Psychopharmacologic and Behavioral Treatments for Functional Gastrointestinal Disorders

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KEYWORDS

- Functional gastrointestinal disorders
- Irritable bowel syndrome • Psychopharmacologic agents
- Behavioral treatments • Brain-gut axis • Treatments

Functional gastrointestinal disorders (FGIDs) are best conceptualized with a biopsychosocial model in which psychosocial factors in addition to GI physiologic factors contribute to the experience of the illness and subsequent behaviors.[1] Modalities such as brain imaging and neurotransmitter research demonstrate that FGID symptoms result physiologically from a dysregulated brain-gut axis.[2,3] For example, neurotransmitters such as serotonin (5-hydroxytryptamine [5-HT]), norepinephrine (NE), corticotropin releasing factor, and opioids, among others, modify both motility and sensation in the gut. This has made psychopharmacologic and behavioral therapies particularly attractive treatment strategies. Their benefit also lies in managing associated psychological disturbances commonly associated with FGIDs.[4] The use of psychotropic agents for FGIDs has grown significantly in the last 2 decades. At least 1 in 8 patients with irritable bowel syndrome (IBS) is offered an antidepressant.[5] In addition, behavioral treatments are an area of increasing research and practice in the management of FGIDs, especially at the severe and refractory end of the spectrum. However, proper treatment is challenging due to insufficient understanding of

All authors report no conflict of interest with regard to financial interests or affiliations with institutions, organizations, or companies as related to this manuscript, and no products or services are discussed.

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Gastrointest Endoscopy Clin N Am 19 (2009) 151–170
doi:10.1016/j.giec.2008.12.001 giendo.theclinics.com
1052-5157/08/$ – see front matter

the complex nature of these disorders, lack of well-designed drug studies, and variability among the treatment efficacy end-points. In addition, lack of therapists in the community dealing with GI disorders makes behavioral treatments less approachable. Lastly, there is insufficient understanding and knowledge of these disorders among physicians and specialists in primary care, which hinders early and effective approach to management.

We discuss the rationale, mechanisms, efficacy, and practical aspects of psychopharmacologic, behavioral, and combination treatments in the management of FGIDs with a focus on some of the more recent work in this field.

RATIONALE FOR THE USE OF PSYCHOPHARMACOLOGIC AND BEHAVIORAL TREATMENTS

The most commonly used psychotropic agents for FGIDs are antidepressants, especially tricyclic antidepressants (TCAs). The rationale for their use in FGIDs is highlighted in **Box 1**. Several reviews and meta-analyses have shown that antidepressants achieve both pain reduction and global symptom improvement in IBS and other FGIDs.[6] Notably, the analgesic effect appears independent of the actions on mood disturbance, and it occurs before improvement in psychological symptoms.[7,8]

Second, in higher dosages, these agents treat psychiatric diagnoses such as depression or anxiety disorder or psychological distress, which, in turn, can improve global symptoms and health-related quality of life (HRQOL). However, clinical improvement with antidepressants, though correlated with psychological scores, is independent of psychological improvement.[7] This indicates a separate but complementary mechanism of action, that is, central analgesia, over treatment of mood disturbance with these agents.

Finally, and in addition to their central effects on mood and pain modulation, these agents also affect gut motility. TCAs with NE and anticholinergic action show a prolongation of the orocecal transit time, thus improving diarrhea symptoms.[7,9] In contrast, selective serotonin reuptake inhibitors (SSRIs) reduce orocecal transit time, which may help constipation-predominant symptoms.[9]

The rationales for the use of behavioral treatments relate primarily to modifying maladaptive cognitions (ie, persistent thoughts and beliefs) or behaviors that impair

Box 1
Potential benefits for use of psychopharmacologic agents in FGIDs

Central effects:

1. Alters central pain perception—analgesia or antihyperalgesia
2. Therapeutic effects on mood—to manage general anxiety, hypervigilance, symptom-related anxiety, agoraphobia, and increased stress responsiveness
3. Treatment of associated psychiatric disorders—depression, posttraumatic stress disorder (PTSD), somatization
4. Treatment of associated sleep disturbances

Peripheral effects:

1. Peripheral analgesic effects—alters visceral afferent signaling
2. Effect in GI physiology (motility and secretion) via effects on cholinergic, noradrenergic, and serotonergic pathways
3. Smooth muscle effects on viscera—for example, gastric fundic relaxation