

Consensus Opinions on Diagnosis and Treatment of Irritable Bowel Syndrome with Integrated Traditional Chinese and Western Medicine (2017)

Professional Committee on Digestive Diseases, Chinese Association of Integrative Medicine

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- Irritable bowel syndrome (IBS) is a common clinical functional bowel disease. In 2003, the 15th National Academic Conference on Integrated Traditional Chinese and Western Medicine on Digestion held in Chongqing issued *the Protocol of Diagnosis and Treatment of Irritable Bowel Syndrome with Integrated Traditional Chinese and Western Medicine (draft)*. Following the publication of the IBS Rome III Diagnostic Criteria by the Rome Committee in 2006, the Association issued the *Consensus Opinions on Diagnosis and Treatment of Irritable Bowel Syndrome with Integrated Traditional Chinese and Western Medicine (2010)*. At present, the Rome IV Criteria has been published. According to the Rome IV Criteria, experts of the Association have revised the *Consensus Opinions on Diagnosis and Treatment of Irritable Bowel Syndrome with Integrated Traditional Chinese and Western Medicine (2010)* based on the recent research progress in the treatment of IBS with integrated traditional Chinese and western medicine.

The Delphi method was adopted in this revision for the discussions on related issues in the diagnosis, treatment and evaluation of IBS. After three rounds of feedback and revisions, several opinions on the diagnosis, treatment and evaluation were integrated to form the *Consensus Opinions on Diagnosis and Treatment of Irritable Bowel Syndrome with Integrated Traditional Chinese and Western Medicine (2017 Revised Version)* (Voting Choices: ① Fully agree; ② Agree, but with certain reservations; ③ Agree, but with greater reservations; ④ Disagree, but with reservations; ⑤ Completely disagree. If $>2/3$ of the people chose ①, or $>85\%$ of the people chose ①+②, then it would be adopted as a passed clause), and final approval was conducted by core expert group. The full text is as follows.

1 Concept

IBS is a functional bowel disease, manifested as recurrent abdominal pain,, which is associated with defecation or accompanied by changes in bowel habits. Typical abnormal bowel habits may be manifested as constipation, diarrhea, or constipation alternating with diarrhea, and meanwhile may have symptoms of abdominal bloating / bloating ^[1]. There is a lack of organic lesions that can be detected by routine clinical tests to explain these symptoms.

Expert Consensus on Irritable Bowel Syndrome in China (2015) defines IBS as “a functional bowel disease, with abdominal pain, abdominal bloating, or abdominal discomfort as the main symptoms. There is improvement in symptoms after defecation, often accompanied by changes in bowel habits [frequency and/or traits]. There is a lack of organic lesions that can be detected by routine clinical tests to explain these symptoms”, and it is believed that “abdominal bloating”

is more common in the Chinese population and should be included in the definition^[2]. According to the differences in the current main symptoms of IBS, the TCM disease name of IBS is divided into “diarrhea”, “constipation”, “abdominal pain”, etc.

2 Western Medicine Diagnostic Criteria

2.1 Clinical Manifestations

Typical symptoms of IBS mainly include abdominal pain, diarrhea, constipation, and so forth according to their types, and combined with upper gastrointestinal symptoms such as heartburn, early satiety, nausea, vomiting, and so on^[3-4], and there may be other systemic symptoms such as fatigue, backache, palpitation, difficulty in breathing, frequent urination, urgent urination, sexual dysfunction, etc. Some patients have obvious tendency of anxiety and depression^[5-6]. There are often no specific clinical signs.

2.2 Diagnostic Criteria

2.2.1 Western medicine diagnostic criteria for IBS (Rome IV)

Recurrent abdominal pain, with average frequency of at least 1 day per week in the last 3 months, accompanied by the following 2 or more items: ① Associated with defecation; ② Accompanied by changes in the defecation frequency; ③ Accompanied by changes in stool property (appearance). The symptoms have appeared at least 6 months before diagnosis, and those appeared in the recent three months meet the above diagnostic criteria.

Rome IV has made some adjustments to IBS diagnostic criteria, mainly including: ① “Symptoms improved after defecation” in Rome III is adjusted to “associated with defecation”; ② Frequency is adjusted from previous “at least 3 days per month” to “at least one day per week”; ③ The word “onset” is deleted from the accompanying symptoms. The *Expert Consensus on Irritable Bowel Syndrome in China (2015)* still recommends the application of Rome III criteria.

2.2.2 IBS classification (Rome IV)

Bristol Stool Form Scale should be used for IBS subtype diagnosis. IBS subtypes should be classified based on the Bristol stool form when patients defecate abnormally. IBS subtype classification will be more accurate when patients have abnormal defecation at least 4 days per month. The dominant type of bowel habits refer to number of days at which at least one abnormal defecation appeared based on stool form [IBS classification is related to abnormal bowel habits (IBS-C, IBS-D, and IBS-M). In addition, patients should discontinue medications for abnormal defecation at the time of assessment].

① IBS with predominant constipation (IBS-C): $>1/4$ (25%) of stool is type 1 or type 2 based on Bristol Stool Form Scale, and $<1/4$ (25%) of stool is type 6 or type 7. ② IBS with pre-dominant diarrhea (IBS-D): $>1/4$ (25%) of stool is type 6 or type 7 based on Bristol Stool Form Scale, and $<1/4$ (25%) of stool is type 1 or type 2. ③ IBS with mixed bowel habits (IBS-M): $>1/4$ (25%) of stool is type 1 or type 2 based on Bristol Stool Form Scale, and $>1/4$ (25%) of stool is type 6 or type 7. ④ IBS Unclassified (IBS-U): Patients meet the diagnostic criteria for IBS, but their bowel habits cannot be accurately classified into any of the three types above, so it is called unclassified.

Expert Consensus on Irritable Bowel Syndrome in China (2015) holds that type 1 to type 3 stool should be included when diagnosing IBS with predominant constipation according to the Bristol Stool Form Scale.

2.2.3 Diagnosis approaches

The diagnosis of IBS should be based on the following 4 main aspects: ① Clinical history; ② Physical examination; ③ Minimum laboratory tests; ④ Colonoscopy or other appropriate examinations (conducted when there are clinical indications).

As many disease symptoms are similar to IBS (e.g. inflammatory bowel disease, celiac disease, lactose intolerance, and microscopic colitis), limited laboratory tests are needed to accurately identify these diseases.

2.2.4 Warning signs

In the diagnosis of IBS, attention should be paid to warning signs, and targeted inspections should be conducted to rule out related diseases. *Expert Consensus on Irritable Bowel Syndrome in China (2015)* proposes that the warning signs of IBS include: New patients >40 years of age, hematochezia, positive result of fecal occult blood test, anemia, abdominal mass, ascites, fever, weight loss, and family history of colorectal cancer. For patients with warning signs, targeted selection of coatingther examinations is required to exclude organic diseases.

3 TCM Syndrome Differentiation

The clinical subtypes of IBS should be distinguished clinically, differentiation and treatment based on syndrome differentiation should be coatingther conducted in clinical subtypes. Clinical differentiation should "examine the evidence and seek the cause", For IBS-M or IBS-U, it is especially necessary to rely on the shown symptoms. This consensus has listed the common syndrome types of each subtype to provide a reference for the clinical practice. It should be clarified that these common syndrome types are not all that appeared in the clinical practice, and the consensus does not exclude other types of syndrome.

3.1 IBS-D

(1) Liver qi Inhibiting the Spleen Syndrome

Main Symptoms: ① Immediate diarrhea after abdominal pain, pain relief after diarrhea; ② The onset of the disease is associated with mood changes.

Secondary Symptoms: ① Bowel sounds and flatus; ② Fullness in chest and hypochondrium with scurrying pain; ③ Abdominal bloating and discomfort.

Tongue and Pulse: Light red or dull tongue, thin white coating; thin pulse.string

Syndrome Type Determination: With 2 Main Symptoms plus 1-2 Secondary Symptoms, or with the first Main Symptom plus 3 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

(2) Spleen and -Stomach Weakness Syndrome

Main Symptoms: ① Loose stools after meals; ② Fear of raw or cold food and drink.

Secondary Symptoms: ① Abdominal bloating and borborygmus; ② Easy to sweat; ③ Reduced or poor appetite; ④ Fatigue and laziness to speak.

Tongue and Pulse: Pale tongue, or with tooth marks, white coating; thin and weak pulse.

Syndrome Type Determination: With 2 Main Symptoms plus 2 Secondary Symptoms, or the first Main Symptom plus 3 Secondary Symptoms, and refer to the Tongue and Pulse for Diagnosis.

(3) Spleen and Kidney Yang Deficiency Syndrome

Main Symptoms: ① Diarrhea at dawn; ② Abdominal pain when feeling cold, and pain relief after getting warm.

Secondary Symptoms: ① Feeling sore and weak in the waist and knees; ② Indigestible food in stool; ③ Cold extremities.

Tongue and Pulse: Fat and pale tongue, with tooth marks on the sides, slippery and white and slippery coating; deep and thin pulse.

Syndrome Type Determination: With 2 Main Symptoms plus 2 Secondary Symptoms, or the first Main Symptom plus 3 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

(4) Large Intestine DampnessHeat Syndrome

Main Symptoms: ① Immediate diarrhea after abdominal pain; ② Urgent or uncomfortable diarrhea.

Secondary Symptoms: ① Uncomfortable in the epigastric region; ② Thirst without desire to drink; ③ Dry and sticky mouth; ④ Burning pain in anus.

Tongue and Pulse: Red tongue, yellow and greasy coating; slippery and rapid pulse.

Syndrome Type Determination: With 2 Main Symptoms plus 2 Secondary Symptoms, or the first Main Symptom plus 3 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

(4) Damp heat of large intestine

3.2 IBS-C**(1) Liver Qi Stagnation Syndrome**

Main Symptoms: ① Abdominal pain accompanied by defecation, dry and hard stools, difficulty in defecation; ② Worsened constipation when in a bad mood.

Secondary Symptoms: ① Chest and hypochondrium are uncomfortable; ② Abdominal pain and bloating; ③ Frequent belching, which is obvious especially when in a bad mood.

Tongue and Pulse: Pale or dull tongue, thin and white coating; pulse string.

Syndrome Type Determination: With 2 Main Symptoms plus 2 Secondary Symptoms, or the first Main Symptom plus 3 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

(2) Large Intestine Dryness Heat Syndrome

Main Symptoms: ① Abdominal pain accompanied by defecation, constipation; ② Dry and hard stools.

Secondary Symptoms: ① Abdominal pain, which is obvious when being pressed; ② Dry mouth with bad breath.

Tongue and Pulse: Red tongue, yellowish coating with less fluid; thready rapid pulse.

Syndrome Type Determination: With 2 Main Symptoms or plus 2 Secondary Symptoms, or with the first Main Symptoms plus 2 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

3.3 IBS-M

Cold and Heat Syndrome

Main Symptoms: ① Abdominal pain accompanied by defecation, diarrhea alternating with constipation.

Secondary Symptoms: ① Abdominal bloating and borborygmus; ② Bitter mouth; ③ Slumped anus; ④ Ungratifying defecation.

Tongue and Pulse: Dark red tongue, white and greasy coating; thin or slippery pulse.

Syndrome Type Determination: With 1 Main Symptoms plus 2 Secondary Symptoms, and refer to the Tongue and Pulse for diagnosis.

4 Treatment

4.1 Treatment goal

The goal of IBS treatment is to relieve symptoms and improve patients' quality of life.

4.2 Conventional Western medicine treatment

4.2.1 Maintenance of good doctor-patient relationship

Good communication between physician and patients, as well as the explanation of the symptoms, are superior to those of the control group in terms of short-term and long-term symptom improvement [7]. Physicians should explain to patients: ① IBS is a functional disease, and there is no evidence to indicate that IBS can directly progress into severe organic diseases or malignant tumors; ② Symptoms of IBS are prone to recur, and the impact on patients is mainly reflected in the quality of life of patients; ③ Lifestyle adjustments should be emphasized for IBS.

Through lifestyle adjustments and proper drug therapy, IBS symptoms of most patients can be improved ideally.

4.2.2 Adjustment of lifestyle, dietary habits and psychological condition

Adjustments of lifestyle and social behavior, such as reducing alcohol and tobacco consumption, paying attention to rest, adequate sleep and other behavioral improvements, can reduce IBS symptoms [8].

The restricted food categories include: ① Food rich in ingredients such as FODMAPs (i.e. short-chain carbohydrates that are difficult to absorb, such as fructose, lactose, polyols, fructan, oligosaccharides) [9]; ② High-fat, spicy, hot and numbing food and food with heavy spices; ③ Food with high dietary fiber may be effective for constipation (but disadvantageous to abdominal pain and diarrhea); cold food may aggravate diarrhea; ④ Once the food allergen is identified, foods containing the allergen ingredient should be avoided.

4.2.3 Drug therapy

With respect to drug therapy for IBS, appropriate drugs are selected mainly according to the symptoms. Common drugs include antispasmodics, antidiarrheals (diarrhea-predominant), prokinetics, laxatives, intestinal microecologies, etc. For patients with obvious anxiety or depression, anxiolytics and antidepressants can be used.

- (1) Antispasmodics: ① Selective calcium channel blockers for gastrointestinal smooth muscle, which are applicable to diarrhea-predominant IBS patients or patients with spastic constipation, such as: pinaverium bromide, 50mg/time, tid, po; otilonium bromide, 40mg/time, bid or tid, po. ② Ion channel modulators: This kind of drugs can directly act on multi-ion channels in cell membranes and have bidirectional regulation effect on smooth muscle movement, so they are applicable to all types, especially for IBS with mixed bowel habits or IBS unclassified, such as: trimebutine maleate, 100mg/time, tid, po.
- (2) Antidiarrheals: Applicable to diarrhea, such as: Loperamide, 2mg/time, tid or qid, po; Diphenoxylate, 1-2 tablets/time, bid or tid, po; Smecta, 3-6g/time, tid, po.
- (3) Prokinetics: Applicable to abdominal bloating and IBS with predominant constipation, such as: mosapride, 5-10mg/time, tid, po; itopride, 50mg/time, tid, po.
- (4) Laxatives: Bulk laxatives can be tried for IBS-C, such as: calcium polycarbophil, 1g/time, tid; methylcellulose and hydrocil instant can also be selected, as well as permeable laxatives such as polyethylene glycol, lactulose, etc. Stimulant laxatives should be used with caution.
- (4) Antidepressants: Antidepressants can be tried for those with psychological factors such as depression, and selective serotonin (5-HT) reuptake inhibitors (SSRIS) are used more.
- (5) Gastrointestinal microecologies: Applicable to IBS patients with intestinal flora imbalance. Common drugs include Si Lian Kang (tetralogy of viable bifidobacterium tablets), Bifico (bifid-triple viable capsules), Golden bifid (live combined bifidobacterium and lactobacillus tablets), Zheng Chang Sheng (bacillus licheniformis capsules), Bioflor (Saccharomyces boulardii sachets), etc.
- (6) Antibiotics: Rifaximin can improve the general symptoms of not Constipation-predominant IBS and the symptoms of abdominal bloating and diarrhea.

4.3 TCM Treatment

4.3.1 TCM Syndrome Differentiation Treatment

(1) IBS-D

① Liver qi Inhibiting the Spleen Syndrome

Rules of Treatment: Suppressing the liver and supporting the spleen.

Prescription: Modified Pain Relief Essential Prescription Plus Flavor (*Danxi's Experiential Therapy*). Largehead atractylodes macrocephala; Radix Paeoniae Alba, radix saposhnikoviae, tangerine peel, etc.

② Spleen and Stomach Weakness Syndrome

Rules of Treatment: Invigorating the spleen and supplementing qi.

Prescription: Modified Shenling Baizhu Powder (*Taiping Huimin Heji Ju Fang (Prescriptions of the Bureau of Taiping People's Welfare Pharmacy)*). Modification: Codonopsis pilosula, largehead atractylodes rhizome, poria, pulp of lotus seed, semen coicis, fructus amomi, platycodon grandiflorum, white hyacinth bean, Chinese yam, honey-fried licorice root, etc.

③ Spleen and Kidney Yang Deficiency Syndrome

Rules of Treatment: Tonifying the spleen and kidney.

Prescription: Fuzi Lizhong Decoction (*Taiping Huimin Heji Ju Fang (Prescriptions of the Bureau of Taiping People's Welfare Pharmacy)*) combined with modified Sishen Pills (*Nei Ke Zhai Yao*). ("Internal Medicine Abstract") Modification: Herbs: radix aconiti carmichaeli, codonopsis pilosula, largehead atractylodes rhizome, dried ginger, schisandra chinensis, fructus psoraleae, Nutmeg, fructus evodiae, honey-fried licorice root, etc.

④ Large Intestine Dampness Heat Syndrome

Rules of Treatment: Clearing the heat and promoting diuresis.

Prescription: Modified Gegen Qinlian Decoction (*Shang Hai Lun (Treatise on Febrile Disease)*). Modification Pueraria lobata, scutellaria baicalensis, coptis chinensis, honey-fried licorice root, etc.

(2) IBS-C

① Liver Qi Stagnation Syndrome

Rules of Treatment: Soothing the liver and Regulating qi.

Prescription: Modified Liumo Decoction (*Zheng Zhi Zhun Sheng (Standards of Diagnosis and Treatment)*): Agilawood, radix aucklandiae, areca catechu, combined spicebush root, immature bitter orange, raw rhubarb, etc.

② Large Intestine Dryness Heat Syndrome.

Rules of Treatment: Relieving heat and moisturizing the intestines and relaxing the bowels.

Prescription: Modified Maziren Pills (*Shang Hai Lun (Treatise on Febrile Disease)*). Modification Cannabidis semen, radix paeoniae alba, Citrus aurantium rheum officinale, magnolia officinalis, almond, white honey.

(3) IBS-M

Cold and Heat Syndrome

Rules of Treatment: Mildly regulating cold and heat.

Prescription: Modified Wumei Pills (*Shang Hai Lun (Treatise on Febrile Disease)*). Modification Black plum, asarum sieboldii, dried ginger, coptis chinensis, angelica sinensis, radix aconiti carmichaeli, Sichuan pepper, cassia twig, codonopsis pilosula, golden cypress, etc.

4.3.2 Treatment with Chinese Patent Medicine

- (1) Shenling Baizhu Granules: Ginseng, poria, largehead atractylodes rhizome, Chinese yam, white hyacinth bean, lotus seed, coix seed, amomum, platycodon grandiflorum, licorice root. 3-6g/time, 3 times/d, suitable for IBS-D Spleen and Stomach Weakness Syndrome.
- (2) Bupi Yichang Pills: Astragalus membranaceus, codonopsis pilosula, Amomum, Radix Paeoniae Alba, angelica sinensis, largehead atractylodes rhizome, cinnamon, rhizoma corydalis, lychee seed, dried ginger, licorice root, radix saposhnikoviae, radix Aucklandiae, fructus psoraleae, red halloysite. 9g/time, tid, suitable for IBS-D spleen deficiency or spleen and kidney deficiency.
- (3) Ginseng Jianpi Pills: Ginseng, largehead atractylodes rhizome, poria, Chinese yam, tangerine peel, radix Aucklandiae, fructus amomi, astragalus membranaceus, angelica sinensis, spina date seed, polygala tenuifolia. 6g/time, bid. Applicable to IBS-D spleen deficiency and dampness syndrome.
- (4) Shenbei Guchang Capsules: Chinese gall, nutmeg (simmering), myrobalan meat (simmering), fructus mume, radix Aucklandiae, rhizoma atractylodis, poria, cornu cervi degelatinatum, red ginseng. 4 capsules/time, 3 times/d. Suitable for IBS-D spleen and kidney yang deficiency syndrome.
- (5) Sishen Pills: Myristica fragrans, fructus psoraleae, schisandra chinensis, fructus evodiae, jujube. 9g/time, tid, applicable to IBS-D with spleen and kidney yang deficiency syndrome.
- (6) Guben Yichang Tablets: Codonopsis pilosula, largehead atractylodes rhizome, fructus psoraleae, Chinese yam, astragalus membranaceus, baked ginger, angelica sinensis, radix paeoniae alba, rhizoma corydalis, radix Aucklandiae, carbonized sanguisorba root, red halloysite, acacia catechu, licorice root. 8 tablets/time, tid, applicable to IBS-D with spleen and kidney yang deficiency syndrome.
- (7) Tongxiening Granules: radix paeoniae alba, green tangerine peel, allium macrostemon, largehead atractylodes rhizome. 1 bag/time, tid, applicable to IBS-D with liver qi inhibiting spleen syndrome.
- (8) Gegen Qinlian Pills: Root of kudzu vine, coptis chinensis, scutellaria baicalensis, honey-fried licorice root. 6g/time, bid, applicable to IBS-D with dampness-heat of spleen

and stomach syndrome.

- (9) Xianglian Pills: radix aucklandiae, coptis chinensis (processed with fructus evodiae). 6g/time, bid; Applicable to IBS-D with dampness-heat of spleen and stomach syndrome.
- (10) Maren Runchang Pills: Fructus cannabis, bitter almond, rheum officinale, radix aucklandiae, tangerine peel, radix paeoniae alba. 6g/time, tid, applicable to IBS-C with large intestine dryness-heat syndrome.
- (11) Bianbitong: Largehead atractylodes rhizome, cistanche deserticola, fructus aurantii. 1 vial/time, bid, Applicable to IBS-C with kidney and spleen weakness syndrome.
- (12) Simotang Oral Liquid: radix aucklandiae, fructus aurantii, areca catechu, combined spicebush root. 10ml/time, tid, Applicable to IBS-C Stagnation of liver qi syndrome.
- (13) Liuwei Nengxiao Capsules: rheum officinale, fructus chebulae, dried ginger, radix inulae racemosae, saponaria officinalis, gypsum rubrum. 2 capsules/time, bid or tid, applicable to IBS-C with qi depression and intestinal dryness syndrome.
- (14) Wumei pills: pulp of fructus mume, Sichuan pepper, asarum sieboldii, coptis chinensis, golden cypress, dried ginger, radix aconiti carmichaeli, cassia twig, angelica sinensis, ginseng. 2 pills/time, bid or tid, applicable to IBS-M with cold-heat complex syndrome.

4.3.3 Acupuncture therapy

Zusanli (ST 36), Tianshu (S25), Sanyinjiao (SP6) are selected for diarrhea, and reducing method is used for excess syndrome while reinforcing method is used for deficiency syndrome. Pishu (BL20), Zhangmen (LIV 13) are added for weakness of spleen and stomach; Shenshu (BL23), Mingmen (GV 4), Guanyuan (CV 4) are added for spleen-kidney yang deficiency, and moxibustion therapy is also feasible; Ganshu (BL18), Xingjian (LIV 2) are added for liver depression. Back-shu, front-mu point and lower sea point of abdomen are mainly selected for constipation. In general, ^[11] Dachangshu (V25), Tianshu (S25), Zhigou (TE 6), Fenglong (S 40) are selected. Reducing method is suitable for excess syndrome while reinforcing method is suitable for deficiency syndrome, and moxibustion therapy is added for cold syndrome. Hoku (LI 4), Quchi (LI 11) are added for heat constipation; Zhongwan (CV 12), Xingjian (LIV 2) are added for qi stagnation, and reducing method is adopted.

4.4 Key points of treatment with integrated Chinese and Western medicine

At present, the clinical studies on IBS treatment with integrated Chinese and Western medicine mainly focus on the following aspects: ① Study on the relationship between IBS physiopathologic mechanism and TCM syndrome type; ② Study on modern medical mechanism of classical prescription in intervention treatment of IBS; ③ Study on clinical efficacy evaluation of IBS intervention by integrated Chinese and Western medicine. However, relatively mature results that can be transformed into clinical use are rare.

Key points of integration include: ① Insist on combining the diagnosis and classification of modern medicine with the characteristics of TCM diagnosis and treatment of IBS, and adopt the combination of disease and syndrome to carry out IBS clinical and scientific research. ② In terms of treatment, liver stagnation and spleen asthenia are considered to be the basic pathogenesis of IBS-D, and it is related to the mechanisms of visceral hypersensitivity and alteration of intestinal flora of modern medicine. The representative prescription for liver stagnation and spleen asthenia, Tongxie Yao Fang, can be used as the basic prescription for IBS-D, and it can be modified. ③ From the endpoint/outcome of IBS, the disease occurs repeatedly and is difficult to cure completely, and the long-term adjustment of the disease should be emphasized in clinical practice. Chinese medicine can be used to regulate the constitution, combined with modern

medicine to relieve short-term symptoms. ④ Anxiety and depression status in IBS patients is one of the concerns in current clinical practice. Anxiolytics and antidepressant can be added during the conditioning with traditional Chinese medicine.

5 Efficacy assessment criteria

With respect to IBS clinical efficacy evaluation, clinical subtypes should be distinguished, and appropriate efficacy evaluation methods should be determined according to the main clinical types. In clinical efficacy evaluation, the primary efficacy evaluation indices and secondary efficacy evaluation indices should be distinguished.

5.1 Primary efficacy evaluation indices

There are no validated and recognized clinical endpoint/outcome indices. Two aspects are mainly considered in existing evaluation methods: Abdominal pain, abnormal defecation. According to the *Guideline on the evaluation of medicinal products for the treatment of irritable bowel syndrome* [10] of Europe and the *Guidance for Industry: Irritable Bowel Syndrome-Clinical Evaluation of Drugs for Treatment* [11] of the United States, the improvement in abdominal pain and stool property (Bristol Stool Form Scale is recommended) is mainly considered for IBS-D; the improvement in abdominal pain and defecation frequency (frequency of completely autonomous defecation per week) is mainly considered for IBS-C. For abdominal pain, the 0-10 numeric rating scales (NRS) is recommended for patients to grade according to the “degree of the most severe abdominal pain occurred in the past 24 hours”.

For IBS-D, it is defined as effective when 50% of the patient’s course of treatment meets the following criteria: Compared with baseline, the abdominal pain is improved by at least 30% and the number of days at which patients defecating Bristol type 6 or type 7 stool is reduced by at least 50%.

For IBS-C, it is defined as effective when 50% of the patient’s course of treatment meets the following criteria: Compared with baseline, the abdominal pain is improved by at least 30% and completely autonomous defecation is increased at least one time in every week.

For IBS-M or IBS-U, the general evaluation method is still being recommended. If a 7-point scale is used, it will be defined as effective when there are at least 2 levels of improvement in efficacy evaluation; If a 5-point scale is used, it will be defined as effective when there are at least 1 level of improvement in efficacy evaluation. In addition, compared with baseline, the abdominal pain should be improved by at least 30%.

The severity of abdominal pain is evaluated based on the situation every day, and the “degree of the most severe abdominal pain occurred in the past 24 hours” is recorded; defecation frequency is evaluated based on the situation every week. Diary of symptoms can be adopted.

5.2 Secondary efficacy evaluation indices

Secondary efficacy evaluation indices of IBS play a complementary role in the primary efficacy evaluation indices. Secondary efficacy indices can be adjusted according to the objectives of clinical study. Secondary efficacy evaluation indices that can be considered include: IBS symptom severity scales (IBS-SSS), TCM syndrome evaluation, quality of life evaluation,

psychological tests, etc.

5.2.1 Syndrome efficacy assessment criteria

Refer to the efficacy assessment criteria of the *Guidelines for the Clinical Research of New Traditional Chinese Medicine*: Nimodipine method is used for calculation. Efficacy index = (total score before treatment - total score after treatment) / total score before treatment × 100%.
① Clinical recovery: Major symptoms and signs disappear or basically disappear, with efficacy index $\geq 95\%$.
② Markedly effective: Major symptoms and signs have significantly improved, with $70\% \leq$ efficacy index $< 95\%$.
③ Effective: Major symptoms and signs significantly get better, with $30\% \leq$ efficacy index $< 70\%$.
④ Ineffective: Major symptoms and signs show no improvement, or even get worse, with efficacy index $< 30\%$.

5.2.2 IBS-SSS

Rome III standard holds that IBS-SSS is the only IBS symptom scale that has been verified, and its effectiveness, reliability and sensitivity to treatment have been validated^[12]. The scale is divided into two parts in addition to general information and instructions: The first part is the severity assessment, and the total score is calculated from five aspects, i.e. abdominal pain severity, abdominal pain frequency, abdominal bloating severity, defecation satisfaction and impact on life. The total score is 500, and it can be regarded as in remission when it's lower than 75; the critical values while considered mild, moderate and severe are 75-175, 175-300, and >300 , respectively. The second part is other information on IBS where users can detail the defecation frequency, stool property, site of abdominal pain, nature of the abdominal pain and so forth^[13].

5.2.3 Quality of life evaluation criteria

IBS seriously affects the quality of life of patients, and the assessment scales for the quality of life of IBS patients include disease-specific scales and generic scales. Commonly used disease-specific scales include Irritable Bowel Syndrome-Quality of Life Scale (IBS-QOL), while generic scales include SF-36, etc.

IBS-QOL scale was developed by Patrick et al. The scale consists of 34 self-evaluation items, ranging from eight dimensions, i.e. dysthymia, behavior disease, body image, health worry, food avoidance, social reaction, sexual concerns and interpersonal relations, to evaluate the quality of life. The scale has achieved good psychological measurement validity^[14-16]. SF-36 is a generic scale which is currently widely used in the world, and the one commonly used in China is the Chinese version made by Professor Li Lu from Zhejiang University^[17].

Patient Reported Outcomes (PRO) is an evaluation indicator developed based on the health-related quality of life abroad in recent years. Existing PRO scales in China include "Chronic Gastrointestinal Disease Patient Reported Outcome (PRO)" and "IBS TCM Syndrome Scale". The former is patient-centered and used to evaluate the intervention effect on chronic gastrointestinal diseases from six dimensions, i.e., systemic symptoms, dyspepsia, reflux, psychology, defecation and social function. The scale has good reliability and validity^[18]; The latter focuses on the diagnosis and evaluation of IBS syndromes from dimensions such as liver stagnation and spleen asthenia, spleen and stomach weakness, and spleen and kidney yang deficiency, which has good reliability and validity^[19].

5.2.4 Psychological tests

The onset of IBS is closely related to mental and psychological factors, and the measurement of mental state is often used as an auxiliary indicator for the clinical efficacy evaluation of IBS. Commonly used psychological state assessment scales include SAS [20-21], SDS [22], HAMA [23], HAMD [24], etc. The complexity of each scale is different, which should be used as needed.

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