

Management of Dyspepsia in Primary Care

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Abstract

Background: Dyspepsia is defined as having one or more symptoms of epigastric pain, burning, postprandial fullness, or early satiation. Dyspepsia is one of the most common complaints of patients attending a primary care clinic and constitutes at least 40% of cases in a gastroenterology practice.

Aim: This review aims to highlight the most important recent developments in both the investigation and management of dyspepsia in primary care, and to explore recommendations from the latest clinical guidelines.

Methodology: The review is comprehensive research of PUBMED since the year 1992 to 2019.

Conclusion: Dyspepsia is common in the community. It represents a considerable burden to the health service; therefore correct initial management is important. There are several treatment options available for the management of this condition. However, new approaches and therapies for dyspepsia continue to be evaluated, and some suggest promise for the future.

Keywords: *Dyspepsia; Management of Dyspepsia; Primary Care*

Introduction

Dyspepsia is defined as having one or more symptoms of epigastric pain, burning, postprandial fullness, or early satiation [1]. It is also defined as any symptom of the upper gastrointestinal tract (GI), present for 4 weeks or more, including upper abdominal pain or discomfort, heartburn, acid reflux, nausea, or vomiting. The symptoms of dyspepsia may be acute, e.g. in gastroenteritis, or chronic. In the latter case, underlying organic (e.g. ulcer, reflux, pancreatic disease, heart and muscle disease) or functional factors may be responsible [2].

Dyspepsia is one of the most common complaints of patients attending a primary care clinic and constitutes at least 40% of cases in a gastroenterology practice [3]. Of those with dyspepsia, around 40% will seek the advice of their primary care physician. Consultation behavior is influenced, in part, by the frequency and severity of symptoms, and increasing age of the patient. Almost 15% of patients with dyspepsia are referred to secondary care for further investigation and management [4].

Regardless of its definition, the causes of dyspepsia are known to include peptic ulcer disease, gastro-esophageal reflux, and functional dyspepsia. The prevalence of dyspepsia varies considerably between different populations. The lowest prevalence of 7% - 8% is seen in Singapore, South East Asia [5], slightly higher rates are seen amongst the Scandinavians (14.5% [6] and 18.4%) [7,8], prevalence rates of 23 - 25.8% are seen in the US [9] with populations in India (30.4%) [10] and New Zealand (34.2%) [11] having the highest rates.

Patients presenting with predominant epigastric pain or discomfort who have not undergone any investigations are defined as having uninvestigated dyspepsia. In patients with dyspepsia who are investigated, there are 5 major causes: gastroesophageal reflux (with or without esophagitis), medications, functional dyspepsia, chronic peptic ulcer disease (PUD), and malignancy [12].

Dyspepsia represents a considerable burden to the health service, and therefore optimal management of the condition in primary care is essential. The initial management of uncomplicated dyspepsia in the community should consist of either non-invasive testing for *Helicobacter pylori*, so-called 'test and treat', with proton pump inhibitor (PPI)-based triple therapy for those testing positive (PPI and two antibiotics) and 4 weeks of PPI for those testing negative, or empirical PPI for all patients [13].

As with any subacute or chronic illness, the initial evaluation of a patient with dyspepsia begins with a thorough history and physical examination. Management include lifestyle advice, such as healthy eating, weight reduction, exercise, smoking cessation, and avoidance of known precipitants of symptoms such as coffee, alcohol, chocolate, or fatty foods, although there is no evidence from RCTs to support such interventions. GPs should also review prescribed medications for possible causes of dyspepsia, such as non-steroidal anti-inflammatory drugs, corticosteroids, bisphosphonates, theophyllines, nitrates, selective serotonin reuptake inhibitors, or calcium antagonists [14,15].

This review aims to highlight the most important recent developments in both the investigation and management of dyspepsia in primary care, and to explore recommendations from the latest clinical guidelines.

Pathophysiology

Visceral hypersensitivity, impaired gastric accommodation and impaired gastric emptying are commonly reported by patients with functional dyspepsia. Involvement of several other mechanisms has also been suggested, including duodenal hypersensitivity to the luminal contents, small bowel dysmotility, psychological disturbances, central nervous system disorders and *Helicobacter pylori* infection [16-21].

Perhaps the most important contributory factors to dyspepsia are the presence of *Helicobacter pylori* and the use of medications such as NSAIDs. *H. pylori* is strongly associated with peptic ulcer disease and weakly associated with functional dyspepsia. NSAIDs can cause symptoms through gastro-duodenal inflammation/ulceration but can also cause dyspepsia in the absence of mucosal injury. Delayed gastric emptying has been reported by gastric scintigraphy in a large proportion (up to 45%) of dyspeptic patients, especially those with postprandial distress syndrome (PDS) [22,23].

Gastric accommodation is mediated by a vasovagal reflex initiated by food ingestion and generated via the activation of nitrenergic nerves that relax the fundus and upper body of the stomach. Gastric barostat studies revealed that patients with dyspepsia had lower thresholds for first perception, discomfort, and pain during distention of the proximal stomach [24].

The duodenum might play a role in the genesis of dyspepsia symptoms was first suggested by a study that showed that 59% of patients with dyspepsia developed nausea during a brief period of duodenal acid perfusion; the same stimulus failed to induce any symptoms in

healthy control subjects. It has been recognized for decades that dyspepsia is commonly linked with psychological comorbidities, such as anxiety and depression [25].

Comorbid anxiety and depression are thought to not only contribute to the basic pathogenesis of symptoms in some FD sufferers, but also to drive health care-seeking behavior [26].

Evaluation and diagnosis

Patients presenting with predominant epigastric pain or discomfort who have not undergone any investigations are defined as having uninvestigated dyspepsia. In patients with dyspepsia who are investigated, there are 5 major causes: gastroesophageal reflux (with or without esophagitis), medications, functional dyspepsia, chronic peptic ulcer disease (PUD), and malignancy [27].

The patient history should assess the quality, duration and severity of symptoms, as well as the presence of other associated symptoms. A list of current medications, especially nonsteroidal anti-inflammatory drugs (NSAIDs), over-the-counter medications and herbal remedies should be collected. A family history of PUD, alcohol use and psychiatric or psychosocial disorders should be noted [28].

The only instrumental diagnostic examinations thought to be sufficiently accurate are esophagogastroduodenoscopy including investigation for *Helicobacter pylori* and abdominal ultrasonography, accompanied in the presence of additional symptoms of IBS by endoscopic inspection of the colon. These investigations are indicated in cases where the medical history and symptoms are typical and the preliminary laboratory tests such as blood count, electrolytes, and hepatic and renal function, as well as erythrocyte sedimentation rate or CRP and, if applicable, peripheral thyroid parameters are in the normal range [29].

A normal upper endoscopy also helps in dividing dyspepsia into organic and functional. This is often a clinical challenge, since an attribution of endoscopic findings to patients' symptoms is not always straightforward. The decision as to whether endoscopic findings, especially minor abnormalities, should be accepted as an explanation of the patient's complaints or the patient has dyspepsia is often an empirical decision based on subjective personal experience [30].

To measure gastric emptying, scintigraphy, paracetamol absorption test, c13-octanoic acid or *Spirulina* breath tests, ultrasonography, and magnetic resonance imaging (MRI) have been reported. Of those, scintigraphy is the most frequently used [31].

The urea breathe test (UBT) and the stool antigen test are the most accurate noninvasive indirect diagnostic tests for *H. pylori* infection and are recommended especially in low prevalence populations. Unlike serological tests that are only markers for exposure to *H. pylori* and do not differentiate current from previous infection, the UBT and the stool antigen test detect active infection. According to the American College of Gastroenterology guidelines, the UBT is the best non-endoscopic test for documenting *H. pylori* infection [32].

Serologic testing is an indirect test for *H. pylori* infection that detects IgG or IgA antibodies to *H. pylori* and has variable specificity. It is a cost-effective tool, particularly in populations in which the prevalence of *H. pylori* is high. However, it may lead to the over-treatment of patients due to the high rate of false-positive test results [33].

Endoscopy is recommended in patients with dyspepsia who have alarm symptoms suggestive of potentially serious underlying conditions such as PUD, gastric/esophageal cancer and other rare upper gastrointestinal (GI) diseases. Studies from open-access endoscopy practices and outpatient series demonstrate that only a few patients with dyspepsia in fact have PUD, reflux esophagitis and gastric cancer [9,34].

Management and treatment

There are several approaches to the treatment of dyspepsia which may need to be individualized depending on the prevalence of *H. pylori* and PUD in the population: the patient's predominant symptoms, the effectiveness of previous therapy in improving dyspeptic

symptoms, the patient's family history of PUD or gastric cancer, the positive predictive values of noninvasive tests, and in some cases, patient preference [35].

Patients without alarm symptoms who have had symptoms for less than four weeks may be managed initially with reassurance, over the counter medications, and "watchful waiting". In low risk patients who have had symptoms for four weeks or longer, a strategy of testing for *H. pylori* infection and treating the infection in those who are positive is probably cost effective and safe, provided follow up of patients is organized and that an appropriate test is used [36]. Primary care physicians must be aware that a test and treat strategy will not reduce dyspeptic symptoms in many infected patients, including some of those who had peptic ulcer disease. Rather than be disheartened by this, physicians should take the view that they have eliminated the issue of peptic ulcer mortality and treat the residual symptoms accordingly [15].

Empirical therapy with antacids, anti-secretory, and prokinetic agents has long been the traditional approach for most primary care physicians in the initial management of patients with uninvestigated dyspepsia. To date, anti-secretory therapy has largely been with H2 receptor antagonists [37]. An empiric trial of anti-secretory therapy should be administered for 6 to 8 weeks. Those who fail to respond or those with early relapse of symptoms should be referred for specialist evaluation and endoscopy. With their widespread availability and their demonstrated efficacy and safety, PPIs are now the recommended first-line anti-secretory therapy in uninvestigated dyspepsia [38].

Given that patients who do not respond to the first choice of symptomatic therapy may have been misclassified, a switch of treatment, for example from prokinetic to PPI, should be considered. If symptoms still persist following such a switch of therapy, a course of high dose PPI therapy may need to be considered, as discussed above. Otherwise, the patient should be referred for endoscopy, or other treatment options considered, depending on the clinical setting [39]. Initial management of uncomplicated dyspepsia in the community should consist of either non-invasive testing for *Helicobacter pylori*, so-called 'test and treat', with proton pump inhibitor (PPI)-based triple therapy for those testing positive (PPI and two antibiotics) and 4 weeks of PPI for those testing negative, or empirical PPI for all patients [15].

Psychotherapy and behavioral therapy may also provide benefit in selected patients. Hypnotherapy has been shown to be superior to supportive therapy or an H2-receptor antagonist. Applied relaxation therapy, psychodynamic psychotherapy and cognitive therapy have also shown potential benefits, but studies are limited and poorly designed [40].

Fundic relaxors can be considered for people unresponsive to prokinetics. Cisapride relaxes the gastric fundus, but alternative options include the anti-anxiety drug buspirone or the over-the-counter product Iberogast [41].

A variety of complementary and alternative therapies have been suggested for the treatment of dyspepsia. One herbal remedy of interest, which has been evaluated in a single large RCT, is iberogast, also known as STW5. It is a mixture of nine different herbs, including milk thistle, chamomile, peppermint, and liquorice. In healthy volunteers, STW5 stimulated gastric relaxation and increased antral motility, which may account for any potential therapeutic effects in FD [42].

Conclusion

Dyspepsia is common in the community. It represents a considerable burden to the health service; therefore correct initial management is important. There are several treatment options available for the management of this condition. However, new approaches and therapies for dyspepsia continue to be evaluated, and some suggest promise for the future.

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