The management of dyspepsia in primary care

Summary

This Briefing considers possible underlying causes and treatment options for dyspepsia, in a case-study format. It uses the National Institute for Health and Clinical Excellence (NICE) guideline on dyspepsia, supplemented with additional evidence. It does not cover the management of dyspepsia in children or pregnant women, or dyspepsia associated with non-steroidal anti-inflammatory drugs (NSAIDs).

Case study

Mr Parker is a 57-year-old sales manager. He is complaining of intermittent heartburn and epigastric discomfort. This occurs approximately three times a week, especially after large or spicy meals, and at night. For several years he has been buying an antacid/alginate and taking it, as required, to relieve his symptoms, but he is now experiencing more frequent periods of discomfort. His general health is good and he does not take any regular medication. He is overweight (BMI 29kg/m²), drinks two pints of beer each night and is a non-smoker.

What is the diagnosis?

Dyspepsia is a complex of symptoms of the upper gastrointestinal (GI) tract including upper abdominal pain or discomfort, heartburn, acid reflux, nausea or vomiting. Of the adult population, 40% have symptoms of dyspepsia, 5% will consult their GP, and 1% will be referred for endoscopy each year. Where signs or symptoms are sufficient to merit endoscopy, 40% have non-ulcer (functional) dyspepsia, 40% have gastro-oesophageal reflux disease (GORD), and 13% have some form of ulcer detected. Gastric and oesophageal cancers are very rare, occurring in less than 3% of patients who have endoscopy. Many of these cases are detected on hospital investigation, rather than following primary care referral for dyspepsia.

In the past, GORD has been diagnosed symptomatically when patients have predominantly reflux symptoms (e.g. heartburn and/or acid/food regurgitation). However, dyspeptic symptoms are a poor predictor of significant disease. A systematic review conducted for the NICE guideline examined the extent to which symptom patterns in unselected referred patients with dyspepsia could be used to predict final endoscopic diagnosis. Neither individual symptoms, nor symptom clusters, were useful tools to predict peptic ulcer, oesophagitis or functional dyspepsia. Another study (n=1,040) found that, even in patients without dominant heartburn, 37% had oesophagitis. Also, patients presenting with predominantly reflux symptoms were as likely to have duodenal ulcers as those presenting with epigastric pain.

Any patient presenting with symptoms of dyspepsia who has not been investigated by endoscopy is now classed as having uninvestigated dyspepsia, whether reflux symptoms dominate or not. Where investigation occurs, differentiation is possible between GORD, non-ulcer dyspepsia (NUD), peptic ulcer disease (PUD) and cancer. GORD encompasses oesophagitis and endoscopically negative reflux disease (ENRD). If endoscopy is normal, NUD is diagnosed, unless reflux symptoms are predominant, when the diagnosis is ENRD.

Mr Parker has not had an endoscopy, therefore, at this stage he can be classed as having uninvestigated dyspepsia.

But he’s over 55, shouldn’t he be referred for endoscopy?

Widespread use of endoscopy would be expensive and is unlikely to benefit most patients with dyspepsia. For the majority, an endoscopic diagnosis will not alter the treatment received and there is a small, but definite, risk of harm from the procedure. It is essential to prioritise patients and target endoscopy at those who are most likely to benefit.

ALARM signs and symptoms (iron deficiency anaemia, loss of weight, anorexia, recent onset of progressive symptoms, melena or haematemesis, difficulty swallowing) have traditionally been used as predictors for major pathology in patients with dyspepsia (e.g. ulcer with complications or upper GI cancer).
Upper GI cancer is rare, and on average each GP is only likely to see one newly diagnosed oesophageal cancer, and one newly diagnosed stomach cancer, every four years. The incidence of stomach cancer has decreased rapidly over the last 50 years, whilst the incidence of oesophageal cancer has increased.2,4 The reason for these changes is unclear. However, it has been suggested that the reduction in gastric cancer is due to a decline in the prevalence of Helicobacter pylori (H. pylori), and that the increase in oesophageal cancer may be due to an increased prevalence of GORD.3

Less than 1% of upper GI cancers are diagnosed in patients aged below 40 years, and the chance of a dyspeptic patient under the age of 55 having gastric cancer is one in a million.4 Two retrospective cohort studies have examined patients diagnosed with upper GI cancers and discovered that cancer was rarely present in patients under the age of 55 years if they didn’t have ALARM symptoms. Unfortunately, when a cancer was found on endoscopy, it was usually inoperable, even in patients without ALARM symptoms.1

ALARM signs and symptoms are surprisingly common, occurring in around 10% of dyspepsia sufferers presenting in primary care.1,5 In some studies they are seen to predict upper GI cancers or ulcer complications, but in others an association is not found. Once ALARM symptoms are present in a patient with upper GI cancer, the prognosis is poor (less than 10% survival at 5 years).1 A Dutch study of 861 patients with persistent or ALARM symptoms who were referred for endoscopy found that weight loss, dysphagia (difficulty swallowing), smoking and male sex were the only factors that increased the likelihood of malignancy, with dysphagia and weight loss the most reliable predictors.4 However, another study, which evaluated the effectiveness of age and ALARM symptoms for predicting all major endoscopic findings (i.e. tumour, ulcer or stricture) in 3,815 patients with dyspepsia, found that dysphagia and weight loss were not significant predictors. Age (≥45 years), male sex, bleeding and anaemia were only weak significant predictors of cancer, ulcer disease and strictures. In this study, only 21% of the endoscoped patients had significant pathology.7

Although ALARM signs and symptoms are only weak predictors of major pathology, they are almost always present in patients with dyspepsia and upper GI cancer, and are therefore used as indicators for referral.6 The NICE guideline outlines the ALARM signs and symptoms which should be used as indicators for referral in dyspeptic patients (see Panel 1).6

An age cut-off for referral for endoscopy is somewhat arbitrary but has traditionally been used, as the incidence of malignancy rises with age.4,5 However, the NICE dyspepsia guideline now advises that routine endoscopic investigation of patients of any age without ALARM symptoms is not necessary.6 This advice is based on a prospective cohort study of 1,852 patients with dyspepsia referred for rapid upper GI endoscopy by GPs following UK cancer guidelines.4 Patients aged over 55 years who had uncomplicated dyspepsia, without ALARM symptoms, were found to have a reduced risk of cancer compared to other patients within the cohort. Endoscopy in patients with dysphagia or weight loss at any age, plus those aged over 55 with ALARM symptoms, would have detected 99% of the cancers found in the cohort.6

In June 2005, the recommendations on referral for endoscopy in the NICE clinical guideline on dyspepsia1 were amended to bring them in line with those in the NICE clinical guideline on referral for suspected cancer.16 The only major change is the reintroduction of urgent referral for patients aged 55 years and over with unexplained and persistent recent-onset dyspepsia. Routine endoscopic investigation of patients of any age without ALARM symptoms is still considered unnecessary (see Panel 1 and Flowchart, page 3).8

In conclusion, although age and ALARM symptoms are generally poor predictors of major pathology, they raise the index of suspicion in a patient with dyspepsia and slightly increase the likelihood of finding pathology. Therefore, the NICE cancer referral and dyspepsia guidelines use them in an attempt to identify patients who are most likely to have significant disease.

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**Panel 1: Dyspepsia: NICE referral guidance**

Immediate (same day) specialist referral is indicated for patients presenting with dyspepsia and significant GI bleeding (e.g. vomiting large amounts of blood).

Urgent (within two weeks) specialist referral or endoscopy is indicated for a patient of any age if they present with dyspepsia and any of the following:

- chronic GI bleeding (e.g. vomiting small amounts of blood, blood in stools)
- progressive dysphagia (difficulty swallowing)
- progressive unintentional weight loss
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal result.

Routine endoscopic investigation of patients of any age presenting with dyspepsia and without ALARM symptoms is not necessary. However, patients aged 55 years and over should be referred urgently (within two weeks) for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. new symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent — continuing beyond a period that would normally be associated with self-limiting problems (e.g. up to four to six weeks, depending on the severity of signs and symptoms).

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**Routine endoscopic investigation of patients of any age with dyspepsia and without ALARM symptoms is not necessary**

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**Flowchart**
Mr Parker is over 55 but he does not have any ALARM symptoms. His dyspepsia is not of recent onset and it is intermittent rather than persistent. According to the NICE guidelines, it is unnecessary to refer him for endoscopy, as he is unlikely to have significant pathology.

So, how should his uninvestigated dyspepsia be managed?

Medication review and lifestyle advice are important elements of care that should be offered to all patients with dyspepsia (see Panel 2). Community pharmacists often provide the first point of contact for dyspepsia sufferers and can help patients to manage their symptoms (see Panel 3, page 4).

Mr Parker may continue to take his over the counter (OTC) antacid/alginate when he needs it for immediate symptom relief. He should be offered lifestyle advice (e.g. eat healthily, lose weight, reduce alcohol, coffee and chocolate intake, avoid fatty and spicy foods, eat evening meal well before going to bed and raise the head of the bed).

NICE recommendations for the management of patients with uninvestigated dyspepsia are based on the findings of a Cochrane review that considered management strategies for dyspeptic patients with epigastric pain and/or heartburn. This review has recently been updated.1

Possible strategies considered include:
- early endoscopy
- testing for H. pylori and performing endoscopy on patients with a positive result (test and scope)
- testing for H. pylori and eradicating the infection in all those testing positive (test and treat)
- empirical acid suppression therapy.

Endoscopy is not cost-effective in patients without ALARM symptoms and is, therefore, not recommended by NICE.1 Similarly, testing for H. pylori and endoscoping patients whose test is positive has been shown to increase costs for no additional benefit in symptom relief when compared to usual care (a mixture of empirical acid suppression and endoscopy).1,11

Using pooled outcomes from five randomised controlled trials (RCTs), the Cochrane review found that endoscopy-based management might be slightly more effective than an H. pylori test-and-treat strategy in obtaining symptom relief. However, the test-and-treat strategy reduced the number of endoscopies by two thirds compared with prompt endoscopy and, even allowing for the cost of H. pylori testing and eradication, is more cost-effective.1,11 For this reason, H. pylori test and treat was one option supported by NICE.1

Flowchart referral criteria for patients with dyspepsia: adapted from NICE dyspepsia guideline

Three trials have compared an H. pylori test-and-treat strategy with empirical acid suppression in the management of dyspepsia. Pooled results from two trials showed that dyspeptic symptoms were significantly reduced at 12 months with test and treat compared with empirical treatment. The average response rate with empirical acid suppression was 47%, and this increased to 60% with H. pylori eradication (NNT 8).1

However, the studies were carried out in H. pylori positive patients so, in a normal dyspeptic population including H. pylori negative patients, the benefits are likely to be reduced.1,11

NICE guidance recommends that initial strategies for managing uninvestigated dyspepsia are either empirical acid suppression therapy or testing for and treating H. pylori.1 There is insufficient evidence to guide which should be offered first.1 However, acid suppression is becoming more cost-effective as the price of proton pump inhibitors (PPIs) drops. Also, the prevalence of H. pylori is falling steadily in the UK population.12 Young people are less likely to be infected than the elderly (50–80% prevalence in individuals born
Panel 3: Community pharmacists’ role

The NICE dyspepsia guideline includes a flowchart to help guide pharmacists’ management of patients with dyspepsia. The community pharmacist is ideally placed to offer initial and ongoing help including:

- when to consult a GP (e.g. when ALARM symptoms are present or when symptoms have persisted for several weeks and/or OTC medication has not provided adequate symptom relief)
- help with medication (e.g. checking whether or not the patient is taking any drugs which are associated with dyspepsia, including OTC NSAIDs or aspirin)
- advice about lifestyle changes for general health benefits and avoidance of dyspepsia triggers
- use of OTC medication for symptom relief (e.g. antacids/alginate, H₂RAs, omeprazole).

Newer PPIs offer no advantage in terms of clinical efficacy over established PPIs. They are more expensive and have less evidence for long-term safety before 1950 compared with <20% in those born more recently), probably as a result of improved hygiene. This means that, over time, fewer patients with dyspepsia will benefit from eradication therapy, and the test-and-treat strategy is likely to be less cost-effective in younger patients than in the elderly.

The Cochrane review concluded that, for patients presenting with dyspepsia and without an initial diagnosis, PPIs are significantly more effective than antacids or H₂-receptor antagonists (H₂RAs) in reducing dyspeptic symptoms. Approximately 40% of patients improved symptomatically with H₂RAs or antacids, but an additional 20% improved with PPIs. Results for other drug comparisons were either absent or inconclusive. NICE, therefore, recommends the use of PPIs first-line.

If further intervention is necessary following lifestyle advice and medication review, it may be appropriate to either prescribe a full-dose PPI for one month for Mr Parker, or to offer an H. pylori test, and treat if positive, as recommended by NICE.

Which PPI should be prescribed?

It is more important that PPIs are used appropriately, rather than debating which one to use. As with all drugs, the choice of PPI should be based on the principles of the ‘STEPS’ acronym: safety, tolerability, effectiveness, price, and simplicity of use. Table 1 shows the usual daily doses of PPIs to treat symptoms of dyspepsia.

Table 1: Usual daily doses of PPIs for dyspepsia*

<table>
<thead>
<tr>
<th>PPI</th>
<th>High-dose ¹</th>
<th>Full-dose</th>
<th>Low-dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>40mg</td>
<td>20mg</td>
<td>10mg</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>40mg</td>
<td>20mg</td>
<td>-</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>-</td>
<td>30mg</td>
<td>15mg</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>-</td>
<td>40mg</td>
<td>20mg</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>-</td>
<td>20mg</td>
<td>10mg</td>
</tr>
</tbody>
</table>

¹ From BNF 50; September 2005

² High-dose is equivalent to double-dose (twice the strength of full-dose)

An analysis of four RCTs in oesophagitis for the NICE guideline found no evidence that one PPI is more effective than another when compared at appropriate, equivalent doses. Similarly, a meta-analysis of 25 RCTs (n>11,000) found no significant differences between equivalent doses of PPIs in endoscopic healing of GORD or PUD. For example, in one RCT (n=1,306) esomeprazole 20mg was equivalent to omeprazole 20mg in healing GORD. The authors concluded that the decision to choose one PPI over another should be based on cost considerations, rather than arguable differences in clinical efficacy. NICE recommendations for the use of PPIs in the treatment of dyspepsia from 2000 stated that the least expensive PPI should be used. This is currently generic omeprazole.

As newer PPIs offer no advantage in terms of clinical efficacy over established PPIs, they are usually more expensive, and have less evidence for long-term safety, omeprazole 20mg daily for one month is a suitable choice to treat Mr Parker’s symptoms. He should be advised to return if his symptoms do not respond, or if he subsequently relapses.

What about testing for H. pylori?

The prevalence of H. pylori infection is about 40% in the UK population, and it probably causes no harm in the majority of people. However, up to 95% of duodenal ulcers (DU) and over 70% of gastric ulcers (GU) are associated with the bacterium and it is a risk factor for gastric cancer (antrum and body). Eradicating H. pylori can cure PUD and this is the main reason for establishing H. pylori status. (See Panel 4, page 5 for management of PUD). The potential to reduce the risk of gastric cancer developing and to ameliorate NUD is more contentious. A Cochrane review (13 RCTs, n=3,186) concluded that eradication therapy had a statistically significant effect on symptom reduction in patients with NUD. However, the effect size was small and most H. pylori positive patients with NUD still had symptoms after receiving eradication therapy. The NNT to cure (no symptoms or mild symptoms not interfering with daily activity) one patient of NUD using H. pylori eradication therapy was 18. This test-and-treat strategy is likely to be cost-effective in patients with NUD because courses of eradication therapy are short, while acid suppression often requires long-term treatment. However, it should be remembered that, for many patients with uninvestigated dyspepsia or NUD, testing for and treating H. pylori will not be curative. (See Panel 5, page 6 for management of NUD).

There is currently no evidence that H. pylori status should be investigated in patients with GORD. RCTs have found no difference between H. pylori eradication therapy and...
placebo for symptom relief in *H. pylori* positive patients with GORD. In one RCT (n=190), the relapse rate at 12 months was 83% in both the *H. pylori* eradicated and placebo groups. Contrary to earlier views, there is now evidence that *H. pylori* eradication does not cause an increase in GORD in patients with PUD or NUD, and does not exacerbate symptoms in patients who already have GORD.

Several non-invasive tests for *H. pylori* are available for use in primary care, avoiding the need for endoscopy and biopsy to confirm infection. Carbon-13 (13C)-urea breath tests and stool antigen tests are more accurate than laboratory-based serological tests (positive predictive values: 88% vs. 84% vs. 64%, respectively). Stool antigen tests using monoclonal antibodies appear to be more accurate (sensitivity and specificity of 96% and 97%, respectively) than those using polyclonal antibodies (sensitivity and specificity of 90% and 94%, respectively). However, the availability of stool antigen testing varies across the country. 13C-urea breath tests can be prescribed, and are likely to be more acceptable to patients than stool antigen testing. Near-patient serological tests for *H. pylori* are not recommended because of their inadequate performance.

*H. pylori* tests have limitations. Firstly, not all infected patients have *H. pylori*-associated disease (e.g. PUD). Secondly, as the prevalence of *H. pylori* falls, *H. pylori* tests become less accurate at predicting disease. In younger patients who have a low pre-test probability of infection, false positive results become more likely, resulting in unnecessary treatment. The role of *H. pylori* and *H. pylori* tests in the management of dyspepsia has been covered more fully in a MeReC Bulletin.

A Drug and Therapeutics Bulletin has reviewed non-invasive tests for *H. pylori*. It concluded that diabact UBT appears to be the 13C-urea breath testing kit of choice on the basis of cost and convenience. This kit does not require ingestion of orange juice or separate citric acid tablets before the test, and post-ingestion samples are collected after 10 minutes, compared to 30 minutes for other tests. 13C-urea breath tests are fairly easy to use but patients should be supervised by an appropriately trained member of staff.

Where it is necessary to re-test to confirm eradication, the 13C-urea breath test should be used. There is currently insufficient evidence to support the use of the stool antigen test as a test of eradication. Serological tests cannot be used to confirm eradication because the antibody persists in the blood for a long period.

A patient due to undergo breath or stool antigen testing should not take antibacterials for at least four weeks before testing, and antisecretory drugs (e.g. PPIs and H2RAs) for at least two weeks before testing. These treatments can suppress *H. pylori* and make a false negative result more likely. The patient should fast for at least six hours before the breath test.

For patients who test positive for *H. pylori*, NICE recommends a seven-day, twice-daily course of treatment consisting of a full-dose PPI, with either metronidazole 400mg plus clarithromycin 250mg, or amoxicillin 1000mg plus clarithromycin 500mg. These regimens achieve the same eradication rate and are effective in 80–85% of patients. The metronidazole-clarithromycin regimen may induce resistance to both the antibiotics, whereas amoxicillin resistance does not appear to increase following use of the amoxicillin-based regimen. For patients who require a second course of eradication therapy, a different regimen should be chosen from that used initially.

Mr Parker found that omeprazole 20mg daily initially relieved his symptoms, but they have recurred following a one-month course. Following a two-week period without taking a PPI or H2RA, it is appropriate to test for *H. pylori* and, if the test is positive, prescribe eradication therapy.

He still has symptoms. What now?

NICE advises that, if symptoms return after initial care strategies for uninvestigated dyspepsia, PPI therapy should be stepped down to the lowest dose necessary to control symptoms. Patients should be encouraged to use the treatment as required to manage their own symptoms, either on demand or intermittently.

On demand therapy for dyspepsia is where treatment is taken when required in response to symptoms, and is stopped once symptoms have resolved, often after a few days. In
Panel 5: Management of non-ulcer dyspepsia (NUD)

Non-ulcer (functional) dyspepsia is diagnosed in patients whose endoscopic investigation has excluded gastric or duodenal ulcer, malignancy or oesophagitis, and who do not have predominant reflux symptoms.1

At endoscopy, the majority of patients are diagnosed with NUD or ENRD (normal endoscopy plus reflux symptoms) and are likely to require long-term treatment.1 A Cochrane review found that:20

- 1 week of treatment is not effective
- after two to eight weeks therapy, PPIs were more effective at curing dyspepsia (minimal or no symptoms) than placebo (NNT 9)
- there was no statistically significant difference in terms of dyspepsia cure between full and low-dose PPIs. Full-dose PPIs are more costly
- H2RAs were more effective at relieving dyspepsia symptoms than placebo (NNT 8), but this may be overestimated due to publication bias
- prokinetic drugs appear to be effective but the data is unreliable and could be due to publication bias. Evidence is based on trials using cisapride (no longer available), not metoclopramide or domperidone
- antacids are no more effective than placebo in reducing symptoms of NUD, but data is from one RCT only.

The NICE guideline recommends:1,9

- testing for and eradicating H. pylori if present. Routine re-testing is unnecessary (See under What about testing for H. pylori?, page 4)
- a low-dose PPI or H2RA for one month, if symptoms persist or recur, followed by as required therapy at the lowest possible dose
- considering a trial of a prokinetic instead of the antisecretory drug, if PPIs or H2RAs provide inadequate symptom relief.

Panel

Generic omeprazole is currently the least expensive PPI and it seems reasonable to suggest that it can be used as required for symptom relief.

If the response to a PPI is inadequate, NICE recommends a trial of H2RA or prokinetic therapy, since individual patients may respond to one of these.1

As Mr Parker has already responded to omeprazole, it is appropriate to prescribe the lowest dose necessary (e.g. omeprazole 10mg) and encourage him to use it on demand or intermittently.

His symptoms are persisting. Should I refer him now?

NICE advises that, in some patients with an inadequate response to therapy for uninvestigated dyspepsia, it may become appropriate to refer them to a specialist for a second opinion.4 However, the benign nature of dyspepsia should be emphasised.

Patients undergoing endoscopy should not take a PPI or an H2RA for a minimum of two weeks beforehand4 because acid suppression therapy can mask or delay the detection of gastric and oesophageal adenocarcinoma.1

Mr Parker still does not have any ALARM symptoms, but initial treatment strategies have failed. In view of his age and the persistence of his symptoms, it is not unreasonable to refer him for endoscopy in order to obtain a diagnosis.

Following endoscopy, Mr Parker is diagnosed with mild oesophagitis.

How should oesophagitis be managed?

About half of all patients with GORD symptoms have endoscopically determined oesophagitis and half have ENRD (see Panel 6, page 7 for management of ENRD). Management of oesophagitis aims to heal mucosal inflammation and resolve symptoms. Although the severity of symptoms does not predict the severity of oesophagitis, oesophageal healing does show strong correlation with symptom resolution.7

NICE recommends full-dose PPI therapy for one to two months to heal oesophagitis.8 Evidence shows that PPIs are more effective than H2RAs, which are more effective than placebo. There is a consistent pattern of benefit across studies and pooled results suggest that healing occurs in 22% of patients taking placebo, 39% of patients on H2RAs and 73% of patients on PPIs. This equates to an NNT of 2 for PPIs and 6 for H2RAs, compared with placebo.1 It is unclear what timescales these, and subsequent, NNTs relate to, but studies of endoscopic healing are likely to be relatively short term (4–12 weeks).

contrast, intermittent therapy refers to a two- to four-week course of treatment in response to recurring symptoms.1
Although antacids are commonly used, there is surprisingly little evidence for their efficacy in GORD. The best evidence is for antacid/alginate combinations, which appear to be better than placebo for symptom relief in patients with GORD (NNT 3) but inferior to H2RAs (NNT 6). One small RCT compared cisapride with placebo and found that cisapride was more effective for healing oesophagitis (NNT 6). However, cisapride has been withdrawn in the UK due to concerns over arrhythmia in patients with heart disease, and the effects of other prokinetics (e.g. metoclopramide, domperidone) have not been studied in GORD.1

In patients whose symptoms have not responded to PPIs at one month, there may be additional benefit in increasing the duration of therapy to two months. Studies that gave oesophagitis healing rates at four and eight weeks were analysed for the NICE guideline. Average healing rates increased from 68% at four weeks to 84% by eight weeks, but there was significant heterogeneity between the studies.1

A meta-analysis of 10 RCTs (n=10,176) conducted for the NICE guideline compared double-dose with full-dose PPI and found that doubling the dose of a PPI only has a small effect on healing rates for oesophagitis at four weeks.1 The average healing rate was increased from 72% to 77% (NNT 19). Post-hoc sub-group analysis of two studies suggests that larger gains may be seen in patients with severe oesophagitis (Los Angeles grade C or D). Therefore, double doses are only appropriate if there is endoscopic evidence of severe oesophagitis.1

It is estimated that 60–80% of patients with successfully treated GORD will symptomatically relapse within one year if they are not provided with maintenance therapy.1 However, this also means that 20–40% can be returned to self-care and may not require prescribed medication. Evidence currently suggests that the most effective therapy to prevent relapse is a full-dose PPI, the next best is a low-dose PPI, then an H2RA. NICE analyses found that, over 6- to 12-month follow-up, full-dose PPIs:1

- reduced the rate of relapse from 79% to 24% when compared with placebo (NNT 2)
- were more effective than low dose PPIs (relapse rate 15% vs. 28%, NNT 8)
- were more effective than H2RA therapy (relapse rate 20% vs. 59%, NNT 3).

However, NICE advises that, if symptoms recur following initial treatment of GORD, a PPI should be offered at the lowest dose possible to control symptoms, on an as required basis.1 H2RA or prokinetic therapy may also be considered as alternatives if there is an inadequate response to a PPI, since individual patients may respond to them.

Mr Parker should be offered a full-dose PPI (e.g. omeprazole 20mg) for one or two months to heal the oesophagitis. If his symptoms recur after stopping treatment, it would seem sensible to try a 10mg dose of omeprazole for on demand or intermittent use before reverting to 20mg, as some patients’ symptoms do respond to low doses and the risk of adverse effects will be minimised.1

What about long-term management of patients taking PPIs?

Despite theoretical concerns that long-term acid suppression may lead to adverse effects, (e.g. atrophic gastritis, gastric cancer and vitamin B12 deficiency) long-term PPI therapy is not thought to be harmful.12,13

An international cohort study of 230 patients (mean age 63 years) with severe reflux oesophagitis, who received ≥20mg omeprazole daily for up to 11 years (mean 6.5 years, range 1.4–11.2 years) found no evidence of serious adverse effects. Metaplasia was rare and no dysplasia or neoplasms were observed. H. pylori infection was associated with an increased incidence of inflammation, gastritis and atrophy, whereas few changes were seen in H. pylori negative patients.20

Some experts recommend that H. pylori eradication should be considered in patients on long-term maintenance therapy with PPIs, but there is currently no consensus on this issue. The decision to eradicate H. pylori should be made on an individual basis, taking into consideration the patient’s preference and likely risk of gastric cancer.21 However, if NICE guidance is followed, the majority of patients will have been tested and, if necessary, may be prescribed PPIs for up to one year.22

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The management of dyspepsia in primary care

Patients should be seen at least annually to discuss symptoms, review medication and reinforce lifestyle advice.

• advising patients to avoid precipitants they attribute to their dyspepsia where possible.
• offering patients an annual review of their condition, encouraging them to try stepping down or stopping treatment.
• a return to self-treatment with antacid/alginate therapy may be appropriate, either prescribed or purchased OTC, and taken as required.
• offering lifestyle advice, e.g. healthy eating, weight reduction and smoking cessation.

There is no evidence to suggest that it is unsafe for Mr Parker to take a PPI long-term. However, he should be encouraged to reduce the use of prescribed medication by using the lowest effective dose, by trying as required, and returning to self-treatment with antacid or alginate therapy when appropriate. Mr Parker is likely to require long-term management of his dyspepsia symptoms and should, therefore, be seen at least annually to discuss his symptoms, review and/or revise his medication and reinforce lifestyle advice.

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References