ORIGINAL ARTICLE

Gastro-oesophageal Reflux Disease: An Update

T Murphy, EK Donaldson, M Mills, M Arthurs, MG Lee

ABSTRACT

Gastro-oesophageal reflux disease (GERD) is a disorder in which reflux of stomach contents causes troublesome symptoms and/or complications and which affects health-related quality of life. It is one of the commonest disorders and appears to be increasing in incidence. The mechanisms leading to reflux are complex and multifactorial. The lower oesophageal sphincter (LES) is an important part of the gastro-oesophageal barrier. Transient LES relaxations (TLESRs) lead to reflux as these vagally mediated motor patterns cause relaxation of the LES and also result in oesophageal shortening and inhibition of the crural diaphragm. Heartburn and regurgitation are the characteristic symptoms of GERD. A clinical diagnosis of GERD can be made with typical symptoms. Oesophagitis is seen in a minority of patients with GERD. Lifestyle modification is widely advocated for patients with GERD. For short-term relief of symptoms of mild GERD, antacids/alginates are frequently used but they do not heal oesophagitis. Both histamine 2 receptor antagonists (H2RA) and proton pump inhibitors (PPI) have been shown to heal and prevent relapse of oesophagitis, although PPIs have been shown to be superior. The PPIs are the recommended first-line therapy for erosive oesophagitis and initial management of non-erosive reflux disease. Maintenance PPI therapy should be given to patients with oesophagitis, those who have recurrence of symptoms after discontinuation of medication and for those with complications of GERD.

Keywords: Gastro-oesophageal reflux, GERD, sphincter, symptoms

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INTRODUCTION

Gastro-oesophageal reflux disease (GERD) is one of the commonest disorders seen by gastroenterologists and primary care providers (1). Although GERD is a common and recognized problem, the actual definition has proven problematic (2–5). In order to promote uniformity, recommendations have been put forward to adopt the Montreal classification and the LA classification of erosive oesophagitis, allowing for a standardization of terminology and classification (6, 7). Gastro-oesophageal reflux disease is a disorder in which reflux of stomach contents causes troublesome symptoms and/or complications.

Although GERD has been described throughout the world, the prevalence of GERD reported varies in different geographic areas. Gastro-oesophageal reflux disease is one of the most common digestive diseases in the Western World and appears to be increasing in incidence, with typical symptoms occurring in 15–20% of the population (8, 9). In a Canadian population-based survey, 17% of respondents had symptoms in the previous three months, with 13% having moderate to severe symptoms (10). In a review of population-based studies of GERD worldwide, the prevalence of weekly symptoms increased until 1995 then plateaued from 1995–2009, except in a Norwegian study where there was an absolute increase of 5% (8, 9, 11). In Europe, in Spain, 15% of the population suffers from GERD symptoms weekly, while the prevalence in Germany was 18%. The prevalence of gastro-oesophageal symptoms is higher in Central and West Asia than in East Asia. There is little data from the African continent, with only Tunisia reporting 24% (5, 12, 13). In Jamaica, 44% of healthy individuals had experienced recent heartburn (14). In another study in Jamaica, weekly symptoms of GERD were present in 18.6% and symptoms of moderate or greater severity were reported in 11.7% (15).

Gastro-oesophageal reflux disease arises from the reflux of acid across an incompetent lower gastro-oesophageal sphincter with or without a hiatal hernia, leading to symptoms (4, 7). Gastro-oesophageal reflux disease can be

From: Department of Medicine, The University of the West Indies, Kingston, Jamaica.

Correspondence: Professor MG Lee, Department of Medicine, Faculty of Medical Sciences, The University of the West Indies, Kingston 7, Jamaica. E-mail: michael.lee@uwimona.edu.jm

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subdivided into oesophageal syndromes, which include symptomatic GERD, oesophageal injury and extra-oesophageal syndromes. Patients may have typical symptoms of GERD but have no oesophageal injury on investigation. This is also known as symptomatic reflux disease or non-erosive oesophageal disease [NERD] (7); it is the most common type of reflux disease, accounting for up to 60% of patients. Oesophagitis is seen in a minority of patients with GERD (16). When oesophagitis or oesophageal injury is present as a result of GERD, the condition may also be complicated by Barrett's oesophagus, oesophageal strictures and adenocarcinoma of the oesophagus. However, the risk of malignancy is very low in patients with Barrett's oesophagus (10). Extra-oesophageal associations for GERD such as chronic cough, laryngitis, asthma and dental erosions have been described, while proposed associations for GERD include pharyngitis, sinusitis, otitis media and pulmonary fibrosis (17).

It is well established that troublesome GERD affects health-related quality of life (HRQoL). In fact, GERD patients commonly experience substantial reductions in both physical and psychosocial aspects of HRQoL, as well as work productivity (16). Impairments in HRQoL are seen whether or not reflux oesophagitis or Barrett's oesophagus is present, and are comparable with or worse than those seen in patients with other chronic diseases such as heart disease, diabetes and cancer. Surveys in primary care and in the community highlight disrupted sleep, reduced concentration at work and interference with physical activities such as exercise, housework and gardening (16). The health deterioration associated with GERD is comparable to people with arthritis and chronic heart failure (17, 18). In addition, frequent nocturnal reflux is associated with decreased sleep, significantly impaired productivity and low HRQoL scores. Factors that appear to impact HRQoL include female gender, increased body mass index (BMI) and nocturnal symptoms (12, 13, 19).

The natural history of GERD remains unclear, with minimal data of adequate duration available. In a Swedish study over a 10-year period, it was reported that there was no significant change in symptoms over time. It did not appear that age and gender had an influence on the occurrence of symptoms, suggesting that the overall occurrence of GERD appeared stable from 1988–1995 (3). The natural history of patents with NERD indicates that progression to oesophagitis is uncommon, and there is no evidence to the development of Barrett's oesophagus (20).

The mechanism through which GERD symptoms are generated is complex and multifactorial. Inherent in the function of the gastro-oesophageal barrier is prevention of acid, secreted by the proximal stomach, from entering the oesophagus during variations of gastro-oesophageal pressure. The gastro-oesophageal apparatus, which consists of the lower oesophageal sphincter (LES) and crural fibres, functions as a one-way valve during swallowing while also allowing venting of air during transient lower oesophageal sphincter relaxations (TLESRs). The LES is an important part of the gastro-oesophageal barrier and consists of two separate components: a tonically contracted intrinsic circular muscle, which relaxes during swallowing, secondary peristalsis and TLESRs. The diaphragmatic crura is the extrinsic component that exerts pressure on the internal sphincter (21). Transient lower oesophageal sphincter relaxations lead to reflux as these vagally mediated motor patterns cause relaxation of the LES while also resulting in oesophageal shortening and inhibition of the crural diaphragm (21). Transient lower oesophageal sphincter relaxations are triggered by activation of the vagal afferents in the cardia of the stomach with gastric distention being an important precipitant.

In mild GERD, in which the percentage of time the pH in the oesophagus is less than 4 is usually below 15%, the reflux of acid occurs mainly post-prandially, resulting in symptoms during daytime hours. In contrast, in patients with severe GERD, there is an associated greater oesophageal acid exposure. A greater proportion of the reflux in severe disease occurs in the absence of TLESRs, when there is a prolongation of low LES pressure and raised intragastric pressure, resulting in excessive distal oesophageal acidification (21). The role of a hiatal hernia in GERD is well documented. The hiatal hernia causes the gastro-oesophageal junction to become displaced in a position that is proximal to the intrinsic sphincteric component of the LES. There is accompanying disruption of the phreno-oesophageal ligaments, leading to an overall impairment in oesophageal clearance, acid emptying, trapping of acid in the hernia sac, re-reflux of acid post peristaltic waves, loss of the flap valve mechanism and decreased LES pressure during straining (21–23).

SYMPTOMS

Heartburn and regurgitation are the characteristic symptoms of GERD. Heartburn indicates retrosternal burning pain or discomfort which may arise from the epigastrium or lower chest and radiate upwards, often most marked post-prandially (5). Regurgitation is the other cardinal symptom of GERD in which there is reflux of acidic gastric contents with or without small amounts of food into the mouth and/or hypopharynx (7, 18). Patients with GERD frequently have co-existing symptoms such as epigastric pain, epigastric burning and nausea (7, 10).

A less common symptom of GERD is chest pain which is usually central, may be radiating and may mimic angina pectoris. Gastro-oesophageal reflux can cause episodes of chest pain that resemble ischaemic cardiac pain, without accompanying heartburn or regurgitation (17).

Waterbrash is the secretion of a large volume of saliva in response to acid reflux/regurgitation and is sometimes seen in GERD. Globus sensation describes a sensation of a lump in the throat in the absence of objective dysphagia or odynophagia. Dysphagia usually indicates a complication

suggestive of oesophageal luminal narrowing. Odynophagia describes pain on swallowing and may be a manifestation of oesophagitis, whether GERD-related or due to other pathology.

Atypical symptoms may occur with GERD. However, the relationship of these symptoms to GERD may not always be obvious and may only become evident with a careful history and physical examination. The following symptoms may be seen in some patients with GERD: hoarseness, laryngitis, chronic dry cough especially nocturnal, asthma, earache, dental erosions and halitosis. It is important to note that night-time heartburn with sleep disturbance may occur in patients with GERD (7, 17).

Clinically, GERD severity is determined by the frequency and severity of symptoms or by the presence and extent of reflux-related lesions such as oesophageal erosions, ulceration, haemorrhage, strictures and Barrett's epithelium (10). Symptomatically, mild disease applies to patients who have infrequent symptoms (less than three times weekly) and of low intensity and duration with minimal effect on daily activities or HRQoL. In contrast, moderate or severe disease refers to more frequent, intense or prolonged symptoms that have a significant effect on daily activities or HRQoL (10).

DIAGNOSIS

A clinical diagnosis of GERD can be made with typical symptoms and GERD is frequently diagnosed based on symptoms alone (7). Upper endoscopy is indicated in patients with alarm symptoms and in patients with a high risk for or symptoms suggestive of complications (1). Alarm symptoms include weight loss, bleeding and dysphagia. Endoscopy in these patients may reveal a complication of GERD or another upper gastrointestinal pathology (24). Endoscopy may be considered for patients with GERD for ten years or more to screen for Barrett's epithelium (10). Endoscopy is also considered in patients who do not respond to usual therapy or have atypical symptoms. A barium swallow/meal is not a useful tool in the diagnosis of GERD but may indicate moderate to severe oesophagitis, hiatus hernia or an alternative diagnosis.

Patients presenting with chest pain should have cardiac evaluation prior to therapy or investigation for GERD. Ambulatory oesophageal pH monitoring is indicated before consideration for endoscopic or surgical therapy in patients refractory to PPI treatment and when the diagnosis is in question (1). Oesophageal pH monitoring must be performed after stopping acid suppressive therapy for at least five days as the refluxate may not be acidic while on acid suppressive medication (24). Oesophageal manometry is used mainly for preoperative evaluation and to exclude motility disorders which may present with some GERD-like symptoms.

TREATMENT

In the management of GERD, a patient-centred approach is recommended (7). A presumptive diagnosis of GERD can be made in the setting of typical symptoms and empirical therapy started (1). Importantly, effective treatment of GERD can help to reverse the adverse effects of GERD on HRQoL. Studies have also shown that, by ameliorating reflux symptoms, acid inhibitory therapy significantly improves the emotional, psychosocial as well as physical aspects of patients' HRQoL (16).

Lifestyle modification is widely advocated for patients with GERD, but there are no randomized studies evaluating the efficacy of these measures. However, lifestyle changes may be prescribed in specific individuals including during pregnancy. Lifestyle change is necessary and weight loss is recommended for patients who are overweight (1, 25). Cessation of smoking, decreasing excess alcohol intake, reducing chocolate, coffee, citrus and any other foods which seem to play a role in the onset, severity and duration of symptoms should be considered in patients with GERD. Also, avoiding large meals, elevation of the head of the bed by 4–6 inches and eating three hours prior to recumbency may be helpful, especially in patients with nocturnal GERD (1).

For short-term relief of symptoms of mild GERD, antacids/alginates are frequently used but they do not heal oesophagitis (26, 27). Therefore, antacids/alginates may be used in symptom control of GERD but are not sufficient for effective long-term management where step-up therapy is necessary. They can be used alone in patients with non-erosive GERD or in combination with other medications for rapid symptom control.

Alginate-based formulations usually contain sodium or potassium bicarbonate. A foam is formed when alginate comes in contact with gastric acid, and the foam floats on the surface of gastric contents, creating a neutral pH barrier (27). Prokinetic medications like metoclopramide and domperidone increase lower oesophageal sphincter pressure, increase oesophageal and gastric peristalsis and promote gastric emptying (28). Baclofen and lesogaberan were developed as selective GABA-B agonists based on their inhibition of transient lower oesophageal sphincter relaxation (28). Although there is controversy regarding the use of these agents, they can be used in combination with histamine 2 receptor antagonists (H2RA) and proton pump inhibitors (PPIs) especially in patients who demonstrate significant regurgitant symptoms. Patients may respond to combination acid suppressant and prokinetic therapy with improvement in HRQoL (28). Potential side effects must be discussed with the patients (29).

Both H2RA and PPIs have been shown to heal and prevent relapse of oesophagitis, although PPIs have been shown to be superior (27). The overall complete healing of erosive lesions, healing rate and complete heartburn relief for patients with oesophagitis is superior with the use of PPIs compared to H2RA (1).

Histamine 2 receptor antagonists are effective in the management of mild to moderate GERD (30). The duration

of therapy is four to 12 weeks. Medication may be given once or twice daily. No particular agent is recommended over another. They can be used as maintenance therapy for patients with NERD who experience relief of symptoms but H2RA may lead to tachyphylaxis with prolonged use (1). They can be added to PPIs for individuals with night-time symptoms.

Proton pump inhibitors are the recommended first-line therapy for erosive oesophagitis and initial management of NERD. A four- to eight-week course is recommended for NERD and an eight-week course is recommended for healing erosive oesophagitis (1). There is no difference between the PPIs in efficacy and they should be given 30–60 minutes before breakfast (1). Omeprazole-sodium bicarbonate, which is an immediate release formulation, has been shown to more effectively control nocturnal gastric pH (31). Dexlanzoprazole, a dual delay release PPI, can be given any time of day regardless of food intake (1).

The dose of PPI can be increased to twice daily in those who do not fully respond to initial treatment. Patients with NERD may be less responsive to anti-secretory medications than patients with oesophagitis (20). Patients with oesophagitis are given at least eight weeks of therapy for healing, followed by maintenance. Maintenance PPI therapy is also given to patients who have recurrence of symptoms after discontinuation of medication and for those with complications of GERD (1). Patients with NERD who have responded symptomatically to PPI can be followed long term with on-demand or intermittent therapy with recurrence of symptoms, whereby PPI is restarted until symptoms resolve or given for a set interval (1).

Surgical treatment options are available for long-term management of GERD. However, for best results, it is generally recommended for patients who respond to PPI therapy (1). It is less effective than medical therapy for some patients with GERD. Relapse rates are high for return to PPI use after five years post surgery. Potential surgical candidates should have manometry and pH testing done to confirm the diagnosis before consideration for surgery (1).

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