Is a proton pump inhibitor (PPI) the GP's gastroscopy?

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Introduction

Gastro-oesophageal reflux disease (GORD) and dyspepsia are two of the most common gastrointestinal conditions seen in general practice. GORD symptoms have been shown to occur on a weekly basis in 20% of a Minnesota, USA population.[1] In a Swedish study of a random sample of 1 000 adults, 45% reported reflux symptoms in the preceding three months.[2] The prevalence of GORD has increased markedly over the past few decades, with possible causes being increased fat intake, obesity, the use of oestrogens and smoking.

Dyspepsia prevalence is estimated at 25-40%, accounting for about 2-5% of GP visits. Only one in four patients consults a GP about the symptoms.[3] The similarities in the clinical picture of GORD and functional dyspepsia are further complicated by the overlap between these conditions. Sixty percent of patients experiencing reflux symptoms of heartburn and regurgitation will demonstrate no endoscopic abnormalities.[4] These patients are referred to as having non-erosive reflux disease (NERD). Females predominate in the overlap group and tend to be about one decade younger than their GORD counterparts. This overlap is not surprising, given the high prevalence rates of these conditions.

Before deciding on a strategy to investigate or treat empirically, one needs to make a working diagnosis. The subsequent management pathway then becomes easier for both doctor and patient. This review will attempt to define, for the general practitioner, the place of the "PPI test" in these conditions. ***(SA Fam Pract 2005;47(2): 24-28)***

Dyspepsia

Dyspepsia is defined in the Rome criteria as pain or discomfort in the upper abdomen that has been present for at least 12 weeks, which need not be consecutive, in the last 48 weeks. No organic lesion must be present to account for the symptoms. The patients should not have irritable bowel symptoms, such as altered bowel pattern or relief of pain after a bowel movement.[5]

Dyspepsia may present with intermittent or episodic pain in the upper abdomen. Other symptoms include early satiety, belching, nausea, postprandial pain and bloating. Mucosal lesions, such as peptic ulceration, are found in only 20% of patients. Those without pathology found at endoscopy are referred to as having "functional dyspepsia". Those not investigated have "uninvestigated dyspepsia".

The causes of functional dyspepsia are poorly understood, and this uncertainty is reflected in the wide range of treatments that may be tried in this condition. Possible causes include delayed gastric emptying, loss of gastric fundic accommodation, increased sensitivity of the gastric antrum to distension and acid hypersensitivity. A higher rate of anxiety, depression and hypochondriasis is found in some patients with functional dyspepsia. Symptom-based subgrouping into ulcer-like, reflux-like and dysmotility-like has been attempted, although there is a too-wide overlap between these subtypes for this approach to be clinically useful.[6] Before considering investigation or drug therapy, patients should be given advice about their lifestyle, e.g. stopping smoking, modest alcohol consumption, regular meals and exercise, and avoiding potentially harmful drugs where possible (NSAIDs).

It is usually at this point that the

doctor has to face the question: Does the patient warrant further investigation, or is a trial of therapy in order? It is perhaps easier to begin with guidelines that would identify the patients who require immediate endoscopy.

Indications for prompt referral for endoscopy

The following are indications that the patient should be referred for endoscopy:

1. Dyspepsia that has not responded to an adequate trial of therapy
2. Dyspepsia with symptoms or signs (red flags) suggesting serious organic disease, or in patients over 45 years of age:
   - Unintentional weight loss
   - Abdominal mass
   - Patients with previous peptic ulcer
   - Dysphagia or odynophagia
   - Persistent vomiting of unknown cause
   - Gastrointestinal bleeding
   - Iron deficiency anaemia
   - Dyspeptic patients on NSAIDs and/or anticoagulants

Management of dyspepsia: empirical therapy

Two strategies are commonly employed in the empiric treatment of the dyspeptic patient: acid suppression or *Helicobacter pylori* eradication.

1. Acid suppression therapy

A single short course of a PPI is administered for a period of two to four weeks. This treatment will usually be effective in those patients with GORD and peptic ulcer disease.[7] Reflux oesophagitis is the most common diagnosis in dyspeptic patients, being seen in up to 43%. The prevalence of peptic ulcer disease is declining, with an estimated one to two per 1 000 in primary care in England and Wales.[8]

In patients with functional dyspepsia, acid suppression therapy has shown only a modest benefit over a placebo.[9] Relapse rates leading to endoscopy after initial acid suppression therapy are about 50% within one year. This therapy does, however, leave a significant number of patients without further symptoms and requiring no further evaluation or treatment.

Endoscopy performed while the patient is symptomatic and before any therapy is administered is still considered the 'gold standard'. Endoscopy performed after one month of therapy may yield a false-negative result, with the ulcer having healed during the treatment period.

2. Helicobacter-based strategies

Testing for *H. pylori* in the management of dyspepsia can be done as part of either a test-and-treat or a test-and-scope strategy, with the aim of detecting patients with a peptic ulcer while reducing the number of normal endoscopies. These strategies will not be discussed in detail. Many factors have to be taken into account, including the background prevalence of *H. pylori* infection, the accuracy of the tests performed and the pre-test probability of peptic ulcer. The incidence of *H. pylori* peptic ulcer is declining in western populations. The test-and-treat strategy has been shown to be cost effective. A small benefit has been shown in the recently updated Cochrane database.[10]

The PPI test in GORD

A thorough and accurate history is the

Figure 1: Algorithm for PPI test in GORD (Modified from Bytzer[17])

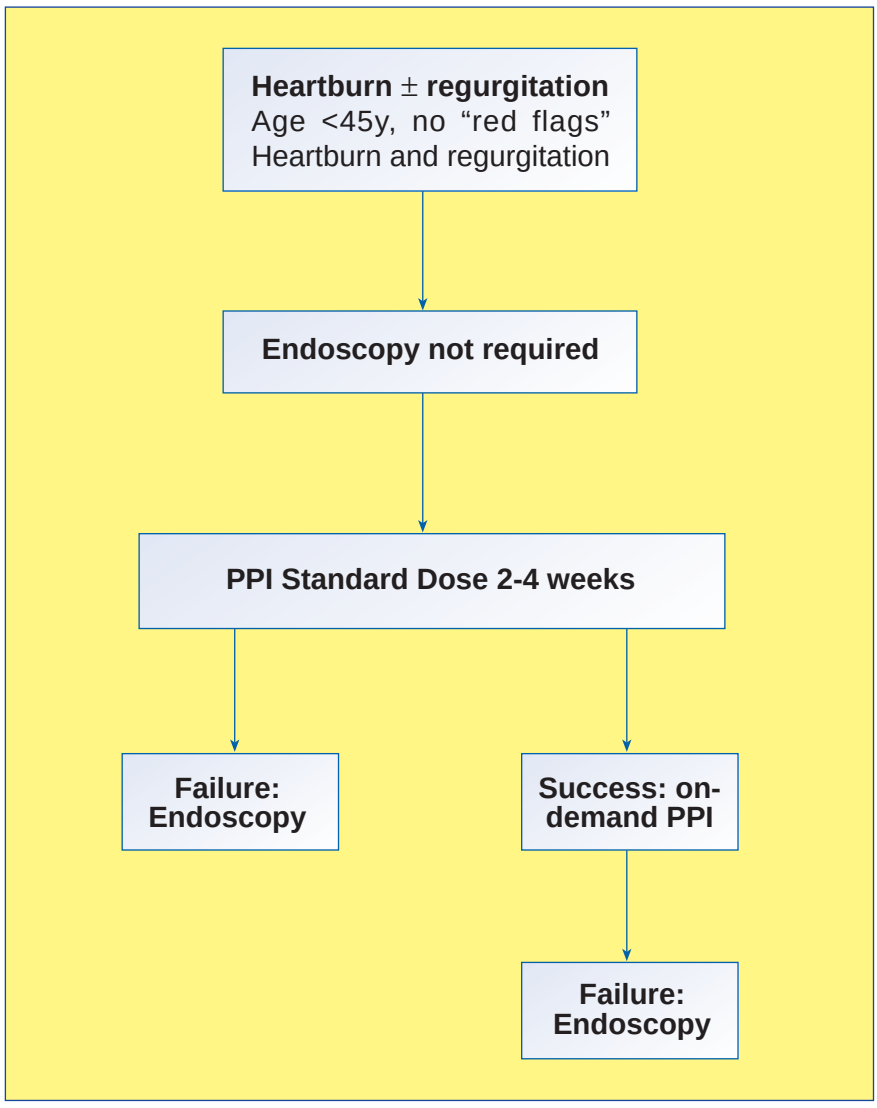

Table I: Published trials of empiric PPI therapy in GORD

Author	Study Type	Conclusion	Comments
Numans et al.[11]	Meta-analysis	Negative	Study: PPI vs. symptom index, 24 H pH, endoscopy
Johnsson et al.[12] N=44	Esomeprazole 40mg daily, or 20mg bd, or placebo 14 days	Positive	Endoscopy and 24h pH. 7-day therapy sufficient for positive test
Juul-Hansen et al.[13] N=68	Lansoprazole 60mg daily for 7 days	Sensitivity: 97% Specificity 6%	Insufficient specificity to be sole diagnostic criterion.
Inadomi et al.[14] N=117	Complete symptom resolution on high-dose PPI, then stepped down to Omeprazole 20mg or lansoprazole 30mg daily	79% reported no recurrent symptoms on lower dose Complete relief in 66%, 63% and 35%.	Validates "step-down" approach
Meineche-Schmidt[15] N=829	Omeprazole 40mg or Omeprazole 20mg or Placebo daily X 2 weeks	Relapse in 12m follow-up was high, ± 65%	Lower health-care utilization in responders vs. non-responders throughout 12m follow-up

cornerstone of GORD diagnosis. GORD typically presents with heartburn, best described as a burning pain that rises in the chest, usually after a meal. Many GORD patients, however, will not give a typical history, and other clues to the diagnosis must be sought. It is essential to enquire about the supra-oesophageal manifestations of GORD, including chronic cough, hoarseness, asthma and chest pain.

PPIs have made the management of GORD relatively easy, because of their wide availability and safety. An empirical trial of PPI therapy is often the best test for defining the presence of GORD.[7] A poor response to the PPI would raise some doubt as to the accuracy of the diagnosis and would indicate a need for further investigation, such as endoscopy or pH-metry. One should be wary of referring a patient for anti-reflux surgery in the face of a poor response to PPI therapy.

The indications for endoscopy in suspected GORD patients are broadly similar to those outlined above in the approach to the dyspeptic patient. In GORD, however, one has patients at risk of oesophageal adenocarcinoma. This malignancy arises in a columnar-lined or Barrett's oesophagus. Barrett's is usually associated with longstanding reflux symptoms and tends to be more frequent in middle-aged white males with longstanding reflux symptoms. The risk of adenocarcinoma in patients with Barrett's oesophagus is about 0.5% a year. Patients with Barrett's are advised to enter a surveillance programme in an attempt to diagnose high-grade dysplasia or early cancer, thus increasing the possibility of surgical resection or endoscopic ablation and cure.

The published trials of empiric PPI therapy in GORD give somewhat conflicting results (see Table I). The approach is nonetheless reasonable, given the savings achieved in an already stretched healthcare budget.

A cost-effectiveness study performed by Gerson et al. in patients with uncomplicated GORD showed that initial treatment with a PPI, followed by on-demand therapy, was more cost effective than:

- Lifestyle modification and antacids.
- H_2RA treatment.
- Step-up from H_2RA to PPI.
- Step-down from PPI to H_2RA.
- PPI-continuous therapy.[16]

Patients responding to a trial of PPI therapy should be given the drug for a fixed period (two to four weeks), before an attempt is made to stop or reduce the dosage or step down to a weaker acid-suppressant medication.

Conclusions

1. Alarm symptoms and signs should be carefully elicited, and patients should be referred for further evaluation by a gastroenterologist.
2. The PPI test using the standard (full) dose once daily or the maintenance dose twice daily is useful in determining the acid-related nature of the symptoms.
3. The PPI test must be followed for a short fixed period not exceeding two to four weeks. A seven-day treatment period is often sufficient to prove the link to acid reflux.
4. Treatment should then be stopped, or stepped-down, preferably to "on-demand" therapy.[17]

See CPD Questionnaire, page 46

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