinical diagnosis and the efficiency of treatment [8]. Under endoscopy at the early stage of the disease, 2 ~ 3 mm diameter round shallow pitting ulcers or Afta aphthous ulcer can be seen with surrounding mucosa hyperemia and

redness. After the disease progresses, the ulcer increases and deepens, and merges with each other to form longitudinal ulcer. The relatively specific endoscopic manifestations include cobblestone changes, annular, multiple, segmental stenosis, and inflammatory polyp hyperplasia. Capsule endoscopy is very sensitive to the judgment of abnormal mucosa, but its specificity is low, and it is not applicable to all CD patients. For patients with stenosis, there is a certain risk. Wireless video capsule endoscope has the advantages of no radiation, no pain, no sedation, easy outpatient use and high patient satisfaction. When traditional diagnostic tools such as endoscope cannot make a clear diagnosis, it can be mainly used. During the development of CD, some patients may involve the upper digestive tract. This type of CD usually presents insidiously without obvious symptoms. Gastroscopy is often used, under which worm etched ulcer, longitudinal ulcer, slub like appearance, stenosis and fistula can be seen [9].

### **2.3 Pathological diagnosis**

Based on the principle of multi-point and multi-segment sampling, CD mucosal biopsy is the most main diagnostic basis of CD. Its pathologic findings are typically non-caseous granulomas that are more easily detected on biopsy in about 30% of cases and are more common in smaller ulcers. In addition, common pathological features include segmental lesions, the presence of inflammatory cell infiltration in the inherent membrane, and submucosal broadening, marked fibrosis, whole-wall inflammation, fissured ulcers, and whole-layer lymphatic follicles in the intestinal wall [10, 11].

### **2.4 Imaging diagnosis**

Imaging also plays a very important role in the diagnosis of CD. CT small intestine imaging or magnetic resonance enterography is the first choice for imaging examination, which is mainly used to evaluate inflammatory lesions in the small intestine. Magnetic resonance enterography is expensive but has the advantage of avoiding radiation and using no iodized contrast agents. The use of contrast-enhanced ultrasound can effectively improve the detection sensitivity of color Doppler ultrasound, which is outstanding in the diagnosis of the combined sensitivity and specificity of CD activity [12]. The sensitivity of small intestinal barium contrast is low and only suitable for dynamic observation in patients with intestinal cavity stenosis, and for the primary medical unit cannot conduct CT small intestinal imaging examination. Barium enema is not used much at present and has been replaced by colonoscopy.

### **2.5 Laboratory examination and diagnosis**

The blood counts are used to monitor anemia in CD patients. The concentration of calcium protective protein in feces was associated with neutrophil infiltration in the intestinal mucosa, it has a strong sensitivity and specificity for CD diagnosis. As an inflammation marker, C-reactive protein and other inflammatory markers are used simultaneously to monitor disease activity to assess disease activity.

## **3. TCM diagnosis of CD**

Although there is no corresponding name of CD in ancient Chinese medical books, there are abundant discussions about it, so the TCM diagnosis of CD was mainly based on symptom diagnosis. According to the main symptoms, CD is diagnosed as abdominal pain, diarrhea, bowel carbuncle, hemafecia, anal fistula, spouting bleeding from anus and other diseases [13, 14].

## **4. TCM etiology and pathogenesis of CD**

### **4.1 Etiology**

CD is associated with a number of pathogenic factors, either alone or in combination. Exogenous pathogenic factors, improper diet, emotional disorders, chronic physical deficiency were the main causes [14]. Exogenous pathogenic factors, such as cold, dampness and heat invade the body, resulting in blood stasis and abdominal pain and diarrhea. Unclean food, or overeating, or eating greasy and cold food can cause damp-heat or cold-dampness accumulating in stomach and spleen, blockage of abdomen Qi, producing diarrhea, bowel carbuncle; Internal injury of emotions, such as moodiness and worry leads to stagnation of qi induce pain easily; Weakness, prolonged illness or excessive fatigue, resulting in weakness of the spleen and stomach, transport and transformation weak that induce abdominal pain and diarrhea. CD mainly occurs in the intestine. In the theory of TCM, CD is also closely related to the spleen, stomach, liver and kidney, and is mainly caused by lesions in middle-jiao and lower-jiao.

### **4.2 Pathogenesis**

The basic pathogenesis of CD is a mixture of deficiency and excess, cold and heat [15]. The deficient root include the deficiency of natural endowments, the deficiency of spleen and kidney, or the prolonged illness and overwork; Damp-heat accumulation, qi stagnation, phlegm and dampness, blood stasis are all belong to excessive superficial. The basic pathogenesis of CD varies according to the main symptoms. If abdominal pain is the main manifestation, the basic pathogenesis is exogenous pathogenic factors of coldness, wetness, heat, it result in qi stagnation, blood stasis, viscera and qi adverse, pain [16]; If the main manifestation is diarrhea, the basic pathogenesis is spleen deficiency and overabundance of dampness [16, 17]; If the main manifestation is intestinal carbuncle, the pathogenesis includes accumulation of dampness and heat, blood stasis, and the accumulation of phlegm and blood stasis [14].

## **5. TCM syndrome differentiation and treatment of CD**

According to the Guidelines of Traditional Chinese Medicine Diagnosis and Treatment of Digestive Diseases compiled by the Committee of Spleen-stomach Diseases of The Chinese Association of TCM in 2006, the common TCM syndromes of CD include the syndrome of liver-stagnation and spleen-deficiency, the syndrome of deficiency and cold of spleen and stomach, the syndrome of yang deficiency of spleen and kidney, the syndrome of cold-dampness impairing spleen splenic function, the syndrome of qi stagnation and blood stasis syndrome, the syndrome of damp-heat accumulation [18, 19].

### **5.1 Syndrome of liver-stagnation and spleen-deficiency**

The main symptoms are anorexia, belching, right abdominal pain or periumbilical distension pain and diarrhea while during abdominal pain and relief of pain after diarrhea. Acute abdominal pain, loose stools, belching and eat less, tongue reddish, and pulsed strings. Its attacks or exacerbations are often caused by irritation or nervous tension. The principle of treatment is soothing the liver and strengthening the

spleen. The main prescriptions are Chaihu Shugan powder and Shenlinbaizhu powder [20] including bupleurum, *Codonopsis pilosula*, poria cocos, Chinese yam, white lablab album, atractylodes macrocephala koidz, fructus aurantii, lotus seed, amomum, coix seed, rhizoma cyperi, pericarpium citri reticulatae, radix paeoniae alba, platycodon grandiflorum, radix glycyrrhizae. Patients with anorexia can add fried hawthorn, malt; Patients with nausea and vomiting can add pinellia ternate, inula flower.

## 5.2 Syndrome deficiency and cold of spleen and stomach

The main symptoms are dull abdominal pain, prefer warm and pressing, prolonged diarrhea, bowel bloating and abdominal distension, vomiting of clear water, loss of appetite, sallow complexion, dizziness, cold limbs, fatigue, pale tongue, thin and white coating, and slow and sunken pulse. The principle of treatment is to warm stomach and strengthen spleen. The main prescription is Shenling Baizhu powder and Fuzi Lizhong pill [21], including fried semen coicis, fried atractylodes macrocephala koidz, poria cocos, *Codonopsis pilosula*, radix paeoniae alba, lotus seed, Chinese yam, bupleurum, giant typhonium rhizome (decocted first), corydalis yanhusuo, common bletilla pseudobulb, amomum (decocted later), honey-fried radix liquiritiae, dried ginger, panax notoginseng powder (take with water). Patient with frequency of defecation can be added nutmeg, *Terminalia chebula*; Patient with bloody stool can be added roasted ginger charcoal, patient with mucus stool can be added atractylodes.

## 5.3 Syndrome of deficiency of spleen and kidney yang

The main symptoms are dull abdominal pain, irregular pain attacks and stop, prefer warm and pressing, thin pus around the anus, dull anal pain, loose stool, or diarrhea at dawn, loss of appetite, fatigue, cold limbs, soreness of waist and polyuria, pale tongue, or fat tongue with teeth marks, white coating, sunken or thin and weak pulse. The principle of treatment is warming kidney and strengthening spleen. The main prescription is Changyangan soup [22], including astragalus membranaceus, poria cocos, *Codonopsis pilosula*, rhizoma bletillae, pseudo-ginseng, cooked monkshood, fructus psoraleae, *Myristica fragrans*, epimedium, fructus chebulae, radix glycyrrhizae.

## 5.4 Syndrome of cold dampness impairing spleen

The main symptoms are acute abdominal pain, loose stool or water stool, or dysentery with blood and pus, heavy head and body, pale tongue, white and greasy coating, soft and slow pulse. The principle of treatment is clearing damp and strengthening spleen. The main prescription is Weiling soup, including atractylodes rhizome, dried tangerine peel, magnolia officinalis, polyporus umbellatus, rhizoma alismatis, cortex cinnamomi, atractylodes macrocephala koidz, radix glycyrrhizae.

## 5.5 Syndrome of qi stagnation and blood stasis

The main symptoms are immovable abdominal lumps, abdominal distension or pricking, loose or bloody stools, purplish or petechial tongue, string and thin and hesitant pulse. The principle of treatment is regulating qi and dispersing blood stasis. The main prescription is infradiaphragmatic stasis-expelling decoction, including peach kernel, safflower, radix rehmanniae, radix angelicae sinensis, red peony, fructus aurantii, *Platycodon grandiflorum*, radix glycyrrhizae, radix bupleuri, radix scrophulariae.

## 5.6 Syndrome of damt-heat accumulation

The main symptoms are abdominal pain refusing to press, brown and smelly stool, or diarrhea with blood and pus, distending pain and scorching hot anus, thirsty and drinking cold, few and yellow urine, red tongue, yellow greasy coating, string and slippery or slippery and rapid pulse. The treatment principle is clearing heat and expelling damp. The main prescription is Baitouweng soup, including pulsatilla, coptis chinensis, phellodendron, ash bark.

Chinese herbal medicine.

Name	Pharmacological effects
Bupleurum	Diaphoresis; prevent malaria
<i>Codonopsis pilosula</i>	enrich blood; immunity enhancement
Poria cocos	Calm; promote healthy digestion
Chinese yam	Improve immune and digestive function
White lablab bean	Antibacterial and antiviral
<i>Atractylodes macrocephala</i> koidz	Adjust gastrointestinal motility; inhibit ulcer
Fructus aurantii	Increases gastrointestinal motility and contractility rhythms
Lotus seed	Immune regulation; improve digestive function
Amomum	bacteriostatic action; peristalsis enhancement
Coix seed	Eliminate edema; immune regulation
Rhizoma cyperi	Relaxes intestinal smooth muscle; anti-inflammatory
Pericarpium citri reticulatae	Promote secretion of digestive juices; relieve asthma
Raidix paeoniae alba	Antibacterial activity; analgesic
Platycodon grandiflorum	Dilate blood vessels; antitussive expectorant
Radix glycyrrhizae	Regulate immunity; inhibit ulcer; protect liver
Fried hawthorn	Help digestion; stop diarrhea
Malt	Help digestion; antifungal
Pinellia ternate	Antitussive expectorant; inhibit ulcer
Inula flower	Relieve asthma; antitussive expectorant
Giant typhonium rhizome	Anti-inflammatory; sedation; expectorant
Corydalis yanhusuo	Spasmolysis, analgesia; suppression of gastric ulcer
Common bletilla pseudobulb	Hemostasis; protect gastric mucosa
Dried ginger	Inhibit ulcer; dilate blood vessels
Panax notoginseng powder	Promote blood clotting; dilate blood vessels
Nutmeg	Antibacteria; anti-inflammatory
<i>Terminalia chebula</i>	Antibacteria; antitumor; antidiarrhea
Roasted ginger charcoal	Hemostasis; acesodyne
<i>Atractylodes</i>	Adjust gastrointestinal motility; diuresis
<i>Astragalus membranaceus</i>	Strengthen immune system; inhibit ulcer; improve substance metabolism
Cooked monkshood	Cardiac; antishock; dilate blood vessels
Fructus psoraleae	Antibacteria; improve immune system
Epimedium	Improve immune system; delay the progression of renal failure

Name	Pharmacological effects
Magnolia officinalis	Promote the secretion of digestive fluids; anti ulcer
Polyporus umbellatus	Diuresis; enhance immunity
Rhizoma alismatis	Diuresis; anti-inflammatory
Cortex cinnamomi	Cardiotonic; anti ulcer; anti-inflammatory
Peach kernel	Reduce vascular resistance and improve hemodynamics; relax bowels
Safflower	Dilate blood vessels; excited uterus; anticoagulation
Radix rehmanniae	Hemostasis; antibiosis; immuno-enhancement
Radix angelicae	Anti-microbico; Antipyretic analgesic
Sinensis	Promote hematopoietic function; immunity enhancement
Red peony	Antithrombus; reduce blood lipid; liver protection
Radix scrophulariae	Antibiosis; dilate coronary arteries
Pulsatilla	Anti-microbico; anti-inflammatory; immunity enhancement
Coptis chinensis	Resistance of pathogens; Antipyretic; antineoplastic
Phellodendron	anti-microbico; excite gastrointestinal smooth muscle
Ash bark	Anti-inflammatory; analgesic; diuresis

## 6. Chinese patent medicines

A large number of studies and clinical evidence show that TCM has obvious curative effect and function in the treatment of CD. The following is a brief summary of commonly used Chinese patent medicines.

### 6.1 Bolus for strengthening intestines and relieving diarrhea

It has the effect of harmonizing liver and spleen, astringent intestine to relieve pain [23] and commonly used in patients with disharmony of liver and spleen, diarrhea and abdominal pain, and nonspecific ulcerative colitis.

### 6.2 Salvia ligustrazin injection

It has the effect of activating blood circulation and removing blood stasis, improving microcirculation. The cure rate can be improved by improving the high coagulation state of CD patients [24].

### 6.3 Warming kidney and invigorating spleen granules

It has the effect of strengthening spleen and tonifying kidney. It can improve the humoral immunity of patients also used to diseases caused by the deficiency of spleen and kidney.

### 6.4 Tripterygium wilfordii polyglycoside tablet

It has the effect of dispelling wind and detoxifying, dehumidifying and detumescence, relaxing tendons and dredging collaterals. Studies have shown that it can effectively improve the clinical symptoms of CD patient [25], but its toxicity of liver and kidney should be valued.

### **6.5 Sishen pill**

It has the effect of warming kidney and dispelling cold, astringent intestine and relieving diarrhea and commonly used for diarrhea caused by deficiency of kidney yang, the symptoms are borborygmus, intestinal distension, diarrhea at dawn, anorexia and indigestion, continuous diarrhea, yellowish complexion and cold limbs.

### **6.6 Dark plum pill**

It has the effect of smoothing liver and regulating intestine, clearing the upper Jiao and warming lower Jiao and used for patient with chronic dysentery, the symptoms are abdominal pain, dysentery, vertex headache, attack intermittently, irritation and vomiting, extremities cold.

### **6.7 Peaceful gastroenterology tablets**

It has the effect of invigorating spleen and kidney, warming stomach and relieving pain, astringent intestine and relieving diarrhea, and used for patient with diarrhea of deficiency of spleen and kidney Yang, the symptoms are irregular stool, diarrhea at dawn with mucus, abdominal distention and pain, epigastric discomfort, and distention of lower abdominal.

### **6.8 Buzhong Yiqi pill**

It has the effect of invigorating and benefiting spleen qi and lifting collapsed qi, be used for diarrhea caused by weakness of spleen and stomach and collapse of middle qi.

### **6.9 Guben Yichang tablets**

It has the effect of invigorating spleen and warming kidney, astringing intestine to relieve diarrhea, and be used for chronic diarrhea caused by spleen deficiency or Yang deficiency of spleen-kidney, the symptoms are chronic abdominal pain and diarrhea, loose stools, anorexia and abdominal distension, weak waist, fatigue and cold limbs.

### **6.10 Aucklandia and coptis tablets**

It has the effect of clearing away heat and eliminating dampness, promoting qi circulation to relieve pain, and be used for dysentery caused by dampness-heat of large intestine, the symptoms are stool with pus and blood, tenesmus, fever and abdominal pain.

### **6.11 Fuzi Lizhong pill**

It has the effect of warming spleen dispersing cold, relieving diarrhea and pain, and can be used for cold syndrome of spleen and stomach, the symptoms are anorexia and abdominal distension, abdominal pain and nausea, weak pulse, cold limbs, or headache attacked by cold, and any chronic disease caused by cold.

### **6.12 Zhuche pill**

It has the effect of nourishing Yin and blood, tonifying qi and strong intestine, removing blood stasis and generating muscles. The symptoms are dull abdominal

pain, persistent diarrhea, stool with pus and blood, low fever in afternoon, dizziness, insomnia, night sweats, irritability, weight loss and fatigue, red tongue, thin and less coating, thin and rapid pulse.

## 7. Acupuncture and moxibustion treatment of CD

Acupuncture therapy is widely applicable to mild and moderate CD patient with no age or gender restrictions, but not for patients with severe CD, in pregnancy and lactation, with mental disorders, with severe tumors, or patients with serious diseases of the heart, liver, kidney, brain and hematopoietic system [26], they need adopt appropriate western medicine to save lives and avoid critical situations.

The basic acupoint prescriptions for CD treatment include Tianshu (ST25), Zusanli (ST36), Shangjuxu (ST37), Guanyuan (RN4), Qihai (RN6), Zhongwan (RN12) [27]. Patients with syndrome of liver depression and spleen deficiency can add Taichong (LR3) and Pishu (BL20); Patients with syndrome of deficiency and cold of spleen and stomach can add Shangwan (RN13) and Xiawan (RN10); Patients with syndrome of yang deficiency of spleen and kidney were added with Mingmen (DU4), Pishu (BL20) and Shenshu (BL23); Patients with syndrome of cold dampness disturbing spleen can add Yanglingquan (GB34) and Fenglong (ST40); Patients with syndrome of qi stagnation and blood stasis can add Taichong (LR3) and Qihai (SP10); Patients with syndrome of dampness-heat accumulation can add Quchi (LI11) and Hegu (LI4). During the acupuncture treatment, the abdomen of CD patients is usually the main part, including the legs and back. The treatment is normally performed for about 20-30 minutes each time, once every other day. If the patient is in serious condition, the curative effect can be enhanced once a day.

Acupuncture therapy is mainly targeted at excess, heat syndrome and relatively simple symptom. For patients with syndrome of intermingled deficiency and excess, acupuncture therapy often combines with moxibustion therapy. The research of Wu Huang research group showed [28, 29] that moxibustion can effectively improve the clinical symptoms and the quality of life of CD patient. The methods were mainly acupuncture at Tianshu (ST25), Zhongwan (RN12), Qihai (RN6). Mix the powder of aconite, cinnamon, salvia miltiorrhiza, safflower, costusroot, coptis chinensis and borneol; add yellow rice wine and mix it to form a thick paste; Make a medical cake in a mold and place it at the above acupoints, and place moxa cone on medical cake, moxibustion twice for each acupoint; Combined with acupuncture at Zusanli (ST36), Shangjuxu (ST37), Sanyinjiao (SP6) and Gongsun (SP4), the goal of synergetic treatment and enhanced curative effect was finally achieved.

## 8. Other therapies

In addition to TCM, Chinese patent medicine, acupuncture and moxibustion treatment methods, there are other unique therapies, and the effect is also very effective. Through clinical controlled experiments, Songnian proved [30] that auricular application can effectively alleviate the abdominal pain of CD patients. Enema administration combined with internal medicine can greatly improve the curative effect of CD [31]. Hu Zhengchao and et al. [32] have found that Chinese medicine fumigation, external washing and sitz bath could effectively alleviate the symptoms of anal fistula patients with CD, not only improving local blood

circulation, but promoting the healing of anal fistula canal. In addition, fecal flora transplantation is also a new treatment method for CD combined with Chinese medicine, it works by transplanting fecal material from a healthy donor into the patient's gut to restore the intestinal flora diversity and thus achieve a good therapeutic effect [33].

## **9. Criteria of efficacy evaluation**

### **9.1 Crohn's disease activity index (CDAI)**

CDAI can be used to evaluate the disease activity and the efficacy of CD, including five aspects of the patient's general condition, such as abdominal pain, diarrhea, abdominal mass and complications [34]. The higher the total score, the more serious the disease. A score of  $\leq 4$  indicates remission, a score of 5-8 indicates moderate activity, and a score of  $\geq 9$  indicates severe activity. It can be scored in three stages before, during and after treatment to dynamically observe the changes of the disease.

### **9.2 Overall efficacy of TCM syndromes**

The total score of TCM syndromes was used to evaluate the clinical symptoms of abdominal pain, diarrhea, pus and blood stool, tenesmus, belching, nausea and vomiting and fever. The total scores before and after treatment was compared, if the total score decreased by  $\geq 90\%$  compared with that before treatment, it is judged as clinical remission. If the total score decreased by  $\geq 70\%$  and  $< 90\%$ , it is judged as significant effect; if the total score decreased  $\geq 30\%$  and  $< 70\%$ , it is judged to be valid; if the total score decreased  $< 30\%$ , it is judged to be invalid.

### **9.3 Endoscopic score**

Simplified endoscopy score for CD (SESCD) can be used for diagnosis and efficacy evaluation of CD. The score items mainly include ulcer size, ulcer area, affected intestinal area, intestinal lumen stenosis and the condition of mucosal healing. The lower the score, the better the mucosal healing degree. A score  $\leq 3$  is remission, a score 4-10 is mild activity, a score 11-19 is moderate activity, and a score more than 20 is severe activity [35].

### **9.4 Quality of life assessment**

Inflammatory bowel disease quality of life questionnaire (IBDQ) was used for CD evaluation, including intestinal symptoms, systemic symptoms, emotional ability and social ability. Scores were recorded for both the pre-treatment and post-treatment stages, with higher scores indicating better quality of life.

### **9.5 Assessment of anxiety and depression**

Self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were used to evaluate the severity of the anxiety and the depressive symptoms of CD patients. Scores were performed according to the symptoms, and the patients were divided into mild, moderate and severe by 50 score. Scores were recorded before and after treatment. Scores below 50 after treatment indicated efficacy.

## **9.6 Long-term efficacy**

The development of CD is a long-term and progressive process. The clinical efficacy evaluation should combine the short-term with long-term efficacy. In addition to the general clinical symptoms, it is also important to observe the status with the ulcer of intestinal mucosa and actively prevent perianal lesions it should also focus on the observation of intestinal mucosal ulcer and the active prevention of perianal lesions of CD patients.

## **10. Prevention and care**

### **10.1 Diet control**

Improper diet is one of the major causes of CD. In TCM, dampness, heat and cold pathogens easily invade the body through improper diet, damage spleen and stomach, and accumulate in intestines. Therefore, CD patients should pay attention to their daily diet, light and easy digestible food is better, avoid eat irritating food, try not to eat or eat less fat and greasy food, or raw and cold food.

### **10.2 Psychological adjustment**

CD is a chronic disease in the developing course of disease, patients are prone to anxiety or depression that aggravating the symptoms of body and mind. Therefore, in the process of diagnosis and treatment, attention should be paid to the psychological and emotional intervention of the patients to avoid negative emotional stimuli, relieve their anxiety or depression situation, guide the correct understanding of disease with good positive attitude [36, 37].

### **10.3 Adjust lifestyle**

CD is persistent and prone to relapse, so it is important to adjust lifestyle, control risk factors and change improper habits. Smoking is an important factor for CD patient, which often aggravates the disease and more likely to cause complications. For CD patients, the first step is to quit smoking, adjust lifestyle, and eliminate risk factors. In addition, patients should have regular daily life, reasonable work and rest, moderate diet, maintain the spleen and stomach, do proper exercise, avoid fatigue, adjust emotions, comply with four seasons, and maintain healthy energy [38].

### **10.4 Regular review and follow-up**

The development of CD is a long-term process, attention should always be paid to physical changes through outpatient, inpatient follow-up, telephone follow-up, and regular review, to understand the recurrence of disease, cancer prevention.

## **11. Conclusion**

The cause of CD is still unclear, it is mainly related to improper diet, disorder emotion, attack of external evil, internal deficiency in TCM theory. The main pathogenesis is deficiency of spleen and kidney combined with damp-heat

accumulation, qi stagnation, phlegm and dampness and blood stasis. The holistic concept and syndrome differentiation are the general principles of TCM treatment, the diagnostic criteria of CD are generally accorded to the consensus Opinions on the Diagnosis and Treatment of Inflammatory Bowel Disease as the reference, and comprehensive judgments are mainly made based on the clinical symptoms, endoscopy results, imaging examinations and pathological tissues of the patients. For example, the concentration of fecal calprotectin was positively correlated with CDAI score, SEC-CD score, CD clinical activity and mucosal healing, it could objectively reflect the inflammatory activity of CD [39]. Imaging diagnostic techniques, magnetic resonance imaging (MRI) and computerized tomography (CT), can be used to assess the activity of CD by showing changes in the thickness of the intestinal wall, abnormal intensification of the intestinal wall, intestinal segment stenosis, abnormal increase in mesenteric vessels, enlarged lymph nodes, fistulas, ulcers, and abscesses [40]. According to the symptoms and characteristics of different syndromes of CD, corresponding treatment methods were adopted, among which Chinese herbal medicine and acupuncture and moxibustion treatment were the most common and had significant curative effects.

With the development of TCM treatment of CD in recent years, certain progress and achievements have been made in clinical and experimental research, such as the gray matter structure of CD patients had significant changes, which was correlated with anxiety and depression status and course of disease [41]. In resting-state, the brain abnormal activities in insula and MCC of CD patients are different between remissive CD patients with and without abdominal pain, and are closely related to the severity of abdominal pain [42], aberrant functional connectivity of the amygdala may be involved in processing of visceral pain and sensation, and emotion in CD [43]. Herb-partition moxibustion combined with acupuncture can improve the clinical common symptoms of abdominal pain, diarrhea, fatigue and anorexia for mild and moderate CD [26]. Both treatments of electro-acupuncture and moxibustion improved cortex-subcortical coupling in remissive CD patients, but electro-acupuncture regulated homeostatic afferent processing network, while moxibustion mainly regulated the default mode network [44]. In CD rats, moxibustion can up-regulate the A20 expression level and down-regulate the expression of TNFR1, TRADD, and RIP1, and increase cell apoptosis in the intestinal epithelial barrier [45]. It is important to relieve the damage of intestinal mucosal barrier and maintain its functional integrity for patients [46]. Many experimental studies have shown that moxibustion can significantly down-regulate the expression of NF- $\kappa$ B P65, TNF- $\alpha$  and IL-1 in the colon tissue of CD model rats [47] and down-regulate the proteins expression of MCP-1 and IL-8 to reduce the expression of downstream inflammatory factors, relieve intestinal inflammation, and improve the morphological structure of colon tissue [48].

However, the pathogenesis of CD is still unclear, there is a lack of prospective studies even large sample and multicenter clinical trials, which still need to be further studied and explored.

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## **Conflict of interest**

There is no conflict of interest among authors.

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