REVIEW ARTICLE

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Irritable Bowel Syndrome: Epidemiology, Etiopathogenesis and Current Treatment Approaches

Abdullah Ozan Polat[1*], Mustafa Sevindik[2]

[1] *Department of Family Medicine, University of Health Sciences, Gaziosmanpaşa Training and Research Hospital, Istanbul, Türkiye.*
[2] *Department of Biology, Engineering and Natural Sciences Faculty, Osmaniye Korkut Ata University, 80000 Osmaniye, Türkiye.*

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ABSTRACT: Irritable Bowel Syndrome (IBS) is a common and chronic gastrointestinal disorder involving interactions between the gut and the brain. IBS is characterized by symptoms such as recurrent abdominal pain, changes in bowel habits, and bloating. Although the etiopathogenesis of the disease is not fully understood, it is known that changes in the gut microbiota, low-grade inflammation, visceral sensitivity, and gut-brain axis dysfunction play an important role. The ROME IV criteria are used as the basis for the diagnosis of IBS, and the duration and characteristics of the symptoms are among the main determinants. IBS is clinically divided into four subtypes: predominantly constipated (IBS-C), predominantly diarrheal (IBS-D), mixed type (IBS-M), and unclassifiable (IBS-U). Treatment approaches are individualized and include various methods such as dietary and lifestyle changes, pharmacological treatments, and therapies targeting the gut microbiota. In recent years, studies on the effectiveness of gut microbiota-based treatments and neuromodulatory drugs in the management of IBS have increased. Additionally, peppermint oil, Iberogast, and other herbal products are increasingly being investigated for their potential benefits in relieving IBS symptoms. This review aims to comprehensively address the pathophysiology, clinical features, diagnostic criteria, current treatment approaches, and the role of herbal therapies in IBS.

Keywords: Irritable Bowel Syndrome, gut-brain axis, microbiota, ROME IV, treatment, herbal treatment

INTRODUCTION

Irritable Bowel Syndrome (IBS) is a common and chronic gastrointestinal disorder involving interactions between the gut and the brain. Clinically, it is characterized by recurrent abdominal pain and irregular bowel habits. The ROME IV criteria, developed by an international group of experts in the diagnosis and management of gastrointestinal dysfunction, are used as a clinical guide for the diagnosis of IBS and similar disorders (Ford et al., 2014). To establish the diagnosis, the patient must have abdominal pain at least one day per week for at least three months, and this pain must be associated with defecation and show changes in the frequency or consistency of defecation. Bloating is commonly reported in IBS patients, but is not considered a mandatory criterion for diagnosis (Drossman et al., 2016).

Irritable Bowel Syndrome (IBS) affects approximately 10-20% of the population worldwide. Regional differences are observed, with the highest prevalence rate reported in South America at 21%. However, limited epidemiological data on IBS in many countries make it difficult to make a comprehensive assessment of the global prevalence of the disease (Ford, 2020).The prevalence of IBS in the United States has been reported to be higher than previous estimates and is 6.1% (Almario et al., 2023). Epidemiological studies conducted in Turkey have shown that IBS is more common in women, with prevalence rates ranging from 6.2% to 19.1% (Karaman et al., 2003).

ETIOPATHOGENESIS

Irritable bowel syndrome (IBS) is defined as a functional disorder of the gastrointestinal tract and is characterized by abdominal pain, bloating, and changes in bowel habits without an anatomical defect (Karantanos et al., 2010; Lee et al., 2014). Although the pathophysiology of IBS is complex and not fully understood, several factors are known to contribute to this condition (Barbara et al., 2004; Karantanos et al., 2010; Lee et al., 2014). Visceral tenderness, abnormal intestinal motility, and brain-gut interaction are among the classical pathophysiological concepts of IBS. In addition, new areas of research such as genetic factors, diet, gut microbiota, low-grade inflammation, and intestinal endocrine cells also contribute to the pathophysiology of IBS (Lee et al., 2014; El-Salhy, 2015; El-Salhy, 2020).

Alterations in the gut microbiota and low-grade inflammation play an important role in IBS, especially after infection (Barbara et al., 2004; Ng et al., 2018). It is thought that the decreased density of intestinal endocrine cells in IBS patients, genetic factors, diet, and factors such as gut microbiota may affect the regulatory signals of these cells, leading to gastrointestinal motility

*ozanpolat1987@gmail.com

and secretion disorders (El-Salhy, 2015; El-Salhy, 2020). In addition, the presence of autoantibodies and immune activation may play an important role in the development of IBS (Zhang et al., 2024).

The pathophysiology of IBS is a complex process based on multifactorial interactions, and many new research areas are currently conducting studies to better understand these mechanisms. The roles played by dysbiosis in the intestinal microbiota, increased intestinal permeability, and immunological factors in IBS are becoming increasingly important. In particular, disruptions in the intestinal epithelial barrier and dysregulation of the mucosal immune response are among the notable mechanisms in the pathogenesis of IBS.

Recent studies have shown that the interaction between the intestinal microbiota and the brain-gut axis may be decisive not only on gastrointestinal symptoms but also on the psychological symptoms (anxiety, depression) accompanying IBS (Peppas et al., 2021). The effects of microbiota-derived metabolites, especially short-chain fatty acids (SCFA) and tryptophan derivatives, on neuroinflammation and intestinal motility have been observed in different ways in IBS patients (Banfi et al., 2021).

In addition, recent genome-wide association studies (GWAS) have identified some genetic variants associated with IBS and have shown that genes associated with neurotransmitter regulation in particular may be effective in the pathophysiology of IBS (Camilleri and Katzka, 2012; Gros et al., 2021). These findings suggest that IBS is not a disease limited to the intestines, but should also be considered as a neuro-gastroenterological disorder. In the future, individualized medicine approaches, microbiota-based therapies, and pharmacological and neuromodulatory treatments targeting the gut-brain axis may offer more effective and targeted approaches in the management of IBS. In this direction, a better understanding of the gut microbiota and immune response will help to more clearly define the place of treatment options such as probiotics, prebiotics, and fecal microbiota transplantation in the treatment of IBS.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

There is no definitive test for diagnosing IBS. Diagnosis begins with a comprehensive medical history, physical examination, and tests. The ROME IV criteria should be questioned (Palsson et al., 2020).

"Current ROME IV criteria are used for diagnosing IBS."

Diagnostic Criteria

Recurrent abdominal pain must occur at least once a week for the past three months on average and must be accompanied by two or more of the following criteria:

1. Associated with defecation

2. Associated with a change in defecation frequency

3. Associated with a change in stool form (Figure 1)

A) Type 1: Small, discrete, round, and hard lumps

B) Sausage-shaped, lumpy but hard stools

C) Sausage-shaped, soft and shaped stools with cracks on the surface

D) Piecemeal, soft, irregular-edged stools

E) Soft, pureed stools with particles

F) Completely liquid, no solid parts

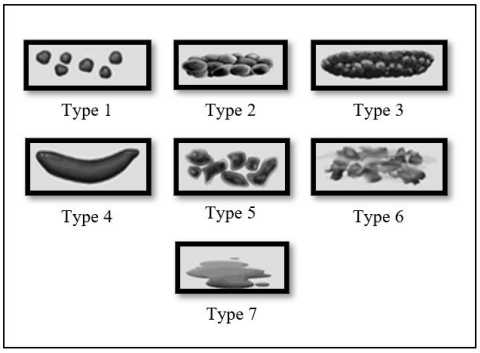

Figure 1. *Bristol Stool Form Scale* (Patel et al., 2015).

IBS Subtypes

IBS subtypes are differential classifications based on the most prominent bowel habits and symptoms of individuals with IBS. There are four IBS subtypes, each of which is equally common:

Predominantly Constipated IBS (IBS-C): This subtype is a form in which constipation symptoms predominate. IBS-C patients generally exhibit more body dysfunction and psychological symptoms.

Predominantly Diarrheal IBS (IBS-D): This subtype, in which diarrhea predominates, is associated with less body awareness and fewer psychological symptoms. IBS-D patients generally have a lower quality of life.

Mixed IBS (IBS-M): This subtype, in which constipation and diarrhea alternate, has been reported as the most common subtype in some studies.

Unclassified IBS (IBS-U): This subtype, in which there is no distinct predominant symptom, is less common (Saha, 2014; Wang et al., 2022).

Diarrhea-predominant individuals (IBS-D): These individuals have more than 25% of their stool movements associated with Bristol Stool Form Scale (BSFS) type 6 or 7.

Constipation-predominant individuals (IBS-C): These individuals have more than 25% of their stool movements associated with type 1 or 2.

Mixed type (IBS-M): More than 25% of their stool movements are associated with type 1 or 2, and the other 25% are associated with BSFS type 6 or 7. Unclassified Subtype (IBS-U) Symptoms vary (Dean et al., 2005).Uses a range of symptoms to ensure that symptoms are not caused by a condition other than IBS (Palsson et al., 2020).These symptoms are often referred to as “alarm signs” or “alarm symptoms.”

These features include:

Alarm Symptoms

Some symptoms should be questioned to ensure that the symptoms are not caused by a condition other than IBS. These symptoms are often referred to as “alarm signs” or “alarm symptoms”.

These characteristics include (Ford et al., 2020):

• Development of new symptoms at age 50 or older

• Presence of blood in the stool (red or black, tarry stools)

• Fever, chills or night sweats

• Symptoms that occur at night and disrupt sleep

• Unintentional weight loss

• Change in typical IBS symptoms (such as new and significant pain)

• Accompanied by abnormal laboratory results (anemia, leukocytosis, high CRP and sedimentation rates, etc.)

• Family history of cancer, inflammatory bowel disease or other gastrointestinal diseases such as celiac disease.

Differential Diagnosis of IBS

“Diseases to exclude include (Ivashkin et al., 2022):”

• Inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis) should be excluded.

• A recent history of intestinal infection within the past few months should be considered.

• Gallbladder disease, pancreatitis, stomach ulcers or gastric reflux, and other gastrointestinal disorders should be excluded.

• Overactive bladder or urinary tract infections, especially in those with urinary symptoms, can cause symptoms similar to IBS.

• In female patients, IBS symptoms can be confused with gynecological conditions.

• IBS symptoms can overlap with certain psychiatric disorders.

• Exclusion of these diseases, along with patient history, physical examination, and laboratory tests, helps ensure a correct diagnosis of IBS (Mansoor et al., 2024).

TREATMENT

The main goal of IBS treatment is to reduce symptoms and improve quality of life. Depending on the severity of symptoms, a variety of strategies can be implemented (Halkjær et al., 2018; Almario et al., 2023).

Lifestyle and Dietary Changes:

• Avoid trigger foods that worsen symptoms.

• Include high-fiber foods in your diet.

• Drink plenty of fluids to maintain adequate hydration.

• Exercise regularly to promote bowel regularity.

• Make sure to get enough sleep.

Dietary Restrictions

If bloating and gas are a problem, eliminate high-gas foods. This includes carbonated and alcoholic beverages, along with certain gas-producing foods (Fukudo et al., 2021).

Eliminating gluten: Some individuals may notice that their symptoms improve when they eliminate gluten (found in rye, barley, and wheat), even if they do not have celiac disease.

FODMAPs (Disaccharides, Fermentable Oligosaccharides, Monosaccharides, and Polyols): These specific carbohydrates, found in certain grains, vegetables, fruits, and dairy products, can trigger symptoms in susceptible individuals (Aroniadis et al., 2019).

Consult a Dietitian

A dietitian can provide guidance and support in implementing dietary changes effectively.

Stress Management

Use stress management techniques such as meditation, yoga, breathing exercises, or psychotherapy if stressors worsen your symptoms.

Medications

Fiber supplements: Psyllium supplements (such as Metamucil) can help relieve constipation when combined with fluids (Johnsen et al., 2018).

Laxatives: If fiber alone does not relieve constipation, laxatives such as magnesium hydroxide or polyethylene glycol may be recommended.

Antidiarrheal medications: Over-the-counter options such as loperamide are available to help manage diarrhea. They may also prescribe bile acid sequestrants, such as cholestyramine, colestipol, or colesevelam, but these can cause bloating (Johnsen et al., 2018; Halkjær et al., 2018).

Anticholinergic drugs: Drugs such as dicyclomine are effective in relieving painful intestinal spasms and may be prescribed to individuals who have diarrheal attacks. Possible side effects include constipation, dry mouth, and blurred vision (Halkjær et al., 2018).

Tricyclic antidepressants: These drugs can treat depression and reduce pain by inhibiting neurons that regulate bowel function. When symptoms of diarrhea and abdominal discomfort occur without depression, your health care provider may

recommend lower doses, usually imipramine, desipramine, or nortriptyline. Possible side effects include dizziness, blurred vision, lightheadedness, and dry mouth (Lembo et al., 2022).

SSRI antidepressants: Selective serotonin reuptake inhibitors, such as fluoxetine or paroxetine, may be helpful for depression and pain with constipation (Holvoet et al., 2021).

Pain medications: Severe pain or swelling may be relieved with medications such as pregabalin or gabapentin (Halkjær et al., 2018; BouSaba et al., 2021).

Specific Medications for IBS

Alosetron (Lotronex): A drug that works by reducing the strain on the colon and slowing the transit time in the lower intestine. It is designed for severe diarrhea-predominant IBS in women who have not responded to other treatments. It is not approved for men and is associated with rare but significant side effects and should be considered when other treatments have been exhausted (Quraishi et al., 2017; Xu et al., 2019).

Eluxadolin: Reduces muscle contractions and fluid secretion in the intestine, reducing diarrhea, and increases muscle tone in the rectum. Common side effects include nausea, abdominal discomfort, and mild constipation. However, it is important to note that eluxadolin has been associated with a potentially serious condition such as pancreatitis, which may occur more frequently in some individuals (Lembo et al., 2022; Qin et al., 2022).

Rifaximin: An antibiotic that works by reducing bacterial growth and relieving diarrhea (Lembo et al., 2022).

Lubiprostone: Increases fluid secretion in the small intestine, making it easier for stool to pass. It is usually prescribed to women with severe IBS-C who have not responded to other treatments (Chang et al., 2022; Biniszewska et al., 2024).

Linaclotide: It also helps with the passage of stool by increasing fluid secretion in the small intestine. It can cause diarrhea as a side effect; however, it is thought that this side effect can be alleviated when taken 30-60 minutes before meals (Chang et al., 2022; Biniszewska et al., 2024). It is important to remember that the effectiveness of these treatment options can vary from person to person. Therefore, close collaboration with other physicians is necessary to create an appropriate personalized treatment plan (Ladabaum et al., 2012; Irvine et al., 2017; Singh et al., 2018).

Use of herbal products in the treatment of IBS

The use of herbal products in the treatment of Irritable Bowel Syndrome (IBS) is gaining increasing attention due to the limited effect of traditional treatment methods. IBS is a common functional bowel disorder characterized by abdominal pain and changes in bowel habits (Porwal et al., 2024). Herbal treatments show promising results in alleviating these symptoms. Common herbal solutions used in this context are listed below.

Menta piperita (Peppermint Oil)

The effect of peppermint oil on IBS symptoms is related to menthol, one of the main components it contains. Menthol has an antispasmodic effect by blocking calcium channels in intestinal smooth muscles and can regulate intestinal motility. In addition, menthol is thought to have analgesic and anti-inflammatory properties, thus reducing visceral pain and improving the quality of life of patients. However, there are still some uncertainties regarding the pharmacokinetics and optimal dosage of peppermint oil (Rahimi and Abdollahi, 2012; Hawrelak et al., 2020). While most studies evaluate short-term effects, more research is needed on its long-term use, potential adverse effects, and effectiveness in different IBS subtypes. It should also be noted that peppermint oil may increase gastroesophageal reflux symptoms in some individuals, and should be used with caution, especially in patients with a history of reflux.

In recent years, enteric-coated peppermint oil capsules have been shown to have a more direct effect on intestinal smooth muscle and to increase its effectiveness by protecting against stomach acid. These formulations are considered a potential therapeutic option in the treatment of IBS, providing better tolerability than classical peppermint oil preparations. In the future, long-term, large-scale randomized controlled trials should be conducted to examine the effects of peppermint oil on IBS more comprehensively.

STW 5 (Iberogast) and STW 5-II

STW 5 is a combination of nine medicinal plant extracts used in the treatment of functional gastrointestinal disorders. These herbs include *Iberis amara* (bitter lettuce), *Melissa officinalis* (lemon balm), *Matricaria recutita* (chamomile), *Carum carvi* (caraway), *Mentha × piperita* (peppermint), *Glycyrrhiza glabra* (licorice), *Angelica archangelica* (angelica herb), *Silybum marianum* (milk thistle) and *Chelidonium majus* (swallowtail) (Khayyal et al., 2001; Schempp et al., 2006; Allam et al., 2015). STW 5 is particularly effective in the treatment of gastrointestinal disorders such as functional dyspepsia and irritable bowel syndrome (IBS) (Germann et al., 2006; Thumann et al., 2024). STW 5-II is a modified formulation of STW 5 and does not contain three of the plant extracts (Silybum marianum, Chelidonium majus, and Glycyrrhiza glabra). Despite this, it has been reported to be as effective as STW 5 clinically (Khayyal et al., 2001; Schemann et al., 2021). STW 5-II has a clinically proven effect, especially in the management of disorders such as irritable bowel syndrome and functional dyspepsia (Elbadawi et al., 2001; Elbadawi et al., 2022; Andresen et al., 2024). The effects of STW 5 and STW 5-II on gastrointestinal function are explained

by the synergistic interactions of the herbal components they contain. In particular, Iberis amara has been shown to accelerate gastric emptying and regulate intestinal motility thanks to its prokinetic effect (Gwee et al., 2021). Components such as lemon balm, chamomile and mint can reduce intestinal muscle spasms and relieve visceral sensitivity with their antispasmodic and anti-inflammatory properties (Valussi, 2012; Lashgari et al., 2024). It is thought that cumin and angelica may alleviate bloating and dyspeptic symptoms due to their carminative effects (Maurya et al., 2017; Das et al., 2023).

There is evidence that the effects of STW 5 and STW 5-II on IBS and functional dyspepsia are not only limited to motility regulation, but may also play a neuromodulatory role in the gut-brain axis. For example, it is suggested that the bioactive components contained in licorice root and celandine may support mucosal barrier function and reduce low-grade inflammation in the intestine (Wu et al., 2023; Lashgari et al., 2024).

However, further studies are needed on the long-term safety of STW 5 and STW 5-II and specific dosage optimizations of individual components. In particular, it is important to clarify the safe dose ranges of Chelidonium majus, which has been reported to have potential effects on liver enzyme levels (Moro et al., 2009). Future randomized controlled trials may help us better understand the effects of these herbal combinations on the gut microbiota and their relationship with the gut-brain axis.

Aloe vera and Asafoetida

Aloe vera and asafoetida are herbal products that offer potential benefits in the management of digestive problems such as irritable bowel syndrome (IBS). Aloe vera is generally known for its intestinal soothing and inflammation reducing properties. The polysaccharides it contains can support the health of the digestive system by protecting the intestinal lining. It can also relieve IBS symptoms such as constipation due to its effects on regulating bowel movements (Joseph and Raj, 2010).

Asafoetida (*Ferula assa-foetida*) is a spice widely used in traditional medicine for its digestive problems relieving properties. It is thought to help reduce gas, bloating, and cramping in particular. The antispasmodic properties of asafoetida can help relax the intestinal muscles, which may be beneficial in the management of IBS symptoms (Hawrelak et al., 2020).

The effectiveness of these herbal products may vary depending on individual responses and severity of the condition. Therefore, it is important to consult a healthcare professional before considering herbal treatments for IBS symptoms. Furthermore, the use of such herbs should be considered as a supportive approach in conjunction with other treatment methods.

Other some plants

The combination of *Mentha longifolia* (new mint), *Cyperus rotundus* (black sand grass), and *Zingiber officinale* (ginger) stands out as an effective approach for relieving IBS symptoms. The unique mechanisms of action of each herb suggest that this combination may provide synergistic benefits.

The antispasmodic effects of *Mentha longifolia* may help relax intestinal muscles, leading to reduced cramping and pain. Additionally, peppermint oil may relieve bloating by reducing gas accumulation in the digestive tract (Sevindik, 2018).

Cyperus rotundus is a traditional herb often used to treat digestive disorders and abdominal discomfort. Thanks to its anti-inflammatory and antispasmodic properties, it can play an important role in the management of IBS symptoms (Peerzada et al., 2015).

Zingiber officinale is another important plant known for its benefits to digestive health. Ginger is known for its properties that relieve nausea and stomach discomfort. It can also support digestion by regulating bowel movements (Shahrajabian et al., 2019).

The fact that this herbal combination provides comparable results to standard treatment methods is an important discovery in terms of the integration of herbal medicine with modern medicine. However, it should be remembered that each individual may respond differently to herbal treatments. Therefore, it is recommended to consult a health professional before using herbal treatment methods. In addition, more clinical research is needed so that the effectiveness and safety of these herbs can be better understood.

CONCLUSION AND FUTURE PERSPECTIVES

Irritable Bowel Syndrome (IBS) poses a significant clinical challenge in terms of diagnosis and treatment processes due to its complex etiology and multifaceted symptoms. Today, multidisciplinary methods such as dietary and lifestyle changes, pharmacological treatments and psychosocial approaches are used in the management of IBS. However, there is no effective and definitive treatment method for every patient, and personalized treatment approaches are becoming increasingly important due to the differences in symptoms among individuals. Recent studies have revealed important findings to better understand the role of intestinal microbiota, brain-gut axis and genetic factors in the pathogenesis of IBS. In particular, it has been shown that treatment approaches focusing on intestinal microbiota, such as probiotics, prebiotics, fecal microbiota transplantation and individualized dietary strategies, may be effective in alleviating IBS symptoms. In the future, more effective treatment options may be offered with the more widespread use of personalized medical approaches in the treatment of IBS, the development of therapeutic approaches that take into account individual differences in intestinal microbiota and the discovery of new

pharmacological agents. In addition, studies on herbal treatments, neuromodulatory drugs, and new therapeutic strategies targeting the gut-brain axis may provide alternative and supportive approaches in the management of IBS. Adopting a multidisciplinary approach in the treatment process of IBS is of great importance to improve the quality of life of patients and make symptom management more effective. Future large-scale clinical studies will contribute to the development of personalized treatment strategies by providing a better understanding of the disease.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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