Inflammatory Bowel Disease:
Medications and Mental Health

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Inflammatory bowel disease (IBD) is an inflammatory condition of the small and large intestine which may be subcategorized into two major types: Crohn's disease (CD) and ulcerative colitis (UC). While CD is primarily a transmural inflammation of the GI mucosa that may occur along any part of the GI tract, UC is a mucosal inflammatory condition that is limited to the rectum and colon. The etiology of IBD can be divided into four main categories:

- environmental,
- genetic,
- infectious and
- immunologic (both autoimmune and non-autoimmune).

Once underlying disease is present, there may be specific exposures or factors that trigger the patient to experience a flare up in disease.[1] Some of the most common triggers include stress, diet (*e.g.*, fatty or greasy foods), infections, smoking, or medications (*e.g.*, NSAIDs, certain antibiotics) (Figure 1).[1,2] However, as with any disease, there is a disease component that often is not considered in the diagnosis. What impact does the diagnosis of CD or UC mean to the patient, their lifestyle, quality of life and family/support networks? As a medical model, we are reflecting here on a biopsychosocial disorder, which requires a similar treatment intervention.

Symptoms

With respect to symptoms, it is important to note the difference between CD and UC. In CD, the small intestine is primarily affected and the classic triad of symptoms includes chronic diarrhea, abdominal pain and weight loss (Figure 2). In UC, on the other hand, the colon is primarily affected and the classic triad of symptoms includes chronic diarrhea, abdominal pain and rectal bleeding (Figure 3). Extraintestinal symptoms that are common to both CD and UC include joint pain/swelling, eye inflammation and skin lesions. Some of the common clinical assessments and tests used to diagnosis patients with IBD include examining the number of stools per day, stool tests, barium contrast x-rays, endoscopy (gastroscopy/colonoscopy) and tissue biopsy.[1]

Some of the most common triggers include stress, diet, infections, smoking, or medications.

While patients with IBD have a normal life expectancy, it is a chronic disease that requires long-term therapy. There are various classes of medications that can be used to treat IBD, including: 5-ASA agents, antibiotics, steroids, immunologic agents and biologic agents.[1] Each has a specific role (*i.e.*, inducing remission, maintenance of remission, or both) and associated pros and cons to its use (Table 1). Initiation of medications in patients with IBD is important because they serve to control inflammation, improve symptoms, improve quality of life, prevent relapse, reduce complications and reduce the need for surgery.[1] These benefits of treatment should,

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Table 1

Pros and cons of IBD treatment

Drug Class	Purpose	Pros	Cons
5-aminosalicylic acid agents	Induces remission Maintenance of remission	- Maintains remission in mild to moderate UC - Maintains remission in CD after medical treatment and/or surgery - Few side-effects - Relatively inexpensive - Used orally or rectally - Safe for all ages	- Rare allergies or side-effects - Not effective for severe disease - Not helpful after steroid use (particularly in CD)
Antibiotics	Maintenance of remission	- Treats mild to moderate symptoms of CD - Used for fistula and perianal CD - Reduces recurrence after surgery - Oral or IV	- Not effective in UC - Metronidazole • Neuropathy • Coated tongue • Yeast infections - Ciprofloxacin • Yeast infections • Tendon injury
Steroids	Induces remission	- Induces remissions in UC and CD - Fast onset - Oral, IV, or rectal (enema) - Inexpensive	- No maintenance benefits - Numerous side-effects: • Fat deposits • High BP • Diabetes • Osteoporosis • Acne • Cataracts • Depression - Potential growth delay in children
Immunologic agents: azathioprine and 6-mercaptopurine	Maintenance of remission	- Effective maintenance treatment for UC or CD • Can treat fistulas in CD - Steroid-sparing agents - Relatively inexpensive	- Slow onset - Requires continuous monitoring with blood tests • Can lower blood counts and immunity - Occasional allergies • Pancreatitis • Fever
Immunologic agents: cyclosporine	For symptomatic patients only	- Effective in severe UC - Works rapidly	- Kidney damage - Increased infections - Seizures - High BP
Immunologic agents: methotrexate	Induction of remission Maintenance of remission	- More effective if given as a weekly injection - Steroid-sparing agents	- CANNOT be used when planning or during pregnancy - Common side-effects: • Nausea • Flu-like symptoms on the day of injection - Rare side-effects: • Liver disease • Pneumonia
Biologic agents: infliximab	Induction of remission Maintenance of remission	- Induces and maintains remissions in CD - Rapidly relieves symptoms and fistula drainage - Steroid-sparing agent - Last-line therapy • But effective when all other therapies fail	- Given as IV infusion - Infusions reactions in 10%-20% of patients • Usually manageable - Development of antibodies and loss of response - Reactivation of TB and other rare infections - Very expensive

IBD: Inflammatory bowel disease UC: Ulcerative colitis CD: Crohn's disease

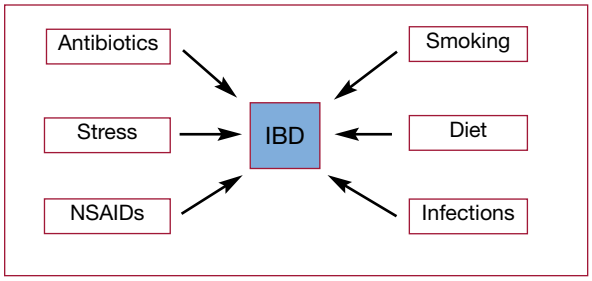

Figure 1. External IBD triggers.

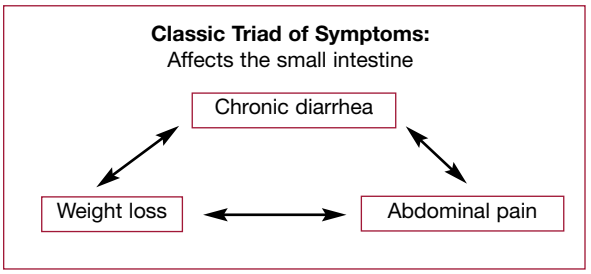

Figure 2. Crohn's disease classic triad of symptoms.

however, be carefully weighed with some of the costs of treatment: short-term side-effects, long-term toxicity and the financial burden some of these medications can place on the patient. These potential costs of treatment should be carefully weighed because patient nonadherence bears an even greater cost—risk of relapse (Table 2).

While medication is important for symptom control and maintaining quality of life in IBD, it is only one piece of the puzzle. IBD is not just a disease, but as noted above it leaves patients with a disease secondary to the vast impact it can have on every facet of the patient's life. In fact, 74% of patients with IBD believe that psychosocial factors contribute to their disease course[3] and it has been found that the frequency of psychological disturbances in IBD is 50% higher compared to other chronic diseases.[4] Regaining a sense of being at ease not only requires that the physical course of the disease be controlled, but it also requires that the psychological and social complications associated with IBD are appropriately addressed. A recent study by Pizzi, *et al* found that 18% of subjects had concurrent depression/anxiety with IBD and that these psychiatric issues had the biggest impact on the patient's overall mental health. Overall, this study found that mental health scores were especially low in patients with IBD compared to a sample of patients with other diseases.[5] Other Canadian research has shown that mood disorders, such as depression and anxiety, have been shown to occur in 27.3% of patients with UC and 31.3% of patients with CD.[6]

The strength of evidence for a causal link between stress, depression and the course of IBD has also been evaluated as it has been suggested that higher disease activity is associated with a higher occurrence of depressive and anxiety symptoms in these patients.[3] A review of the literature found that there are persistent findings of an association between depression and IBD.[3] Interestingly, a recent study by Persoons, *et al* in 2005 found that management of major depressive disorder (MDD) should be part of the treatment plan for a patient with CD because MDD is a risk factor for failure of infliximab to induce remission in CD.[7]

Interface between IBD and mental health

The interface between IBD and mental health may be secondary to a dysregulation of the central nervous system, gut and functioning of the immune system via the hypothalamic-pituitary-lymphocyte axis.[2] Specifically, it is hypothesized that psychological disease may alter the bowel flora and the body's immune response to dietary antigens as the immune system may have increased responsiveness under conditions of psychological distress.[2] It has also been hypothesized that psychological distress may also stimulate mast-cell degranulation and histamine release, which

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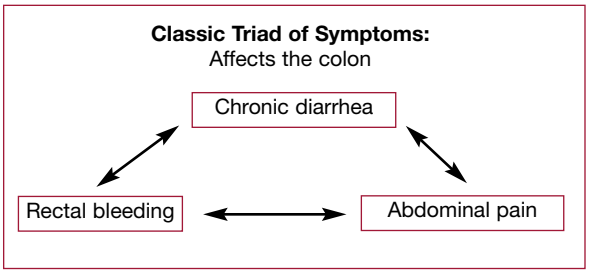

Figure 3. Ulcerative colitis classic triad of symptoms.

may also contribute to an upregulation of the immune system.[2] Finally, the occurrence of mental health disorders in IBD patients may even be secondary to some of the medications being used to treat their IBD. Steroids (*e.g.*, prednisone) can cause decreased peripheral and central serotonin secretion and may potentially lead to depression or mood disorders.[8] Therefore, it is essential to pay close attention to psychological factors and the medications being used in IBD patients because these elements may also affect disease activity and place the patient at higher risk for disease exacerbation.[9]

Conclusion

In conclusion, what we had historically perceived to be a point on a line is actually a continuum, where IBD interfaces with mental health and depression. As stated above, the two are very interlinked and the severity of one often directly correlates with the severity of the other. Pain also aggravates depression and the whole cycle continues. A valuable learning point is that if we address the patient as a whole, they get better as a whole. Biopsychosocial treatment modalities address all components: the biology of the disorder, psychological ramifications, the societal component and, finally, being able to obtain a quality of life that they expect and deserve.

Table 2
Risks vs. benefits of treatment

Benefits

- Control inflammation
- Improve symptoms
- Improve quality of life
- Prevent relapse
- Reduce complications
- Reduce surgery

Risks

- Short-term side-effects
- Long-term toxicity
- Cost

For references, please contact **cme@sta.ca**