

Additional considerations for gastro-oesophageal reflux disease

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Abstract

Gastro-oesophageal reflux disease (GORD) is a common condition worldwide. It is characterised by numerous upper gastrointestinal tract symptoms, but patients mainly present with heartburn and regurgitation. Various causes have been linked to the pathophysiology of GORD. Some of them are well known, while others are less frequently implicated. Oesophageal inflammation is the result of the inadequately managed suppression of gastric acid caused by the retrograde flow from the stomach through the lower oesophageal sphincter, which may result in complications, including stricture formation, Barrett's oesophagus, erosive oesophagitis and adenocarcinoma. The incidence per region and country varies significantly, and is dependent on the population demographics. GORD is responsible for an impaired general health score in affected individuals, and has a negative impact on economic productivity in society. Treatment may range from unscheduled self-medication to complicated laparoscopic surgery. This article describes some of the associated factors, revised definitions and the role of surgery in the management of GORD.

Keywords: gastro-oesophageal reflux disease, glucocorticoid, GORD, *Helicobacter pylori*, obstructive sleep apnoea syndrome, quality of life

Introduction

Gastro-oesophageal reflux disease (GORD) is a quotidian upper gastrointestinal tract disorder, characterised by dyspepsia (indigestion, belching, bloating, nausea, early satiation and postprandial fullness), epigastric pain or heartburn (substernal burning sensation or chest pain), and regurgitation (casting up of incompletely digested food).¹ Oesophageal inflammation (oesophagitis) is the most frequent complication if left untreated, and may result in stricture formation, Barrett's oesophagus and adenocarcinoma.

As with many common medical conditions, continuous research into the causality and association of other pathological conditions with GORD has changed dramatically over the last few decades. Oesophagitis and hiatus hernia were regarded as the main cause of reflux in the medical literature 40 years ago.² Soon thereafter, it was linked to the impairment of vagal function, with the assumption that it was a motility disorder characterised by sphincter and peristaltic dysfunction.^{3,4} More recently, symptomatic episodes of GORD were shown to be a consequence of an acid peptic disorder, with approximately 80% of the cases being the result of acid reflux via various mechanisms.⁵ Elucidation of alternative and additional mechanisms is by technological and diagnostic advancements being available in modern clinical research. Thus, it is evident that GORD is a condition with features of multiple pathological

causes, culminating in the reflux of gastric acid through the lower oesophageal sphincter, and resulting in heartburn and regurgitation.

In an attempt to obtain international evidence-based consensus on a unifying definition of GORD, the Montreal definition was adopted in 2006.¹ The aim of this global consensus definition was to simplify disease management, encourage collaborative research and conduct generalisable studies and clinical trials when assisting patients, physicians and regulatory authorities. The new definition states that GORD is a condition "which develops when the reflux of stomach contents causes troublesome symptoms and/or complications". It is independent of endoscopic findings and revolves around a patient-centred approach in which discrete syndromes, such as laryngitis, coughing, asthma and dental erosions, are recognised. The threshold for severity and response to treatment of these conditions is based on analysis of "quality of life" datasets.⁶ Although endoscopic evaluation is not required for the Montreal definition, its usefulness is still pertinent in distinguishing between erosive and nonerosive oesophagitis. Applying the Montreal definition, a diagnosis of GORD can be made if antacids such as histamine 2-receptor antagonists (H₂RAs) or proton-pump inhibitors (PPIs) provide adequate symptomatic relief. Patients without symptom improvements should be referred for further investigation and the exclusion of other possible causes.

Incidence

It is estimated that 20–30% of the world's population suffers from GORD, with children aged ≤ 14 years accounting for 1%.^{7,8} However, there is a significant variation in incidence in different countries and regions. Risk factors and population demographics have an influence on its prevalence. Symptom profiles for blacks and whites are very similar. However, black patients appear to have a lower incidence of developing oesophageal strictures, erosions or ulcers, compared to white populations. There seems to be a considerably lower incidence rate in African and Asian countries, compared to that in Western and European regions. This might be the result of under-reported cases, an inability to access medical facilities and unexplored opportunities with respect to gathering epidemiological data.^{9,10} With an appreciation that South Africa is a multicultural society, and in the absence of documented reliable data, the incidence of GORD in patients experiencing weekly episodes of heartburn or regurgitation could range from 5–20%.

Causes and associations

The pathogenesis of GORD and peptic ulcer disease are well described, and involve many thoroughly documented causes, such as alcohol use, smoking, obesity, infection with *Helicobacter pylori*, the use of nonsteroidal anti-inflammatory agents and glucocorticosteroids.¹¹ Several additional variables have recently been linked to GORD, while some of the traditional causes have been refined. This implies that mere treatment with PPIs or gastric acid suppressants might not be adequate in reducing the symptoms in every patient with a diagnosis of GORD.

Obstructive sleep apnoea syndrome

Obesity, which is often associated with sleep disorders, is undoubtedly a risk factor for the development of GORD.¹² The variables associated with the prevalence of GORD symptoms in patients with obstructive sleep apnoea syndrome and primary snoring was evaluated in a recent study in order to elucidate whether or not sleep disorders contribute to GORD. The severity of snoring (mild, moderate and severe) does not lead to an increase in the severity of GORD symptoms (heartburn or acid regurgitation), regardless of the body mass index (BMI) of an individual. However it was found that female gender, obesity and sleepiness were related to GORD.¹³

Glucocorticoid therapy

Glucocorticoid therapy inhibits prostaglandin synthesis, thereby compromising the physiological defence mechanism rendered by the gastric mucosa against endogenously secreted hydrochloric acid. Considerable controversy still exists regarding the effect of the dose and short-term use in the development and exacerbation of GORD and peptic ulcer bleeding. Patients administered a dose of between 4 mg and 12 mg methylprednisone per day, or equivalent, for ≥ 14 days had a 1.84-fold increased risk of developing GORD, compared to control groups.¹⁴ Therefore, short-term exposure to low-dose

glucocorticosteroids is significantly associated with GORD and peptic ulcer bleeding.

Helicobacter pylori

Infection with *H. pylori* is a major cause of GORD and functional dyspepsia in approximately 40–90% of patients.¹⁵ Eradication of this organism is responsible for greater symptomatic improvement in patients with additional microscopic duodenitis, than in those with uncomplicated and non-erosive acid reflux. Although *H. pylori* is historically associated with gastric carcinoma, its presence does not increase the risk of cancer developing in patients with heavy alcohol consumption and who binge drink.¹⁶ In contrast, it was demonstrated that patients with diabetic nephropathy displayed a higher incidence of *H. pylori* infection, and therefore had a higher risk of developing gastric carcinoma than patients who consumed alcohol or with uncomplicated type 2 diabetes mellitus.¹⁷

Impact on quality of life

Patients suffering from heartburn and regurgitation often report its negative impact on their lifestyle. Affected individuals may exhibit impaired social functioning, sleep disturbances, reduced productivity in the work environment and interference with physical activity.¹⁸ It is estimated from international studies that GORD accounts for an average of almost seven hours of work being lost per week in the working population, thereby contributing to a negative impact on the economy.⁸ It has been shown that patients who predominantly have heartburn symptoms experience more severely impaired daily activities, sleeping habits and lower general health scores than those who predominantly have regurgitation symptoms.¹⁹ Therefore, it is important for clinicians to properly assess the predominant complaint in order to optimise treatment and prognosis.

Treatment and response

The key to the successful treatment of GORD depends upon the ability to adequately control gastric acid secretion, whatever the cause may be. Various treatment options exist, but PPIs are the frontier of current medical management. Their popularity, effectiveness and presumable safety can be seen with the recent down scheduling of lansoprazole and pantoprazole from schedule 4 to schedule 2 substances, and by including their availability in the latest South African standard treatment guidelines and essential drug list. However, a limitation has been imposed, and the supply may not exceed a treatment period of 14 days, after which referral to a physician is mandatory. The current guidelines still advocate endoscopy for nonresponsive cases, and the presence of warning signs (weight loss, persistent vomiting, dysphagia, anaemia, a palpable mass and haematemesis) to exclude gastric or duodenal carcinoma, and re-assessment of the GORD diagnosis.²⁰

Refractory reflux symptoms

The treatment of refractory oesophagitis has shifted towards the treatment of PPI refractory symptoms (subendoscopic oesophagitis, weak acid reflux events and alternative diagnosis).

Refractory GORD is a diagnosis which can be made in the absence of any endoscopic findings, including the escalation of PPIs to a twice-daily dosing schedule, where the patient still remains symptomatic. Refractory reflux and partial response to PPI therapy can be as high as 32%, and is more common in females.⁸ Psychogenic factors, such as co-morbid anxiety and depression, hyperalgesia and allodynia may contribute to the increased symptom burden, which includes abdominal discomfort, indigestion and altered bowel habits, which are easily confused with GORD.

Medical versus surgical treatment

According to a 2010 Cochrane review, it was shown that laparoscopic fundoplication surgery was more effective for the short- and medium-term management of moderate to severe GORD, compared to medical treatment with PPIs or H₂RAs. Significant improvement was shown following surgical intervention in adults with refractory symptoms. However, the benefit of surgery in the long term is still undetermined.²¹ Surgery as a treatment option should be based on patient and surgeon preference, after taking into account the unpredictable risks associated with any surgical procedure.

Conclusion

Increased awareness of GORD should be advocated in order to improve the health status of individuals suffering from heartburn and regurgitation, leading to unnecessary work absence and reduced productivity. Family physicians and general practitioners should be vigilant in diagnosing and treating GORD by understanding the epidemiological and economic impact that this disease has on society. Being familiar with new treatment options and previously unknown associations is pertinent in the current medical diagnosis and management of GORD.

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