

## TOPIC HIGHLIGHT

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# Drug treatment of functional dyspepsia

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## Abstract

Symptomatic improvement of patients with functional dyspepsia after drug therapy is often incomplete and obtained in not more than 60% of patients. This is likely because functional dyspepsia is a heterogeneous disease. Although great advance has been achieved with the consensus definitions of the Rome I and II criteria, there are still some aspects about the definition of functional dyspepsia that require clarification. The Rome criteria explicitly recognise that epigastric pain or discomfort must be the predominant complaint in patients labelled as suffering from functional dyspepsia. However, this strict definition can create problems in the daily primary care clinical practice, where the patient with functional dyspepsia presents with multiple symptoms. Before starting drug therapy it is recommended to provide the patient with an explanation of the disease process and reassurance. A thorough physical examination and judicious use of laboratory data and endoscopy are also indicated. In general, the approach to treat patients with functional dyspepsia based on their main symptom is practical and effective. Generally, patients should be treated with acid suppressive therapy using proton-pump inhibitors if the predominant symptoms are epigastric pain or gastroesophageal reflux symptoms. Although the role of *Helicobacter pylori* (*H pylori*) in functional dyspepsia continues to be a matter of debate, recent data indicate that there is modest but clear benefit of eradication of *H pylori* in patients with functional dyspepsia. In addition, *H pylori* is a gastric carcinogen and if found it should be eliminated. Although there are no specific diets for patients with FD, it may be helpful to guide the patients on healthy exercise and eating habits.

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**Key words:** Functional dyspepsia; Drug treatment;

*Helicobacter pylori*; Predominant symptoms

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## INTRODUCTION

Symptomatic improvement of patients with functional dyspepsia with current drug therapy is left with many unmet needs. This is because functional dyspepsia is a heterogeneous disease and a uniform response to drug treatment can therefore not be achieved. There are many possible factors to explain the difficulties achieving adequate symptom relief these patients<sup>[1-3]</sup>. The issues to be addressed when treating patients with functional dyspepsia: (1) Definition and classification of dyspepsia (Rome I, Rome II); (2) Associated upper and lower GI symptoms; (3) Predominant symptom (e.g. reflux, abdominal pain); (4) Number of symptoms; (5) Presence of alarm features (anemia, weight loss, dysphagia); (6) Co-morbidities; (7) Drug interactions; and (8) *Helicobacter pylori* (*H pylori*) status. One of the main factors that warrants clarification is the definition of dyspepsia. Although great advance has been achieved with the consensus definitions of the Rome I and II criteria, there are still some aspects about the definition of functional dyspepsia that require clarification. The Rome criteria explicitly recognise that epigastric pain or discomfort must be the predominant complaint in patients labelled as suffering from functional dyspepsia. However, this strict definition can create problems in the daily primary care clinical practice, where the patient with functional dyspepsia presents with many complex rather one simple symptom because on the average, patients with dyspepsia seen in primary-care settings report 5.5 abdominal symptoms, which also may vary over time<sup>[4,5]</sup>. In addition, patients with functional dyspepsia presenting to the primary care doctor are different than patients being evaluated at tertiary medical centres<sup>[1,2,6-9]</sup>. Before starting drug therapy it is recommended to provide the patient with an explanation of the disease process and reassurance. Ruling out an organic cause of their disease by endoscopy can lead to improved acceptance of the disease process. In general, the approach to treat patients based on their main symptom is practical and effective. The general approach is to treat patients with

acid suppressive therapy with proton pump inhibitors if the predominant symptom is epigastric pain or if there are gastroesophageal reflux symptoms present. The role of *H pylori* in functional dyspepsia continues to be a matter of debate. Nevertheless, recent data indicate that there is a modest but significant benefit in eradication of *H pylori* in functional dyspepsia. Although there are no specific diets for patients with FD, it may be helpful to guide the patients on healthy exercise and eating habits.

## PROBLEMS WITH THERAPEUTIC TRIALS

The literature is full of reports on drug therapies for functional dyspepsia and the list of drugs used to treat functional dyspepsia is long<sup>[10-30]</sup> (Table 1). One of the most frustrating aspects about therapies in functional dyspepsia is that most medical treatments available to date have been shown to be of no or only limited efficacy. Furthermore the results of most of these studies do not apply to our current standards anymore. First, the definition of functional dyspepsia has changed over time. Second, most studies are difficult to interpret because of lack of rigorous design criteria, either because of small sample size, poor design, not blinded or not placebo-controlled. Smaller studies tend to show more efficacy than well-controlled larger ones. Abraham *et al* has demonstrated that the quality of trials has an impact on the efficacy estimates of treatment<sup>[31]</sup>. The authors performed a systematic review of randomized controlled trials of dyspepsia investigated using endoscopy from 1979 to 2003 using the Jadad score and Rome II guidelines<sup>[31]</sup>. They found that poor quality trials suggested a benefit of prokinetic therapy, which was not confirmed in high quality trials. Also there was a marked benefit of H2-receptor antagonist therapy in poor quality trials, but a marginal benefit in good quality trials. Two high quality trials suggested a limited benefit with the use of proton pump inhibitors, with no poor quality trials to provide a comparison<sup>[31]</sup> are (1) Setting where study was conducted (primary care, tertiary centre); (2) Size of study; (3) Duration of recruitment; (4) Duration of therapy; (5) Clinical endpoint: complete response versus partial response to therapy; (6) Short versus long-term response; (7) Follow-up after finishing therapy; (8) Quality of meta-analysis or systemic review (i.e. inclusion of abstract, contact of primary author, use of effective therapies to eradicate *H pylori*, etc); (9) Good clinical practice standards; (10) Publication bias (negative studies are less likely to be published); and (11) Publications before 1992 (definitions of dyspepsia have changed, older studies were too small or used drugs that are not current any more). The issues to be addressed when interpreting trials of drug therapy in functional dyspepsia. In order to clarify issues, meta-analyses of various approaches to treat functional dyspepsia have been conducted. Interestingly, even meta-analyses performed in the same period have yielded completely opposite results<sup>[32,33]</sup>. Third, it is also very important to remember that functional dyspepsia tends to be a chronic condition<sup>[6,34]</sup>. In most studies therapy has been only given for short periods of time. There are essentially no studies evaluating chronic therapies for functional dyspepsia. And finally, the placebo effect in pa-

**Table 1 Drug therapies used in the therapy of functional dyspepsia**

Acid suppression therapy
Proton pump inhibitors <sup>1</sup>
Omeprazole
Lansoprazole
H2 blockers
Cimetidine
Ranitidine
Famotidine
Simethicone
Herbal therapies
Iberogast (Iberis, peppermint, Camomille)
Artichoke leaf extract
Xinwei decoction
Ganaton (itorpide hydrochloride)
Capsaicin
Motility agents
Cisapride
Domperidone
Mosapride
Erythromycin
<i>H pylori</i> eradication
Antidepressants
Serotonin reuptake inhibitors (SSRI)
Amitryptiline
Placebo

<sup>1</sup>Other PPI such as esomeprazole, rabeprazole and pantoprazole are also used to treat functional dyspepsia, but the largest and most significant trials reported to date have used either omeprazole or lansoprazole.

tients with functional dyspepsia is high. Therefore, most studies comparing a new therapy to no therapy will likely show a marked benefit for the treatment arm. But on the other side, clinicians treating patients with dyspepsia are many times confronted with the option of no therapy and any form of therapy, and will likely choose to give some form of therapy, because of the possibility of achieving a symptom response (similar or slightly better than placebo) in a significant percentage of patients.

## CLINICAL PREDICTORS OF TREATMENT RESPONSE

In functional dyspepsia it has been suggested that there are associations between pathophysiologic mechanisms and symptoms (i.e. clinical presentation)<sup>[1-3,5]</sup>. These mechanisms include gastroesophageal reflux, delayed gastric emptying, impaired gastric accommodation to a meal, hypersensitivity to gastric distension, altered response to duodenal lipids or acid, abnormal duodenojejunal motility or central nervous dysfunction<sup>[1]</sup>. Therefore, it seems logical to hypothesize that the clinical presentation of patients with functional dyspepsia can guide therapy and even predict the response to therapy. The problem is that there is much overlap and interaction of these mechanisms, and their relevance for the individual patient is uncertain, especially because of the variability of symptoms over time<sup>[34]</sup>. Meineche-Schmidt *et al* showed that patients with functional dyspepsia usually have a combination of symptoms and the predominant symptom may vary over time<sup>[6]</sup>. Nonetheless, there are some studies which tried to address response to therapy based on the predominant symptom<sup>[35-37]</sup>. In a random

starting day trial including 301 patients with functional dyspepsia, Bytzer *et al* found that this sort of trial may be a valuable tool to identify response to acid suppression in dyspeptic patients<sup>[35]</sup>. In this study the only predictor of response was symptoms suggesting gastroesophageal reflux<sup>[35]</sup>. In another similar trial, Madsen *et al*<sup>[36]</sup> also found that response to therapy was more in patients with associated symptoms of gastro-oesophageal reflux<sup>[36]</sup>. Nonetheless, the same authors later showed that reproducibility of this study design was imperfect, mainly because of the strict criteria used to evaluate response and overall low response rates<sup>[37]</sup>. Lack of symptom stability in patients with functional dyspepsia further impairs the value of the random-starting-day trial and only patients with frequent and stable symptoms should be evaluated in this design<sup>[37]</sup>.

## ***H pylori* ERADICATION**

Although, the aim of our article is aimed mainly at describing drug therapies for functional dyspepsia, the role of *H pylori* therapy in patients with functional dyspepsia deserves a comment. Today it is clear that *H pylori* is the main cause of peptic ulcer disease but its role in non-ulcer dyspepsia is not well known. The effect of *H pylori* eradication on the symptoms of non-ulcer dyspepsia show somewhat conflicting results<sup>[2]</sup> Until the mid-nineties most studies evaluating *H pylori* eradication in the therapy of functional dyspepsia did not meet adequate methodological criteria. Since then there have been few well done prospective, randomized double-blind, placebo controlled trials of adequate size that evaluate the efficacy of *H pylori* eradication in functional dyspepsia<sup>[2,38-43]</sup> (Table 2). The ELAN study (European multi-centre trial) and a single-centre trial from Scotland suggested modest superiority of eradication therapy versus acid suppressive therapy with PPI alone<sup>[38,39]</sup>. The ELAN study further suggests that if patients were classified as responders (dyspepsia score of 1) or non-responders, there was a higher proportion of responders (44%) in patients with successful eradication compared to patients without eradication (36%)<sup>[38]</sup>. In the Scottish study it is likely that the high response occurred because of high prevalence of peptic ulcer disease<sup>[39]</sup>. The other studies evaluating elimination of *H pylori* in functional dyspepsia have had negative results<sup>[40-43]</sup> (Table 2). But recent well done meta-analysis and Cochrane Database systematic reviews show that there is a small but significant benefit of eliminating *H pylori* in patients with dyspepsia<sup>[44,45]</sup>. In the most comprehensive and thorough systematic review published to date, Moayyedi *et al* identified through electronic searches of the Cochrane Controlled Trials Register (CCTR), MEDLINE, EMBASE, CINAHL and SIGLE all randomized controlled trials evaluating *H pylori* eradication in functional dyspepsia and concluded that *H pylori* eradication therapy has a small but statistically significant effect in *H pylori* positive non-ulcer dyspepsia<sup>[44]</sup>. As demonstrated by Moayyedi *et al*<sup>[45]</sup>, other systematic reviews have included trials that used drug regimens known to be ineffective for *H pylori* eradication, have failed to include recent trials, have not contacted

**Table 2** Role of *H pylori* eradication in functional dyspepsia

Author	Name of study (if any)	Year	Type of study	No pts	Follow-up (mo)	Response
Mc Coll		1998	Singlecenter	218	12	Yes
Blum	OCAV	1998	Multicenter	438	12	No
Talley	ORCHID	1999	Multicenter	278	12	No
Talley		1999	Multicenter	170	12	No
Malfertheiner	ELAN	2001	Multicenter	180	12	Yes
Koelz	FROSCH	2003	Multicenter	181	6	No

authors for further information, have included abstracts, and have assumed that dropouts were treatment failures.

## **ACID SUPPRESSIVE THERAPY**

### ***H2* receptor antagonists**

Several studies and a large meta-analysis have demonstrated a slight advantage of H2-blockers over placebo or motility agents for treating functional dyspepsia<sup>[2,10-18]</sup>. In the large meta-analysis 22 studies met the inclusion criteria, 15 of which reported H2-blockers to be superior to placebo. Although many of the analyzed studies suffered from sub-optimal study design the odds ratio in favor of H2-blockers was 1.48 (95% confidence interval (CI): 0.9-2.3), for global assessment of dyspepsia symptoms, 2.3 (95% CI: 1.6-3.3) for improvement of epigastric pain, and 1.8 (95% CI: 1.2-2.8) for complete relief of epigastric pain. In most studies standard doses of H2-blockers were used but the duration of therapy was not longer than 8 wk<sup>[18]</sup>. Larger studies evaluating higher doses of H2-receptor antagonists and of longer duration may be necessary to determine the exact effect of H2-blockers on functional dyspepsia, but because PPI have been shown to be superior to placebo or H2-blockers in the therapy of functional dyspepsia, it is likely that we will not see major H2-blocker studies for the therapy of dyspepsia in the future<sup>[19-27]</sup>.

### **Proton pump inhibitors**

In a large primary care study, Meineche-Schmidt showed that in patients with presumed acid-related un-investigated dyspepsia, a standard dose of omeprazole 20 mg/d was significantly more effective than placebo in treating their self-worded main dyspepsia complaint<sup>[19]</sup>. In this study, 9% of the patients had sole reflux-like symptoms while the rest had other accompanying symptoms and would be considered to have dyspepsia. In fact, patients had on average more than five symptoms. As no initial endoscopic investigations were made, patients could have had a variety of possible diagnoses such as gastroesophageal reflux disease, ulcer disease, or functional dyspepsia. The recent CADET-PE study showed that if patients had endoscopic abnormalities (i.e. esophagitis), these were findings that predicted an appropriate response to acid suppression therapy<sup>[20]</sup>.

The largest studies evaluating PPI for the therapy of functional dyspepsia are: the CADET-HN, OPERA,

Table 3 Role of acid suppression using PPI in functional dyspepsia

Author	Name of study	Year	Type of study	PPI	No pts	Follow-up	Response
Bolling-Sternevald	PILOT	1996	Multicenter	Omeprazole <i>vs</i> placebo	197	2 wk	Yes
Jones		1997	Multicenter	Lanzoprazole <i>vs</i> ranitidine	432	4 wk	L better than R
Talley	BOND	1998	Multicenter	Omeprazole <i>vs</i> placebo	642	4 wk	Yes
Talley	OPERA	1998	Multicenter	Omeprazole <i>vs</i> placebo	606	4 wk	No
Meineche-Schmidt	ENCORE	1999	Multicenter	Omeprazole <i>vs</i> placebo	567	3 mo	Yes
Peura		2004	Singlecenter	Lanzoprazole <i>vs</i> placebo	921	8 wk	Yes
Veldhuyzen	CADET-HN	2005	Multicenter	Omeprazole (O), ranitidine (R), cisapride(C), placebo	512	4 wk	O better than R, C or placebo

BOND, PILOT, ENCORE and lansoprazole studies<sup>[21-26]</sup> (Table 3). In the CADET-HN study, 512 *H pylori* negative patients were randomised to omeprazole, ranitidine or cisapride for 4 wk. The proportion of patients who were responders at 4 wk and 6-mo was significantly greater for those receiving omeprazole (31%), compared with cisapride (13%) or placebo (14%), and ranitidine (21%,  $P=0.053$ ). In the BOND and OPERA multi-center trials 1262 patients with functional dyspepsia were randomized in a double-blind, placebo-controlled design in two studies with identical protocols to omeprazole 20 or 10 mg a day or identical placebo for 4 wk<sup>[21,22]</sup>. Complete symptom resolution was observed in 38% of patients taking omeprazole 20 mg/d, 36% on omeprazole 10 mg/d and 28% of patients on placebo. The Scandinavian Pilot study was a double blind, randomized, placebo controlled trial that evaluated the effect of gastric acid inhibition using omeprazole 20 mg twice daily in 197 patients recruited from gastroenterology practices in Bolling-Sternevald *E et al*<sup>[23]</sup>. Patients were excluded if they had a known gastrointestinal disorder, predominant symptoms indicating GERD, or the irritable bowel syndrome, as were patients with heartburn/regurgitation as their only symptom. Complete symptom relief was achieved in 32% of patients treated with omeprazole 20 mg/d compared with 14% of patients on placebo<sup>[23]</sup>. The ENCORE study addressed the consequences of relieving symptoms in patients with functional dyspepsia once they are off therapy<sup>[24]</sup>. In this study 567 patients from the OPERA study were followed for as additional three months during which time treatment was given at the discretion of the investigator. Responders had fewer clinic visits than non-responders (1.5 *vs* 2.0 mean visits) and fewer days on medication (mean, 9 d *vs* 23 d) over the 3-mo period (both,  $P<0.001$ ). The quality of life in responders was better at study entry and persisted over 3 mo (all,  $P<0.001$ ) Two large studies using lansoprazole have been published<sup>[25-26]</sup>. Jones *et al* performed a double-blind, parallel group, randomized, multi-center study in 32 general practices in the UK<sup>[25]</sup>. The investigators randomized 213 patients with symptoms of reflux-like or ulcer-like dyspepsia to receive lansoprazole 30 mg daily, and 219 to receive ranitidine 150 mg b.i.d. for 4 wk. After 2 wk 55% of the lansoprazole patients and 33% of the ranitidine group were symptom-free ( $P=0.001$ ) with corresponding 4-wk figures of 69% and 44%, respectively ( $P=0.001$ ). In the lansoprazole group, at 4 wk, 80% of patients were free of daytime heartburn and

81% of night-time epigastric pain, compared with 55% ( $P=0.001$ ) and 65% ( $P=0.01$ ) in the ranitidine group<sup>[25]</sup>. Peura *et al*<sup>[26]</sup> compared the efficacy of lansoprazole with placebo in relieving upper abdominal discomfort in 921 patients with functional dyspepsia in a blinded-randomized trial and moderate upper abdominal discomfort on at least 30% of screening days<sup>[26]</sup>. In contrast to the study of Jones *et al*, none of the patients had predominant symptoms suggestive of gastroesophageal reflux or endoscopic evidence of erosive or ulcerative esophagitis, or gastric or duodenal ulcer or erosion. Patients were assigned randomly to receive lansoprazole 15 mg ( $n=305$ ), lansoprazole 30 mg ( $n=308$ ), or placebo ( $n=308$ ) daily for 8 wk. At wk 8, significantly greater mean reductions in the percentage of days with upper abdominal discomfort were reported in patients treated with lansoprazole 15 mg (35%) or 30 mg (34%) compared with those treated with placebo (19%) ( $P<0.001$ ). Similarly, more patients treated with lansoprazole 15 mg (44%) or 30 mg (44%) reported complete symptom resolution at 8 wk than did placebo-treated patients (29%,  $P<0.001$ ). Improvement of upper abdominal discomfort, however, was seen only in patients who had at least some symptoms of heartburn at enrollment<sup>[26]</sup>.

### Prokinetic agents

Although delayed gastric emptying is considered a major pathophysiological mechanism in functional dyspepsia, the efficacy of prokinetic drugs to treat this dyspepsia has not been clearly established<sup>[1-3]</sup>. Problems with studies evaluating prokinetic agents include small sample size, patient heterogeneity, and poor quality design. Nevertheless, prokinetic agents such as metoclopramide, cisapride, mosapride citrate, itopride hydrochloride and domperidone continue to be widely used for the therapy of functional dyspepsia worldwide<sup>[1,2,27-30,46-48]</sup>. Due to its severe cardiac side effects, cisapride is not currently available in most of Europe and North America. Recent reviews and meta-analyses suggest that domperidone and cisapride are more effective than placebo<sup>[49-51]</sup>. Veldhuyzen *et al*<sup>[49]</sup> performed a meta-analysis to determine the efficacy of cisapride and domperidone in functional dyspepsia in placebo-controlled trials that included more than twenty patients<sup>[49]</sup>. For cisapride, 17 studies met the inclusion criteria. For all outcome measures, there was a statistically significant benefit in favor of cisapride: global assessment of improvement by the investigator or patient, epigastric pain, early satiety,

abdominal distension, and nausea. There were insufficient data to determine whether there is a relationship between improvement in gastric emptying and response to treatment. For domperidone, four of eight studies could be used for the analysis of global assessment of improvement by the investigator. This showed an OR of 7.0 in favor of domperidone. Although both cisapride and domperidone appear to be efficacious in the treatment of functional dyspepsia, this conclusion was largely based on global assessment by the investigator, which is not an optimal outcome measure. The effect of other prokinetic drugs, such as erythromycin, alosetron and tegaserod on functional dyspepsia have been inconsistent<sup>[52,53]</sup>.

### Antidepressants

Antidepressants have been only marginally explored in functional dyspepsia. Serotonin re-uptake inhibitors (SSRI) have the potential of relieving functional dyspepsia because they increase the availability of synaptically released 5-HT (pro-motility) not only at the central nervous system, but also at the level of the enteric nervous system<sup>[1-3]</sup>. Amitriptyline and 5-HT<sub>3</sub> receptor antagonists have been investigated mainly in IBS and the few studies performed in functional dyspepsia have provided conflicting results<sup>[54-56]</sup>. Also, kappa-opioid receptor agonists might be useful for functional dyspepsia because of their antinociceptive effects, but available results in functional dyspepsia are inconclusive. Other receptors that represent potential clinical targets for antagonists include purinoceptors (i.e., P2X<sub>2/3</sub> receptors), NMDA receptors (NR2B subtype), protease-activated receptor-2, the vanilloid receptor-1, tachykinin receptors (NK(1)/NK(2)) and cholecystokinin (CCK)(1) receptors<sup>[1,2]</sup>.

### Herbal Medications

Among the herbal medications, one of the best evaluated in prospective studies is Iberogast<sup>®</sup><sup>[57,58]</sup>. Iberogast<sup>®</sup> is a combination of herbal medicines, which include Iberis, peppermint, and chamomile<sup>[58]</sup>. Meta-analysis of double-blind, randomized clinical studies that evaluated the efficacy of the herbal preparation Iberogast<sup>®</sup> in patients with functional dyspepsia demonstrated a clear and highly significant overall therapeutic effect of Iberogast<sup>®</sup> in the treatment of functional dyspepsia<sup>[57,59]</sup>. All studies had the same duration and used the same dosage of active treatment and the same primary outcome measure, a dyspepsia-specific gastrointestinal symptom score. Of the 592 trial participants, 196 were treated with Iberogast<sup>®</sup> and 192 with placebo or cisapride (positive control). The individual studies all showed a substantial improvement of symptoms with Iberogast<sup>®</sup> but varying results regarding its statistically significant superiority to placebo<sup>[57]</sup>. There are many other herbal medications used in the therapy of functional dyspepsia<sup>[59-61]</sup>. These include the traditional chinese herbal medicine Xinwei Decoction, ganaton (itorpide hydrochloride), capsaicin (red pepper) and artichoke leaf extract (ALE)<sup>[59-61]</sup>. It is paradoxical to consider red pepper as a potential therapy for FD, but capsaicin, through its desensitization of gastric nociceptive C-fibers may alleviate dyspeptic symptoms<sup>[61]</sup>. Nonetheless, most studies using herbal medications are too small to allow us to reach conclusions regarding their efficacy to

treat functional dyspepsia.

### Hypnotherapy

Hypnotherapy was shown to be effective in irritable bowel syndrome, with long-term improvements in symptomatology and quality of life<sup>[62]</sup>. In another study aimed to evaluate the efficacy of hypnotherapy in functional dyspepsia, the data demonstrate an advantage of hypnotherapy over placebo and medical treatment<sup>[62]</sup>. Although hypnotherapy is time consuming and requires intense involvement by both physician and patient, it is an option that deserves further evaluation in future studies.

In summary, functional dyspepsia is a heterogeneous disease with variable response rates to therapy. Although the main aim of therapy is to obtain complete and long-lasting relief of symptoms, in many patients there is only partial relief or the relief is only of short-term duration. Long-term improvement with drug therapy occurs in a minority of patients. Before starting drug therapy it is recommended to provide the patient with an explanation of the disease process and reassurance. Ruling out an organic cause of their disease by endoscopy can lead to improved acceptance of the disease process. In general, the approach to treat patients based on their main symptom is practical and effective. The general approach is to treat patients with acid suppressive therapy with proton pump inhibitors if the predominant symptom is epigastric pain or if there are gastroesophageal reflux symptoms present. The role of *H. pylori* in functional dyspepsia continues to be a matter of debate. Nevertheless, recent data indicate that there is a modest but significant benefit in eradication of *H. pylori* in functional dyspepsia. The overall data indicates that symptomatic improvement of patients with functional dyspepsia with current drug therapy is left with many unmet needs. Thus, more studies are needed to better understand this condition as well as to study more therapeutic possibilities.

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