It’s Not Just About the Gut: Managing Depression and Anxiety in Inflammatory Bowel Disease

Anxiety and depressive disorders are prevalent in the community, and even more common in individuals with chronic disease, contributing to the role impairment and disability often seen in chronic illness. Higher rates have also been found in inflammatory bowel disease, and these conditions can have a detrimental effect on disease course. Routine screening for anxiety and depression in IBD patients has been encouraged. Practical recommendations for managing these conditions when treating the patient with IBD are discussed, including consideration of screening and initiating evidence-based pharmacological or psychological treatment.

INTRODUCTION
Anxiety and depression are the most common psychiatric disorders, with one year prevalence rates of 18% and 10% respectively (1), and highest prevalence in young adulthood. These disorders are seen at even higher levels in persons with chronic illnesses such as cardiac disease, diabetes, and arthritis. While anxiety and depression carry a high disease burden in themselves, much of the disability and role impairment seen in chronic medical conditions is associated with comorbidity with these psychiatric conditions (2,3). There is a growing recognition of the need for management of both the physical and mental conditions in the care of the patient (4).

ARE DEPRESSION AND ANXIETY MORE COMMON IN IBD?
Given the stress associated with a chronic illness and the historical observations of psychiatric comorbidity in IBD, there was a long held assumption that depression and anxiety played a causal role and were present at higher rates in IBD patients than in the general pop-
It’s Not Just About the Gut

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #62

ulation. That assumption was challenged in the 1990s with careful reviews that criticized study design flaws in prior empirical work and recommended better accounting for disease severity (5–7). Recent reviews, assessing more rigorous clinic and community studies that have used appropriate control groups or population-based case comparisons, have converged on the conclusion that there are higher rates of depression and anxiety in IBD, but that there is little evidence to date of an etiological contribution (8,9). Nevertheless, experimental studies with animal models are suggesting common and potentially causal pathophysiological mechanisms for inflammatory processes and depression in particular (10,11).

WHAT ARE THE RATES OF THESE DISORDERS IN IBD?

Estimates of rates have been variable, depending on the measure used, with self-report and single item scales often yielding higher estimates. Structured psychiatric diagnostic interviews are considered the gold standard for identifying anxiety and depressive disorders. A recent study by our group directly compared the levels of anxiety and depression in a population-based IBD cohort to the levels in the community using a matched sample of controls from a national health survey (12). The same structured diagnostic interview was used to determine lifetime prevalence rates for both samples. Those with IBD were at least twice as likely to have experienced a depressive disorder at some point in their lifetime compared to those of similar age and background who did not have IBD, with rates of 27% compared to 12%. There was also a trend to a higher lifetime prevalence of panic disorder for those with IBD, with almost double the level compared to the community (8.0% vs 4.7%). Other large population-based studies have had similar findings of significantly higher rates of depression and anxiety in the IBD sample than in controls (13,14).

WHAT ARE THE EFFECTS OF DEPRESSION AND ANXIETY IN INFLAMMATORY BOWEL DISEASE?

Dealing with a chronic illness can be a major life stressor, and stress is in turn a risk factor for anxiety and depression (15). The period around the onset of the disease, as well as periods of disease flare, are times of higher risk for depression and anxiety in IBD (13,16). While psychiatric symptoms may settle as the IBD flare resolves, it is not clear that this occurs for all affected patients and there is no good ability to predict who might still require clinical support for depressive or anxiety symptoms. Depression in particular has been found to have a detrimental effect on disease course, with a greater likelihood of more frequent or earlier relapse (17). There is evidence of significantly poorer adherence to treatment regimens by those with a comorbid psychiatric disorder (18). Finally, overall quality of life, those aspects of daily living and well-being that are of such importance to the individual, has also been found to be compromised (19,20).

SHOULD COMORBID ANXIETY OR DEPRESSION BE MANAGED WITHIN IBD CARE?

Updated consensus guidelines for Crohn’s disease management have included a recommendation to assess for anxiety and depression and to identify appropriate treatment as needed (21). Similar recommendations have been made for routine screening of depression in heart disease and diabetes (22,23). A small qualitative study of 18 gastroenterologists found that half of those surveyed had directly treated their IBD patients for anxiety or depression (24), but there has been no systematic evaluation of how widespread the practice is or how consistently that has been done for all patients in need. Gastroenterologists have been encouraged to expand their patient care models to provide oversight of more general health maintenance, with attention to comorbid health issues including psychiatric concerns (25). With anxiety and depression often occurring or intensifying in the context of diagnosis or escalating GI disease, the physician managing the inflammatory bowel disease is the logical entry point for care of both. However, patients interested in or in need of psychological care often do not mention to their physician when they are experiencing symptoms of anxiety or depression, and as a result these conditions frequently go unrecognized and untreated.

(continued on page 15)
These psychiatric conditions are readily treatable, however, with well-established response to pharmacological and psychological therapies (26,27). The second-generation antidepressants are broadly effective for both anxiety and depression (28) and include the selective serotonin reuptake inhibitors (SSRIs; e.g., citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) and the serotonin norepinephrine reuptake inhibitors (SNRIs; e.g., duloxetine, venlafaxine). Similarly, cognitive behavioral therapy, a class of psychotherapy that targets changes in behavior (e.g., activation, avoidance reduction, improved self-care, problem solving) and patterns of negative thinking that affect biological and emotional processes, has strong empirical support for efficacy with both conditions (29). Both pharmacological and psychological interventions have been identified as first line treatments for anxiety and depression (26,27).

ARE ANXIETY AND DEPRESSION IN IBD RESPONSIVE TO TREATMENT?

While the empirical support for the efficacy of antidepressants, based on numerous randomized controlled trials and meta-analyses, is strong in the general literature, there is more limited evidence on treatment in the context of IBD. A recent review identified only 12 studies in the prior 15 years that have assessed the use of antidepressants in IBD (30), half of which were case reports. The findings from these studies were favorable, noting good response of the psychiatric conditions, albeit based on small numbers. The additional observation in several of the studies that disease activity was also positively affected is still a very preliminary finding, although lab-based work using rodent models of colitis has raised the possibility of a protective role for antidepressants in inflammatory processes (31).

There has been some attention to the use of psychological therapies in IBD, with controlled studies examining psychodynamic and cognitive behavioral applications (32), and recent exploration of hypnotherapy for steroid nonresponders (33). In the subset of studies that selected for patients with comorbid anxiety or depression and assessed outcomes using evidence-based treatments for these conditions, results were positive. Cognitive behavioral therapy resulted in significant improvement in depression and anxiety, with sustained benefits one year later, across both adolescent and adult samples (34,35). The adolescent study identified a trend toward corresponding improvement in disease activity, but those findings are very preliminary.

SCREENING FOR ANXIETY AND DEPRESSION IN THE IBD PATIENT

Since patients may be reluctant or embarrassed to raise any concerns about their mental health and distress, incorporating brief screening questions into a health systems review at the clinic visit can facilitate early identification and intervention, as well as communicate to the patient that their overall health is of concern. Alternatively, validated screening measures can be administered in the waiting room, as even brief scales have been found to be effective at identifying problems (36). The latter approach is often more practical in high volume centres, considering that staff time may be required to distribute, collect and score the scale.

Common patterns often seen in patients who are having difficulty coping with illness can include:

• Withdrawal from normal activities due to distress about the illness, including decreased physical activity and reduced time with family/friends.
• Putting life on hold until all medical avenues have been exhausted.
• Loss of focus on personal direction and goals.
• Persistent worry that the medical problems will never be stabilized or resolved.
• Anger and frustration about having the illness.

The use of three or four questions in the clinical review, such as those listed below that ask generally about coping and then specifically about salient symptoms of anxiety and depression, can be useful in flagging issues.

• How have you been coping recently? Have there been any major stresses for you?
• Have you noticed that you feel nervous or tense much of the time? OR Do you experience problems with stress or worry?
• Have you felt down or depressed most of the day OR Do you find that you have decreased interest in the things you usually enjoy?
It’s Not Just About the Gut

**INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #62**

**Table 1. Early intervention with anxiety and depression: behavioral steps**

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understanding and acceptance of disease</td>
<td>• Patients who <em>accept</em> the disease and focus on coping rather than cure manage better over time; those who do not move beyond frustration and anger are at risk for anxiety and depression.</td>
</tr>
<tr>
<td></td>
<td>• Provide well-designed education materials and/or good quality web-based resources to the patient regarding the disease and distress.</td>
</tr>
<tr>
<td></td>
<td>• Ask the patient about disease-related worries and provide information related to those concerns.</td>
</tr>
<tr>
<td>Diarrhea management</td>
<td>• Bowel symptoms can be embarrassing; ask directly how the patient is managing.</td>
</tr>
<tr>
<td></td>
<td>• Encourage behavioral steps that promote mobility such as carrying a ‘safety kit’ (e.g., toilet paper; change of clothes, air freshener).</td>
</tr>
<tr>
<td></td>
<td>• Encourage regular use of toilets when away from home to minimize phobic avoidance and activity restrictions.</td>
</tr>
<tr>
<td>Pain management</td>
<td>• Chronic pain can escalate depression and anxiety, and vice versa.</td>
</tr>
<tr>
<td></td>
<td>• When pain is pronounced, determine if it represents active disease that requires escalation of immune therapy, or is functional and may respond to alternative approaches.</td>
</tr>
<tr>
<td></td>
<td>• Address unrealistic beliefs about pain and treatment such as “it will never go away” or “I should only use pain medicine when the pain is so awful I can’t stand it”.</td>
</tr>
<tr>
<td></td>
<td>• Review principles of pain treatment with the patient: when pain is intermittent, analgesic medication may be of benefit PRN; if pain is constant, some may require chronic regular maintenance dosing. Use of analgesics in anticipation of challenging activities, and in combination with adjuvant medications or behavioural approaches where indicated can be considered.</td>
</tr>
<tr>
<td>Maintaining physical and social activities</td>
<td>• Encourage participation in regular physical activity and enjoyable social or leisure activities; increased activity in both areas is generally associated with improved mood.</td>
</tr>
<tr>
<td></td>
<td>• The physician is in a good position to advise on what is ‘safe’ in the context of the patient’s disease and energy.</td>
</tr>
<tr>
<td>Problem solving</td>
<td>• Patients with depression and anxiety are especially vulnerable to coping with these illness-related challenges such as financial strain with excessive worry rather than solution-focussed action.</td>
</tr>
<tr>
<td></td>
<td>• A few minutes spent on practical problem solving can help the patient to develop a more effective approach.</td>
</tr>
<tr>
<td>Focus on life goals</td>
<td>• Encourage a re-focus from symptoms to important areas in the patient’s life such as work, education, caring for family, or other personal goals</td>
</tr>
<tr>
<td></td>
<td>• Have patient identify and implement small, measurable steps toward these goals.</td>
</tr>
</tbody>
</table>
If the patient acknowledges symptoms or difficulties, then further probing is important to determine severity, persistence and level of interference. Typical anxiety symptoms include acute or chronic sympathetic arousal, excessive worry, and behavioral avoidance, whereas depression is characterized by depressed or agitated mood, anhedonia, cognitive interference (e.g., concentration difficulties), and somatic changes (e.g., low energy, loss of sexual interest, change in sleep) (37). When any of these clusters of symptoms have been consistently present for more than a few weeks, and are disrupting daily functioning, some level of intervention can be of benefit (See Figure 1).

EARLY INTERVENTION IN THE CLINIC

If the patient is having difficulty coping, or is experiencing symptoms of anxiety or depression, it can be helpful to normalize the experience by explaining the condition and its common occurrence with acute symptoms or chronic disease. Nevertheless, as effective coping can improve health, functioning, and quality of life, it can also be important to emphasize the need to deal with these concerns. Effective approaches to management of anxiety and depression often focus initially on practical problem solving and engaging the patient as much as possible in valued and enjoyable daily activities in spite of emotional distress (also described as behavioral activation) (38). The consulting physician is well-positioned to facilitate patient coping in a number of areas, as described in Table 1, to help mitigate distress. Not all of these areas need to be addressed with every patient; those aspects to be reviewed will depend on the assessment of the patient.

When the symptoms are more severe or interfering, more specific treatment may be required. Patient preference is strongly associated with treatment uptake and adherence (39), so it is important to review the treatment options with the patient, considering both the pharmacological and psychological approaches, and the availability through the GI specialist, the family physician or other health care providers (shown in Figure 1). Discussion of the advantages and disadvantages of the different treatments (see Table 2) with the patient can facilitate decision-making. If the IBD physician is not comfortable initiating treatment for these disorders, communication with the primary care physician regarding the identified need for initiating this therapy becomes important, to ensure that treatment is pursued. Alternatively, the IBD physician may need to identify an appropriate health care professional with whom to consult who can or will initiate such therapy.

INITIATING PHARMACOTHERAPY

If the patient is receptive to antidepressant medication, the IBD physician may choose to directly initiate treatment. That decision often hinges on the level of physician comfort and experience with these medications, the clinic time to provide early monitoring, and the availability of a family physician or mental health specialists who could provide treatment. There is no clear recommendation for a particular antidepressant medication over others related to efficacy. Recent comparative meta-analyses have suggested that buproprion has lower rates of sexual dysfunction and weight gain (40) and sertraline has a higher acceptability profile overall with significantly lower rates of treatment dropout in the acute treatment phase (41).

Medication is typically titrated gradually over the first several weeks, to facilitate side effect tolerance. As the clinical benefits are typically realized only some weeks into treatment, and side effects are evident early in treatment, it is important to educate the patient both regarding the potential lag time in symptom improvement, and the expected side effects. Gastrointestinal side effects such as nausea, dyspepsia or cramps can be of particular concern to the IBD patient, but tend to be dose-related and often settle in the early weeks of treatment. Weight gain and sexual dysfunction can be more persistent. The absolute risk for a more severe side effect, an upper gastrointestinal bleed, is low, with 0.05% of cases estimated to be attributable to the use of antidepressants (42). However, large epidemiological studies have found that the relative risk of an upper GI bleed is modestly elevated with the use of SSRIs and SNRIs, with the risk increasing significantly when antidepressants were used concurrently with NSAIDs or NSAIDs + aspirin, and the risk was substantially reduced when acid-suppressing agents were used (42,43).
It’s Not Just About the Gut

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #62

Figure 1. Managing anxiety and depression in IBD care.
(continued on page 23)
REFERRAL TO SPECIALIST SERVICES

As shown in Figure 1, treatment of anxiety and depression for the IBD patient can be provided by other health care clinicians, including the family physician or a mental health specialist such as a psychologist or psychiatrist, depending on the preferred treatment approach. Networking with clinicians who regularly treat anxiety and depression, and who are familiar with inflammatory bowel disease can facilitate the consultation process and patient acceptance.

If the patient prefers a medication approach, the majority of patients with anxiety and depression are usually treated in primary care, although treatment has been found to be more comprehensive in specialty care (44). If the patient prefers psychological treatment, it is important that the providers are familiar with evidence-based psychotherapies for anxiety and depression. Timely access or availability may also be considerations. Certainly, choice of a health care provider for either mode of treatment may depend on very practical factors such as insurance coverage and location.

While some clinicians recommend combining pharmacological and psychological treatments, research supporting this approach is limited and combining treatment often does not improve outcome. There is some indication that the benefit of the lower relapse rate in psychological treatments is lost in a combined approach when the medication is discontinued (45). An alternative is to start with the approach that is preferred by the patient or most quickly available and then add in another treatment component if response to the first treatment is not adequate.

When the patient is referred elsewhere for treatment, it is important to follow up, ideally within two months, to ensure that the patient has engaged in treatment and to evaluate response to treatment. Patients often encounter difficulty moving forward with new treatments, so it is best to identify problems early in the process.

CONCLUSIONS

In sum, with patient-focused care that is attentive to the whole patient, physicians managing patients with IBD need to consider the impact of psychiatric conditions on their patients’ disease, well being, and quality of life. The use of evidence-based treatments has been shown to be effective in improving outcomes. However, the choice of treatment should be guided by the patient’s preferences and circumstances. 

Table 2.

The Pros and Cons of Evidence-based Treatments for Anxiety and Depression

<table>
<thead>
<tr>
<th>Pharmacological (e.g., SSRIs SNRIs)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pros:</strong></td>
</tr>
<tr>
<td>• Demonstrated effectiveness.</td>
</tr>
<tr>
<td>• Accessible in primary care settings.</td>
</tr>
<tr>
<td>• Less expensive in short term</td>
</tr>
<tr>
<td>• Requires minimal effort by patient.</td>
</tr>
<tr>
<td><strong>Cons:</strong></td>
</tr>
<tr>
<td>• Return of symptoms after discontinuation of treatment is common</td>
</tr>
<tr>
<td>• Side effects can be unpleasant, particularly enduring side effects such as weight gain and sexual dysfunction</td>
</tr>
<tr>
<td>• Patients taking IBD-related medications may be reluctant to add further medication.</td>
</tr>
<tr>
<td>• Medication costs may not be covered in the health system or insurance plan; higher cost with longer term use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychological (e.g. Cognitive Behavior Therapies)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pros:</strong></td>
</tr>
<tr>
<td>• Demonstrated effectiveness</td>
</tr>
<tr>
<td>• Well accepted by patients</td>
</tr>
<tr>
<td>• Treatment is time limited, often 8-16 sessions</td>
</tr>
<tr>
<td>• Improvements are well-maintained after treatment completion</td>
</tr>
<tr>
<td><strong>Cons:</strong></td>
</tr>
<tr>
<td>• Less readily available than medication options, as not all therapists are trained in evidence-based protocols for anxiety and depression.</td>
</tr>
<tr>
<td>• Requires more time and effort by the patient.</td>
</tr>
<tr>
<td>• Adjustments are necessary for patients with limited education or cognitive abilities.</td>
</tr>
<tr>
<td>• Costs may not be covered in the health system or insurance plan; higher cost in the short term.</td>
</tr>
</tbody>
</table>

\(^1\)SSRI – selective serotonin reuptake inhibitor, SNRI—selective norepinephrine serotonin reuptake inhibitor. Another antidepressant, bupropion, has been found to be effective for depression, but has not been evaluated for anxiety disorders. Bupropion has the lowest rates of sexual dysfunction and weight gain relative to other antidepressants (40).
of life. Treating physical symptoms may be more complicated or recalcitrant in the setting of either depression or anxiety. To provide optimal care in managing these patients, it can be of benefit to develop a strategy to identify the early signs of these conditions and to address treatment needs, and integrate that into usual care. Depression and anxiety are readily responsive to pharmacological or psychological treatment. Initiating interventions directly in the clinic, including behavioural steps or medication, can expedite care. Alternatively, physicians managing patients with IBD can identify and network with other health care professionals who may direct the care regarding these concerns in their patients.

Acknowledgements

The authors acknowledge the contribution of Kate Walsh (BA Hons) for her assistance in the literature searches and reference preparation, and the contributions of James Bolton, (MD, FRCPC) and Peter Thomson (BSc, PharmD) for their assistance with information regarding pharmacological treatments.

References


It’s Not Just About the Gut

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #62

Fellows’ Corner is open to Trainees and Residents ONLY.

Section Editor: C. S. Pichumoni, M.D.

Send in a brief case report. No more than one double-spaced page. One or two illustrations, up to four questions and answers and a three-quarter to one-page discussion of the case. Case to include no more than two authors. A $100.00 honorarium will be paid per publication.

Case should be sent to:
C. S. Pitchumoni, M.D.
Chief, Gastroenterology,
Hepatology and Clinical Nutrition
St. Peter’s University Hospital
254 Easton Avenue, Box 591
New Brunswick, NJ 08903
E-mail: pitchumoni@hotmail.com

Practical Gastroenterology reprints are valuable, authoritative, and informative. Special rates are available for quantities of 100 or more.

For further details on rates or to place an order: visit our Web site at:
www.practicalgastro.com