Management of Functional Dyspepsia

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The Rome III consensus committee defined dyspepsia as the presence of any of the following symptoms: postprandial fullness, early satiation, epigastric pain, and epigastric burning.1 Episodes of dyspepsia (Greek dys: bad, peptein: digestion) occur occasionally in every individual, but the entity of functional (“non-ulcer”) dyspepsia is a more chronic condition, present for at least 3 months in the preceding year.1 It is divided into two clinical categories – postprandial distress syndrome and epigastric pain syndrome.

Functional dyspepsia (FD) does have an impact on quality of life.3 Despite periods of remission, the symptoms trouble the patient on a long-term basis.4

In the management of these patients, establishing rapport and building confidence patiently is vital. Initial management consists of careful history-taking that elicits all the symptoms, paying particular attention to the ones that trouble the patient the most. This is important because the management ultimately aims to control symptoms rather than reverse pathology or permanently “cure” a disease. Asking pointed and specific questions tells the patient that the doctor understands the situation. Predominance of typical reflux symptoms (heartburn, regurgitation) classifies these patients as having gastro-oesophageal reflux disease (GORD). Attention should be paid to medication history, including over-the-counter medications, NSAIDs, and complementary and alternative medicines.

A detailed physical examination reassures the patient and helps rule out structural findings. Upper gastrointestinal (GI) endoscopy is recommended for those with alarm (“red flag”) features – recurrent vomiting, dysphagia, weight loss, GI blood loss, symptom onset after age 50 years, family history of GI malignancy.1,5,6 An endoscopic catch-all diagnosis of “gastritis” or “duodenitis” is often loosely made; it provides a handle for the treating physician and a label for the distressed patient to cling to, but is hopelessly subjective and so should be discouraged.

**Treatment**

Explaining the entity to the patient is key. The goal of treatment is to help the patient accept, diminish, and cope with the symptoms.7 For the majority of patients the treatment is symptom-based.8,9

**General measures**

Commonsense lifestyle modifications are usually prescribed to these patients but there are no systematic studies to establish benefit from these.10 Measures include eating on time, avoiding heavy / fatty meals,11 moderation in intake of spices,12 caffeine and alcohol, restricting use of NSAIDs, and avoiding smoking and tobacco in any form.13 In those with sedentary lifestyle / professions, periodic light exercise during the day should be encouraged.

**Pharmacological measures**

Drug therapy is based on controlling the pathogenetic mechanisms that are known to be associated with FD, i.e., delayed gastric emptying, impaired gastric accommodation, and gastric hypersensitivity particularly to acid. However, the proof of efficacy with pharmacological agents is limited.

**Antacids**: Randomised studies have failed to show benefit of antacids over placebo in the treatment of FD.14-15 They are probably more effective in treating patients with undiagnosed GORD.16 However, many patients are satisfied with the relief they obtain from commercial (especially the liquid) formulations during episodes. This may be independent of the acid-neutralising effect, and may even be attributed to mucoprotective effect or to the antiflatulent agents that are often combined in these formulations. The truth may never be known because future controlled studies with antacids are unlikely, considering that they fly off the shelf in any case! Patients should be informed that antacids containing aluminium and magnesium salts are not recommended for long-term use.

**Histamine H2 receptor antagonists (H2RA):** Many studies have evaluated the efficacy of H2RA in FD. Compared to placebo, H2RA were more likely to improve global symptoms (odds ratio 1.48, 95% CI 0.9 to 2.3) and epigastric pain (OR 1.8, 95% CI 1.2 to 2.8).17 In another meta-analysis significant benefit was found with H2RA, with a relative risk reduction of 23% and with number-needed-to-treat of 7.18 In the studies included in these meta-analyses patients with gastro-oesophageal reflux were not specifically excluded.19,20

**Proton pump inhibitors (PPI):** Several reports have described relief of symptoms with PPI in patients with FD.21-23 A meta-analysis of eight randomised controlled trials confirmed that this class of drugs was superior to placebo in symptom control, with number-needed-to-treat of 10 and relative risk reduction of 13%.24 These numbers may not compare favourably with those for H2RA probably reflecting a more stringent inclusion of true FD and exclusion of GORD. The benefit was greatest in those with ulcer-like or reflux-like symptoms; there was no significant benefit in patients with dysmotility-like symptoms.21,22

At this stage it is pertinent to discuss the therapeutic relevance of the Rome III clinical classification of FD into epigastric pain syndrome and postprandial distress syndrome, which correspond closely to the ulcer-like and dysmotility-like subgroups in earlier classifications. Response to H2RA in FD could be predicted based on symptom reproduction with acid infusion into the stomach.25 This observation suggests that a subgroup of patients with FD have symptoms arising from the presence of acid in the stomach (the “epigastric pain syndrome” or “ulcer-like” group) and so would respond to acid neutralisation or suppression. Others would probably need alternative or additional treatment (prokinetic agents). Making this distinction clinically is critical to treatment approach.

**Cytoprotective or mucoprotective agents:** Sucralfate has been tried in FD with some benefit,26 other studies have failed to show any superiority over placebo.27-28 Misoprostol also has not been found to be useful in patients with FD.29

**Prokinetic agents:** The finding of abnormal gastric emptying (presumably corresponding to the dysmotility-like clinical group) in some patients with FD provided the rationale for using this class of drugs. A systematic review of the use of cisapride and domperidone for FD revealed that both these drugs the global improvement in symptoms was significantly more

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than for placebo.58 (Cisapride has since been withdrawn due to safety concerns.) Other types of prokinetic agents have not been found to be too useful in FD.30 Tegaserod, a 5HT4 agonist, showed some benefit as compared to placebo in a phase 3 trial, but was also recently withdrawn due to concerns about ischemic events.31 Itopride, a dopaminergic agonist, showed some promise in an initial trial.32,33

Although data are lacking, many patients claim relief from the bloated sensation accompanying the postprandial distress syndrome, with the use of antiflatulent agents (simethicone, methyl polysiloxane) and sometimes with probiotic supplements; the latter would suggest a contribution to symptoms from unfavourable gut flora (fermenters?).

Anti-Helicobacter pylori therapy: The pathogenetic role of H. pylori in FD is controversial, with most authorities now accepting a limited role for it. Studies analysing the role of H. pylori eradication in the long-term relief of symptoms in FD have given mixed results.34-40 A Cochrane meta-analysis reported a 10% pooled relative risk reduction as compared to placebo at 12 months’ follow up, with number-needed-to-treat of 15.

Psychotropic drugs: The role of antidepressants and anxiolytics in FD is not clear. Systematic reviews have suggested that these drugs may have some benefit.41 A randomised, placebo-controlled trial of venlafaxine (a selective serotonin and norepinephrine reuptake inhibitor) found that it was no more effective than placebo in improving symptoms. Low-dose tricyclic antidepressant drugs or trazodone have an uncertain benefit but may improve commonly associated symptoms such as insomnia and fibromyalgia.42 It is important to note that tricyclics appear to be effective at doses well below their currently used doses for depressive disorders and thus may be effective in patients without obvious psychiatric abnormalities.

Drugs Under Development

Gastric fundus-relaxing drugs: Administration of the 5-HT1A receptor agonist sumatriptan has been shown in pilot studies to induce relaxation of the gastric fundus. Other fundus-relaxing drugs are buspirone, clonidine and citalopram. Preliminary data are promising, but there is insufficient data available presently to recommend their routine use.43,44 Acotiamide is a new drug that enhances fundal accommodation and has been found to be useful in a pilot study.45

Visceral analgesics: Visceral analgesics, such as the serotonin-receptor antagonists, the somatostatin analogue octreotide, and the kappa receptor opioid agonist fedotizone, have been tried in the management of functional digestive disorders such as FD and irritable bowel syndrome,46-48 none of them was found to be very effective.

Psychological therapy: Studies have shown that psychological therapy (cognitive-behavioural therapy, hypnotherapy, psychotherapy, group support with relaxation training) has benefited selected patients. However, most of these studies have biased patient recruitment and problematic statistical analysis.49-51

Complementary and alternative medicine: A systematic review of studies involving herbal and natural products, acupuncture, and homeopathy suggested a benefit from peppermint oil and STW5 (a European multi-herbal preparation that includes peppermint and caraway). However, the quality of the supporting evidence is considered to be generally low. More research is needed before we can recommend these therapies. Unfortunately, despite the plethora of such medications available in India, scientific evaluation is lacking.

Practical Approach to Managing Functional Dyspepsia

It should be remembered that no drug or group of drugs is universally effective for FD. Also, there is no long-lasting relief assured with any treatment approach, and length of treatment depends on duration and frequency of relapses.

All patients should be reassured and given lifestyle and dietary modification. Those with severe symptoms or those who do not respond to these measures should be prescribed acid suppression with an H2RAs or PPI for an initial period of four weeks. Prokinetic agents (and/or antiflatulents, although data are lacking) should be prescribed if postprandial distress is the predominant symptom. If the patients still do not respond, testing for H. pylori and eradicating it if positive is a reasonable strategy, although data are inadequate. In patients in whom significant symptoms persist despite these therapies, a trial of low-dose tricyclic antidepressant may be considered even in the absence of overt anxiety or depression. In motivated patients psychological treatments like psychotherapy, hypnotherapy or relaxation therapy can be tried. A counsellor’s, or even a psychiatrist’s, opinion should be considered in those in whom the symptoms severely impact daily functioning.

In all cases, it must be emphasised that success with therapy depends to a large extent on physician-patient bonding, patient understanding of the disease (particularly its long-term benign nature despite the morbidity) and acceptance of limitations in treatment strategies, with a motivation to overcome the impairment in quality of life.

References

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