Heartburn, gastro-oesophageal reflux disease and nonerosive reflux disease

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Abstract
Recognising nonerosive reflux disease (NERD) as a distinct presentation of gastro-oesophageal reflux disease (GORD) has been one of the most important developments in the field of GORD. Therapeutic modalities still focus on acid suppression for the management of heartburn, GORD and NERD. However, there is growing recognition that other therapeutic treatments should be considered for NERD.

Introduction
After eating, food is carried from the mouth to the stomach through the oesophagus. The oesophagus is a tube-like structure that is made of tissue and muscle layers that expand and contract to propel food to the stomach through a series of wave-like movements. At the lower end of the oesophagus, where it joins the stomach, there is a circular ring of muscle called the lower oesophageal sphincter (LOS). After swallowing, the LOS relaxes to allow food to enter the stomach and then contracts again to prevent food and acid from refluxing back into the oesophagus. However, sometimes the LOS does not close properly, allowing the stomach contents to leak into the oesophagus and/or mouth.1,4 While the lining of the stomach is resistant to the irritant effects of acid, that of the oesophagus is readily irritated by acid.4 The dominant pathophysiological mechanisms that cause gastro-oesophageal junction incompetence are transient lower oesophageal sphincter relaxations, a hypotensive lower oesophageal sphincter and anatomic disruption of the gastro-oesophageal junction, often associated with a hiatal hernia.2

Gastro-oesophageal reflux disease
GORD is a chronic disease that develops when the reflux of stomach acid causes troublesome reflux-associated symptoms and/or complications.6-7 The most common symptom of GORD is heartburn.1 Heartburn is experienced as a burning sensation in the centre of the chest, which sometimes spreads to the throat.4 People who experience heartburn at least two to three times a week may have GORD.1

Other less common symptoms of GORD include the following:1,3,4,6
- Burning in the throat, or an acid taste in the throat.
- Difficulty in swallowing.
- Stomach or chest pain.
- Vomiting.
- A persistent sore throat.
- Persistent hoarseness.
- An unexplained cough.
- Dental disease.
- Recurrent lung infection.
- Chronic sinusitis.
- Waking up with a choking sensation.

The severity of GORD appears to increase with time. Most patients with GORD fall into one of two categories, nonerosive reflux disease (NERD) or erosive oesophagitis. While making a separation between erosive oesophagitis and NERD on a clinical level is difficult, there are physiological, pathophysiological, anatomical, and even histological characteristics that are unique to NERD. Furthermore, NERD and erosive oesophagitis diverge in their response to anti-reflux treatment.7

Erosive oesophagitis
For some patients GORD can cause erosive oesophagitis, a condition that causes inflammation, swelling, or irritation of the oesophagus. It has been found that less than half of patients with GORD suffer from oesophagitis and most patients have NERD.5

Nonerosive reflux disease
Patients experience the typical symptoms of gastro-oesophageal reflux disease caused by intra-oesophageal reflux with NERD, but they do not have visible oesophageal mucosal injury, such as erosion or ulceration, which can be detected by conventional endoscopy. The dominance of acidic reflux in the aetiology of the symptoms of NERD is underlined by the widespread agreement that if the symptoms of a patient do not respond to acid suppressive medication, or cannot be proven to be associated with
an oesophageal acid exposure on pH testing, then a diagnosis of NERD is unlikely.7

Clinical studies have demonstrated that heartburn severity and intensity are similar in patients with erosive oesophagitis and those with NERD. A recent study found that NERD patients had a significantly higher prevalence of functional bowel disorders, such as functional dyspepsia and irritable bowel syndrome, psychological disorders and a positive acid perfusion test. Patients with erosive oesophagitis tended to experience a higher prevalence of hiatal hernia, greater oesophageal acid exposure and more oesophageal dysmotility. The absence of a diaphragmatic hernia suggests that transient lower oesophageal sphincter relaxation is likely to be the predominant mechanism for gastro-oesophageal reflux in most patients with NERD. In contrast to GORD, in the case of NERD, women predominate, and as a group, they are younger by a decade. Only 10% of those with NERD have been found to have erosive oesophagitis over time. It is very unlikely that NERD is a precursor to, or a factor in, the early development of erosive reflux disease.7 The two conditions appear to be distinct. Patients with NERD are thought to comprise a heterogeneous group in which the two most important mechanisms are considered to be the reflux of acid and non-acid contents and oesophageal mucosal hypersensitivity.7,8

**Management of gastro-oesophageal reflux disease**

Depending on the severity of the GORD symptoms, treatment may involve one or more of the following: lifestyle changes, medications or surgery.4 Initial treatment for mild acid reflux includes lifestyle changes, dietary modification and using non-prescription medications, including antacids, alginates, histamine 2-receptor antagonists (H2RAs) and proton-pump inhibitors (PPIs).1

**Lifestyle changes and dietary modifications**

Lifestyle modifications aim to enhance oesophageal acid clearance, minimise the incidence of reflux events, or both.6 Lifestyle changes and dietary modifications include:1,3-5,8

- **Eating smaller meals:** Eating large meals may cause the stomach to become overdistended. This increases upward pressure against the oesophageal sphincter, causing acid reflux.

- **Avoiding acid reflux-inducing foods:** Some foods may cause relaxation of the LOS, promoting acid reflux. Excessive caffeine, chocolate, peppermint and fatty foods may cause bothersome acid reflux in some people.

- **Avoiding lying down for three hours after a meal:** Eating three or more hours before bedtime will help to minimise reflux. Gravity helps to keep the stomach contents from backing up into the oesophagus. Lying down with a full stomach makes reflux more likely.

- **Avoiding smoking:** Saliva helps to neutralise refluxed acid and is one of the body’s defences against damage to the oesophagus. Smoking inhibits the production of saliva and reduces the amount of saliva in the mouth and throat. Smoking also stimulates the production of stomach acid and can weaken the reflux of acid and non-acid contents and oesophageal mucosal hypersensitivity.7,8

- **Raising the head of the bed:** By elevating the head of the bed, the head and shoulders are raised higher than the stomach, allowing gravity to prevent acid from refluxing. The head of the bed can be elevated by placing bricks, blocks or anything that is sturdy securely under the legs at the head of the bed to raise it. A foam wedge under the mattress or a wedge pillow to elevate the shoulders and head may also be used. Bed elevation is important for individuals with nocturnal or laryngeal symptoms.

**Medication**

Acid-suppressive medication regimens include, in increasing order of potency, over-the-counter (OTC) antacids, alginates and H2 antagonists at non-prescription strength, prescription-strength H2 antagonists and PPIs. Symptom severity and previous treatments can guide the selection of an initial acid suppressive regimen in patients with mild to moderate GORD. The most common and effective treatment of oesophagitis and GORD is to reduce gastric acid secretion with either an H2 antagonist or a PPI.8

**Antacids**

Antacids are usually the first agents recommended to relieve heartburn and other mild GORD symptoms. Antacids are typically used for short-term relief of acid reflux. However, the stomach acid is only neutralised briefly after each dose, so antacids only offer short-term symptom relief.6,5 Antacids alone won’t heal an inflamed oesophagus that has been damaged by stomach acid.9 Many brands on the market use different combinations of three basic salts: magnesium, calcium and aluminium, with hydroxide or bicarbonate ions to neutralise the acid in the stomach. Magnesium salts can lead to diarrhoea and aluminium salts can cause constipation. Aluminium and magnesium salts are often combined in a single product to balance these effects.6,5

**Alginates**

Alginates are used in combination with antacids to prevent acid reflux. These medicines work by covering the stomach contents with foam or a raft to prevent reflux, and are effective in mild to
Prescription.13 Pantoprazole and rabeprazole are PPIs that are available with a prescription.9,13 They block the action of H₂, which usually signals the stomach to produce acid after eating. H₂ antagonists have a slower onset of action when compared to antacids, but they provide longer relief.1,12 OTC medications include cimetidine, e.g. Lenamat OTC®, and ranitidine, e.g. Zantac 75®. Stronger versions of these medications are available with a prescription.8,13

Patients with moderate to severe symptoms of acid reflux, complications of GORD, or mild acid reflux symptoms which have not responded to lifestyle modifications and the above-described medications, usually require treatment with prescription medications. Most patients are treated with a PPI. Although some PPIs are available OTC, their use in this setting is restricted to 14 days. Patients who suffer from persistent or recurring symptoms are best referred to the doctor for comprehensive symptom assessment.10

Proton-pump inhibitors

Currently, PPIs are considered to be the most effective therapeutic modality for GORD. These agents have consistently been demonstrated to be more effective than any other acid-suppressant agent in healing erosive oesophagitis and relieving GORD-related symptoms in clinical trials. The superior efficacy of PPIs has also been observed in patients with NERD.7 PPIs block acid by reducing the body’s production of gastric acid, allowing time for damaged oesophageal tissue to heal.6 PPIs have a slower onset of action than H₂ RAs, but they relieve symptoms for longer periods.12 These medicines are most helpful for people who have heartburn often, e.g. for more than two days of the week.1 OTC PPIs include lansoprazole, e.g. Lanzor HB capsules®, Lansoloc OTC capsules® and Lancap® 15 mg. Esomeprazole, omeprazole, pantoprazole and rabeprazole are PPIs that are available with a prescription.13

Patients with NERD, as compared to those with erosive oesophagitis, demonstrate a highly variable and unpredictable symptomatic response rate to anti-reflux treatment. This is likely to explain the high percentage of patients with NERD who fail PPI treatment.7

Currently, novel therapeutic modalities are under consideration for patients with GORD, and specifically those with NERD. Main areas of interest include improving acid suppression, reducing the transient lower oesophageal sphincter relaxation rate, decreasing oesophageal sensitivity and enhancing oesophageal motility.7

Surgical treatment

Because of the effectiveness of medical therapy, the role of surgery has become more complex. Anti-reflux surgery may be considered in patients who require high doses of PPIs to control symptoms, particularly in young patients who may require lifelong therapy. However, whether surgery is beneficial for patients who have failed therapy with a PPI remains controversial. In general, anti-reflux surgery involves repairing the hiatus hernia and strengthening the lower oesophageal sphincter. The most common surgical treatment is the laparoscopic Nissen fundoplication. This procedure involves wrapping the upper part of the stomach around the lower end of the oesophagus.1,14 Patients who have undergone fundoplication may continue to use antisecretory medications.14

Response to anti-reflux surgery has been shown to be different between patients with NERD versus those with erosive oesophagitis. Clinical studies which compared the outcome of anti-reflux surgery in patients with erosive oesophagitis versus those with NERD demonstrated that 91% vs. 56% reported heartburn resolution and 94% vs. 79% were satisfied with surgery, respectively.7

Conclusion

Some people may be able to manage their acid reflux by dietary modifications, lifestyle changes and/or by taking non-prescription medication. The pharmacist can play an important role in helping the patient to select an appropriate medication that will help relieve and treat the symptoms of heartburn or GORD. The pharmacist can also offer practical advice on measures to prevent recurrence of the condition. However, if the symptoms persist or the condition worsens, the patient should be referred to the doctor.

References