BMJ MASTERCLASS FOR GPs

Dyspepsia and *Helicobacter pylori*

Rupal Shah

GP principal
Battersea, London
roo.tindall@hotmail.com

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Dyspepsia is common; up to 40% of adults in the United Kingdom have the condition. A general practitioner will see on average 210 patients with dyspepsia each year (around 4% of all consultations) and will refer about one in 10 of these patients for more investigations. Around 10-20% of people who use non-steroidal anti-inflammatory drugs will develop peptic ulcer disease that can be detected with endoscopy. The annual cost of drugs that inhibit acid secretion in the UK is about £500m.

What should I already know about this condition?

Dyspepsia is not a diagnosis. It is a term used to describe a range of symptoms, from upper abdominal pain to heartburn, nausea, bloating, and retrosternal pain. Most dyspepsia is "functional," which means no abnormalities are found on endoscopy. The National Institute for Health and Clinical Excellence (NICE) has produced clear guidelines on when you should refer patients for endoscopy (see below). Of those patients referred for endoscopy, some 30% have normal findings, and only 2% of endoscopies reveal malignancy. The most common abnormal findings on endoscopy are¹:

- Gastritis, duodenitis, and hiatus hernia (together making up 30% of endoscopic diagnoses)
- Oesophagitis (10-17%)
- Duodenal ulcer (10-15%).

Infection with *Helicobacter pylori* causes most duodenal ulcers (95%) and gastric ulcers (70%). It is also likely to cause around 9% of dyspepsia cases where no ulcers are detected. Treating patients for *H pylori* infection is more likely to benefit those whose main symptom is gastritis than those with acid reflux as their most prominent symptom.

Which test should I do?

Urea breath test

The urea breath test is the most accurate way to detect *H pylori*, with a sensitivity of 95% and a specificity of 95%. You should advise patients to stop taking antibiotics for at least four weeks before the test, to stop proton pump inhibitors at least two weeks before, and to stop histamine H₂ receptor antagonists at least one day before. Several different urea breath tests are available on an FP10 prescription, but at a cost of £15-£20. In addition, patients may need to be supervised during administration of the urea breath test, with extra costs incurred in terms of appointment time with a practice nurse or healthcare assistant.

PRACTICAL TIPS

- Dyspepsia is common, and most patients with dyspepsia do not need referral. Of those referred for endoscopy, some 30% are normal, and only 2% show malignancy. Mortality from endoscopy is 0.0001–0.0005%
- For dyspepsia without alarm symptoms, to "test and treat" for *Helicobacter pylori* or to give a proton pump inhibitor empirically is more economical than referral for endoscopy
- Review patients who have been taking acid suppression treatment for more than six weeks, to step down or stop treatment if feasible
- Gastric ulcers found during endoscopy usually need at least 4 weeks' treatment with a full dose proton pump inhibitor as well as *H pylori* eradication. Patients should then have a repeat endoscopy because of the small (2%) risk of cancer
- For patients at high risk of peptic ulcer disease (elderly, with a history of ulcers, or taking drugs that can cause ulcers) who test positive for *H pylori*, consider giving eradication treatment before starting regular treatment with non-steroidal anti-inflammatory drugs

Stool antigen test

With a specificity of 91.9% and a sensitivity of 92.4%, stool antigen tests are almost as good as the urea breath test. You should advise patients to stop taking antibiotics for at least four weeks before the test, proton pump inhibitors at least two weeks before, and histamine H₂ receptor antagonists at least one day before.

Serology

Serology is much less specific than the urea breath test and leads to about four times as many false positive results. Patients do not need to stop taking proton pump inhibitors before having the blood test.

Endoscopy

If you decide to refer your patient for an endoscopy (see below), you should advise them to stop taking proton pump inhibitors and histamine H₂ receptor antagonists two weeks before the procedure.

What new evidence do I need to know about?

Bristol helicobacter project, 2006

In a sample of people from Bristol, about 15% tested positive for *H pylori* and were randomised to eradication treatment (ranitidine 400 mg plus clarithromycin 500 mg twice daily for two weeks) or to placebo.²

This is the first in a series of occasional articles featuring BMJ Masterclasses. BMJ Masterclasses are designed to provide general practitioners with up to date information on managing common medical problems. For more information contact Dr Cath McDermott, editor of BMJ Masterclasses (CMcDermott@bmjgroup.com)

The study found

- Of the 787 people in the eradication group, 55 (7%) consulted for dyspepsia over the two year follow-up, compared with 78/771 (10%) of people in the placebo group (number needed to treat 33)
- NHS costs were £84.70 greater per participant in the eradication group over the two years
- The cost of screening in practice is likely to be £1500–£2000 per successful treatment and is unlikely to be offered to patients who do not have symptoms of dyspepsia.

Bottom line

Would screening the general population for *H pylori* be cost effective? Probably not.

CADET-Hp trial

This randomised controlled trial looked at the efficacy of the “test and treat” strategy for anyone presenting with symptoms of moderate or severe dyspepsia in the preceding month.³ It found that, of those patients who received one week of eradication treatment, 50% were symptom-free after one year, compared with 36% of those given a proton pump inhibitor alone.

Bottom line

“Test and treat” is likely to be more effective than treating patients with proton pump inhibitors alone in patients with uninvestigated dyspepsia.

Bristol helicobacter project, 2004

Previous studies have shown that eradicating *H pylori* in patients with symptoms of reflux might increase symptoms.⁴ In this study, people who tested positive for *H pylori* were randomised to eradication treatment (clarithromycin 500 mg and ranitidine bismuth citrate 400 mg twice daily) for two weeks or to placebo.⁵ The study found

- After two years, treatment did not improve the symptoms of patients who had heartburn or reflux at the start of the study
- People who did not have any symptoms to start with did not have any side effects as a result of the treatment.

Bottom line

Although eradicating *H pylori* does not benefit patients with heartburn or reflux, it does not worsen their symptoms.

Endoscopic view of a perforated gastric ulcer

Cochrane review: initial management strategies for dyspepsia⁶

Bottom lines

- Proton pump inhibitors are more effective than both histamine H₂ receptor antagonists and antacids for treating dyspepsia
- Initial endoscopy is associated with a small reduction in the risk of recurrent dyspeptic symptoms compared with *H pylori* test and treat (odds ratio 0.75), but is not cost effective (mean additional cost of endoscopy is £214 (€319, \$401))
- Test and treat may be more effective than acid suppression alone (relative risk 0.59 (95% confidence interval 0.42 to 0.83))

What new guidelines have been produced over the past two years?

NICE guidelines on managing dyspepsia in adults in primary care (2004, updated 2005)⁷

You should refer under the “two week rule” (that a patient must be seen by a specialist within two weeks of referral) anyone with any of the following alarm symptoms:

- Chronic gastrointestinal bleeding
- Unintentional weight loss
- Difficulty swallowing
- Persistent vomiting
- Iron deficiency anaemia
- Epigastric mass
- Suspicious findings after barium meal.

You should also refer urgently patients older than 55 years with dyspepsia that is persistent (lasting four to six weeks), unexplained (for example, not related to taking non-steroidal anti-inflammatory drugs), or of recent onset, even in the absence of alarm symptoms. You should consider referring for urgent endoscopy patients with iron deficiency anaemia, persistent vomiting, or weight loss even if they do not have symptoms of dyspepsia.

Patients with dyspepsia who do not have alarm symptoms—After you have reviewed patients’ current treatments and offered lifestyle advice, first line treatments for people with dyspepsia are (a) empirical treatment with a proton pump inhibitor or (b) testing for and treating *H pylori*. There is not enough evidence to advise on which of these you should offer first.

Patients with gastro-oesophageal reflux disease shown on endoscopy—You should prescribe a full dose proton pump inhibitor for one or two months. If symptoms recur after initial treatment, offer a proton pump inhibitor at the lowest dose possible to control symptoms, with a limited number of repeat prescriptions.

Patients with peptic ulcer disease shown on endoscopy—You should (a) stop any treatment with non-steroidal anti-inflammatory drugs, (b) start a full dose proton pump inhibitor or histamine H₂ receptor antagonist for two months, and (c) offer eradication treatment if *H pylori* is present.

Patients with dyspepsia without peptic ulcer disease on endoscopy—You should arrange for these patients to have initial treatment for *H pylori*, followed by management

NICE guidance on managing uninvestigated dyspepsia (adapted from *Managing dyspepsia in adults in primary care*⁹)

of their symptoms, and monitoring perhaps every three months. You should not offer routine retesting after eradication.

Which eradication regimen to use—For patients who test positive for *H pylori* (by urea breath test, stool antigen test, or laboratory based serology), you should recommend a seven day, twice daily course of eradication treatment consisting of a full dose proton pump inhibitor with either (a) metronidazole 400 mg plus clarithromycin 250 mg or (b) amoxicillin 1 g plus clarithromycin 500 mg.

Practical management tips

Review patients who have been taking acid suppression treatment for more than six weeks. This is important for assessing their need to continue treatment. Try to step down treatment (for example, advise patients to take a proton pump inhibitor only when they have symptoms) or stop it when feasible.

Patients with gastric ulcers shown during endoscopy usually need at least one month of treatment with a full dose proton pump inhibitor in addition to *H pylori* eradication treatment. After a month's treatment, arrange for these patients to have a repeat endoscopy because of the small (2%) risk of cancer.

In patients at high risk of peptic ulcer disease who test positive for *H pylori*,⁸ consider giving eradication treatment before starting treatment with non-steroidal anti-inflammatory drugs. Such patients include:

- Elderly people
- People with a history of peptic ulcer disease

- People taking other drugs that can cause peptic ulcer disease.

When should I refer my patient?

The NICE guidelines on managing dyspepsia in adults in primary care offer guidance on who to refer urgently (see above). Also consider referring patients who do not respond to treatment outlined in the figure.

Common pitfalls

Remember to consult the NICE guidelines on which patients to refer for endoscopy. Do not underestimate the risks associated with non-steroidal anti-inflammatory drugs: about 10-20% of people who use these drugs regularly will develop peptic ulcer disease that is detectable by endoscopy, and some 1-1.5% of regular users develop serious complications such as perforation or major bleeding.⁹

Offer patients older than 65 who need regular non-steroidal anti-inflammatory drugs some form of gastric protection, possibly a proton pump inhibitor or misoprostol.¹⁰

Other people at high risk of peptic ulcers whom you should consider for gastric protection include those

- With history of a gastroduodenal ulcer, gastrointestinal bleeding, or perforation
- With serious comorbidity, especially chronic lung disease
- Taking other drugs that might increase the risk of adverse gastrointestinal events. These include bisphosphonates, selective serotonin reuptake inhibitors, corticosteroids, calcium channel blockers, and nitrates.

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ADDITIONAL EDUCATIONAL RESOURCES

- National Institute for Health and Clinical Excellence: www.nice.org.uk
- Scottish Intercollegiate Guidelines Network: www.sign.ac.uk
- Clinical Evidence: www.clinicalevidence.com
- British Society of Gastroenterology: www.bsg.org.uk
- BMJ Journals: www.bmjournals.com
- Drug and Therapeutics Bulletin: www.dtb.org.uk

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