Irritable bowel syndrome

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Abstract

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic abdominal pain associated with a change in frequency and form of stool. IBS is common, with a population prevalence of around 10%, and causes a reduction in quality of life. Its pathophysiology remains incompletely understood, although abnormal communications within the brain–gut axis are considered to be important. IBS can be subclassified according to predominant bowel habit and/or pain. Treatments are directed towards improving symptoms and are multifaceted. Dietary and lifestyle modification, pharmacotherapy and psychological interventions can be useful in managing the disorder.

Keywords Functional gastrointestinal disorders; irritable bowel syndrome; MRCP

Key points

- Irritable bowel syndrome (IBS) is a common disorder characterized by abdominal pain, bloating and change in bowel habit
- IBS can be subclassified according to the predominant bowel habit
- Although the pathophysiology of IBS remains incompletely understood, disordered interactions in the brain–gut axis are central
- Treatment is multimodal and targeted at improving the most bothersome symptoms

Introduction

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal (GI) disorder characterized by abdominal pain, bloating, distension and a change of bowel habit. IBS accounts for >40% of new gastroenterology outpatient clinic referrals, although most patients are diagnosed and managed in primary care. The Rome Foundation, a multinational group of experts, regularly updates the formal definition of IBS. This process is now in its fourth iteration, and Table 1 shows the most recent definition of IBS.[1]

Epidemiology

IBS is common, with a reported worldwide prevalence of around 10%, with most incident cases occurring in the 18–34-year age group. This variability in reported prevalence is probably because of differing diagnostic criteria. UK data suggest an incidence of 4 per 1000 population per annum. In the UK, IBS is associated with significant healthcare expenditure, estimated in total as approaching £320 million per annum, and these costs are even higher in the USA. IBS is associated with heightened lost work/school days through both absenteeism and presenteeism (i.e. where a sufferer is present in the workplace but is not productive because of bothersome symptoms).

Pathophysiology

The underlying cause of IBS remains incompletely understood and is likely to be multifactorial.[2] A number of studies have shown that a significant proportion of patients with IBS display increased sensitivity of the GI tract to distension, an epiphenomenon referred to as visceral hypersensitivity. Similarly, alterations in stress-responsive physiological systems, such as the autonomic nervous system and hypothalamus–pituitary–adrenal axis, have been implicated in changes to visceral sensitivity and can contribute to differences in motility of the GI tract. So too can changes in the central nervous system, personality traits, environmental influences and genetic factors.

IBS can develop after an episode of gastroenteritis, where it is termed post-infectious IBS. Post-infectious (PI-) IBS is particularly common after *Campylobacter*, *Shigella*, *Escherichia coli* and *Salmonella*. Up to 30% of those suffering a bout of gastroenteritis can develop chronic PI-IBS; independent risk factors are the severity of the initial infection and concomitant psychiatric comorbidity. The microbiota has recently been an area of intense research interest in IBS. For instance, preliminary studies have shown that IBS is associated with changes in the microbiota to produce an increase in Firmicutes-associated taxa, associated with a reduction in *Bacteroides*-related taxa.

In addition, personality traits such as neuroticism, as well as childhood abuse, have also been associated with a higher predisposition to the development of IBS.

Clinical features

IBS is a symptom-based diagnosis based on stereotypical symptoms including abdominal pain associated with a change in stool form or frequency. Symptoms typically wax and wane and are often exacerbated by stress.[3] These changes in defecatory patterns allow IBS to be subtyped into the following discrete disorders: IBS-diarrhoea (IBS-D), IBS-constipation (IBS-C), IBS-mixed (IBS-M) (with alternating between diarrhoea and constipation) and IBS-unclassified (IBS-U) (Figure 1).

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Rome IV diagnostic criteria for IBS

Recurrent abdominal pain on average at least 1 day per week in the preceding 3 months, associated with two or more of the following:

- Relation to defecation
- Association with a change in frequency of stool
- Association with a change in form (appearance) of stool

Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis.
Source: http://theromefoundation.org.

Table 1

Alarm symptoms that should prompt further investigation

- Abnormalities on clinical examination such as a palpable abdominal mass
- Unintentional weight loss
- Rectal bleeding or a mass on rectal examination
- Change in bowel habit for >6 weeks in patients aged >60 years
- History of recent antibiotic use
- Raised inflammatory markers
- Family history of colorectal carcinoma or ovarian cancer

Table 2

Patients also frequently report significant abdominal bloating and distension. Extra-GI symptoms, such as dysmenorrhoea, migraine, dyspareunia and lassitude are also common. IBS is frequently associated with co-morbid disorders such as fibromyalgia, depression and other unexplained medical syndromes. Additional co-morbid functional GI disorders, such as functional dyspepsia, are also frequently seen.

IBS-D is the most common subtype, accounting for approximately 40% of all cases. Although IBS is more common in women overall, recent data suggest that the subtype of IBS-D is more common in men. Healthcare-seeking in patients with IBS largely depends on the severity of symptoms and its implications for quality of life. Female patients tend to have increased healthcare-seeking in IBS.

Differential diagnosis

Although the symptoms of IBS are typical, they are not specific, and therefore it is important to exclude alarm ('red flag') symptoms (Table 2). In the absence of these, IBS can be positively diagnosed without a need for extensive and invasive investigations.

The differential diagnosis of IBS-like symptoms is broad and includes inflammatory bowel disease, coeliac disease, bile acid diarrhoea, chronic idiopathic constipation, pelvic floor disorders and lactose intolerance. Thus, particularly in the context of diarrhoeal symptoms, screening blood tests such as a full blood count, erythrocyte sedimentation rate, C-reactive protein concentration, haematinics and tissue transglutaminase are important tests for the differential diagnosis. Although not specifically included in the Rome IV diagnostic criteria, faecal calprotectin measurement can also be valuable in excluding inflammatory bowel disease.

Bile acid diarrhoea is an important differential diagnosis of IBS-D. Approximately one-third of patients meeting the diagnostic criteria for IBS have bile acid diarrhoea.[4] These patients respond well to bile acid sequestrants, such as colestyramine or colesevelam. Bile acid diarrhoea should be considered in patients who have undergone a terminal ileal resection and in those with a prior cholecystectomy. It can be diagnosed using the nuclear medicine 23-seleno-25-homotaurocholic acid (SeHCAT) test, with a 7-day SeHCAT retention of <10% supporting a positive diagnosis of bile acid diarrhoea.

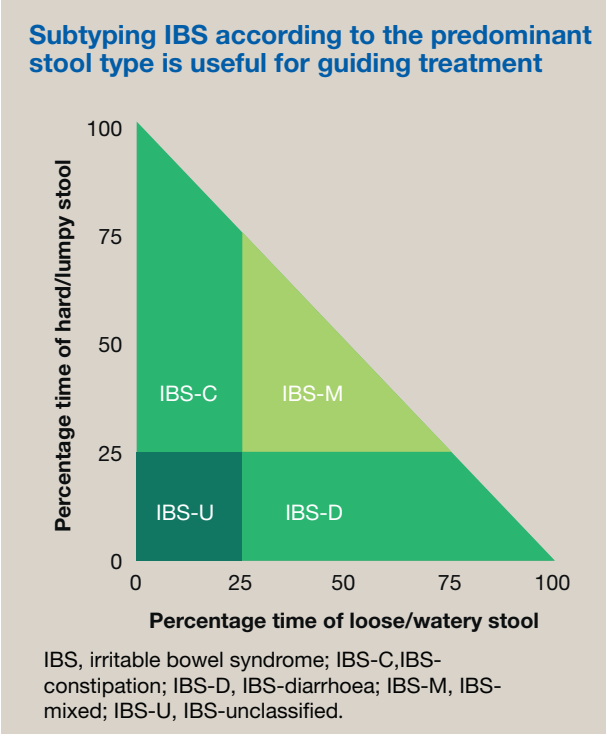

Figure 1

Management of irritable bowel syndrome

General approach and patient–doctor relationship

Typically, patients seek healthcare when the symptoms of IBS begin to impact on their quality of life. Patient education, sharing of information and support are very important throughout when making a diagnosis of IBS, as is developing a positive doctor–patient relationship. Within this, a supportive approach to the patient's symptoms is pivotal, as patients have sometimes experienced negative attitudes from other healthcare professionals. In addition, the involvement of other members of the multidisciplinary team, including dietitians, psychiatrists and psychologists, can be useful; this clearly depends on the severity and chronicity of a particular patient's symptoms and the availability of local services. Patients often find it very helpful, and indeed reassuring, to have discussions around the underlying pathophysiology and natural history of IBS.[5]

Diet and lifestyle

Patients with IBS frequently report that certain dietary components, such as bread and dairy products (which are high in

fermentable carbohydrates), worsen their symptoms. In IBS management, it is important to promote healthy regular meals with good fluid intake, although caffeine should be limited in patients with IBS-D.

Given that a diet high in fermentable carbohydrates can worsen symptoms, considerable research effort has been given to developing dietary intervention that reduce the intake of fermentable oligo-, di-, monosaccharides and polyols (FODMAPs). Reducing the intake of FODMAP foods reduces fermentation in the GI tract, with a resulting decrease in intraluminal gas production. This in turn leads to reduced pain and bloating. High-FODMAP foods include fruits such as apples and peaches, garlic, onion and sweeteners. Reduction of FODMAP intake can reduce symptoms in IBS. However, the low-FODMAP intervention is not a 'diet for life', and food groups should be gradually reintroduced in a systematic manner to ascertain an individual's list of 'triggers foods'. This intervention is complex and is most effective when undertaken by a trained dietitian.

Pharmacotherapy

The main objective of pharmacotherapy in IBS is to reduce the most bothersome symptoms, such as constipation, diarrhoea and pain.

Constipation — in IBS-C, simple laxatives such as senna, bisacodyl, polyethylene glycol-based preparations and sodium docusate can be effective in improving constipation. Lactulose should be avoided as it often worsens abdominal distension. In patients who do not respond to these interventions, linaclotide, a guanylate cyclase-C agonist, has been demonstrated to have efficacy. Linaclotide improves constipation but also has a beneficial effect on abdominal pain and bloating, and can serve as a second-line therapy in these patients if simple laxatives have not proved sufficient beyond a 12-month period.

Diarrhoea — loperamide, an opioid receptor agonist that does not cross the blood–brain barrier, is useful in the management of diarrhoea by reducing colonic motility, thereby allowing more water to be absorbed across the wall of the GI tract. This leads to harder, drier stools and reduces defecatory urgency. Serious adverse events are relatively uncommon. Individuals who do respond to treatment can be given eluxadoline, which is a μ- and κ-opioid receptor agonist and δ-opioid receptor antagonist. This dual mechanism explains its antidiarrhoeal and abdominal pain-modulating action without causing profound constipation. Eluxadoline has been shown to reduce abdominal pain and improve stool consistency, although it is contraindicated in patients who have had a prior cholecystectomy.

Pain — abdominal pain in IBS can be one of the most challenging symptoms to treat effectively. Antispasmodics can be useful in reducing pain. Hyoscine, for instance, reduces acetylcholine binding at muscarinic receptors, which results in smooth muscle relaxation, although it can worsen constipation. Calcium channel blockers also reduce smooth muscle contraction, and preparations containing peppermint oil can reduce symptoms.

A summary of the treatments for IBS

General approach
- Development of doctor–patient relationship encompassing support and education

Constipation
- Simple laxatives (senna, bisacodyl, polyethylene glycol-based preparations, docusate)
- Linaclotide

Diarrhoea
- Loperamide
- Eluxadoline

Dietary and lifestyle changes
- Regular healthy meals, reducing caffeine intake
- Low-FODMAP intervention (needs to be dietitian-led)

Pain
- Antispasmodics (e.g. hyoscine in IBS-D, peppermint-based preparations in IBS-C)
- Tricyclic antidepressants (e.g. low-dose amitriptyline in IBS-D)
- Selective serotonin reuptake inhibitors (e.g. citalopram in IBS-C)
- Psychological therapies such as gut-focused hypnotherapy

Treatment needs to be individualized, with a focus on improving the most bothersome symptoms.

Table 3

Tricyclic antidepressants, such as low-dose amitriptyline (e.g. 10 mg at night), have efficacy in reducing pain in IBS, although amitriptyline should be avoided in IBS-C because of its anticholinergic adverse effects. In this context, selective serotonin reuptake inhibitors, such as citalopram, can reduce pain and discomfort. The role of gabapentin, pregabalin and selective noradrenergic reuptake inhibitors (e.g. venlafaxine, duloxetine) in managing pain in IBS is not yet clear.

Psychotherapy — psychologically targeted interventions, in particular gut-focused hypnotherapy, have been shown to be very effective in reducing symptoms in patients with recalcitrant symptoms. Table 3 summarizes these interventions. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 30-year-old woman presented with a 3-month history of abdominal pain and loose watery stools following a cholecystectomy.

What is the investigation of choice?

A. Serum tissue transglutaminase (TTG)
B. Colonoscopy
C. Faecal calprotectin
D. Thyroid function tests
E. 23-Seleno-25-homotaurocholic acid (SeHCAT) scan

Question 2

A 42-year-old man presented with abdominal pain and constipation. He was found to have a diagnosis of irritable bowel syndrome with constipation. He had tried senna and polyethylene glycol (PEG)-based laxatives with no improvement in his symptoms.

What is the best treatment option?

A. Lactulose
B. Low fermentable oligo-, di-, monosaccharides and polyols (FODMAP) diet
C. Gut-focused hypnotherapy
D. Linaclotide
E. Bisacodyl

Question 3

A 26-year-old woman presented with a 6-month history of abdominal pain, bloating and diarrhoea. Standard investigations are normal. Her pain is particularly problematic and disturbs her sleep at night.

Which of the following is the best treatment option for the most likely diagnosis?

A. Peppermint oil
B. Loperamide
C. Gut-focused hypnotherapy
D. Amitriptyline
E. Low fermentable oligo-, di-, monosaccharides and polyols (FODMAP) diet