# The Use of Antidepressants in the Treatment of Irritable Bowel Syndrome and Other Functional GI Disorders

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**What are functional GI disorders?**

There are more than twenty functional disorders of the GI tract. Of these, IBS is the most common and most thoroughly studied. These disorders are characterized by abnormal changes in the movement of the muscles of the intestines (abnormal motility), an increase in the sensations produced by intestinal activity (visceral hypersensitivity), and brain-gut dysfunction, especially difficulties in the brain's ability to regulate painful signals from the GI tract. With IBS, a person's awareness and interpretation of these activities may be abnormal (abnormal perception).

**Abnormal Motility**

Instead of the normal muscular activity (motility) of digestion, IBS patients may experience spasms and cramping. If the motility is too fast it may result in diarrhea, and if it is too slow it might result in constipation. These two conditions may also produce abdominal discomfort or pain in IBS patients. Abnormal motility can also be associated with abdominal cramping, belching, urgency, or other unpleasant GI symptoms.

**Visceral Hypersensitivity**

For IBS patients, there can also be increased sensitivity of the nerves in the GI tract. This can develop after a gastrointestinal infection or an operation that causes injury to the nerves in the intestine. This results in a lower threshold for experiencing intestinal sensations, leading to abdominal discomfort or pain. In those with visceral hypersensitivity, the stretch put on the intestines from eating even small amounts of food may produce discomfort.

**Brain-Gut Dysfunction**

When the nerve impulses from the gut reach the brain, they may be experienced as more severe or less severe based on the regulatory activities of the brain-gut axis. Signals of pain or discomfort travel from the intestines up to the brain.The brain has the ability to "turn down" the pain by sending signals that block the nerve impulses produced in the GI tract. Recent studies, including brain imaging research at our Center, have shown that this ability to turn down the pain is impaired in patients with IBS. In addition, the pain can become more severe when an individual is experiencing psychological distress. Often this may occur because of stresses in life or even the stress and frustration of the GI symptoms. This brain-gut dysfunction can be remedied with either psychological treatments or antidepressants or a combination of both.

**Why are antidepressants used to treat IBS?**

Some medicines can have more than one action (benefit) in treating medical problems. For example,

aspirin can be used to treat headaches, muscle aches and fever, but it can also help prevent heart attacks. Although antidepressants were developed to treat depression, research studies have shown that they can also be effective as analgesics (drugs that reduce pain). Antidepressants are, therefore, used to treat such chronic painful conditions as migraine headaches, diabetic neuropathy and fibromyalgia. Similarly, antidepressants are effective in treating symptoms of IBS and other functional GI disorders. Patients who have taken antidepressants for their IBS symptoms have reported significant improvement in their abdominal pain and reduction in other IBS symptoms, such as diarrhea, constipation, bloating, nausea or urgency.

**How do antidepressants work in IBS?**

The brain is always monitoring and processing all that goes on in the body. As already noted, antidepressants are known to work at the level of the brain and spinal cord to block pain messages between the GI tract and the brain, thereby reducing visceral hypersensitivity. In effect, there is recovery of more normal brain-gut function, possibly by helping the brain send down signals to block incoming pain impulses, a natural response. Much like treating diabetes with the insulin that is missing, antidepressants may help recover the brain's ability to respond to pain signals properly.

Certain antidepressants can also help regulate abnormal bowel functions like diarrhea and, constipation, as well as other IBS symptoms. The tricyclic antidepressants (TCA's) help with diarrhea and the serotonin reuptake inhibitors (SSRI's) help treat constipation. Furthermore, these medicines can help with other problems such as anxiety and depression, which are often associated with chronic painful disorders.

Finally, a recent observation relates to growing knowledge that antidepressants may also stimulate nerve cell growth and possibly restore more normal nerve functioning in the brain and intestines over time. This is why at our Center we might recommend treatment for a year or two before tapering off the medication.

**When are antidepressants used for IBS?**

Patients with mild IBS symptoms do not usually need antidepressants. Their symptoms may be controlled by other treatments. Patients with moderate or severe IBS may benefit from taking an antidepressant medication either alone or in combination with other treatments.The full effects (benefits) of antidepressants typically take four to six weeks to occur. Usually, low dosages are used at the onset and gradually increased as needed. In some cases the low dose is sufficient to improve symptoms.

**Which antidepressants are used for IBS and what are their possible side effects?**

Traditionally, the most frequently prescribed antidepressants fell into one of two large groups -- Tricyclics (TCA's) and Selective Serotonin Reuptake Inhibitors (SSRI's). More recently, a newer

group, Serotonin-Norepinephrine Reuptake Inhibitors (SNRI's), has also been shown to be effective in treating these disorders.

TCA's have been on the market for many years, are relatively inexpensive, and have been used more frequently in treating functional GI disorders. TCA's include:

- *Amitriptyline (Elavil)*
- *Imipramine (Tofranil)*
- *Desipramine (Norpramin)*
- *Nortriptyline (Pamelor) and others.*

When first taking antidepressants, some people may notice some side effects, but these usually go away in a few days or weeks as the body gets used to the medicine. Common side effects of TCA's are dry mouth or, at times, difficulty sleeping, difficulty urinating, sexual difficulties, constipation, dizziness and/or drowsiness.

The SSRI's have been available for a shorter period of time and can also be useful in treating IBS along with associated symptoms, such as depression or anxiety, though may not be as helpful as the other classes of medications for pain. SSRI's include:

- *Citalopram (Celexa)*
- *Escitalopram (Lexapro)*
- *Paroxetine (Paxil)*
- *Sertraline (Zoloft)*
- *Fluoxetine (Prozac)*

Common side effects of SSRI's may include nervousness, vivid dreams, sleep disturbances, sexual difficulties, and/or diarrhea.

The SNRI's are a relatively new class of medications that are effective in treating pain like the TCA's but without the side effects of TCA's. SNRI's include:

- *Venlafaxine (Effexor)*
- *Duloxetine (Cymbalta)*
- *Desvenlavaxine (Pristiq)*
- *Milnacipram (Savella)*

Duloxetine has been marketed not only for depression but for treating peripheral neuropathy, fibromyalgia and other types of pain. Preliminary studies suggest it is helpful for visceral (i.e., bowel) pain, as well. Common side effects include nausea, headache and, rarely, changes in liver chemistry tests. Milnacipran is an SNRI that is actually marketed for treatment of pain (fibromyalgia) but not as an antidepressant.

Other types of antidepressants that may be used to treat IBS are:

- *Bupropion (Wellbutrin)*
- *Mirtazipine (Remeron)*
- *Trazodone (Desyrel)*

**What are common concerns about taking antidepressants?**
Some people are concerned that these medications are addicting, or they may alter mental functioning. They are not addictive and do not change your personality or your thinking. Your physician will choose a particular antidepressant based on a combination of factors including your major IBS symptoms of diarrhea or constipation, associated emotional symptoms (anxiety, depression), your general medical health, possible side effects (SSRI's have fewer effects on the heart), and possibly your previous experience with other antidepressants. Finally it is important to remember that these medications are being used within GI to treat functional GI symptoms, not emotional difficulties, and this occurs often in lower dosages than for treating major depression. Nevertheless even in low dosages it may help to reduce stress or symptoms of emotional distress often resulting from the chronic symptoms of IBS and other FGIDs.

**How long will you need to take antidepressants?**
This varies from person to person. Some IBS patients may only need to take an antidepressant for 6 months to a year. Others, especially those with a longer history of IBS, may need to take them longer. This decision will depend on how the patient responds to the antidepressants, and whether IBS symptoms recur when the medication is stopped or decreased.

**Other Treatments for IBS**
First-line therapy for IBS is often lifestyle modification. Keeping a diary of foods, situations and emotions that may trigger IBS symptoms can be helpful. You and your physician can develop strategies to help manage your symptoms. These can include helpful dietary changes, such as:

- eating small, more frequent meals
- avoiding high fat foods
- increasing or decreasing fiber
- eliminating other problematic foods

Medications that act directly on the GI tract can be used for specific symptoms, such as antispasmodic medications, which are used to treat abdominal cramping and pain. These include:

- *Hyoscyamine (Levsin)*
- *Dicyclomine (Bentyl)*
- Alosetron (for diarrhea and IBS-D)

*Loperamide (Imodium)* is a medication that slows gut motility, can be effective in treating diarrhea, and is available without a prescription. For more severe diarrhea in association with IBS, *Alosetron* may be prescribed to help reduce diarrhea and pain.

*For mild constipation, Milk of Magnesia* is safe and effective for patients and is available over the counter. It is important to avoid stimulant laxatives, such as senna or cascara, since they may have a negative effect on the bowel and can cause more problems with cramping and pain.

For severe constipation, your doctor may prescribe *Miralax*, which is a Polyethylene Glycol Solution (PEG), similar to what was once used prior to colonoscopies to thoroughly clear out the bowel. Miralax is modified so that it can be taken in small amounts on a regular basis. *Lubiprostone* is also prescribed as a prescription medication used to treat IBS-C or chronic constipation.

Psychological treatments have also been used to reduce pain and other GI symptoms. Your doctor can refer you to a specialist who can help you with these psychological treatments. Various techniques are used to improve management of symptoms, such as:

- Relaxation Therapy
- Hypnosis
- Cognitive-Behavioral Therapy (CBT) which can be useful in understanding how specific thoughts may have a negative effect on managing an illness.

**Future Treatments**

Newer medications that act at nerve receptors in the GI system may become available shortly. Drugs that can block pain from the intestines are currently being studied, and some appear to be more effective for diarrhea-predominant or constipation-predominant IBS. As more information becomes available about these new medicines, we will communicate this information to you.

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