



Review Article

Update in diagnosis and management of irritable bowel syndrome

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ABSTRACT

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by a lack of structural or biochemical abnormalities. The current diagnosis of IBS is based on the Rome IV criteria, and it is recommended to approach IBS patients using a multidimensional clinical profile (MDCP). The pathophysiology of IBS is multifactorial and involves motility disorders, genetic factors, immune responses, visceral hypersensitivity, brain-gut dysregulation, and altered intestinal microbiota. The management of IBS includes both nonpharmacologic and pharmacologic therapies. Nonpharmacologic therapy options include physical activity, low fermentable oligosaccharides, disaccharides, monosaccharides, and polyol diet, as well as cognitive behavioral therapy. Pharmacologic therapy options include probiotics, antidepressants, antispasmodics, and new agents. In clinical practice, a multidisciplinary strategy, including nonpharmacologic or/and pharmacologic treatment for IBS, is emphasized. Therefore, clinicians should carefully consider the underlying pathophysiology before selecting an appropriate therapeutic option for the treatment of IBS. In other words, individualized treatment plans are necessary for managing IBS.

KEYWORDS: *Irritable bowel syndrome, Management, Pathophysiology*

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by symptoms such as abdominal pain or discomfort and changes in bowel habits, including stool consistency or frequency. These symptoms occur without any detectable structural or biochemical abnormalities. IBS is more commonly seen in females and younger individuals. A recent meta-analysis report indicated that the global prevalence of IBS was 9.2% based on the Rome III criteria and 3.8% based on the Rome IV criteria [1]. Interestingly, a recent epidemiological study from Taiwan showed a decreasing trend in the incidence and prevalence of IBS from 2012 to 2018 [2]. However, it is important to note that these data were obtained from the National Health Insurance Research Database using the ICD-9 coding, rather than based on the Rome criteria, raising doubts about the accurate diagnosis of IBS.

IBS has a significant impact on health-related quality of life and is often accompanied by psychological comorbidities such as anxiety and depression [3-6]. In Taiwan, female IBS patients with a history of sexual abuse had a higher prevalence of anxiety, depression, and sleep disturbances [7]. Furthermore, IBS results in substantial direct and indirect costs worldwide [8]. IBS patients often visit doctors more frequently and undergo extensive diagnostic investigations [9,10]. They

also experience increased absenteeism and impaired work productivity [11,12]. Therefore, it is crucial to enhance our understanding of IBS, as this can help reduce unnecessary medical examinations and provide better care for patients.

PATHOPHYSIOLOGY

Biopsychosocial model

Drossman DA first introduced a biopsychosocial model to enhance our understanding of this condition [13]. This model emphasizes the interconnections among biology, cognition, behavior, and the environment. Figure 1 illustrates how these factors interact and contribute to the development of IBS.

Visceral hypersensitivity and brain-gut axis dysregulation


IBS patients exhibit lower pain thresholds in their colon compared to healthy controls, as evidenced by several studies [14-17]. These studies have demonstrated that IBS patients have lower sensory thresholds during rectal balloon distension. In addition, a meta-analysis study revealed that IBS patients display an increased activation of the brain regions associated with emotional arousal and endogenous

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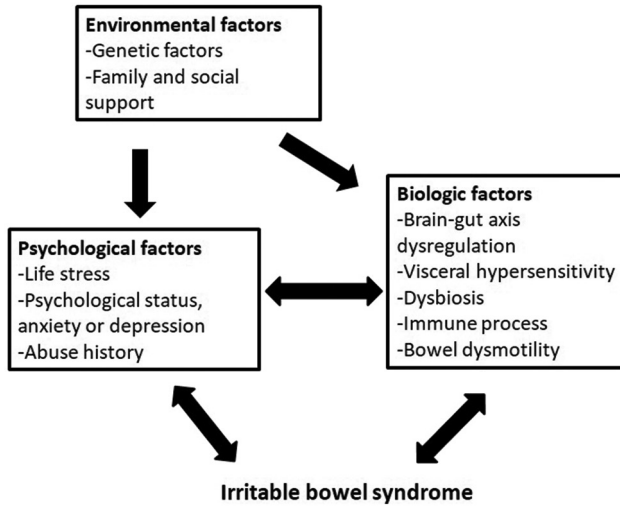


Figure 1: The biopsychosocial model of irritable bowel syndrome

pain modulation in response to rectal balloon stimulation, in comparison to healthy controls [17]. Therefore, the brain's processing of noxious stimuli from the gut and the bidirectional communication between the brain and gut are crucial factors in the pathophysiology of IBS. Furthermore, several studies have indicated a high prevalence of comorbid anxiety and depression disorders among individuals with IBS [3,18-20].

Gastrointestinal microbiota

Postinfectious IBS has been considered one of the etiologies of IBS. As a result, altered fecal microbiota has been proposed as one possible cause of IBS [21-24]. In a systemic review, Pittayanon *et al.* showed that IBS patients had increased an abundance of family *Enterobacteriaceae* (phylum *Proteobacteria*), family *Lactobacillaceae*, and genus *Bacteroides*, but a decreased abundance of uncultured *Clostridiales* I, genus *Faecalibacterium* (including *Faecalibacterium prausnitzii*), and genus *Bifidobacterium* [25].

Bowel dysmotility

Altered bowel transit is a distinctive feature observed in different subtypes of IBS. For example, diarrhea-predominant IBS (D-IBS) is characterized by rapid bowel transit, whereas constipation-predominant IBS (C-IBS) is associated with sluggish bowel transit [26]. Serotonin (5-HT) in the bowel plays a multifaceted role in regulating motor and sensory functions through the enteric nervous system, thereby influencing intestinal motility [27,28]. Plasma levels of 5-HT vary between D-IBS and C-IBS, with higher levels detected in D-IBS and lower levels observed in C-IBS [29,30].

Immune process

IBS patients exhibit distinct immune system characteristics compared to healthy controls, including cytokine imbalances, immune cell activation, and increased gastrointestinal membrane permeability. A meta-analysis study revealed that IBS patients had elevated levels of the pro-inflammatory cytokine tumor necrosis factor- α , while the levels of the

anti-inflammatory cytokine interleukin (IL)-10 did not show significant differences [31]. Moreover, IBS patients demonstrated an increased presence of inflammatory cells in the intestinal mucosa, indicating a potential state of low-grade inflammation. In addition, IBS patients exhibited heightened gastrointestinal membrane permeability. Colonic mucosal mast cell counts and increased membrane permeability were found to be correlated with abdominal pain and disease severity [32].

Genetic factors

IBS may have a genetic component, as indicated by twin studies that have demonstrated a higher concordance rate in monozygotic twins compared to dizygotic twins [33-35]. Among the genes investigated, the serotonin transporter gene polymorphism (5-HTTLPR) has been one of the most extensively studied in relation to IBS [36-39]. However, the findings of these studies have yielded conflicting results [37].

DIAGNOSIS

The current diagnosis of IBS is based on the Rome IV criteria [40,41]. According to these criteria, patients must experience recurrent abdominal pain, occurring at least once per week for the past 3 months, with symptom onset at least 6 months before diagnosis. The pain should be associated with two or more of the following: changes in defecation, stool frequency, or stool appearance (form). It is also important to employ a multiple dimensional clinical profile (MDCP) approach when treating IBS patients [42]. Before diagnosing IBS, it is crucial to thoroughly investigate warning signs [43]. These include the onset of symptoms after the age of 50, unintentional weight loss, overt gastrointestinal bleeding, recent changes in bowel habits, palpable abdominal mass or lymphadenopathy, and a family history of colon cancer or inflammatory bowel disease.

Based on the predominant bowel habits during days with abnormal bowel movements, IBS can be classified into four subtypes: D-IBS, C-IBS, mixed (M-IBS), and unclassified (U-IBS). The diagnostic criteria for IBS according to the Rome III and Rome IV are provided in Table 1 [44]. In the Rome IV, the term "abdominal discomfort" has been omitted from the definition due to its imprecise nature. Abdominal pain should occur at least once per week during the past 3 months. The phrase "improvement with" defecation has been revised to "related to" defecation as some patients may experience an increase or maintenance of pain. In addition, the term "onset" has been removed from the associated changes in stool frequency and appearance.

The sensitivity and specificity of the Rome IV criteria are 62.7% and 97.1%, respectively, while those of the Rome III criteria are 73.1% and 93.1%, respectively [45]. The estimated prevalence of IBS is significantly lower when using the Rome IV criteria (5.7%) compared to the Rome III criteria (10.7%) [45]. This aids in identifying true IBS patients and avoiding overdiagnosis.

MANAGEMENT

Table 2 presents the treatment strategies for IBS.

Table 1: The Rome III and Rome IV diagnostic criteria for irritable bowel syndrome

Rome III	Rome IV
Recurrent abdominal pain or discomfort at least 3 days/month associated with two or more of the following criteria	Recurrent abdominal pain at least once/week associated with two or more of the following criteria
Improvement after defecation	Related with defecation
Onset associated with a change in the frequency of stool	Associated with a change in the frequency of stool
Onset associated with a change in the form (appearance) of stool	Associated with a change in the form (appearance) of stool
Symptoms onset at least 3 months in the past 6 months	

Table 2: Treatment strategies for irritable bowel syndrome

Nonpharmacologic	Pharmacologic
Patient reassurance and education	First-line
	Antidiarrheals (D-IBS)
Stress management	Laxatives (C-IBS)
Low-FODMAP diet	Antispasmodics
Probiotics	Antidepressants (TCAs and SSRIs)
Physical activity	Second-line new agents
	Linaclotide (C-IBS)
	Rifaximin (D-IBS)
	Eluxadoline (D-IBS)
	Asimadoline (D-IBS)

FODMAP: Fermentable oligosaccharides, disaccharides, monosaccharides, and polyol, D-IBS: Diarrhea-predominant irritable bowel syndrome, C-IBS: Constipation-predominant irritable bowel syndrome, TCAs: Tricyclic antidepressants, SSRIs: Selective serotonin reuptake inhibitors

Dietary and lifestyle advice

Patient reassurance and stress reduction

IBS is a benign disease without a reduction of life expectancy or any correlation with the development of organic diseases [46]. Therefore, patient education and reassurance are warranted, and these will ease their anxiety. A positive patient–physician relationship can improve symptom control [46]. Stress reduction also has been shown beneficial effects on IBS symptoms [47,48].

Low fermentable oligosaccharides, disaccharides, monosaccharides, and polyol diet

The low fermentable oligosaccharides, disaccharides, monosaccharides, and polyol (FODMAP) diet involve reducing the consumption of poorly absorbed short-chain carbohydrates and low gas-producing foods. Unabsorbed fructose, polyols, and lactose can increase small intestinal water content, while indigestible fructans and galacto-oligosaccharides may lead to microbial fermentation in the colon, triggering symptoms in IBS patients [49]. The low FODMAP diet is a dietary therapy that should be supervised by a nutritionist. Halmos *et al.* demonstrated that a low FODMAP diet can improve bloating, abdominal pain, and flatulence in IBS patients [50]. In a recent meta-analysis of 13 randomized controlled trials (RCTs), a low FODMAP diet was found to be the most effective dietary therapy for reducing abdominal pain severity and abdominal bloating in IBS patients [49]. Ideally, the low FODMAP diet

should be followed for 4–6 weeks, as long-term restrictions may increase the risk of inadequate nutrition.

Probiotics

Probiotics have been shown to have a beneficial effect on global symptoms, abdominal pain, bloating, and flatulence in IBS patients [51]. However, the specific species and strains of probiotics that are most effective for treating IBS remain uncertain.

Physical activity

In 2011, Johannesson *et al.* reported that physical activity can improve symptoms of IBS [52]. IBS patients experienced relief from abdominal distress and extracolonic symptoms after engaging in 12 weeks of physical activity. Their subsequent study revealed the long-term positive effects of physical activity on IBS symptoms [53].

Pharmacological treatments

Antidiarrheals and laxatives

Basically, we can choose drugs according to the predominant symptoms of IBS. For instance, antidiarrheals including loperamide and bile acid sequestrants such as cholestyramine were prescribed for D-IBS, while laxatives were used for C-IBS [54]. Treatment goals targeted to decrease the symptoms and improve the quality of life. Therefore, these medications could be temporarily stopped and should be evaluated if patients still needed them.

Antispasmodics

Antispasmodics are smooth muscle relaxants that act on the gastrointestinal tract, including antimuscarinic, anticholinergic agents, and calcium channel blockers. They can improve symptoms of IBS, particularly relieving cramping distress, due to their spasmolytic effects. Ford *et al.* demonstrated that antispasmodics, specifically otilonium and hyoscine, can improve IBS symptoms [55]. In Taiwan, Chang *et al.* revealed that otilonium is as effective as mebeverine in improving IBS symptoms, including abdominal pain, flatulence, and bloating [56].

Tricyclic antidepressants and selective serotonin reuptake inhibitors

Due to the pathophysiology of IBS mentioned earlier, antidepressants such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have been shown to have pain-modulating effects on both the central and peripheral nervous systems [57,58]. In a systematic review and meta-analysis conducted by Ford *et al.*, it was found that both TCAs and SSRIs can alleviate IBS symptoms, with an estimated number needed to treat of 4.5 and 5, respectively [59]. The most commonly reported adverse effects of these antidepressants are drowsiness and dry mouth.

Second-line new agents

Rifaximin is a nonsystemic antibiotic that possesses gut-modulatory and anti-inflammatory effects [60]. In May 2015, it was approved by the US Food and Drug Administration for the treatment of D-IBS. Several studies have demonstrated its efficacy and safety profiles [61-64]. Linaclotide, a guanylate cyclase-C agonist, acts as a secretagogue in the

gastrointestinal tract. Some studies have shown its beneficial effects on C-IBS [65-68]. Eluxadoline and asimadoline, both targeting opioid receptors, are utilized for the treatment of D-IBS [69-73]. However, it is important to note that these newer agents are currently not available in Taiwan.

Psychological intervention

Cognitive behavioral therapy (CBT) is a psychological therapy that incorporates various components, including psychoeducation, relaxation strategies, cognitive restructuring, problem-solving skills, and exposure techniques [74]. A meta-analysis and systematic review of 20 RCTs demonstrated that CBT can improve gastrointestinal symptoms in both short-term and long-term for individuals with IBS [75]. However, the widespread use of CBT is limited due to the scarcity of well-trained gastrointestinal psychology therapists. In Taiwan, Internet-delivered CBT for young female IBS patients showed a positive impact on reducing anxiety and depression, although it did not have a significant effect on IBS symptoms [76].

CONCLUSIONS

IBS is a complex disease with no specific etiology. The possible pathophysiological mechanisms include visceral hypersensitivity, dysregulation of the brain-gut axis, dysbiosis of intestinal microbiota, bowel dysmotility, immune responses, and genetic factors. The biopsychosocial model provides a comprehensive framework for understanding this disease. In clinical practice, a multidisciplinary approach that incorporates nonpharmacological and/or pharmacological treatments is emphasized for managing IBS. Therefore, health-care providers should carefully consider the underlying pathophysiology before selecting an appropriate therapeutic option. In other words, individualized treatment plans are necessary for effectively managing IBS.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

There are no conflicts of interest.

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