

Consensus Statement on Depression, Anxiety, and Functional Gastrointestinal Disorders

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Functional gastrointestinal disorders such as irritable bowel syndrome (IBS) are commonly encountered in primary care, and IBS accounts for over 50% of new consultations with gastroenterologists. IBS and other related functional gastrointestinal disorders are often associated with psychiatric disorders, most frequently anxiety and depression. The evolving disease model for IBS, based on alterations in brain-gut interactions, potentially explains, at least in part, why this association is so commonly observed.

Central to the proposed model is an uncontrolled cycle of positive feedback between the brain and the gut, potentially initiated by pathologic events in either the central nervous system (CNS) or the enteric nervous system (ENS). According to the model, individuals with increased CNS arousal could experience gastrointestinal distress and increased motility via CNS-mediated autonomic outflow. Visceral afferent input to the locus ceruleus and other critical brain structures via vagal afferents via the ENS could create the uncontrolled cycle of gastrointestinal distress and CNS arousal.

At our consensus meeting on depression and anxiety disorders in general medicine, the International Consensus Group on Depression and Anxiety reviewed anxiety, depression, and functional gastrointestinal disorders from the perspectives of both the gastroenterologist and the psychiatrist. This article sets out our consensus views on the detection of depression and anxiety in gastroenterology as well as management issues in the light of the evolving disease model and identifies further areas for research.

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PRESENTATION

IBS and other functional gastrointestinal disorders are typically worsened by stressful life events such as bereavement, breaking up of close relationships, relocating, or getting a new job. In many cases, it is a major life event that first prompts IBS sufferers to consult a physician about their gastrointestinal symptoms.

IBS patients frequently report prior traumatic events, including sexual and/or physical abuse or other severe acute stressors. Exposure to a situation in which there is a threat of death or serious injury can result in persistent gastrointestinal symptoms. There is evidence, for example, that victims of rape often experience moderate to severe gastrointestinal symptoms, persisting for at least 3 months after the assault.

Patients with new-onset IBS tend to exhibit more concomitant anxiety than depression. Patients with IBS that is persistent or resistant to treatment are likely to exhibit both depression and anxiety. IBS often co-occurs with other functional disorders such as chronic fatigue, a spectrum of pain syndromes including chronic pelvic pain (a syndrome of altered visceral perception, like IBS) and fibromyalgia (a syndrome of altered somatic perception), noncardiac chest pain, interstitial cystitis, and migraine headache.

Patients with IBS exhibit "visceral hyperalgesia," which can be demonstrated experimentally via rectal distension procedures. Using this paradigm, IBS patients consistently report pain or discomfort at stimulus intensity levels that are lower than the discomfort thresholds observed in normal volunteers.

Research Needs

There is evidence that some neurobiological abnormalities such as increased secretion of corticotropin-releasing factor may play a role in the etiology or modulation of anxiety, depression, posttraumatic stress disorder (PTSD), and IBS.¹ Potential pathogenic associations between IBS, anxiety, depression, and PTSD require further investigation.

Further studies are needed to understand the reduced cortisol response in IBS patients, which is also observed in subjects who develop PTSD after exposure to an acute trauma.

IMPACT OF ANXIETY AND DEPRESSION ON PROGNOSIS

IBS is comorbid with psychiatric disorders such as panic, anxiety, and depression in 50% to 90% of IBS patients. This high level of comorbidity is theoretically consistent with shared pathophysiologic mechanisms for the disorders. The presence of anxiety or depression has a significant adverse effect on the outcome of IBS, with patients suffering from concomitant anxiety and depression showing less improvement in abdominal pain, distension, and diarrhea (but not constipation) in response to treatment interventions.² The poor response in IBS patients with anxiety and depression may be secondary to the strong association between the severity of psychiatric symptoms and the severity of IBS symptoms. There appears to be a self-perpetuating cycle of interaction, such that anxiety and depression increase the severity of IBS symptoms while chronic IBS symptoms increase anxiety and particularly depression.

The adverse effect of anxiety and depression on outcome underlines the importance of including psychological assessments in studies of treatment intervention in IBS.

RECOGNITION OF ANXIETY AND DEPRESSION

It is important for general physicians and gastroenterologists to appreciate that brain-gut interactions are implicated in the etiology and exacerbation of IBS. Directing effort at the recognition and treatment of concomitant anxiety and depression may prevent the progression of increasing severity of psychiatric and gastrointestinal symptoms. Although gastroenterologists are increasingly aware of the importance of psychological factors and the need for psychosocial support of their patients, they are not always equipped to deal confidently with emotional issues. Also, medical outpatient clinics generally focus almost exclusively on investigations for organic disease and may limit the opportunity for physicians to explore with their patients any psychological problems associated with gastrointestinal symptoms.

Sufferers from IBS tend not to present with psychological complaints and are reluctant to acknowledge the impact of psychological factors. IBS patients who persistently attribute their symptoms to physical illness alone may benefit from education about the involvement of stress and psychological factors in exacerbating and perpetuating this painful syndrome.

A large percentage of IBS patients show autonomic abnormalities similar to those of patients with anxiety and depression. IBS patients share certain abnormalities in regional brain activity with PTSD patients and depressed patients and show evidence of fear conditioning toward visceral sensations and marked alterations in brain circuits involved in fear conditioning. However, in approximately 50% of IBS patients, anxiety remains undetected using current standardized instruments. Apparently, IBS is a disorder in which anxiety is focused on an internal stimulus. The use of an instrument to assess sensitivity to bodily sensations could be useful, in addition to the use of traditional measures of anxiety.

Two self-administered screening instruments are the Somatosensory Amplification Scale,³ a 10-item questionnaire to assess sensitivity to uncomfortable visceral and somatic sensations, and the Illness Attitudes Scale,^{4,5} which consists of 9 subscales designed to assess fears, attitudes, and beliefs associated with abnormal illness behavior and hypochondriacal concerns. Validation studies^{6,7} of these scales in general medical and general practice patients have demonstrated satisfactory internal consistency and stability for each of the scales and a high degree of intercorrelation of their scores.

MANAGEMENT ISSUES

IBS patients are reported to have more firmly held health worries than depressed patients attending psychiatric clinics.⁷ They worry about their symptoms, fear that they might have cancer or other serious illness, and are preoccupied with bodily symptoms. Pronounced health worries contribute to a poorer outcome from treatment of IBS, as do concomitant psychiatric symptoms and a lack of psychosocial support. Those patients who accept that stress may contribute to their IBS symptoms tend to have a more favorable outcome than those who attribute symptoms solely to physical illness.

We suggest that it is important for clinicians to inquire routinely about acute or chronic sustained psychological stress that may contribute to fluctuations in the IBS symptoms of their patients. It is helpful for patients to understand why they have their symptoms and what makes them worse. There are brief, specific questionnaires for traumas such as sexual abuse that can be applied and may identify the need to refer the patient to a psychiatrist for further assessment. One example is the Davidson Trauma Questionnaire,⁸ a self-rating scale that assesses exposure to a wide range of traumata, as well as age at occurrence of traumata and identification of the worst event. We recognize the lack of data on the importance of trauma assessment in the management process. Clearly, if the patient has, for example, comorbid PTSD, it should be treated. If IBS appeared during or soon after a severe trauma, it may be helpful to make the patient aware that IBS can be related

to what they have experienced. Patients should also be told that numerous environmental cues, which may remind them consciously or unconsciously of that trauma, might exacerbate their symptoms via conditioned fear pathways that modify intestinal functioning.

The brain-gut model for IBS provides a rationale for applying similar strategies to the treatment of both gastrointestinal symptoms and symptoms of depression and anxiety. As yet, the clinical data are limited, but they generally show a positive effect of treating IBS patients with psychotropic medication, irrespective of the presence of concomitant psychiatric symptoms or disorders. It is an important message to gastroenterologists and general physicians that treatment with antidepressants or benzodiazepine anxiolytics may benefit patients with functional gastrointestinal disorders, improving gastrointestinal as well as psychological symptoms and overall quality of life.

TREATMENT OPTIONS

No currently accepted standard of care exists for IBS and related functional gastrointestinal disorders. In the past, clinical trials in IBS often have been flawed methodologically, with one of the major issues being the lack of agreement on the definition of efficacy and the lack of validated outcome measures.^{9,10} Another issue is the exclusion of IBS patients with comorbid psychiatric conditions from randomized clinical trials.¹ Since anxiety and depression are present in 90% of the IBS patients who seek treatment, using the presence of these symptoms as an exclusion criterion for trial entry would mean that the results of these clinical trials cannot be generalized.

There is increasing research interest in the appropriate management of IBS and related functional gastrointestinal disorders with different strategies targeted at sites in both the periphery and the CNS.

Psychotherapy

Given the association between severe social stress and the onset of IBS, physicians' support for patients' psychosocial problems and relationships is important in the overall management of IBS. Formal psychotherapy is reported to be an effective treatment, reducing psychological symptoms with a parallel reduction in bowel symptoms.^{11,12} More recent studies^{13,14} support the efficacy of cognitive-behavioral therapy in improving the distress and disability associated with bowel symptoms.

Facilities for providing psychotherapy may not be readily available to gastroenterologists or general physicians, and even when they are, intensive psychological treatment for individual patients is unlikely to become a first-line treatment because it is time consuming and thus expensive. A more cost-effective option is for a psychologist to provide cognitive-behavioral therapy to a group of

patients. Group therapy (8 sessions over 3 months) is reported to produce sustained reduction in abdominal complaints and avoidance behavior.¹⁵

Pharmacotherapy

There have been only a few controlled studies of psychotropic agents in the treatment of IBS.¹ In clinical practice, gastroenterologists often use tricyclic antidepressants in low doses (usually less than 50 mg/day) to treat abdominal pain in IBS patients. Treatment is reported to attenuate somatic symptoms, although the threshold for the perception of visceral pain remains unchanged. Less information exists on newer antidepressants such as the selective serotonin reuptake inhibitors (SSRIs) in IBS patients with or without psychiatric disorders. Some case reports suggest that SSRI antidepressants may be useful for some patients^{16,17}; others suggest exacerbation of IBS may also occur.¹⁸

Benzodiazepines have been found to be effective when anxiety disorders co-occur with IBS. Since their antidepressant effects are minimal, they would not be useful for treating coexisting depression or protecting against emerging depression during extended use. They may work well in combination therapy with antidepressants for comorbid anxiety and depression in IBS patients.

When IBS patients visit a gastroenterologist, they may be reluctant to receive an antidepressant, interpreting this treatment option as meaning that their symptoms are based on psychological factors. Physicians need to educate their patients about the importance of brain-gut interactions in IBS. In our experience, educational efforts directed at explaining the mechanisms and brain circuits associated with pain modulation and IBS symptoms are well received by patients, who will then more readily accept taking medications acting on these circuits. In this approach, it is vital to validate the gastrointestinal symptoms and avoid any implication that patients have a neurotic disorder. Many patients feel that they are labeled as neurotic and are stigmatized by the medical profession, whereas physicians experience frustration with the disorder, related as much to uncertainty about appropriate intervention as intolerance of their patients' complaints.¹⁹ A better partnership between physicians and their patients founded on an appropriate explanation of the disorder will help in achieving a better outcome.

Research Needs

There is a need for well-designed clinical trials, including dose-ranging studies, of SSRIs and other antidepressants in IBS. Further study of responders to treatment could determine whether there are subgroups of IBS sufferers more responsive to one form of treatment than another. For example, there may be one subgroup with a conditioned visceral stimulus fear response that is more likely to respond to benzodiazepines and a second subgroup

more similar to patients with chronic anxiety disorders and more responsive to antidepressants.

The inclusion of appropriate psychological measures in clinical trials could be useful in assessing which of the following aspects of IBS are improved with treatment: pain, depression and anxiety, sensitivity to visceral sensations, gut motility/reactivity locally, or alterations in afferent nerve systems that generate or relay information on abdominal pain.

Finally, further research is needed on the potential role of trauma in the etiology or modulation of IBS. At a minimum, routine screening and referral for treatment, as indicated for traumatic experiences, may assist in the management of IBS patients.

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