The therapy of functional dyspepsia: an update

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Abstract

Functional dyspepsia (FD) is a common disorder of the gut-brain interaction (previously named functional gastrointestinal disorders). Recent data evaluate its prevalence to 7% worldwide. FD is classified into epigastric pain syndrome (EPS) and PDS (PDS). While the diagnosis of FD is standardized thanks to the work of the Rome Foundation committees, the therapy is far from being satisfactory. A recent European guide found few strong recommendations, reflecting the lack of sufficient data for high levels of evidence. This review is presenting possibilities of management of FD. Therapeutic indications should target the main symptoms and be proportionate to the severity.

Keywords: dyspepsia, epigastric pain, functional dyspepsia, postprandial distress disorder, therapy

Introduction

Functional dyspepsia (FD) is a common disorder of the gut-brain interaction (previously named functional gastrointestinal disorders) and 7% of the general population worldwide report FD symptoms [1]. FD is part of a larger group of symptoms labelled as dyspepsia. Dyspepsia is defined as one or more symptoms attributed to the stomach and duodenum, localized in the upper digestive part of the abdomen. According to the etymology, dyspepsia means "difficult digestion" in Greek. Another word for the same condition, coming from Latin, is "indigestion" but this is now rather reserved to the alteration of intestinal digestion and absorption.

Diagnosis

Symptoms included in dyspepsia are epigastric pain, epigastric burn, early satiety, epigastric fullness, anorexia, nausea, emesis but not heartburn. Most patients wrongly make the attribution of dyspeptic symptoms to the biliary system. Dyspepsia may be acute or chronic.

The first step in the diagnosis of dyspepsia is: organic or functional? Upper digestive endoscopy is necessary to rule out the existence of organic conditions.

The second step is to assess the presence of H. pylori infection. According to the Guidelines for the management of *Helicobacter pylori* infection in Italy: The III Working Group Consensus Report 2015 [2], there is strong evidence now that: "HP test-and-treat strategy is appropriate for the initial management of uninvestigated dyspepsia as HP prevalence in adults in Italy is over 20%. This approach is applicable to patients younger than 50 years without alarm symptoms. Evidence level: 1a; Grade of recommendation: A" [2]. *H. pylori* dyspepsia is that dyspepsia where the symptoms disappear after the eradication of the *H. pylori* infection.

The next step is the identification of functional dyspepsia. This is defined according to Rome IV criteria [3] as: the presentation of dyspeptic symptoms fulfilling the following criteria (Table I):

Actually, beside the postprandial distress syndrome including epigastric distension, early satiety, loss of appetite, nausea, symptoms largely attributed to gastroduodenal motility disorders and altered visceral sensitivity and the epigastric pain syndrome including pain, food related, these being attributed to the contact and sensitivity of gastric mucosa to gastric acid, there is the possibility of association between these two subtypes. Patients fulfilling criteria of FD but not

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typical PDS or EPS are considered as having Nonspecific functional dyspepsia NFD.

FD is not the only disorder of gut-brain interaction (DGIB) attributed to the gastroduodenal segment of the gastrointestinal tract. Table II shows other gastroduodenal DGIB according to Rome IV [3].

Table I. Diagnostic criteria for functional dyspepsia according to Rome IV [3].

1. One or more of the following:
• a. **bothersome** postprandial fullness **PDS**
• b. **bothersome** early satiation
• c. **bothersome** epigastric pain **EPS**
• d. **bothersome** epigastric burning
2. No evidence of structural disease
Start more than 3 months, onset at least 6 months, frequency at least 1 day/week

Table II. Gastroduodenal DGIB beside FD [3].

Belching disorders
• a: Excessive supragastric belching
• b. Excessive gastric belching
Nausea and vomiting disorders
• a: Chronic nausea and vomiting syndrome
• b: Cyclic vomiting syndrome
• c: Cannabinoid hyperemesis syndrome
Rumination syndrome

Table III. Statements not endorsed in the therapy of FD [5].

Dietary adjustment improves symptoms in FD.
Proton pump inhibitor therapy is the most appropriate initial therapy for FD.
Proton pump inhibitor therapy is the most effective therapy for EPS.
Prokinetic therapy is the most appropriate initial therapy for FD.
Prokinetic therapy is an effective therapy for FD.
Prokinetic therapy is the most effective therapy for PDS.
Efficacy of prokinetics is not related to their enhancement of gastric emptying rate.
Itopride is effective for FD patients.
Tricyclic antidepressants are effective for epigastric pain syndrome (EPS).
Tricyclic antidepressants are effective for post-prandial distress syndrome (PDS)
Tricyclic antidepressants are not effective for post-prandial distress syndrome (PDS).
Serotonin reuptake inhibitors are effective for FD.
Serotonin reuptake inhibitors are not effective for FD.
Serotonin noradrenaline reuptake inhibitors are effective for FD.
Serotonin noradrenaline reuptake inhibitors are not effective for FD.
Mirtazapine is effective for post-prandial distress syndrome patients with weight loss.
5-HT1A agonists (tandospirone, buspirone, ….) are effective for PDS.
Herbal therapies are effective for FD patients.
Rifaximin is effective for FD patients.
Hypnotherapy is effective for FD patients.
Cognitive behavioral therapy (CBT) is effective for FD patients.
Acupuncture is effective for FD patients.
Mindfulness is effective for FD patients.

Therapy

There are several attempts to treat functional dyspepsia and several algorithms to use. However, the success is less than expected and efficacy of most remedies is reduced [4]. Therefore, the European Society of Neurogastroenterology and Motility (ESNM) undertook an important initiative to create guidelines for FD [5]. The part corresponding to therapy was largely disappointing, as few strong recommendations could be elaborated based on currently existing evidence [5].

We present below the main statements and recommendations of ESNM [5].

Thus, the following statements were not endorsed by the panel of experts (Table III).

The following statements were endorsed by the ESNM experts [5] (see table IV):

Table IV. Statements endorsed in the therapy of FD [5].

HP positive FD patients should receive eradication therapy.
Proton pump inhibitor therapy is an effective therapy for FD.
In case of severe weight loss in FD, nutritional support may be needed.

As it has been observed, although theoretical pragmatic recommendation exist and make sense [6], there is little agreement between experts concerning FD therapy [7]. This situation is due to the lack of strong evidence. More trials, involving more centers from more countries and testing of new drugs are necessary before observing significant progress in the management of FD.

Conclusions

Dyspepsia is a common challenge for physicians. Functional dyspepsia remains an important DGIB in Rome IV. Its investigation should be performed carefully and according to algorithms. Therapy should address symptoms and be adapted to severity. It is difficult to find strong recommendations for therapy as long as evidence is still scarce.

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