Clinical Review: Management of dyspepsia

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Definitions of the term dyspepsia vary but generally describe pain or discomfort in the epigastric region. People with dyspepsia have a normal life expectancy, but symptoms impair quality of life, and affect productivity. In this review we summarise recent evidence, to provide the general reader with an update on how to treat this disorder effectively.

What are the treatment options?

Uninvestigated dyspepsia in primary care or the community

An individual patient data meta-analysis of randomised controlled trials found that—although prompt endoscopy was superior to testing patients with uninvestigated dyspepsia for H pylori, and treating with eradication therapy if positive, in terms of symptom control at 12 months—it was not cost effective. However, it is unclear whether a test and treat approach is preferable to empirical acid suppression first line, because a second individual patient data meta-analysis found no significant difference in symptoms or costs between the two. Current guidelines state that either option can be used. If the prevalence of H pylori in the population is known, it makes sense to use an acid suppression strategy first if prevalence is low (<10%) and an H pylori test and treat strategy if the prevalence is higher. If these strategies are unsuccessful, other options (discussed below) can be considered, or the patient can be referred to secondary care for advice and further investigation if appropriate.

A six month primary care based Dutch trial compared two management strategies for uninvestigated dyspepsia based around empirical acid suppression. One strategy used a step-up approach, starting with antacids, with treatment escalated to H2 antihistamines and then proton pump inhibitors (PPIs) if symptoms remained uncontrolled. The second used a step-down approach, with the drugs given in the reverse order and de-escalated if symptoms improved. Treatment success (adequate relief of symptoms) was similar at six months (72% with step-up/70% with step-down), but costs were significantly lower with the step-up approach. This, together with the small treatment effect in favour of step-up, meant that it came out top in a cost effectiveness analysis.

Another group of primary care patients who may benefit from H pylori test and treat are those who do not consult with dyspepsia very often but who require PPIs long term. A trial screened long term PPI users for H pylori and randomised those who were positive to eradication therapy or placebo. Eradication therapy significantly reduced symptom scores, PPI prescriptions, consultations for dyspepsia, and dyspepsia related costs. The costs of detection and treatment were less than the money saved after two years of follow-up. Sensitivity analysis showed that the prevalence of H pylori would need to be less than 12% before this was no longer cost saving.

It has been estimated that 5% of dyspepsia in the community is attributable to H pylori, so population screening and treatment for this organism could theoretically reduce dyspepsia related costs. Results from follow-up studies of people recruited to two large randomised controlled trials of population based screening (and eradication therapy or placebo if H pylori positive) in the UK suggest this might be the case, with significantly lower costs and fewer consultations after seven to 10 years. However, these studies did not follow up all recruited people successfully, so currently there is insufficient evidence to institute population screening and treatment in the UK.

Peptic ulcer disease

The causal role of H pylori in peptic ulcer disease is well established, and patients with H pylori positive disease should receive eradication therapy. A Cochrane review found that the number needed to treat (NNT) with eradication therapy to prevent one duodenal ulcer relapse (26 placebo controlled trials) was 2 and for gastric ulcer (nine trials) the number was 3. Although there was significant heterogeneity between studies in both analyses, all but one trial showed a significant benefit with eradication therapy. PPI triple therapy (a PPI plus two antibiotics (clarithromycin with amoxicillin or metronidazole)) should be used in areas like the UK where clarithromycin resistance is less than 10%, with bismuth quadruple therapy (bismuth plus PPI and two antibiotics) being given where resistance is higher. Most cases of H pylori negative peptic ulcer disease are caused by NSAIDs, and trials show that PPIs are superior to H2 antihistamines for ulcer healing in this
situation. H pylori negative, NSAID negative peptic ulcer disease is rare and probably requires long term PPI treatment.

**Functional dyspepsia**  
**Diet and lifestyle**  
Food diaries from a small study of 29 patients suggest that people with functional dyspepsia eat fewer meals and consume less energy and fat than healthy controls, but whether this is a cause or a consequence of symptoms is unclear. Although the prevalence of undiagnosed coeliac disease is higher in people with symptoms of irritable bowel syndrome, this is not the case in dyspepsia. It is also unclear whether non-coeliac gluten sensitivity is involved in symptom generation in some patients with functional dyspepsia. Doctors often advise people with dyspepsia to lose weight, avoid fatty food and alcohol, or stop smoking, but there is little evidence that these measures improve symptoms. As a result, drugs are the mainstay of treatment.

**Acid suppression therapy**  
Antacids neutralise gastric acid, the production of which is controlled by gastrin, histamine, and acetylcholine receptors. Once stimulated, these receptors activate proton pumps in the parietal cell. H2 antihistamines and PPIs reduce acid production by blocking H2 receptors or the proton pump, respectively. Because PPIs act on the proton pump itself, these drugs lead to more profound acid suppression than H2 antihistamines or antacids. A Cochrane review has studied the efficacy of acid suppressants in functional dyspepsia. One placebo controlled trial of antacids showed no benefit. Twelve randomised controlled trials of H2 antihistamines versus placebo found that these drugs were effective for the treatment of functional dyspepsia (NNT=7). However, there was significant heterogeneity between studies, which was not explained by sensitivity analysis, and evidence of funnel plot asymmetry, suggesting publication bias or other small study effects. Their efficacy may therefore have been overestimated. Ten trials studied PPIs. Again, there was a significant benefit over placebo, although this was modest (NNT=10). There was significant heterogeneity between studies, with no obvious explanation, but no funnel plot asymmetry. A subgroup analysis conducted according to predominant symptom showed that PPIs were most beneficial in patients with reflux-type symptoms and more effective than placebo in patients with epigastric pain. However, they were no more effective than placebo in those with dysmotility-like functional dyspepsia. Most trials used PPIs for four to eight weeks. This seems a reasonable duration, especially as concerns have been raised recently about the safety of long term PPI use. Observational studies suggest that hip fracture, community acquired pneumonia, and Clostridium difficile infection are more common in PPI users, although all these associations were extremely modest, and direct causation cannot be assumed from studies such as these.

**H pylori eradication therapy**  
The benefit of eradication therapy is less pronounced in functional dyspepsia than in peptic ulcer disease, but treatment is still more effective than placebo. In a Cochrane review of 21 placebo controlled trials the NNT for improvement in symptoms after eradicating H pylori was 14, with no heterogeneity between studies and no evidence of funnel plot asymmetry.

**Footnotes**  
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**References**  