Irritable bowel syndrome: etiology, Pathophysiology, Diagnosis, and treatment

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Senior Research Paper

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Abstract

Objective: This article reviews the literature of Irritable bowel syndrome. Following the overview of epidemiology, etiology, symptomatology, pathophysiology, diagnosis and management, the emphasis was placed on the etiology and conservative management.

Data Sources: The information and studies reviewed were obtained from ChiroACCESS database, ChiroWeb database, EBSCO, Pub Med, Internet, Book and Lecture note.

Reference Selection: The references utilized were selected on the based of applicable information. Only articles published in English and within 10 years were undertaken. But only those that provided important insights or had high further-reading value on have been citied.

Conclusion: The etiology and pathophysiology with irritable bowel syndrome seem to be multifactorial. The mechanisms still remains uncertain. Current medical treatment protocols offer mostly temporary relief of symptoms with unwanted side effects. The conservative natural protocols such as nutrition, botanical medicine, mind-body medicine, exercise and Chinese herbal medicine etc. seem to be benefit to patients with irritable bowel syndrome. The lack of published, peer review documentation supporting the use of conservative care for the treatment of irritable bowel syndrome emphasizes the need for more researches in an attempt to qualify the efficacy of conservative care such as herbal medicine, mind-body medicine, nutrition and chiropractic care.

Introduction

The term "Irritable bowel syndrome" was probably first coined by Peters and Bargen in 1944 (1). Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain is associated with defecation or changes in bowel habit, and with features of disordered defecation and with distension, which are not explained by structural or biochemical abnormalities (33). The irritable bowel syndrome is probably the most common condition seen by gastroentrologists in the developed countries.

The patient's symptoms mainly are pain, bloating, and an altered bowel habit. The disease significantly reduces the quality of life and present huge healthy care problem (9).

The problems with irritable bowel syndrome are multifactorial, the patient is plagued with a disorder that is annoying at the very least and very disruptive to their quality of life in worst cases. The condition also causes multi-billion health care problems. A survey within the residents of Olmsted County, Minnesota done by Talley NJ; Gabriel SE; et al in 1995 reveal that the odds of incurring charges are 1.6 times greater in patients with irritable bowel syndrome having symptoms than those without symptoms.

Overall the average costs incurred by subjects with irritable bowel syndrome were $742 compared with $ 429 for controls and $614 for subjects with some symptoms but inadequate criteria for irritable bowel syndrome (34). The condition accounts for a proximately 2.4-3.5 million visits to doctors every year, and 2.2 million prescriptions are issued in United State (33). It is the second leading cause of work absenteeism in the U.S and brings great social

impaction (30).

Unfortunately, from doctor's point of view, the pathophysiology and etiology of irritable bowel syndrome is still unclear. It is also the frustration of a lack of well defined treatment protocol. The treatments of IBS ranging from allopathic treatment to alternative treatment have been shown to relieve symptoms with no cure. It is a great challenge for both health care professions and patients and not surprisingly no important advances in treatment will exist until the etiology and pathophysilogy are clear understood.

Description of Methology

An automated literature search was conducted using ChiroACCESS database which extends from 1996 to 2002. The subject heading of "irritable bowel syndrome" was entered and 17 records were founded. Then ChiroWeb database was used and "irritable bowel syndrome" was entered as a search phase. 53 matching results showed up. Another automated literature search was conducted using EBSCO host database and entered "irritable bowel syndromes" as searching phrase. 360 items were showed up through standard search. Pub Med database was utilized and put "irritable bowel syndrome" as searching phrase.254 items were displayed.

In addition to the above mentioned resources, five reference books and one Websites were found related to irritable bowel syndrome.

Total 694 resources were obtained. Only articles in English and publish within ten years were undertaken. Only those that provided important insights or had high value have been citied.

In summary 78 resources were undertaken. Among them, 70 articles including abstracts from referred journal, 5 reference books, 1 websites and 2 lecture notes.

Results and Discussion

Irritable bowel syndrome is described as a functional disorder of the gastrointestinal tract. Being a functional disorder, there is no objective evidence of structural change in those areas of the bowel demonstrating clinical symptomatology. The main symptoms are abdominal pain, altered bowel habit and abdominal bloating. The etiology of IBS remains unclear and the treatment is unsatisfactory.

Epidemiology

Irritable bowel syndrome is the most common functional bowel disorder encountered by physicians in primary care. In United State the condition account for 12% primary care. The condition affects about 10%-20% of the adult population in the industrialized world with similar prevalence in Europe, Australia, and Asia. Women with symptoms of the condition visit doctors more common than men, even though both of them have similar prevalence. The prevalence in people over 60 years old is lower. Near 30% of the patient become asymptomatic over time. Only a minority of people with more severe symptoms such as, abdominal pain, greater frequency or other non-gastrointestinal symptoms seek care for the condition (9, 33).

Etiology and Pathophysiology

Many researches and authors such as Talley,Nicholas J; Spiller, Robin and Michael J G Farthing indicated the pathogenesis factors are multifactorial: disruption of central mechanism, abnormal gut mobility and sensitivity, dietary factor, inflammation, psychological factors, genetics and environment. They

all play a part of roll in etiology and pathophysiology. Their importance varies from one patient to another (1, 33).

Altered brain activity: Disruption of central mechanism:

Some research done by Whorwell PJ, McCallum M and Talley Nj, Phillips SF found that patients with irritable bowel syndrome are often accompanied by altered smooth muscle activity, such as nausea, vomiting, early satiety in upper gastrointestinal tract, nocturia, urgency, feeling of incomplete emptying of the bladder, dispareunia in urinary system(35,36). These additional study invoke a hypothesis agreed by Michael J G Farthing that altered the brain activity that modulate the mobility and sensation of gastrointestinal system plays more important roles rather than primary end organ dysfunction in irritable bowel syndrome (33).

In fact several studies reported by Silverman DH, Munakata JA and Mertz H, Morgan V found directly the supportive evidences that comparing to normal people patients with irritable bowel syndrome have relative lower activity in anterior cingulate gyrus which functions to reduce sensory input, This fact well explains why patients have visceral hypersensitivity like abdominal pain, diarrhea, and feeling of incomplete rectal emptying (10, 11).

A recent study was done by Silverman DH; Munakata JA; et al in 12 subjects, half with irritable bowel syndrome. The effects of rectal pressure stimuli on regional cerebral blood flow were evaluated with positron emission tomography. The result showed in healthy subjects the blood flow in the anterior cingulated cortex was significantly related to pain perception and no anterior cingulated cortex response to the non-painful stimuli were seen whereas IBS subjects failed to response to the same stimuli and significant

activity of left prefrontal cortex was observed. The study concluded that patients with IBS have abnormal brain activation both in noxious and painful rectal stimuli (10).

Abnormal gut mobility and sensitivity:

It remains unknown that irritable bowel syndrome is the condition in which altered gut mobility is normally perceived or in which normal mobility is abnormally perceived (33).

It is reported by Ragnarsson G, Bodemar G more than 50% of the patients with irritable bowel syndrome show altered response to eating (37). Three types of bowel habits involved in irritable bowel syndrome were divided: 1) predominantly loose or frequent stools 2) predominantly hard or infrequent stool 3) variable or normal stools. They are all related to disturbed motor function to some extent (38). The study done by Chey WY, Jin HO revealed that patients with diarrhea-predominant symptom have increased sensitivity to cholecystokinin and an excessive response to eating which cause imbalance between mixing of motor patterns and excessive propulsive contraction pattern in gastrointestinal tract which may cause diarrhea symptom (39). Further based on Barrow L and Blackshaw PE study, loxiglumide, a cholecystokinin-1 antagonist, has been proved selectively slow the colonic transit movement in diarrhea- predominant subjects with irritable bowel syndrome (40). By contrast, Cann PA, Read NW, Brown C reported patients with constipation-predominant irritable bowel syndrome show fewer propulsive contraction and longer transit than those of diarrhea-predominant subjects after eating (41). Although altered mobility and transit time in small intestine and colon have been identified, many inconsistencies and

substantial overlap exist between measurements in control group and irritable bowel syndrome group. Michael J G Farthing believes it seems to be no pathophysiological marker existing in the colon and be difficult to suggest that the condition is due to altered gut mobility (33).

Several studies reported by Prior A, Maxton DG and Whitehead WE et al have indicated increased sensitivity to balloon distension of the rectum in subjects with irritable bowel syndrome (14, 42). One study done by Cook IJ et al found the increased sensitivity is not part of global, lower pain threshold as tolerance of cold and other painful stimuli produce either normal or reduced pain perception scores (43). Again not every research can reproduce these founding (44).

Dietary factors:

Many patients with irritable bowel syndrome have many symptoms often seen in dietary intolerance conditions such as, maldigestion, bloating, and abnormal transit over bowel. The most common causing foods seen are milk and wheat. Talley and Jeffer reported the exclusive diet has resulted in symptomatic improvement up to 50% of the patients with functional diarrhea (1, 9), but for a long term, most patients hardly can maintain such a good results.

Because many symptoms seen in lactose intolerance are similar to those with irritable bowel syndrome, it is thought that lactose intolerance may coexist with irritable bowel syndrome and lactose intolerance may exacerbate symptoms (9). The study done by Wahnschafe U et al found that patients with irritable bowel syndrome may have a subtle form of gluten intolerance characterized by normal villi but increased intraepithelial lymphocytes (45).

Also excessive ingestion of short-chain fatty acid many cause prolonged propagated contractions in the ileum and large amount of sorbitol or fructose may stimulate diarrhea and bloating (9).

Inflammation:

Almost 20% of patient with irritable bowel syndrome have an inflammation history, such as gastroenteritis, preceding the onset of symptoms. The inflammation processes produce inflammatory mediators including prostaglandins, bradykinins, 5-hydroxytryptamine, nerve growth factor, adenosine etc. Evidence reported by Hoey indicated these inflammation mediators cause organ hypersensitivity, exaggerated motor response and increase secretions, which lead to diarrhea syndrome (17, 18). Further study done by Dunlop SP, Jenkins D, Spiller RC. found increased serotonin-containing entero-endocine cell in patients with irritable bowel syndrome after infected by campylobacter and possible other organisms (46). 5-hydrixytryptamine released from these entero-endocrine cells play an very important role in primary intrinsic afferent neurons to initiate ascending excitation and descending inhibition. Camilleri M studies showed Alosetron, a serotonin antagonist, improve symptoms of diarrhea- predominant irritable bowel syndrome by delaying transit and relaxing the colon. (47)

Psychological factors:

Michael J G Farthing believes no gut pathophysiological or biochemical marker of irritable bowel syndrome exists and altered smooth muscle activity or hypersensitivity in other parts of the body strongly implicate that central nerve system plays an important role in irritable bowel syndrome(33). Even though the causal mechanism of irritable bowel syndrome and psychological

factors still remains unknown.

Many studies done by Delvaux M, Ali A and Drossman Da revealed some patients with irritable bowel syndrome reported a history of sexual, physical, or emotional abuse (48, 49, 50). The linkage between them is unknown. Talley NJ explained that such a history may be associated with another factor (e g. neuroticism), which predispose to irritable bowel syndrome (51). In addition Scarinci studies found the patients with irritable bowel syndrome who have been abused showed decreased pain thresholds and lower standards for judging noxious stimulus, which indicated increased organ sensitivity (52). Emotional factors can alter the gut function. Acute stress such as an interview or an examination can cause bowel frequency, nausea, vomiting, early satiety and urinary frequency. Heitkemper indicated that chronic sustained stressors such as separation and bereavement are probably more important than acute stresses in establishment of onset and persistence of symptoms in patients with irritable bowel syndrome (12). Compare to healthy people the subjects with irritable bowel syndrome had a significantly increased stress score (53). Another study by Gomborone JE reported that the consulters with irritable bowel syndrome had significantly higher anxiety and depression score than either non-consulters with irritable bowel syndrome or control healthy group. Sixty per cent of the consulters meet the diagnosis criteria of the Diagnostic and Satistical Manual of Mental Disorders. Among them were major depression (50%), anxiety disorder (43%), and dysthymia (7%) The consulters judged their own suffering to be more frequent, prolonged, sever and disruptive to daily living than the non-consulters (54). The exact mechanism of interaction between psychological factors and irritable bowel

syndrome is still unknown and warrant the further exploration.

Genetics and environment factors:

A few study by Locke GR and his colleagues suggested IBS tended to cluster in families (55). Studies by Levy RL et al and Morris-Yates A reported that the monozygotic twins have twice chance to get irritable bowel syndrome compared with dizygotic twins (56,57) and a few study by Woodman CL revealed that an increased prevalence of psychiatric disorders in relatives of patients with irritable bowel syndrome (58).

The environment factors may play more important role than genetic factors. An interaction between genetics and environment factors seems to be probable. The research done by Chan J, et al revealed that genes controlling downregulation of inflammation might be different in some subjects with irritable bowel syndrome, which could account for susceptibility to the irritable bowel syndrome after infection (59).

Symptomology and Diagnosis

The symptoms presenting clinical in irritable bowel syndrome may include some combinations of :1)abdominal pain; 2) altered bowel function; 3) colonic mucus hyper secretion; 4) symptoms of dyspepsia. 5) varying degrees of anxiety or depression or fatigue(15,16).

In the early stage irritable bowel syndrome was diagnosed by exclusion. In 1978 Heaton's research group in Bristol established Manning criteria.

Manning criteria:

1) Pain relieved by defecation

2) Looser stools at pain onset

3) More frequent stools at pain onset

4) Visible abdominal distension

5) Passage of mucus

6) Feeling of incomplete rectal emptying.

Based on an absence of organic disease on follow-up, presence of two or three symptoms, referred to as the Manning criteria.

Some experts disagreed on their use due to its lower validity especially in men and more symptoms present in the condition. In 1999 based on consensus-based approach, a group of international experts coined Rome 2 criteria as a standardization of entry criteria into clinical studies (1).

Rome 2 criteria:

Pain or discomfort for 12 weeks of the previous 12 months associated with two of the following three:

1) Relief with defecation

2) Looser or more frequent stools

3) Harder or less frequent stools.

Symptoms that cumulatively lend support to the diagnosis:

1) Abnormal stool frequency (more than 3 bowel movements per day and less than 3 bowel movements per week)

2) Abnormal stool form (lumpy/hard or loose/ watery)

3) Abnormal stool passage (straining, urgency, or feeling of incomplete rectal emptying)

4) Passage of mucus

5) Bloating or feeling of abnormal distension.

Some evidence suggests that inclusion of absence of alarm indications with

Rome criteria increase diagnostic certainty, with one report showing 100% specificity for the condition; although sensitivity was substantially lower (60).

Alarm indications that suggest organic disease is more likely than irritable bowel disease: (1)

1) Age of onset older than 50 years
2) Progressive or very sever or non-fluctuating symptoms
3) Nocturnal symptoms (e g, diarrhea, pain) waking the patient from sleep
4) Persistent daily diarrhea
5) Rectal bleeding or evidence of anemia
6) Unexplained weight loss
7) Recurrent vomiting
8) Positive family history of colon cancer
9) Fever
10) Abnormal physical examination (apart from mild abdominal tenderness), e g. skin rash, anemia, mouth ulcers, rectal mass, pain on tensing abdominal wall muscles

Most patients do not need extensive tests for organic diseases. A complete patient history and careful physical examination can give positive diagnosis of irritable bowel syndrome. A further test should be done unless there are alarm indicators or important conditions which may be confused with irritable bowel syndrome. Sigmoidoscopy is needed to rule out ulcerative colitis. Biopsy may be necessary in patients with predominant diarrhea to rule out collagenous or microscopic colitis. If patients are over 50 years old with new onset symptoms a colonoscopy or a double-contrast barium enema with sigmoidoscopy is indicated to check colon cancer. Any bleeding, anemia, weight loss,

steatorrhea, vomiting, fever and a family history of colon cancer require appropriate further examination.

For the laboratory work, a thyroid-stimulating hormone level should be measured to exclude hyperthyroidism (diarrhea) and hypothyroidism (constipation). Lactose intolerance test and lactose hydrogen breath test may be needed to rule out lactase deficiency. For severe acute abdominal pain a plain abdominal radiograph is necessary to check bowel obstruction or other pathological conditions. For female with mid-menstrual cycle pain and disturbed defecation, gynecological examinations are needed to exclude endometriosis or fibroids. Pelvic inflammatory disease should be considered if vaginal discharge is present (9).

Once a firm diagnosis has been made, subsequent testing has an extremely low yield and should not be undertaken unless symptoms have changed (9).

Management

Irritable bowel syndrome is pathologically characterized as a result of abnormal mobility, visceral hypersensitivity, and brain-gut deregulations. Therefore, a comprehensive approach to irritable bowel syndrome patient care should incorporate medications, nutrition and botanical medicine, behavioral modalities, as well as other therapies.

Medications:

The response to placebo is approximately 40%-70% in irritable bowel syndrome, in part due to the fluctuating nature of the condition and spontaneously improvement.

For patients with postprandial abdominal pain, antispasmodics or alternatives

such as hyoscyamine, belladonna dicyclomine are useful when taken 30-60 minutes before meals to reduce the gastrocolonic response. The side effects include dry mouth, blurred vision, and urinary retention.

For patients who do not respond to dietary fiber for treatment of constipation, lactulose or milk of magnesium may helpful. Misoprostil, a prostaglandin analogue, is very useful in sever cares but commonly induce diarrhea.

Stimulant Laxatives have potential side effects such as water and electrolyte loss and damage to the colonic menteric plexus, therefore should be avoided.

Loperamide and bile acid-sequestering agent such as cholestyamine is used to treat diarrhea.

Activated charcoal can reduce flatus after lactulose challenge in normal individuals. Tricyclic antidepressants are particularly useful in resistant patients or patients with chronic pain (9, 32).

As mentioned above, Medications used in irritable bowel syndrome treatment have some side effects. Drugs must be prescribed sparing in irritable bowel syndrome treatment based on necessity (9).

Nutrition and botanical medicine:

<u>High dietary fiber intake:</u>

High fiber diets are commonly recommended. (61) A high fiber intake is proved to be efficacy for constipation in irritable bowel syndrome. Several studies indicated that role of fiber in gastrointestinal tract include delaying gastric emptying, slowed small bowel transit, decreased colonic transit time because of the water holding capacity, viscosity or gel-forming capacity, bulking capacity and bacterial fermentation of fiber (61, 62). A research done by A.P. Manning found after six weeks controlled trial with high or low wheat

fiber in twenty-six IBS patients, there was significant improvement in symptoms and objective change in colonic motor activity in high fiber group and no such changes occurred on low fiber regimen. This indicated increased fiber diet might only beneficial to patients with low fiber diet (63). However, several double-blind studies failed to find supportive evidence that addition of bran to the diet improved symptoms (64). In a survey of 100 patients, 55% subjects reported that wholemeal wheat and bran products made symptoms worse, while only 10% of subjects stated them better. Among the sources of fiber, citrus fruit may be the most offenders while proprietary fiber products (e g. psyllium) demonstrated some improvements, with 39% of patient improvement and 22% worse. These negative finding may be caused by some patients react adversely to certain dietary fibers (65). Patients with irritable bowel syndrome vary in their response to fiber diets. The dose of dietary fiber should be individually adjusted to each patient's response.

Avoid refined carbohydrates and sugar

Refined carbohydrates decrease the physical buffering function of fecal bulk due to lack of dietary fiber, subsequently, provokes smooth muscle spasm (66). The survey done by Jarret GM et al. reported that comparing 18 women having irritable bowel syndrome with 37 normal controls, a high intake of refined carbohydrates may contribute to irritable bowel syndrome, while calorie, fat, and protein intakes were designed to be silimar (67).

Dietary sugar may contribute to the irritable bowel syndrome too. For instance, sucrose increases bile acid concentrations, decreases intestinal transit time and increases bacteria fermentation, all of which induce the risk of irritable bowel syndrome (69). Fernandez-Banares investigated sugar malabsorption

by using breath hydrogen test. They found 96% of irritable bowel syndrome patients suffered at least one sugar malabsorption and ingestion of that sugar induced irritable bowel syndrome symptoms and signs (68).

Limit dietary fat

Sjolund K et al found the patients with IBS showed excessive and prolonged release of cholecystokinin after ingestion of a fatty meal (70). In addition, Kellow JF et al. reported a small intestinal infusion of a dietary fat decreases intestinal mobility in patients with irritable bowel syndromee and accompanied by abdominal symptoms and signs (71).

Rule out food sensitivities

Food sensitivities induce problems in about 2/3 of irritable bowel syndrome patients. The most common causing foods seen are dairy (40-44%) and grains (40-60%) (75). The exclusive diet has resulted in symptomatic improvement up to 50% of the patients with functional diarrhea (1, 9), but for a long term, most patients hardly can maintain such a good results.

Add probiotic supplement

Lactobacillus acidophilus has been found to effective in irritable bowel syndrome symptom relief, and its effectiveness has been confirmed in a double-blind crossover study even though it may takes several weeks or months (9, 73, 74). The mechanism of action is not sure; the benefits of L acidophilus could be due to its antimicrobial activity when patients have undiagnosed chronic intestinal infections

Botanical medicine

Botanical supplements should be selected based on the nature and location of the patient's symptoms. Teas are best for upper gastrointestinal complaints

while capsules are best used for lower gastrointestinal symptoms.

Carminatives (e g. peppermint, Ginger, Fennel, German chamomile etc.) can relax smooth muscle and reduce abdominal spasms. Several studies showed that peppermint could increase digestive function, relieve nausea, and relax smooth muscle spasm (76, 77).

Bulking agents (e g. Linseed, Psyllium seed and Husk, Wheat Bran etc.) and osmotic Agents (e g. Cascara, Senna pods and leaves) are useful for patients with constipation. Teas made from the dried leaves of berry bushes are commonly used for diarrhea-prediminant irritable bowel syndrome.

Demulcents serve to coat mucosal surface, thereby decreasing inflammation (19, 31).

Other

Increasing Vitamin C, copper and taurine, at least 6-8 glass water per day is necessary. Pantothenic acid and zinc are the gastrointestinal nutrients.

Taking 100mg magnesium every several hours or liquid Ca/Mg is excellent for irritable bowel syndrome. If patient's stools get loose, cut down the dosage (3, 13, 21, 22).

Mind-body medicine and exercises:

Many of patients with irritable bowel syndrome experience an episode of significant stress and anxiety that makes their symptom even worse. Mind-body treatment lays emphasis on patient self-awareness of symptom causing factors and acquiring skills to enhance self-regulation. Cognitive behavioral therapy, interpersonal/dynamic therapy, biofeedback, hypnotherapy and guided imagery, stress management/relaxation training etc. these are

commonly chosen to best match the patient's lifestyle and belief structure (78, 79).

Light to moderate exercises is encouraged for all patients. Physical activity can reduce psychological stress, lessen depression and anxiety and enhance physiological function. One study showed that Yoga is effective in reduction of abdominal pain and irritable bowel syndrome (24).

Chiropractic treatment:

There are not many studies done about chiropractic treatment for irritable bowel syndrome. However several case studies reported chiropractic treatment of bowel dysfunction.

Wagner described a 25 years old female patient with 5 years irritable bowel syndrome history, after chiropractic adjustment in upper cervical and thoracolumbar region the patient reported complete symptom free (26). Two case studies described effectiveness of chiropractic care in constipation treatment of 7-month infant, and 5 years old female (27,28). The another case study suggest that chiropractic adjustment may be effective in treating bowel and bladder dysfunction secondary to lumbar dysfunctional syndrome (29). It is believe that chiropractic manipulation is through somatovisceral reflex pathway to relive symptoms in person with irritable bowel syndrome (19).

Chinese Herb Medicine

Chinese herb medicine has been used for centuries in treatment of functional bowel disorders. The mechanism of action still remains uncertain. Although

several Chinese studies suggest the potential effectiveness of Chinese Herbal Medicine for irritable bowel syndrome treatment, to date, no strong scientific evidence supports the use of Chinese herbal agents in irritable bowel syndrome treatment. There is a randomized, double blind, placebo-controlled study done in 1998 by Alan Bensoussan et al during 1996 to 1997. The study found that comparing to placebo group, the IBS group treated with Chinese Herbal Medicine had significant improvement in IBS score. Chinese herbal formulations individually tailor to the patient showed no more effective than standard CHM treatment (appendix A). On following-up 14 weeks after completion of the treatment, only the individualized CHM treatment group maintained improvement. The study reached conclusion that Chinese herbal medicine appear to offer improvement in symptoms for some patients with IBS (23).

Summary

A lack of awareness and education on the part of the health care profession can Lead to a misdiagnosis for those suffering from the symptoms of irritable bowel syndrome. The etiology and pathophysiology is still poorly understood and current medical treatment offer mostly temporary relief of symptoms with unwanted side effects.

The lack of documentation supporting the use of conservative care for the treatment of irritable bowel syndrome emphasize the need for more research in an attempt to qualify the efficacy of conservative cares such as chiropractic care, body-mind medicine,exercise, nutrition and herbal.

Appendix A

Standard Formula (capsule Ingredients)

Chinese Name	Pharmaceutical Name	Powder Herb (%)
Dang Shen	Codonopsis pilosulae, radix	7
Huo Xiang	Agastaches seu pogostemi, herba	4.5
Fang Feng	Ledebourielle sesloidis, radix	3
Yi Yi Ren	Coicis lachrymal-jobi, semen	7
Chai Hu	Bupleurum Chinense	4.5
Yin Chen	Artemesiae capillaries, herba	13
Bai Zhu	Atractylodis macroaephalae, rhizome	9
Hou Po	Magnoliae officinalis, cortex	4.5
Chen Pi	Citri reticulatae, pericarpium	3
Pao Jiang	Zingiberis offinicinalis, rhizome	4.5
Qin Pi	Fraxini, cortex	4.5
Fu Ling	Poriae cocos, sclerotium (hoelen)	4.5
Bai Zhi	Angelicae dahuricae, radix	2
Che Qian Zi	Plantaginis, semen	4.5
Huang Bai	Phellodendri, cortex	4.5
Zhi Gan Cao	Glycyrrhizae uralensis, radix	4.5
Bai Shao	Paeoniae lactiflorae, radix	3
Mu Xiang	Saussureae seu vladimirae, radix	3
Huang Lian	Coptidis, rhizome	3
Wu Wei Zi	Schisandrae, fructus	7

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