Irritable Bowel Syndrome in Inflammatory Bowel Disease Patients: Prevalence, Etiology, and Treatment

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Abstract: One in 4 patients with endoscopically confirmed quiescent inflammatory bowel disease (IBD) reports persistent gastrointestinal symptoms, which are often compatible with irritable bowel syndrome (IBS). The reporting of these IBS-type symptoms is associated with psychological comorbidity, impaired quality of life, and increased health care utilization. The brain-gut axis, which provides the link between the central nervous system and gastrointestinal tract, may facilitate these relationships. In IBS, dietary manipulation, gut-brain neuromodulators, and brain-gut behavioral therapies may have a beneficial effect on symptom reporting and quality of life. However, evidence supporting their use in patients reporting IBS-type symptoms specifically in IBD is lacking. Despite this, observational studies describing the relationship between mood and inflammatory activity highlight the role of the brain-gut axis in the pathophysiology of IBD. There remains a need for further carefully designed clinical trials of treatments targeting the brain-gut axis in IBD patients reporting IBS-type symptoms, who may be most likely to respond to these therapies. An integrated approach to management, combining treatments targeting inflammatory activity and brain-gut axis dysfunction, has the potential to improve the natural history of symptoms, psychological well-being, and quality of life in this select group of patients with IBD. This article will review the prevalence, impact, etiology, and treatment options for the management of patients with quiescent IBD who report IBS-type symptoms.

Keywords
Inflammatory bowel disease, irritable bowel syndrome, psychological well-being, gut-brain neuromodulators, brain-gut behavioral treatments

Crohn's disease (CD) and ulcerative colitis (UC), collectively termed inflammatory bowel disease (IBD), are chronic inflammatory disorders of the gastrointestinal tract with a combined prevalence of almost 0.5% in Western populations.[1] The etiology of IBD is uncertain and likely multifactorial, with intestinal inflammation resulting from immune activation occurring in genetically susceptible

individuals exposed to an environmental trigger. Medical management aims to suppress immune dysregulation, improve mucosal inflammation, and avoid complications of disease progression, including stricture formation, the development of a fistulizing disease phenotype in CD, and the need for surgery in both CD and UC.

Typical symptoms associated with IBD include alteration in bowel habit, fecal urgency, and passage of blood per the rectum. The natural history of IBD varies significantly but typically consists of episodes of disease activity on a background of disease quiescence. Assessment of disease activity and determination of treatment response are based on a combination of subjective clinical parameters, including patient-reported symptoms, as well as more objective measures of disease activity such as C-reactive protein (CRP), fecal calprotectin (FC), and endoscopic assessment. STRIDE-II defines treatment targets in IBD in terms of immediate, intermediate, and long-term goals that may be used to guide treatment decisions, with shorter-term targets reliant on the interpretation of patient-reported symptoms.[2] Despite this guidance, the use of clinical disease activity assessment tools can be unreliable. The relationship between symptom reporting and objective assessment of inflammatory activity is poor, particularly in CD.[3-5] Moreover, subjective endpoints used in clinical trials of IBD therapies, including clinical response and clinical remission, are associated with high placebo response rates. These rates are attenuated when endoscopic outcome measures are used,[6,7] suggesting that these indices are unreliable when used alone.

The observed discordance between symptom reporting and objective assessment of disease activity may be secondary to the relatively high proportion of patients who report gastrointestinal symptoms in the absence of active mucosal inflammation. This is similar to the situation observed in patients with irritable bowel syndrome (IBS). The prevalence of these symptoms in IBD is variable, with figures between 11% and 64% reported,[8,9] depending upon the method used to define disease remission, the underlying type of IBD, and the criteria used to define IBS.[10,11] The impact of IBS-type symptoms on the natural history of IBD is uncertain, but the reporting of these symptoms is consistently associated with adverse psychological outcomes, including a higher prevalence of anxiety and depression, compared with IBD patients who do not report these symptoms.[9,12-15]

This article will consider the association between symptom reporting and mucosal inflammation, the prevalence and longitudinal impact of IBS-type symptoms in patients with IBD, the role of the brain-gut axis in the development of these symptoms, and hypothetical treatment strategies for patients who report these symptoms.

Prevalence of Irritable Bowel Syndrome–Type Symptoms in Inflammatory Bowel Disease

According to the current gold standard of the Rome IV criteria, the global prevalence of IBS in the general population is 5%.[16] Given this, some of the explanation for any overlap between IBD and IBS-type symptoms could be coincidence. The prevalence of IBS-type symptom reporting in patients with IBD varies substantially, having been reported to be as low as 11%[9] or as high as 64%[8] in different study populations. However, this is still higher than would be explained by chance overlap. Factors affecting the prevalence of these symptoms include the type of IBD, the criteria used to define disease remission, and the criteria used to define the presence of IBS-type symptoms. In a recent systematic review and meta-analysis including 27 observational studies assessing IBS-type symptom reporting in quiescent IBD, the pooled prevalence of these symptoms in all studies was 32.5%.[11] In the same meta-analysis, when studies were restricted to those using endoscopic assessment to determine disease quiescence, the pooled prevalence of IBS-type symptoms dropped to 23.5%. Overall, IBS-type symptom reporting was observed more commonly in CD (36.6%) than UC (28.7%), and the prevalence was lowest when the Rome IV criteria were used to define IBS, compared with previous iterations.[11] Direct comparison of the prevalence of IBS-type symptom reporting using Rome III vs Rome IV criteria has been performed in an observational study, which confirmed these findings.[10] It also highlighted a more severe associated psychological burden in those select patients who met the Rome IV criteria, as has been observed in patients with IBS.[17]

Proposed Etiology of Irritable Bowel Syndrome–Type Symptoms in Inflammatory Bowel Disease

The etiology of both IBD and IBS is uncertain, but pathophysiologic mechanisms responsible for the development of these conditions may be similar. Mucosal inflammation, altered intestinal microbiome composition, activation of the enteric nervous system, and the brain-gut axis are implicated in both diseases.[18-20] Inflammation is the hallmark of IBD. However, proinflammatory cytokines are more abundant in the blood and intestinal mucosa of patients with IBS than healthy controls, suggesting that subclinical systemic and mucosal inflammation may also contribute to the development of IBS.[21] Debate about the role of inflammation in the generation of IBS-type symptoms in IBD is unresolved. In one prospective case-control study, proinflammatory cell infiltrates, enhanced tumor

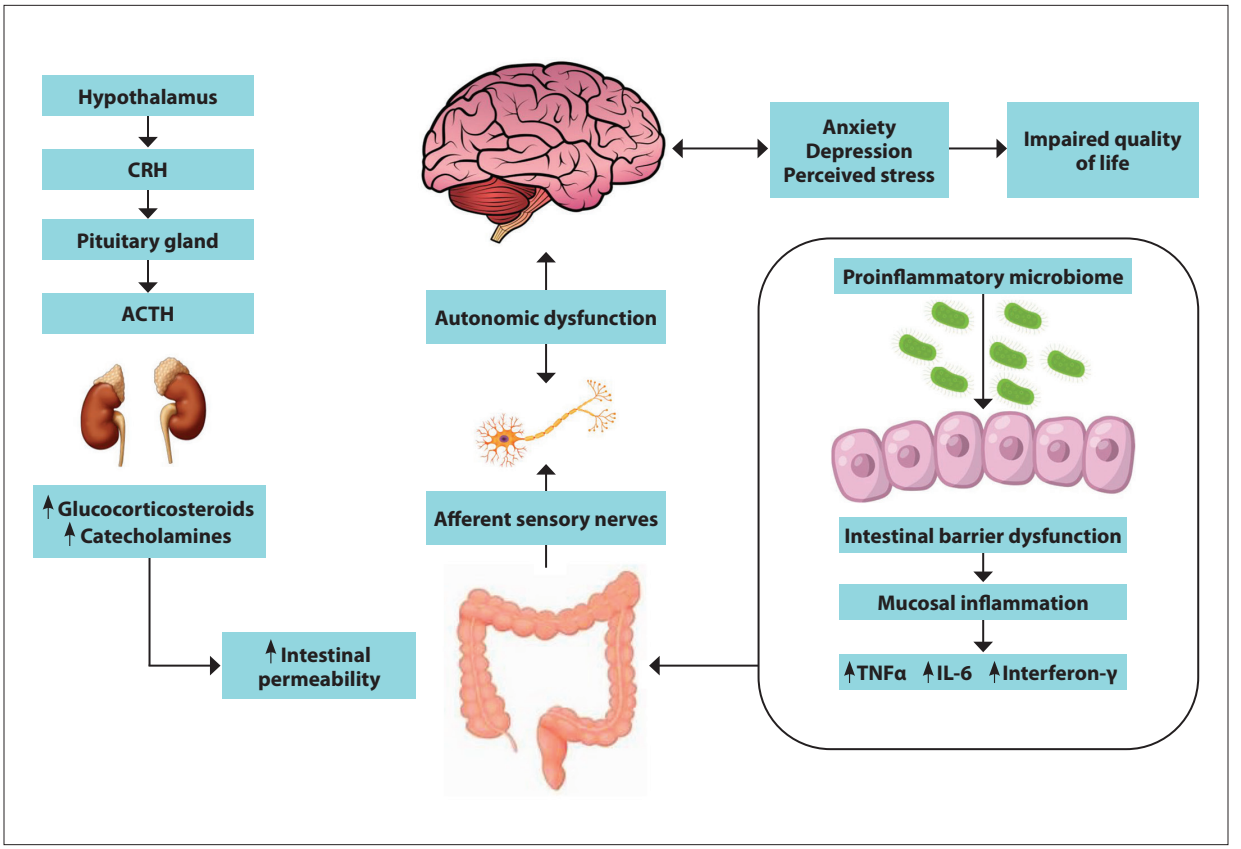

Figure. Proposed neurohormonal pathways of the gut-brain axis.

ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; IL, interleukin; TNFα, tumor necrosis factor alpha.

necrosis factor alpha (TNFα) expression, and increased paracellular permeability were observed in patients with IBD who reported IBS-type symptoms.[22] Despite this, observational studies suggest that the inflammatory burden, assessed endoscopically or with FC, is no greater among patients with IBS-type symptoms than in asymptomatic patients with quiescent IBD who do not report these symptoms.[9,13,23] Additionally, the attenuated symptomatic response to conventional IBD therapies in patients with a limited inflammatory burden,[24-26] as well as the lack of association between IBS symptom reporting and objective adverse disease activity outcomes (including hospitalization and intestinal resection)[12,15] during longitudinal follow-up, suggest that persistent subclinical inflammation in isolation cannot be responsible for the development of these symptoms.

In IBS, interaction between luminal proinflammatory bacterial species and the enteric nervous system leads to activation of afferent sensory nerves and the propagation of visceral hypersensitivity, mediated by the brain-gut axis.[27] Similarly, proinflammatory bacterial species are observed commonly in the lumen and mucosa of patients with IBD and may influence the onset and natural history of the disease in a similar way. Here, a reduction in microbial diversity, specifically butyrate-producing organisms and other anti-inflammatory bacterial species (including *Faecalibacterium prausnitzii*),[28] combined with altered bile acid metabolism[29] and mucosal mucin depletion results in intestinal barrier dysfunction and dysregulation of enteric immunity triggered by exposure to proinflammatory bacterial species.[30] Despite these findings, a cross-sectional study that assessed microbial diversity in patients with IBD reporting IBS-type symptoms failed to identify any significant difference in the abundance of individual bacterial taxa or in overall bacterial diversity between patients who reported IBS-type symptoms and those who did not.[31] Nevertheless, the brain-gut axis may still be implicated in the development of these symptoms, as has been postulated in IBS.[32,33] Anxiety, depression, and perceived stress are often associated with IBS-type symptom reporting in cross-sectional studies,[13,34] but the directionality of the relationship remains uncertain in IBD. Antecedent mood disorders may, therefore, be a risk factor for the development of IBS-type symptoms,

Table. Summary of Evidence for Treatment of IBS-Type Symptoms in Patients With IBD

	Specific therapies	Type of study	Tested in patients reporting IBS-type symptoms?
Biologic therapies	Anti-TNFα antibodies	RCT[24-26]	Indirectly: poor clinical response in symptomatic patients with low inflammatory burden[24-26]
Microbiome therapies	Probiotics	Meta-analysis of RCTs[51]	Yes: improvement in diarrheal symptoms and quality-of-life scores[51]
	Fecal microbiota transplantation	Meta-analysis of RCTs for UC[54]	No
Dietary therapies	Low-FODMAP diet	RCT[65]	Yes: reduction in IBS symptom severity and improved quality-of-life scores[65]
Gut-brain axis–directed therapies	Gut-brain neuromodulators, including selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants	Meta-analysis of case series and RCTs[75]	Possibly: improvements in gastrointestinal symptoms when used in conjunction with optimized medical therapy for UC[76]
	Brain-gut behavioral treatments, including CBT, mindfulness, acceptance and commitment therapy, hypnotherapy, psychodynamic psychotherapy, and solution-focused therapy	Meta-analysis of RCTs[79]	Yes: improvement in quality-of-life scores in one RCT[79]
5-HT$_3$ receptor antagonists	Ramosetron	RCT[84]	Yes: improvement in global symptom severity, pain, and stool frequency in one RCT[84]

5-HT$_3$, 5-hydroxytryptamine-3; CBT, cognitive behavioral therapy; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; RCT, randomized controlled trial; TNFα, tumor necrosis factor alpha; UC, ulcerative colitis.

with the relationship between the disorder and symptoms mediated via the gut-brain axis.

The Gut-Brain Axis: A Target for Therapeutic Intervention in Irritable Bowel Syndrome and Inflammatory Bowel Disease?

The gut-brain axis is a collective term used to describe a series of interconnected neurohormonal pathways comprising the hypothalamus-pituitary-adrenal axis; the central, peripheral, and autonomic nervous systems; and the gastrointestinal tract. These interconnected pathways are instrumental in the pathophysiology of disorders of gut-brain interaction, including IBS, where bidirectional relationships have been described.[32,33] In IBS, antecedent mood disorders, including depression and anxiety, are associated with new onset of symptoms compatible with IBS, and the presence of symptoms compatible with IBS is associated with the development of anxiety or depression de novo. More recently, the same bidirectional relationship between psychological comorbidity and disease activity has been described in patients with IBD.[35,36]

The Figure provides an illustrated overview of the physiologic pathways making up the gut-brain axis. How bidirectional gut-brain interactions may influence the natural history of mental health, disease activity, and IBS-type symptom reporting in patients with IBD is complex and hypothetical. Brain-gut effects may result from hypothalamus-pituitary-adrenal axis activation, triggered by a psychological stressor, leading to secretion of adrenocorticotropic hormone that causes mast cell degranulation and cytokine-mediated intestinal barrier dysfunction.[37] In response to stress, sympathetic nervous system activation and enhanced adrenal medullary secretion of catecholamines may impart proinflammatory effects on the gastrointestinal tract by stimulation of macrophages and mast cells, mediated via nuclear factor κB signaling pathways.[38,39] Cholinergic inhibition of proinflammatory cytokine release is diminished during the stress response,

limiting the anti-inflammatory effects of the vagus nerve.[40]

Propagation of gut-brain effects may be triggered by impaired intestinal barrier function, allowing proinflammatory bacterial lipopolysaccharide-mediated enteric immune activation, resulting in visceral hypersensitivity. This phenomenon is described in patients reporting IBS-type symptoms in IBD, and its presence is associated with psychological distress and female sex.[41] Although the etiology of visceral hypersensitivity is uncertain, perception of visceral pain is thought to involve the spinothalamic, spinoreticular, and spinomesencephalic tracts.[42] Central convergence of each of these pathways has been shown to influence psychological well-being in experimental animal models, providing a feasible link between visceral pain and mood, mediated via gut-brain interactions.[43]

Longitudinal Disease Outcomes in Patients Reporting Irritable Bowel Syndrome–Type Symptoms

Cross-sectional studies describe a consistent association between the reporting of IBS-type symptoms and poor psychological health, including anxiety, depression, and somatization, as well as reduced quality of life.[9,13,34] These relationships appear durable over time[12,14,15] and may provide a target for therapeutic intervention via modulation of altered gut-brain interactions, potentially with the use of neuromodulators. In contrast, in a longitudinal observational study with follow-up extending to 6 years, disease activity outcomes (including flare, escalation in medical therapy, hospitalization, and the need for surgery) were no different in patients in biochemical remission at baseline (defined using FC <250 μg/g) who reported IBS-type symptoms compared with patients who did not.[12,14,15] Although these findings suggest that the natural history of inflammatory activity is not impacted by the presence of IBS-type symptoms, clinician uncertainty regarding whether these symptoms are related to ongoing inflammation may lead to increased health care utilization, as evidenced by an increase in requesting radiologic and endoscopic investigation and increased frequency of hospital clinic attendance, compared with patients who do not report these symptoms.[12,14,15] Furthermore, clinical decision-making based on patient-reported symptoms in isolation may result in inappropriate escalation of medical therapy that is expensive,[44] ineffective for non-inflammatory symptoms,[24] and associated with adverse events.[45-47]

The presence of adverse psychological health, reduced quality of life, and increased health care utilization highlight the need for alternative management strategies, distinct from conventional IBD management, which may improve outcomes in this group of patients.

Management of Patients Reporting Irritable Bowel Syndrome–Type Symptoms in Inflammatory Bowel Disease

Low-grade mucosal inflammation, an abnormal microbiome, and disordered brain-gut axis activity may be implicated in the development of both IBS and IBD.[18] Assessing the benefit of conventional IBD treatments as well as IBS therapies, including probiotics, fecal microbiota transplantation (FMT), dietary interventions, gut-brain neuromodulators, and brain-gut behavioral treatments, in the management of patients with IBD reporting IBS-type symptoms would, therefore, seem logical. The Table provides a summary of possible treatment options for the management of IBS-type symptoms in IBD.

Conventional Pharmacologic Therapies

Numerous randomized controlled trials (RCTs) investigating the effect of pharmacologic therapies, including glucocorticosteroids, 5-aminosalicylic acids, immunomodulators, small molecules, and biologic therapies, have been conducted in IBD; however, no clinical trial of conventional IBD pharmacotherapy has assessed efficacy in the management of IBS-type symptoms specifically. Despite this, several clinical trials have commented on a lack of efficacy of biologic therapy in symptomatic patients with normal CRP or only mild endoscopic activity at randomization.[24-26] These findings suggest that conventional pharmacologic therapies are not effective in the management of symptomatic patients with a limited inflammatory burden and are unlikely to be of benefit in the management of patients who report IBS-type symptoms, when used in isolation. Acknowledging that subclinical mucosal inflammation, independent of IBS-type symptom reporting, is associated with adverse longitudinal disease activity outcomes suggests that conventional pharmacologic therapy has a role in the management of patients who report these symptoms.[48] The efficacy of optimized conventional IBD pharmacotherapy combined with alternative interventions, including dietary treatments, gut-brain neuromodulators, and brain-gut psychological therapies, has not been evaluated in clinical trials to date.

Manipulation of the Intestinal Microbiome

Probiotics may be effective for the treatment of gastrointestinal symptoms in IBS.[49] Their use in IBD has also been assessed in systematic reviews and meta-analyses.[44,50] The efficacy of probiotics, in terms of induction of remission of active disease or prevention of relapse of quiescent disease, appears limited and restricted to patients with UC.

Only 2 studies have sought to assess the effect of probiotics in the treatment of patients reporting persistent

symptoms in otherwise quiescent IBD. An observational study of 43 patients with UC in endoscopic remission meeting the Rome IV criteria for IBS suggested an improvement in diarrhea and quality of life following 4 weeks of treatment with a probiotic preparation comprising *Lactobacillus acidophilus*, *Clostridium butyricum*, *Bacillus mesentericus*, and *Streptococcus faecalis*.[51] A small RCT examining the effects of *Bifidobacterium bifidum* G9-1 for patients with quiescent CD meeting Rome III criteria for IBS reported no improvement in inflammatory burden but improved anxiety scores.[52] These studies are limited by their modest sample size, meaning that firm conclusions cannot be made regarding the benefit of probiotics for IBS-type symptoms in IBD.

The evidence for FMT in both IBS and IBD is limited. In a systematic review and meta-analysis of RCTs of FMT vs placebo conducted in patients with IBS, improvement in symptom severity was observed, particularly in patients receiving FMT delivered via colonoscopy.[53] Similarly, in a meta-analysis of RCTs of FMT vs placebo in 324 patients with UC, short-term improvements in disease activity were noted.[54] No studies have examined the effect of FMT in patients with IBD who report IBS-type symptoms. In addition, FMT remains an experimental intervention in both IBS and IBD.

Rifaximin, a nonabsorbable antibiotic, is an evidence-based intervention for the management of IBS with diarrhea[55] and is recommended as a second-line therapy in national guidance.[56] However, antibiotics are not recommended for the treatment of inflammatory activity in IBD[57,58] and have not been evaluated for the management of IBS-type symptom reporting in IBD.

Dietary Interventions

International consensus guidelines support the use of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) in IBS.[59,60] FODMAPs are osmotically active fermentable carbohydrates, the ingestion of which results in increased luminal water and gas volume,[61] leading to the perception of pain.[62] The low-FODMAP diet is also associated with potentially deleterious alterations in bacterial diversity, including the abundance of *Bifidobacteria.*[63,64] Four studies have considered the low-FODMAP diet as an intervention for the management of IBS-type symptoms in IBD. In an open-label trial of 89 patients with IBD who also fulfilled the Rome III criteria for IBS, participants were randomized to a low-FODMAP or habitual diet.[65] Improved IBS-type symptom burden and quality of life were observed in patients receiving the low-FODMAP diet, compared with patients eating a habitual diet. In a double-blind, crossover, rechallenge RCT, 32 patients with IBD with functional symptoms who had previously responded to a low-FODMAP diet were randomized to a series of 3-day FODMAP challenges, during which time symptom severity and stool output were assessed.[66] Abdominal pain, bloating, flatulence, and fecal urgency scores were all significantly higher during the FODMAP challenge. Conducted over a 4-week period, another RCT of low-FODMAP diet vs sham dietary advice in 52 patients with quiescent IBD who reported functional bowel symptoms demonstrated significantly higher rates of adequate relief of symptoms with a low-FODMAP diet.[64] The fourth RCT assessed the effect of the low-FODMAP diet in patients with IBD with mild disease activity (defined using a combination of FC and clinical disease activity indices) who also fulfilled the Rome IV criteria for IBS.[67] Findings suggested that a low-FODMAP diet was associated with a reduction in median FC and improved symptom burden and quality of life.

Although these RCTs suggest a potential role for the low-FODMAP diet in the management of IBS-type symptoms in IBD, their small sample size, together with issues of blinding and the lack of an active control in some trials, limits the validity and applicability of these findings in clinical practice.

Gut-Brain Neuromodulators

When used at a low dose to regulate brain-gut activity, antidepressants are referred to as gut-brain neuromodulators.[68] They are effective in managing abdominal pain and global symptoms in IBS,[69,70] and their use is recommended by international guidance.[56] The mechanism by which gut-brain neuromodulators are proposed to impart their gastrointestinal effects is multifaceted. Tricyclic antidepressants upregulate peripherally acting neurotransmitters, including serotonin and noradrenaline, which influence visceral sensitivity and gut motility.[71] They may also have anti-inflammatory effects mediated via the vagus nerve,[72] while potentially having a direct effect on circulating inflammatory cytokines, mediated via nuclear factor-κB.[73] Similarly, selective serotonin reuptake inhibitors affect circulating levels of interleukin-6 and TNFα, both of which are implicated in the pathogenesis of IBD.[74]

Although these drugs may be effective in the management of depressive symptoms in patients with IBD in general,[75] only one study has reported the efficacy of tricyclic antidepressants in patients who had ongoing symptoms in otherwise quiescent disease.[76] In this retrospective uncontrolled study, improved symptom severity was observed in 60% of patients with IBD, with a greater response noted in patients with UC compared with CD, suggesting that these drugs may be a beneficial adjunctive therapy in these patients.

Brain-Gut Behavioral Treatments

Brain-gut behavioral treatments are superior to placebo in managing symptom burden in patients with IBS, with cognitive behavioral therapy and gut-directed hypnotherapy interventions having the most evidence for efficacy.[77] These therapies also appear to be effective in the management of pain in patients with IBS.[78]

In IBD, a recent systematic review and meta-analysis of RCTs assessed the efficacy of brain-gut behavioral treatments in the management of disease activity, psychological well-being, and quality of life.[79] Overall, brain-gut behavioral therapies had no impact on disease activity outcomes but were associated with a short-term beneficial impact on anxiety, stress, and quality-of-life scores and a longer-term beneficial effect on depression scores, compared with treatment as usual. Treatment effects were most marked with third-wave therapies such as acceptance and commitment therapy and when included studies were restricted to those recruiting patients with IBD with impaired psychological health, fatigue, or reduced quality of life at baseline.

Only one RCT has sought to examine the effect of a brain-gut behavioral treatment in patients with IBD specifically reporting IBS-type symptoms.[80] The authors reported that multiconvergent therapy was associated with an improvement in quality of life, compared with a waiting list control. However, the sample size of only 27 patients means that definitive evidence is lacking to support the efficacy of brain-gut behavioral treatments in this patient group.

Other Pharmacologic Therapies

Abdominal pain and diarrhea are common presenting symptoms associated with IBS. Pharmacologic management of these symptoms, including the use of antidiarrheal agents and antispasmodics, is considered first-line treatment in IBS.[56] Loperamide, peppermint oil, and hyoscine butylbromide are all evidence-based treatments used in IBS but have not been tested in IBD. Moreover, the use of loperamide is cautioned against in patients with IBD because of a theoretical increased risk of adverse events such as precipitating toxic megacolon, particularly in patients with active disease.[81] No studies have assessed the efficacy of these treatments in patients with IBD reporting IBS-type symptoms, but their use is supported in clinical guidelines, provided that disease quiescence has been confirmed objectively.[82]

5-hydroxytryptamine-3 receptor antagonists, including ondansetron, alosetron, and ramosetron, are also effective in managing IBS with diarrhea.[55,83] An RCT of ramosetron showed beneficial effects on clinical outcomes, including global symptom severity, pain, and stool frequency, in IBD patients reporting IBS-type symptoms.[84]

Summary

The assessment and management of IBD has changed significantly in recent years, and the availability of multiple different advanced therapies has increased the complexity of clinical decision-making in these patients.[46,47] As therapeutic options have evolved, treatment targets have transitioned from subjective[85] to more objective determinants of disease activity,[2] aided by the use of noninvasive markers of intestinal inflammation, including FC. Contemporary medical management is associated with improved clinical outcomes, including a reduction in the observed incidence of the requirement for surgery in both CD and UC.[86,87] Despite this, 1 in 4 patients with endoscopically confirmed disease quiescence continues to report persistent gastrointestinal symptoms.[11] IBS-type symptom reporting does not appear to impact longitudinal disease activity outcomes but is consistently associated with psychological comorbidity, impaired quality of life, and increased health care utilization.[12,14,15] Escalating use of conventional medical therapy is ineffective in treating these symptoms,[24-26] yet the evidence base for alternative management strategies is poor.

Although probiotics, FMT, the low-FODMAP diet, gut-brain neuromodulators, and brain-gut behavioral therapies may be potential adjunctive treatment options, particularly in patients with coexistent mood disorders,[79] the evidence base supporting their use is restricted to data from small RCTs or observational studies, which lack the necessary power to confirm treatment effects definitively. Many of these studies rely on symptom reporting as the sole determinant of disease activity assessment, and the inclusion of patients without IBS-type symptoms in many of these trials may have resulted in an underreporting of their efficacy. Future research should focus on the evaluation of these treatments in well-designed RCTs using objective determinants of inflammatory disease activity and validated measures of psychological well-being and quality of life.

Recognition of the high prevalence of IBS-type symptom reporting, as well as the lack of evidence-based options for the management of these symptoms, highlights the need for additional carefully designed clinical trials in this subgroup of patients. The high prevalence of psychological comorbidity,[88] combined with evidence of a bidirectional relationship between mood and disease activity in IBD,[35,36] reinforces the importance of gut-brain axis interactions in the generation of these symptoms.

Disclosures

The authors have no relevant conflicts of interest to disclose.

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