BEST PRACTICE

ATYPICAL MANIFESTATIONS OF GORD

Introduction
The most recent definition of GORD (ROME IV) is more restrictive than the previous one, limiting this condition to patients with endoscopic features of reflux oesophagitis and/or elevated acid exposure, as determined on functional tests such as oesophageal manometry and pH-impedance studies.1

In clinical practice, the profile of the patient with GORD-like symptoms includes both physical and psychological co-morbidities. Generally, reflux symptoms improve if spicy foods, fizzy drinks and acid-inducing foods are avoided. Weight loss is also helpful, as reflux symptoms occur more commonly in overweight patients.

Treatment typically entails PPI therapy, as this approach is more effective than H2-receptor antagonist therapy. Other medication to improve gut motility can be considered, such as domperidone or metoclopramide. In patients with severe symptoms, consider surgery.

KEY MESSAGES

- Underlying anxiety and psychological conditions should be considered in the case of patients with GORD who do not respond to proton pump inhibitor (PPI) therapy
- Primary care practitioners play a vital role in the evaluation of patients with GORD-like symptoms
- The presence of any ‘red light’ symptoms such as dysphagia, weight loss, stomach pain and/or vomiting should be referred for specialist evaluation
- Patients who do not respond to standard PPI therapy should be referred for further investigation.

Atypical manifestations
Typical symptoms of ‘heartburn’ and reflux do not occur in all patients. “In patients with laryngitis, non-responsive adult-onset asthma, chronic cough and chest pain, gastro-oesophageal reflux may be present but disguised,” Dr Kleyhans noted. Clinicians should have a high index of suspicion for the possible presence of atypical GORD in the patient groups described in Figure 1.
Prevalence of atypical GORD

Firstly, how common are GORD symptoms? It has been estimated that 7% of the population experience daily reflux symptoms, while symptomatic events occur in 40% of people if measured on a monthly time scale. Atypical GORD, on the other hand, occurs in 40-60% of patients with asthma without symptoms of ‘heartburn’. The occurrence of atypical GORD is also as high as 60-90% in the ear, nose and throat patient group. Forty to 75% of patients with chronic cough also experience atypical GORD.

Mechanisms of atypical GORD

The most likely mechanism of atypical GORD is micro-aspiration, described as ‘small volumes of gastric acid resulting in oesophageal irritation’. Vagal effects can also play a role, causing spasm and irritation of the nerve endings in the distal oesophagus. Bile and enzymes are also factors in some patients.

Asthma patients

Acid reflux commonly occurs among asthma patients and may result from either acid or vagal effects or as a side-effect of medication such as theophylline, β₂-antagonists and steroids. Table 1 describes the asthma patient most likely to develop atypical GORD.

Chronic cough and GORD

In patients with a chronic cough lasting longer than three weeks, atypical GORD should be considered after other conditions such as asthma, post-nasal drip and typical GORD are excluded. Characteristics of this cough are as follows. It is present during the day, is a dry cough with little sputum production and is of longer duration. Medication such as ACE-inhibitors as a cause of the cough must be excluded. Chest x-ray is normal (except in smokers) and heartburn occurs in approximately 50% of these patients.
Reflux laryngitis

These patients have the following symptoms: a strained hoarse voice, frequent clearing of the throat, a dry cough and a sore throat, and sometimes dysphagia. Reflux occurs in 10-60% of them and laryngoscopy shows ulcers, nodules, granuloma and leucoplakia.

Non-coronary chest pain

Twenty to 30% of patients with chest pain have normal coronary arteries. GORD is a common cause of chest pain (25-55%), although in some cases a definitive cause cannot be established with certainty. Mobility abnormalities, such as the ‘nutcracker syndrome/spasm’ must also be considered. Pepsin contributes to the development of symptoms, but in 20% of patients with non-coronary chest pain, there are no symptoms of heartburn.

If coronary artery involvement is suspected, an ECG or angiogram should be performed to confirm the diagnosis. For diagnosis, a barium meal is of little value in this situation. Gastroscopy with at least five biopsies is useful, as is pH-monitoring. Clinically the patient can be treated empirically but if symptoms persist, other causes such as angina or Barret’s oesophagus must be explored.

Investigations of atypical GORD

Gastroscopy is helpful in 10-30% of cases of atypical GORD, in contrast with the success rate in typical GORD of 50%. Barium meals are of doubtful value. Twenty-four-hour pH-monitoring has a sensitivity of 70-80% for pinpointing reflux, even though there are no specific tissue abnormalities. Empirical PPI treatment is associated with a ‘false-negative’ rate of 20-50% and even ‘false-positive’ results occur. The rate of ‘false positivity’ is unknown. In the case of suspected non-acidic-related reflux, impedance-pH studies are of value.

If the patient does not improve on therapy, other causes of reflux and other symptoms must be considered. The PPIs are treatment of first choice, although H$_2$-receptor antagonists can be useful; a combination of an H$_2$-receptor antagonist and ranitidine is useful. In typical GORD cases therapy should result in resolution of symptoms in 60-98% of cases. If omeprazole is prescribed, a dosage of 40mg bd is recommended with an expected success rate of 67%. If the patient improves, the dosage of PPI can be halved.

Surgery can be considered if there is little or no improvement with therapy. In cases of typical GORD, surgery has a 93% success rate, which drops in atypical cases to 56%, but which is still a better outcome than that achieved with PPI therapy. The period of PPI treatment is 2-3 months; this is also the case for asthma-related reflux. In the latter case if there is no improvement within a four-month period, the original diagnosis must be re-assessed.

Other gastric abnormalities

Peptic ulcers

PPI therapy is very effective and there is little difference in the success rates achieved with different PPIs. Costs can, of course, influence the selection of the PPI. Normally, a double dose is prescribed.

In the case of concomitant bleeding, there is a difference of opinion with regard to IV or oral therapy (IV therapy consisting of esomeprazole or pantoprazole 80mg loading dose, followed by 8mg/hour for 72 hours). The IV therapy results in a 66% suppression of acid levels at day 5. It should be noted that a single PPI dose does not have an immediate effect and a double dose has a more rapid effect. Therapy should last...
for at least 4-8 weeks. Cases of reflux oesophagitis should be treated for at least 8-12 weeks, with the majority of patients requiring 12 weeks of therapy. Thereafter, a maintenance dose should be considered.

**Helicobacter pylori**

If *Helicobacter pylori* is present (as determined by biopsy, stool or blood sample), therapy may result in the infection moving into the corpus of fundus of the stomach. Eradication therapy consists of either clarithromycin 500mg bd for 7-10 days, or amoxicillin 1g bd combined with a double dose of PPI. In the case of penicillin allergy, metronidazole (500mg bd) is a useful alternative. There is increasing evidence that longer therapy for at least 14 days improves outcome. In cases of resistance, quadruple therapy with bismuth, metronidazole (or clarithromycin), tetracycline and a PPI should be prescribed.

### References