

## Treatment of irritable bowel syndrome in China: A review

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### Abstract

Irritable bowel syndrome (IBS) is a common, chronic, functional gastrointestinal disorder with a high incidence rate in the general population, and it is common among the Chinese population. The pathophysiology, etiology and pathogenesis of IBS are poorly understood, with no evidence of inflammatory, anatomic, metabolic, or neoplastic factors to explain the symptoms. Treatment approaches are mainly focused on symptom

management to maintain everyday functioning and to improve quality of life for patients with IBS. However, prescribed medications often result in significant side effects, and many IBS sufferers (particularly Chinese) do not improve. Instead of taking a variety of conventional medications, many have turned to taking traditional Chinese medicine or integrated Chinese and Western medicine for remedy. A number of clinical trials have shown that Chinese herbal, acupuncture or integrative therapies presented improved treatment outcomes and reduced side effects in IBS patients. The purpose of this review article is to examine the treatment approaches of IBS that have been published in recent years, especially in China, to assess the possible differences in treating IBS between China and other countries. This would provide some useful information of unique treatment approach in clinical practice for physicians in the management of IBS in China, thus offering more treatment options for IBS patients with potentially better treatment outcomes while reducing the medical cost burden.

**Key words:** Irritable bowel syndrome; Integrated treatment; Traditional Chinese medicine; China

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**Core tip:** Irritable bowel syndrome (IBS) is a common, chronic, functional gastrointestinal disorder highly prevalent in the general population, and it is common among Chinese population. The current review examines the differences between IBS treatment approaches in China and Western countries. The review reveals more treatment options in China in using traditional Chinese medicine (TCM) alone or in conjunction with conventional treatments, with the integration of TCM with Western medicine showing rather promising results. Besides providing extra treatment options, this information would foster future research for more effective treatment to provide IBS patients with better outcomes while reducing the financial burden.

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## INTRODUCTION

Irritable bowel syndrome (IBS) is a common, functional gastrointestinal disorder that is highly prevalent in the general population. Depending on the diagnostic criteria used to define the condition, it is reported to affect approximately 5%-20% of the general population worldwide<sup>[1,2]</sup>. Two large population surveys performed in China reported that the prevalence of IBS was estimated to be 7.26% (Manning criteria) or 0.82% (Rome criteria) in Beijing<sup>[3]</sup> and 11.5% (Manning criteria) or 5.67% (Rome criteria) in Guangdong<sup>[4]</sup>.

IBS is characterized by recurrent abdominal pain and discomfort associated with alterations in the frequency or consistency of stool, that present as diarrhea or constipation. Based on the Rome III diagnostic criteria, which classify IBS according to different bowel behaviors, there are four subtypes: IBS-D (diarrhea-predominant), IBS-C (constipation-predominant), IBS-M (mixed), and unspecified IBS (IBS-U)<sup>[1,5]</sup>. Clinically, the complexity and diversity of IBS presentation make treatment difficult. In practice, clinicians generally make treatment decisions for symptom reduction in IBS according to the type and severity of the symptoms. However, many pharmacological treatment approaches are associated with side effects that result in a decreased benefit to the patient in terms of treatment outcomes<sup>[1]</sup>. Hence, IBS sufferers often have absenteeism, reduced health-related quality of life and multiple healthcare-seeking behaviors, leading to great social and economic burdens<sup>[6,7]</sup>.

In terms of health care delivery, China has a unique cultural background in developing traditional Chinese medicine (TCM) as well as an extensive experience in its implementation. In fact, as opposed to other countries, TCM is practiced alongside conventional Western medicine in China. This is reflected by the substantial number of Chinese proprietary herbal medicines included in the National Essential Medicines List in China. Chinese physicians are often trained in both Western and Chinese medicine techniques and often use combined TCM and conventional Western medicine to manage different diseases and disorders. In recent years, due to dissatisfaction with conventional treatments, many IBS sufferers have turned to alternative medicine, particularly TCM or integrated Chinese and Western medicine for remedy. A number of clinical trials have shown that TCM therapies alone or combined with Western medicine produced improved treatment outcomes in IBS patients<sup>[8-19]</sup>. However, as most of these studies were published in China, the results and potential benefits

for IBS treatment using TCM or integrative therapies are little known in other countries.

This review will examine the differences between IBS treatment approaches in China and Western countries, with special attention to clinical research carried out in China, in order to provide alternative treatment options in clinical practice for physicians who manage IBS. Furthermore, we believe that this assessment would also foster and facilitate potential areas of future research for more effective treatment models, thus providing IBS patients with better treatment outcomes while reducing the medical cost burden.

## CURRENT TREATMENT APPROACHES FOR IBS

Although IBS is a highly prevalent disease, there is still no universally accepted satisfactory treatment. As in Western countries<sup>[1]</sup>, treatment approaches in China are also mainly focused on symptom management through lifestyle modification, psychotherapy and pharmacotherapy. The treatment objective is to maintain everyday functioning and improve quality of life. For clinical research, most of the performed clinical trials focused on the comparison between complementary and alternative medicines and on standard care with pharmacological therapies in treating IBS symptoms<sup>[11,20]</sup>. In the following sections, we will provide a brief description of treatment approaches commonly used in China to treat IBS.

### *Lifestyle modification*

The first treatment option normally adopted is lifestyle modification. Common lifestyle modifications include encouraging regular exercise, sharp reductions in drinking, dietary changes, abstinence from alcohol and coffee, and developing regular sleeping habits. Physical activity is frequently used as a primary treatment modality in IBS. This is based on the results of many published studies showing the benefits of physical activity for IBS. A recently published randomized controlled trial (RCT) involving 102 patients with IBS showed that those who were randomized to physical activity group had fewer IBS symptoms compared with the control group<sup>[21]</sup>. Other studies also indicated that physical activity can improve patients' moods and symptoms of fatigue, bloating and abdominal discomfort; regular physical activity can improve defecation patterns and colonic transit times in patients complaining of chronic constipation<sup>[11,22,23]</sup>.

Regarding dietary changes, one Chinese research group reported that certain foods could contribute to IBS symptom onset. After eliminating certain specific food from the diet, the symptoms were alleviated to some extent in IBS patients<sup>[24]</sup>. Other Chinese clinical researchers have also linked the causation of IBS to food through a number of mechanisms, such as an allergy or intolerance to a particular food<sup>[25,26]</sup>, which

**Table 1** Conventional pharmacological treatments for irritable bowel syndrome

Drug category	Drug functions	Examples
Antispasmodics	Antagonists of muscarinic receptors and calcium channels of smooth muscle	Pinaverium bromide, mebeverine, trimebutine maleate
Antidiarrheals	$\mu$ -opioid receptors agonists	Loperamide
Laxatives	Osmotic, stimulant	Bisacodyl, polyethylene glycol, lactulose
Bulking agents	Water binding to increase stool bulk	Methylcellulose, psyllium
Receptor targeted	5-HT <sub>3</sub> receptor antagonists	Alosetron, cilansetron
	5-HT <sub>4</sub> receptor agonists	Metoclopramide, domperidone
Probiotics	To balance intestinal flora	Lactobacilli, bifidobacteriae
Psychiatrics	Tricyclic antidepressants	Amitriptyline, doxepin
	Selective serotonin reuptake inhibitors	Citalopram, fluoxetine
Antibiotics	To inhibit gut microorganisms	Neomycin, rifaximin

is similar to results from a Western study by Brandt *et al.*<sup>[1]</sup>. Patients with IBS are advised to avoid fatty foods, beans and gas-producing foods that may contribute to symptoms of diarrhea, bloating and distension. For some patients with IBS-C, increasing the intake of foods high in soluble fiber can improve symptoms. Individual diet health management plans can be advocated<sup>[27]</sup>.

If such non-pharmacological measures are unsuccessful, pharmacologic interventions are then recommended.

### Psychotherapy

Psychological factors, such as certain depressive and anxiety disorders, play a role in the pathophysiology of IBS. Patients with IBS are more likely to have depression and "abnormal" behavior patterns, including anxiety and somatization symptoms<sup>[28]</sup>. In IBS patients, feelings of frustration, inadequacy and powerlessness in dealing with medically unexplained symptoms can also adversely affect both medical decision making and the physician-patient relationship.

Psychotherapies have been evaluated for their potential application in IBS. Patients, once diagnosed, should be educated and reassured about the non-life-threatening nature of the disease<sup>[14]</sup>. Mind-body therapies, such as hypnotherapy and cognitive-behavioral therapy, are effective in managing IBS symptoms<sup>[22]</sup>. Many Chinese clinical researchers are also focusing on psychological disturbances observed in IBS patients<sup>[14]</sup>. A study by Tang *et al.*<sup>[29]</sup> found that most IBS patients complained of nonspecific somatic symptoms, such as dizziness, insomnia and fatigue. A further study by the same group reported that in young and middle-aged patients (18-57 years), quality of life was negatively correlated with anxiety and depression, but it was not associated with the severity of abdominal pain/discomfort<sup>[30]</sup>. The use of non-drug treatments for IBS is popular with patients who are disappointed by their lack of response to standard drug treatment or concerned about its potential side effects. Therefore, only improving gastrointestinal symptoms may not improve quality of life<sup>[30]</sup>. Clinical evidence has demonstrated that the use of psychological interventions in conjunction with conventional treatment can improve IBS symptoms

and overall quality of life<sup>[26]</sup>.

### Pharmacotherapy

The available pharmacological approaches are mainly targeted at symptom reduction, as there is a wide range of the symptoms that may be experienced. These conventional pharmacological treatments include antispasmodics<sup>[31,32]</sup>, antidiarrheals<sup>[1,33]</sup>, laxatives or bulking agents<sup>[1,5]</sup>, 5-hydroxytryptamine-3 (5-HT<sub>3</sub>) receptor antagonists, 5-HT<sub>4</sub> receptor agonists<sup>[34]</sup>, probiotics<sup>[35]</sup>, tricyclic antidepressants<sup>[36]</sup>, selective serotonin reuptake inhibitors<sup>[37]</sup>, and antibiotics<sup>[38]</sup>. Antispasmodics plus stool consistency modifiers are usually the first-line drug treatment options to treat the major symptoms and defecation. Antidepressants are also commonly used for all subtypes of IBS. As gastrointestinal microbiota are thought to be involved in the pathogenesis of IBS, probiotics, when administered in adequate amounts, can sometimes be beneficial for the patient<sup>[39]</sup>. Table 1 summarizes the conventional pharmacological treatments for IBS in Western medicine<sup>[32]</sup>.

These pharmacotherapeutic treatments are widely used in China, as in Western countries. However, the use of these medications has been limited by side effects, expensive drug costs, and high recurrence rates. In order to reduce symptoms of IBS and improve the quality of life of patients, other more effective therapies with fewer side effects, such as TCM, should be considered.

### USE OF TCM FOR IBS IN CHINA

As a therapeutic discipline, TCM was derived and developed after many centuries of clinical practice and experience of traditional Chinese physicians. In China, many physicians consider TCM superior to the use of conventional Western medicine for IBS treatment<sup>[10,19]</sup>. Long-term clinical practice has accumulated rich experience and has perfected methods of employing TCM to treat the main symptoms of IBS<sup>[19]</sup>. Clinical evidence also shows that a combination of pharmacotherapy with TCM treatments provides the best symptom relief and highest quality of life for IBS patients<sup>[11,20]</sup>. According to the consensus of Chinese

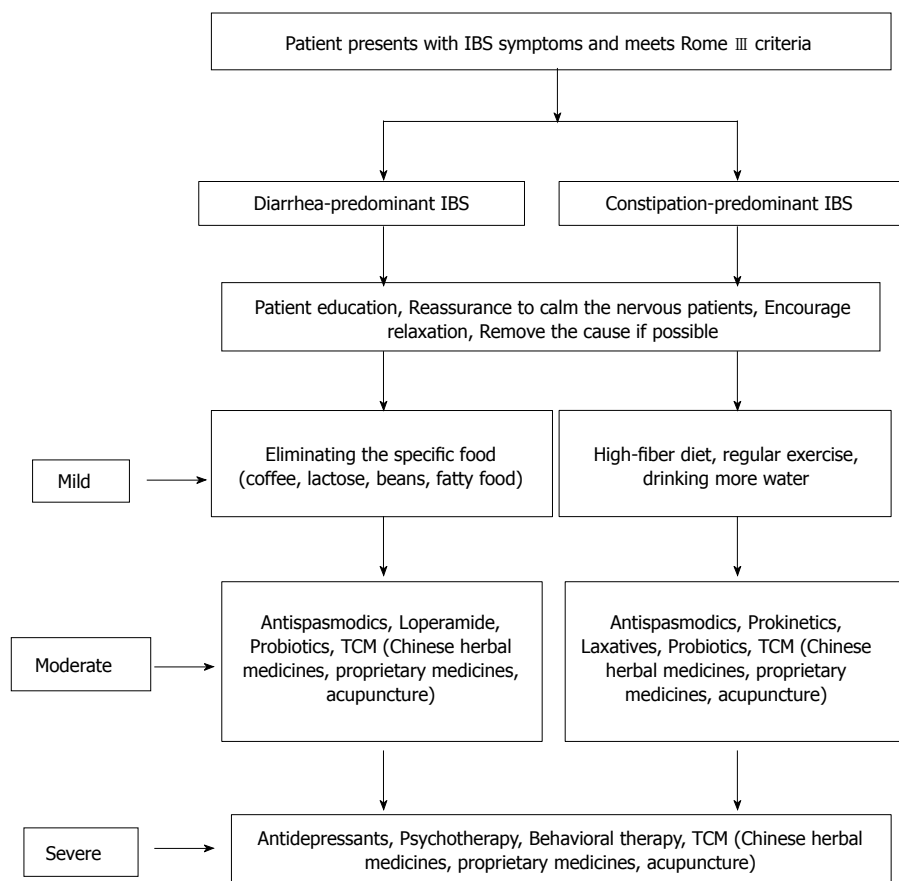


Figure 1 Flow diagram of the treatment of irritable bowel syndrome in China. IBS: Irritable bowel syndrome; TCM: Traditional Chinese medicine.

Society of Gastroenterology and the China Association of Integrative Medicine<sup>[40,41]</sup>, the recommended procedure to treat IBS in China is shown in Figure 1.

### Chinese herbal medicines and proprietary medicines

Unique Chinese herbal mixtures and proprietary medicines have been used in China for a long time. Based on low levels of satisfaction with pharmacotherapy in the management of IBS, an increasing number of patients and practitioners have turned to herbal therapies for symptomatic relief. In recent years, the study of Chinese herbal medicines in managing IBS has gained much progress in China<sup>[13]</sup>. Chinese proprietary medicines, usually formulated as tablets or capsules for convenient administration, are frequently used for patients with special syndromes. TCM represents one aspect of the Chinese medical philosophy, which is characterized by its emphasis on maintaining and restoring balance in the human body. When used appropriately, herbal medicine may provide benefits in relieving symptoms and reducing their recurrence<sup>[14]</sup>. According to the symptoms assessment in TCM, patients might be diagnosed to have the nature of “cold” or “heat”, and whether this nature is “in deficiency” or “in excess”. The syndrome differentiation can then effectively guide the clinical treatment of the individuals with TCM<sup>[19]</sup>. Chinese herbal medicines can then be prescribed for different individuals based on the differentiation of symptoms

according to traditional Chinese medicine diagnostic patterns. Hence, using Chinese herbal medicine is a strategy that provides the patient with individualized and comprehensive treatments<sup>[19]</sup>.

Clinical studies by Chinese researchers have been performed on a number of herbal products either as single herbs or as combined products in managing IBS. The trials showed a significant reduction in abdominal pain and severity compared to placebo, and the herbs appeared to be safe<sup>[42,43]</sup>. Studies also confirmed that Chinese Shugan Jianpi Granules, when compared with Western medicine, showed better efficacy in treating patients with IBS-D<sup>[12,44]</sup>. Another study demonstrated the beneficial effects of herbal Tongxie Yaofang (TXYF) Granules in alleviating abdominal pain and distention, restoring normal stool consistency, reducing the frequency of defecation, and improving mental tension and depression in IBS-D patients<sup>[8]</sup>. Furthermore, another Chinese group had performed a systematic review about the effectiveness of TXYF alone and with different Chinese herbal additions (*e.g.*, TXYF-A) in the management of IBS. They found that in the nine included studies, the TXYF-A group had better results than did the control group<sup>[9]</sup>. The evidence suggested that TXYF-A was useful and effective for IBS treatment. Another group retrieved literature from CNKI and screened effective medical records to establish a database using a structural electronic medical case

collecting system. The methods of Chinese physicians to diagnose and treat IBS were then analyzed. They found that liver depression and spleen deficiency were the main diagnoses of pathogenesis for IBS. Hence, diagnosis and treatment of IBS should be performed clinically according to this pathogenesis, with TXYF used as the basic prescription with modification according to syndrome differentiation<sup>[10]</sup>. According to the results of these studies, Chinese herbal formulas may offer improvements of IBS symptoms globally.

Although treating IBS with TCM appears to be effective, safety is certainly another concern with the use of herbal medicines, as TCM is not without adverse effects. Shi *et al.*<sup>[45]</sup> reviewed RCTs in the literature on IBS treatment with and without herbal medicine and found that herbal medicines had a therapeutic benefit in IBS with few adverse events. However, it is possible that because of the lack of rigorous monitoring, adverse effects including serious events may be under-reported. Hence, the side effects of Chinese herbal medicine such as liver toxicity and renal damage must be monitored. In addition, the long-term therapeutic effect as well as toxicity should be further observed through well-designed studies with larger samples<sup>[46]</sup>. Like using any therapy, clinicians should weigh the potential benefits and uncertainties when advising patients about using herbal medicines.

### Acupuncture

Acupuncture, a well-known old therapeutic modality anchored in TCM, has been used to treat several gastrointestinal symptoms in functional and organic diseases in China for centuries. Acupuncture can regulate visceral reflex activity, gastric emptying, and acid secretion through affecting various endogenous neurotransmitter systems. Studies have shown that the application of acupuncture targeting serotonergic, cholinergic, and glutamatergic pathways in IBS patients can increase the concentration of endogenous opioids, which in turn reduces visceral and global pain perception<sup>[47-49]</sup>.

A number of clinical trials investigating the effect of acupuncture on symptom relief in IBS patients have recently been conducted in China<sup>[50-52]</sup>. One clinical study on acupuncture to treat IBS-D patients with liver-stagnation and spleen-deficiency syndrome found that the clinical symptoms were improved after one week of treatment in the acupuncture group, which had a faster onset of effects than did the medicine treatment group. At the same time, the total effective rate was 90.48% in the acupuncture group compared with 78.95% in the medicine treatment group<sup>[50]</sup>. Another clinical study compared the therapeutic effects of electro-acupuncture with probiotics combined with Deanxit in treating IBS-D. The results indicated that both electro-acupuncture and Western medication could effectively treat IBS-D accompanied with anxiety and/or depression. However, while both groups showed

improvement in IBS symptoms, electro-acupuncture had better long-term therapeutic effects<sup>[52]</sup>. Likewise, a study by Li *et al.*<sup>[51]</sup> compared the therapeutic effects of acupuncture with Western medication on IBS-D symptom severity scores and quality of life scores and found a significant improvement in both scores over the course of four weeks as well as a remarkable reduction of the recurrence rate at 12 wk.

There were also meta-analyses evaluating the efficacy of acupuncture in managing IBS. A meta-analysis of 11 clinical RCTs with 969 patients through retrieval from CNKI and VIP showed the effective rate of acupuncture and moxibustion superior to conventional Western medication treatment<sup>[53]</sup>. Another meta-analysis of six RCTs also confirmed that acupuncture improved the symptoms of IBS, including abdominal pain and distension, sensations of incomplete defecation, times of defecation per day, and consistency of stool<sup>[54]</sup>. All these Chinese clinical trials and systemic reviews showed that acupuncture is beneficial and can achieve an improvement in quality of life for IBS patients. Furthermore, no serious adverse events associated with acupuncture were reported.

Acupuncture has gained increasing acceptance in Western medicine over the past few decades and is therefore an attractive treatment option for IBS. However, the efficiency of acupuncture in IBS is still inconclusive. Although Chinese trials reported greater benefits from acupuncture than from pharmacological therapies, other investigators from Western countries showed no significant differences after treatment with true or sham acupuncture. A recently published systematic review and meta-analysis of randomized controlled trials to estimate the effects of acupuncture for treating IBS found no benefits of acupuncture relative to a credible sham acupuncture control on IBS symptom severity or IBS-related quality of life<sup>[55]</sup>. Due to the conflicting conclusions between the meta-analyses conducted in China and in Western countries, further research is required to more accurately assess the efficacy and mechanism of action of acupuncture for IBS treatment. Future trials may help to clarify whether these reportedly greater benefits of acupuncture relative to pharmacological therapies are due entirely to patients' preferences for acupuncture or to patients' greater expectations of improvement with acupuncture relative to drugs<sup>[55]</sup>.

### Integrated traditional Chinese and Western medicine

In recent years, clinical investigators have paid more attention to integrated traditional Chinese and Western medicine. According to Chinese experts' opinion, the integration of conventional pharmacological therapy and TCM treatment may provide long-term symptom alleviation and highest quality of life to IBS patients.

In fact, the combination of TCM with Western medicine has been used for a long time by Chinese practitioners to treat IBS<sup>[10]</sup>. A number of clinical trials

as well as systematic reviews conducted and published in China have shown that the integrated approach is superior to either treatment alone<sup>[11,16-18,20,56]</sup>. These trials compared use of the combination of Chinese herbal medicines with Western medicine with use of Western medicine alone, and they used global improvement of symptoms as the main outcomes. A clinical study by Sun *et al.*<sup>[18]</sup> reported that TXYF combined with Trimebutine and Bifid Lriple Viable capsules were effective in treating IBS-D. Wu *et al.*<sup>[16]</sup> showed a statistically significant beneficial effect of using a Chinese medication called Anshen Ningchang Tang in combination with Trimebutine over Trimebutine treatment alone. A RCT study showed that Shugan Jianpi Granules, a Chinese herbal medication, reduced the number of gut mucosal serotonin-positive cells in patients with IBS-D, and its effect was enhanced when used in combination with conventional recognition-behavior therapy and symptomatic treatment by Western medicine<sup>[44]</sup>. Another Chinese study also reported a better efficacy of the combination use of psychotherapy and TXYF over TXYF alone<sup>[57]</sup>. All these studies provided evidence to support the efficacy of the combination of TCM with Western medicine in managing IBS. Conceptually, the use of combination therapy with TCM and Western medicine for IBS is in line with recommendation of using combination therapy by America College of Gastroenterology and the British Society for Gastroenterology<sup>[1]</sup>.

Recently, our research group evaluated the clinical efficacy of the combination of TCM and Western medicine in the treatment of IBS *via* a series of meta-analyses. Compared to the Western medicine treatment alone, our results showed that TCM combined with Western pharmacological interventions significantly improved global symptoms of IBS (RR = 1.21; 95%CI: 1.18-1.24). Moreover, the relapse rate was lower, and no serious adverse events were reported. These results would provide further evidence indicating that treating IBS with integrated traditional Chinese medicine with Western medicine showed better efficacy than treating with conventional Western medicine alone.

## CONCLUSION

Despite the wide range of available medications and the continuous development of new drugs, the management of IBS remains a challenge, and to date, no completely effective remedy is available. Compared to treatment options available to physicians in other countries, physicians from China have the additional options in the use of TCM, including Chinese herbal medicines and acupuncture, in addition to conventional medicines available to other countries to treat IBS based on the individual symptoms presented in each IBS patient. These strategies have produced beneficial effects, with lower adverse effects and lower reoccurrence rates. These additional treatment approaches from China may provide good options for

the best symptom relief and highest quality of life to IBS patients. Among these, the integration of Chinese herbal medicine with conventional Western medicine appears rather promising.

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