



## Treating Functional Dyspepsia: What are Your Options?

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### Defining Functional Dyspepsia

Dyspepsia is a common disorder that affects up to 30% of the general population. Symptoms of dyspepsia include upper abdominal pain or discomfort and frequently include symptoms of burning, pressure, or fullness often, but not necessarily, related to meals. Other common symptoms include early feeling of fullness (satiety), nausea, belching, and bloating. While dyspeptic symptoms may develop due to diseases such as peptic ulcer or gastritis, the vast majority of patients with dyspeptic symptoms are ultimately diagnosed as having functional dyspepsia. Functional dyspepsia (FD) is a heterogeneous disorder; in other words a variety of causes can lead to similar symptoms. Some studies suggest that FD is a chronic condition for many patients, with approximately 50% of patients still experiencing symptoms over a 5-year follow-up period.

While the definition of FD has changed somewhat over the years, the disorder is generally regarded as a group of symptoms thought to originate in the upper digestive tract (stomach and upper small intestine) in the absence of any structural or metabolic disease likely to explain the symptoms. Frustratingly, symptoms of FD do not reliably guide therapy.

### Causes of Functional Dyspepsia

The causes of functional dyspepsia are largely unknown and likely multiple. Some evidence exists to implicate a genetic predisposition. Although *H. pylori* infection may produce dyspeptic symptoms in a small subset of patients, there is little data to support this bacterium as a cause of symptoms in a majority of patients.

Psychological factors may influence the symptom experience in some patients with functional dyspepsia.

Changes in gastric function have been identified in many patients with FD. In approximately 40% of patients with dyspepsia, the stomach does not relax normally in response to a meal. This is known as “impaired accommodation” and may be associated with symptoms of fullness and pressure in some patients.

Impaired stomach contractions and abnormal stomach emptying may also be seen in a similar percentage of patients. Impaired stomach emptying has been associated with symptoms of bloating and early feeling of fullness. As many as two-thirds of patients with functional dyspepsia have heightened perception of stomach activity, which is termed visceral hypersensitivity. While frequently seen, visceral hypersensitivity in functional dyspepsia has not been strongly associated with any specific symptoms.

### Treatment Options

**Diet** – Most patients with FD have symptoms associated with the ingestion of food. As such, a variety of dietary recommendations are often made, although no clinical trials have formally evaluated specific dietary interventions for the treatment of FD. There are limited data to suggest that dietary fat may induce or exacerbate symptoms and patients often report improvement by eating low-fat meals, and more frequent, smaller meals.

**Eradication of *H. pylori*** – Although testing and treating *H. pylori* infection is recommended and often employed, the eradication of *H. pylori* infection generally does not improve symptoms outside of those associated with peptic ulcer disease. In patients with FD, there is little benefit beyond placebo in eradicating *H. pylori* infection and a recent analysis found that only one out of every fourteen *H. pylori*-infected patients with FD would benefit from treatment.

**Acid-lowering Medications** – H<sub>2</sub> blockers such as ranitidine (Zantac), cimetidine (Tagamet), nizatidine (Axid) or famotidine (Pepcid) are the initial agent used by many primary care providers, and are marginally better than placebo at improving upper-center abdominal (epigastric) pain, although they do not improve other dyspeptic symptoms. If H<sub>2</sub> blockers fail to improve symptoms, most doctors then use a proton pump inhibitor (PPI) – omeprazole (Prilosec), lansoprazole (Prevacid), rabeprazole (Aciphex),

pantoprazole (Protonix), or esomeprazole (Nexium). Short-term risks of this strategy are low, and this may provide relief of symptoms in a small number of people, many of whom may have had silent acid reflux. As a group, PPIs are approximately 10% better than placebo at improving dyspeptic symptoms. However, long-term use of PPIs can be expensive. There is emerging data suggesting that long-term PPI use – when combined with other risk factors – may place some patients at increased risk for *Clostridium difficile* colitis, community acquired pneumonia, and hip fractures. Nonetheless, overall risk of long-term PPI use seems to be relatively small.

***Prokinetic and Antiemetic Agents*** – Patients with nausea will respond to medications that target that specific symptom. Limited data suggests that symptoms of early feeling of fullness, upper abdominal fullness, and discomfort after eating may respond to the use of medicines that increase gastrointestinal motility (prokinetic agents). The drugs metoclopramide (Reglan) and domperidone (Motilium) are now the most commonly employed agents. Unfortunately, metoclopramide often has significant side effects including anxiety, drowsiness, decreased libido, and breast tenderness as well as movement disorders. Domperidone is not commercially available in the United States although it is widely used throughout much of the rest of the world. The utility of prokinetic therapy in functional dyspepsia, to date, is largely unproven.

***Centrally Acting Therapies*** – Much of the control of digestive function and sensation is under central nervous system guidance; therapies that target central control mechanisms may have value in relieving symptoms. Tricyclic antidepressants, used in doses lower than required to treat depression, may improve symptoms of dyspepsia in patients who have failed to benefit from treatment with H2 blockers or prokinetics.

Another type of antidepressant, selective serotonin reuptake inhibitors (SSRIs), have not been well studied for the treatment of FD, however they appear effective in the treatment of other functional digestive disorders. Hypnotherapy may improve dyspeptic symptoms in some patients, and a recent study found that hypnotherapy was better than medical therapy and supportive therapy at improving quality of life and symptom scores. Although not well studied, psychological therapies, including cognitive behavioral therapy, may also relieve symptoms of dyspepsia.

## Conclusions

Functional dyspepsia is a common digestive disorder that remains poorly understood. Ongoing investigations seek to define causes and effective therapies. The National Institutes of Health (NIH) has sponsored a nationwide, multi-center study that hopes to better define causes and treatments for FD.

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## February 26, 2009: FDA Requires Boxed Warning and Risk Mitigation Strategy for Metoclopramide-Containing Drugs

**Adverse events:** Frequent and long-term use of metoclopramide has been linked to tardive dyskinesia, a disorder that causes uncontrollable, repetitive movements of the body such as lip smacking, grimacing, tongue protrusion, puckering and pursing of the lips, rapid eye movements or blinking, and rapid movements of the fingers, arms, legs, and trunk.

**People at risk:** Those at greatest risk include elderly people, especially older women, and people who have been on the drug for a long time.

**Recommendations:** Talk to your doctor before you use metoclopramide. The FDA advises avoiding using the drug for a long time (more than 12 weeks) in all but rare cases where you and your doctor decide that the benefits outweigh the risks.