Irritable bowel syndrome: enigmatic for doctors, problematic for patients

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Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder, characterised by chronic abdominal pain and an alteration in bowel habit. The symptoms of IBS can be debilitating and associated with a reduction in quality of life. Although in Europe IBS more often presents in women, men also suffer and this potential diagnosis should not be overlooked.

IBS is characterised by abdominal pain, bloating, distension and a change of bowel habit. It accounts for more than 40% of new gastroenterology outpatient clinic referrals, although the vast burden of disease is managed in primary care. The pathophysiology of IBS remains enigmatic, which unfortunately often results in suboptimal outcomes to treatment, symptom chronicity, over-investigation and patient disillusionment.

EPIDEMIOLOGY

Irritable bowel syndrome is very common, affecting 5–20% of individuals worldwide, most commonly 18- to 34-year-olds. Specific to the UK, one large population-based study of 580,000 primary care patients reported an incidence of four new cases per 1000 patients per annum. IBS is associated with significant annual expenditure, which has been estimated to be in the region of £90–£316 million in the UK. Moreover, IBS is associated with increased absenteeism and presenteeism (ie where an individual is present at work but not productive due to symptoms).

CLINICAL FEATURES

Characteristically, IBS comprises symptoms of recurrent abdominal pain with alterations in stool form or frequency. This can span from constipation (IBS-C), IBS with diarrhoea (IBS-D), IBS with mixed bowel habit (IBS-M) and IBS unclassified (IBS-U).

Figure 1. The different subtypes of irritable bowel syndrome (IBS) are classified according to the predominant bowel habit: IBS with constipation (IBS-C), IBS with diarrhoea (IBS-D), IBS with mixed bowel habit (IBS-M) and IBS unclassified (IBS-U).

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IBS is frequently comorbid with other disorders, such as anxiety, depression and fibromyalgia. Moreover, in patients with IBS, there is often a significant overlap with other functional GI disorders, such as gastro-oesophageal reflux disease and dyspepsia. Symptoms typically wax and wane, such that pain or discomfort typically occurs for approximately three days per week.\(^2\)

IBS is classified into four subtypes, based upon the most prominent bowel habit (Figure 1):

- IBS-constipation (IBS-C)
- IBS-diarrhoea (IBS-D)
- IBS-mixed (IBS-M) (alternating between constipation and diarrhoea)
- IBS-unclassified (IBS-U).

It has previously been suggested that IBD-D is the most common subtype, possibly accounting for around 40% of IBS.\(^7\) Although IBS is considered to be more prevalent in females \textit{per se}, IBS-D is more common in men.\(^7\) Healthcare-seeking in IBS patients is determined by the extent to which the IBS negatively influences quality of life and the presence of comorbidities, rather than mental health status or physical symptoms. However, there are gender differences in healthcare-seeking, such that females consult more frequently in the USA and Europe, in contrast to India, where males consult more readily (Figure 2). The Rome Foundation has sought to systematise the definition of IBS and is now in its fourth iteration (Rome IV; see http://theromefoundation.org) (Box 1).

**AETIOLOGY**

The patho-aetiology of IBS remains incompletely understood. However, research over the last three decades has suggested a number of factors, ranging from changes in the stress-responsive physiological systems (e.g. autonomic nervous system and hypothalamic pituitary adrenal axis), personality traits, aberrancies in the microbiota, environmental influences and genetic factors. With respect to genetics, twin studies show a hereditability of 22–57%.\(^8\)

More recently, genome-wide association studies have demonstrated a number of single nucleotide polymorphisms that are associated with IBS.\(^9\) IBS can develop following an enteric infection, and in such cases is termed post-infectious (PI)-IBS.\(^10\) Following bacterial gastroenteritis, whether from campylobacter, salmonella, shigella or \textit{Escherichia coli}, the majority of patients have self-limiting symptoms; however, 4–32% of patients develop IBS-like symptoms that long outlast this initial infection.\(^11\) Similarly, there has been recent interest in the composition of the microbiota. For instance, it has been shown that in IBS patients there is a relative increase in firmicutes-associated taxa, along with a relative depletion of the bacteroides-related taxa.\(^12\)

Individual factors, such as personality traits or childhood abuse, have also been attributed to the aetiology of IBS.\(^13\) In the case of personality traits, factors such as neuroticism (degree of pessimism/anxiety) have been associated with IBS genesis, with stressful childhood events, including maternal separation (in animal models) and physical abuse additionally implicated in its aetiology.

**DIFFERENTIAL DIAGNOSIS**

When assessing a patient with GI symptoms potentially attributable to IBS, it is critically important to exclude red flag or ‘alarm symptoms’ (Box 2). In the absence of these, IBS can be confidently diagnosed, without the need for extensive or unnecessary investigation. However, given the relative lack of symptom specificity, a broad differential diagnosis is apparent, including coeliac disease, inflammatory bowel disease, bile acid malabsorption, food allergies and lactose intolerance.\(^14\) Thus, particularly in the context of IBS-D, screening blood tests such as a full blood count, ESR, C-reactive

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**Box 1. The Rome IV diagnostic criteria for irritable bowel syndrome**

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

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool

Criteria fulfilled for the past three months with symptom onset at least six months before diagnosis.
Management of IBS

Patient–doctor relationship

As a result of our incomplete understanding of IBS, treatment can be difficult. First and foremost, a positive doctor–patient relationship is key, as this disorder is often chronic. Secondly, a supportive attitude to the patient’s symptomology is important – it is not uncommon for IBS patients to experience negative attitudes from healthcare professionals due to the absence of clinical findings on investigation. Goal-setting can be a useful management step, and it is key to utilise the wider multidisciplinary team, including dietetics, psychiatry and psychology, where available. In addition, patient education around the nature of IBS is central to good management, and there are some excellent web-based resources, eg http://www.theibsnetwork.org.

Diet and lifestyle

Many patients with IBS report that certain dietary components can exacerbate symptoms (eg dairy products, bread or pasta). Therefore, lifestyle and dietary changes are often useful interventions. It is important to take an effective dietary history and look for any symptom-exacerbating foods, but also to emphasise the value of regular meals, encourage fluid intake and limitation of caffeinated drinks to three cups per day, and also to factor in periods of exercise and relaxation.

Above and beyond these general approaches, the reduction of dietary fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) may yield a degree of symptomatic relief. FODMAPs are fermentable carbohydrates, which cause intraluminal gaseous distension and additionally exert an osmotic effect.

Foodstuffs high in FODMAPS include certain fruits (eg apples and peaches), legumes and artificial sweeteners, and their intake should be limited. However, it is our experience that such an intervention is most effectively delivered by a dietician with suitable skills and experience.

Pharmacotherapy

The main objective of pharmacotherapy in IBS is to reduce the most bothersome symptoms, whether pain, bloating, constipation or diarrhoea. For IBS-C, simple laxatives, such as senna or docusate, may be effective in treating symptoms. However, it should be noted that lactulose often makes bloating and distension worse and is generally best avoided. Linacotide (Constella), a guanylate cyclase C inhibitor, is a second-line therapy in patients where simple laxatives have not proved sufficient beyond a 12-month period. Linacotide has been shown to improve not just bowel symptoms, but also abdominal pain and bloating. For IBS-D, loperamide may provide some symptom relief by improving stool consistency and reducing urgency.

Selective serotonin reuptake inhibitors can cause diarrhoea and thus may prove useful in IBS-C. The role of selective noradrenergic reuptake inhibitors (eg venlafaxine and duloxetine), gabapentin and pregabalin in managing pain in IBS is unclear. The role of antibiotics (eg rifaximin) and probiotics in IBS is uncertain. A number of new oral drugs are currently being evaluated, including eluxadoline (a mixed mu opioid-receptor agonist/delta opioid-receptor antagonist) for IBS-D, ondansetron (a 5-HT3-antagonist) for IBS-D, ibodutant (a tachykinin NK2-receptor antagonist) for IBS-D, plicanatide (a guanylate-cyclase C agonist) for IBS-C and elobixibat (leal bile acid transport inhibitor) for IBS-C.

Conclusion

IBS is a common and incompletely understood functional GI disorder. Making a positive diagnosis and subtyping based on predominant bowel habit aids in the guiding treatment, which is largely directed towards improving symptoms.

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References


