

Gastro-Oesophageal Reflux Disease – GORD

Valerie Vella BPharm(Hons), MSc(Clin Pharm)(Aberdeen), MRPharmS

Senior Clinical Pharmacist, St Luke's Hospital, Guardamangia, Malta

Email: valerie.vella@gov.mt

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Symptoms of gastro-oesophageal reflux disease (GORD) have a substantial impact on patients' everyday lives. In the majority of situations patients can be managed empirically with over-the-counter preparations, however some patients presenting with alarm signs will require urgent referral for endoscopic studies.

Introduction

GORD is a collective term embracing all diseases caused by gastro-oesophageal reflux.¹ Gastro-oesophageal reflux is a disorder in which the oesophageal mucosa is damaged by the reflux of gastric or intestinal contents into the oesophagus and results in patient complaints of heartburn and other symptoms such as 'burping up' stomach contents or the taste of bitter contents in the mouth.² Although the classical symptom is "heartburn", at times it presents itself as pain in the centre of the chest, which might mimic cardiac angina² or asthma.¹ Twenty-five percent of adults experience heartburn at least once a month and most of these are treated empirically.³ The prevalence and incidence of GORD has doubled in a period of ten years⁴, and this increase is being linked to dietary and lifestyle changes.⁵

Pathophysiology of GORD

The development of GORD is associated with a disruption of the balance between defensive mechanisms (lower oesophagus closure and oesophageal peristalsis) and aggressive factors (e.g. acid, pepsin, bile salts).²

There are three pathophysiologic mechanisms, which predispose a patient to reflux:

1. a spontaneous transient or sustained relaxation of the lower oesophageal sphincter (LOS);
2. a low resting lower oesophageal pressure;
3. increased gastric pressure.²

GORD is associated with long-term morbidity and mortality.⁵ Complications of GORD are oesophagitis which if severe can cause erosive changes, oesophageal ulcers, strictures, haemorrhage, perforation,

aspiration and the development of Barrett's oesophagus. Barrett's oesophagus predisposes the patient to the development of oesophageal cancer.²

Treatment

The primary aim of treatment is complete clinical remission and prevention of long-term complications. Pharmacists are in an ideal position to monitor, advise and refer patients accordingly.

Lifestyle changes

Some foods are known to irritate the gastric mucosa such as spicy food and citric juices; others may stimulate acid secretion as cola and beer, whereas some are known to lower oesophageal sphincter pressure such as foods with a high-fat content.^{2,6}

Although epidemiological studies fail to show any association between food and GORD, some patients may benefit from avoiding such foods. Some drug therapy such as alcohol, beta-adrenoceptor agonists, diazepam, progesterone, theophylline and verapamil, can also exacerbate GORD.²

Obesity and tight clothes may exacerbate reflux by continuously increasing the gastro-oesophageal pressure gradient.²

Additional advice which may benefit patients with reflux symptoms include, smoking cessation, avoiding meals 2-3 hours before lying down and avoiding bending down.²

Drug therapy

When recommending drug therapy, pharmacists need to keep in mind patient co-morbidities especially in the elderly and also interactions with other medications.

Antacids can provide relief of mild to moderate symptoms associated with GORD because of their ability to neutralise gastric acid and to increase LOS pressure. However antacids have no role in promoting healing of oesophagitis and consequently are only useful in providing symptomatic relief. Antacids should be used only as an adjunct.² Calcium containing antacids should be avoided as they can induce rebound acid secretion.⁷

H₂-Receptor antagonists (H₂RAs) can be effective for management of mild to moderate GORD when used in full doses. Healing rates in patients with

mild pre-treatment oesophageal reflux are significantly better than in those with moderate or severe pre-treatment disease. H₂-antagonists should be administered in daily divided doses because gastric acid suppression or neutralization throughout the day is important in the treatment of reflux disease.²

Proton Pump Inhibitors (PPIs) inhibit gastric acid secretion for a sustained period of time and are highly effective in the treatment of GORD.² In a direct comparison PPIs were found to be more effective than H₂RAs in relieving heartburn in patients with GORD.³ The disadvantages of PPIs are their relatively slow onset of action, limited activity to the post-prandial period and limited efficacy in reducing nocturnal acid secretion.⁸

Sucralfate appears to be effective in resolving mild cases of oesophagitis but it appears less effective in management of severe disease. This drug should be administered four times daily preferably as a suspension because the drug needs to be in direct contact with the damaged mucosa.^{2,7}

Metoclopramide stimulates the motility of the upper gastrointestinal tract without affecting gastric acid secretion. When administered as 10mg four times a day, 30-60 minutes before meals and at bedtimes, it increases gastric peristalsis, which leads to accelerated gastric emptying thus decreasing the intestinal transit. Because of its adverse effect profile and the general lack of gastrointestinal motility dysfunction in adult patients with GORD, its usefulness is significantly limited.^{2,7}

Nocturnal reflux

Patients complaining of night-time GORD should be given particular attention.⁹ Nocturnal reflux designates a greater risk of erosive oesophagitis and additionally these patients have a reduced quality of life as GORD interferes with sleep and consequentially next-day mental and physical functioning.¹⁰ These patients usually benefit from:⁹

- elevating the head of the bed;
- adjusting sleeping position;
- full dose PPI at night;
- low dose PPI on a twice daily regimen; or
- full dose PPI in the morning plus a short intermittent course of an H₂RA at night.

When to refer patients

Patients should always be referred for endoscopy studies if they show any of the following

ALARM signs:^{6,11,12}

- GI bleeding (such as haematemesis, malaena)
- Dysphagia
- Unintentional weight loss
- Abdominal swelling
- Epigastric mass
- Persisting vomiting

Gastro-oesophageal reflux in infants

Gastro-oesophageal reflux and GORD are common in the first months of life and is often linked to the immaturity of the oesophagus and stomach and the higher liquid intake of infants.¹³ Some also claim that genetic factors are involved.¹³ Symptoms include regurge and vomiting. Simple measures like using thickened formulas are useful in reducing regurgitation but occasionally treatment with alginates and PPIs is necessary.¹⁴ The alginate suspension is licensed only for children over the age of two but the alginate oral powder can be used in neonates unless they are preterm.⁷ The only PPI licensed for use in children (over the age of one year) is omeprazole, which is conveniently available in dispersible tablets.¹⁵ Infants with suspected reflux should always be referred.

Pregnancy-associated reflux

It is estimated that 30-50% of all pregnant women experience dyspepsia which is most commonly due to gastro-oesophageal reflux, caused by transient relaxation of the lower oesophageal sphincter. Altered oesophageal motility and increased abdominal pressure may also play a role in the pathogenesis of reflux. Symptoms can occur at any time during pregnancy but are more common and severe during the last trimester.¹⁶

First-line treatment - Lifestyle advice:¹⁶

- Avoid precipitating factors as coffee, fatty foods, alcohol, smoking, spicy foods, citrus products;
- Eat smaller meals;
- Do not eat within 3 hours of bedtime;
- Wear looser clothes;
- Raise head of bed when sleeping.

Second-line treatment – antacids:

When choosing an antacid for a pregnant patient one must bear in mind that not all antacid preparations are licensed for use in pregnancy. Additionally one must remember to choose a low sodium product especially in patients with gestational hypertension and pre-eclampsia.¹⁶ Patients should also be advised to leave a minimum of 2 hours between antacids and iron supplements.^{7,16} Licensed antacids include:

- **Co-magaldrox** (magnesium hydroxide 195mg & dried aluminium hydroxide 220mg/5ml) low sodium. Dose: 10-20ml, 20-60 minutes after food and at bed-time, or when required. Manufacturer advises to avoid in the first trimester, as there is no clinical data on exposed pregnancies.¹⁷
- **Sodium alginate** 500mg/5ml(sugar-free) Dose: 5-10ml, after meals and at bed-time when required. Studies have failed to show any significant adverse effects of this product on the course of pregnancy or on the health of the foetus.¹⁸

Third-line treatment

None of the H₂-receptor antagonists currently on the market are licensed for use in pregnancy. Cimetidine showed inhibition of testicular descent and genital differentiation in pregnant rodents.¹⁹ Ranitidine crosses the placenta and should only be used during pregnancy if considered essential. Surveillance studies do not suggest that ranitidine presents a major teratogenic risk when used in recommended doses but regardless of this it is still unlicensed in pregnancy.²⁰

Omeprazole is now licensed in pregnancy as there is no evidence of adverse effects on pregnancy or on the health of the foetus at a dose of 20mg once daily.²¹ Other proton pump inhibitors are not recommended, as there is insufficient evidence to recommend the use of these drugs in pregnancy.¹⁶

Patients should be referred if:

- symptoms do not respond adequately to lifestyle measures and over-the-counter preparations;
- they are not eating sufficiently or are progressively losing weight;
- they have signs and symptoms of GI bleeding, dysphagia or persisting vomiting.¹⁶

Conclusion

Despite major advances in the understanding of GORD, management remains a challenge, as some patient needs are still unmet.^{8,22} New products, which have a faster onset of action, complete acid inhibition together with improved duration of efficacy, are being developed. These include potassium competitive ATPase blockers (PCABs), histamine H₃ agonists and gastrin antagonists.⁸

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Practice points

- Gastroesophageal reflux is a lifelong disease that requires lifestyle modifications as well as medical intervention.
- Self-treatment with antacids or alginate therapy may be appropriate for immediate relief of occasional heartburn, however their duration of action is less than two hours.
- Magnesium containing antacids should not be used in patients with renal failure.
- H₂ RAs have a delay in onset of at least 30 minutes however they provide heartburn relief for up to 8 hours. Recommend to take preparations before meals known to cause heartburn.
- Proton pump inhibitors are increasingly being used first line as they provide superior efficacy and once-daily dosing regimen.

Social

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- Mr Hilary Paul Agius, BPharm, MBA (Henley), currently General Manager (Pharma), GlaxoSmithKline (Malta).
- Mr Josef N. Grech BPharm(Hons), MSc(Syd), MBA (Henley), MRSC, MIM (Hon), currently Group Chief Executive Officer with a local group of companies with various business interests.
- Ms Josette Sciberras, BPharm(Hons), MBA (Henley), currently Head of Pharmacy Department, St Lukes' and Mater Dei Hospitals.

We would also like to congratulate:

- Ms Louise Azzopardi BPharm(Hons), MPhil(Glasg), Senior Clinical Pharmacist at St Lukes' and Mater Dei Hospitals for obtaining a Masters degree from the University of Strathclyde.
- Ms Ruth Theuma BPharm(Hons), MSc(Clin Pharm)(Aberdeen), Senior Clinical Pharmacist at St Lukes' and Mater Dei Hospitals and MCPP Secretary for obtaining a Masters degree in Clinical Pharmacy from Robert Gordon University, Aberdeen.

We would like to take this opportunity to welcome all the final year pharmacy students into the profession and wish them a successful career. We look forward to having them become members of the College and participating in both educational and social events.