Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Managing Chronic Gastroesophageal Reflux Disease

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EB CME

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The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. A key clinical question based on the AHRQ Effective Health Care Program review is presented, followed by an evidence-based answer and an interpretation that will help guide clinicians in making treatment decisions. For the full review, clinician summary, and consumer summary, go to http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=757.

A collection of Implementing AHRQ Effective Health Care Reviews published in *AFP* is available at http://www.aafp.org/afp/ahrq.

Key Clinical Issue

What are the effectiveness, benefits, and harms of therapies used to address symptoms and prevent adverse long-term outcomes in adults with gastroesophageal reflux disease (GERD)?

Evidence-Based Answer

Proton pump inhibitors (PPIs) are superior to histamine H_2 antagonists for treating chronic GERD. Comparisons among different PPIs or among different dosages and dosing regimens show few consistent differences. Limited studies suggest that continuous daily dosing provides improved symptom control and quality of life at six months compared with on-demand dosing. Surgery appears to be as effective as medication through up to three years of follow-up, but serious adverse effects may be more common with surgical treatments. Evidence to evaluate endoscopic treatments is lacking. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

GERD is defined as the presence of chronic symptoms, with or without mucosal damage, from abnormal reflux of stomach contents into the esophagus. GERD is common, with more than 40 percent of the U.S. population experiencing at least one episode of heartburn monthly.[1] Treatment typically begins with lifestyle modifications. Medical treatment options include a variety of over-the-counter and prescription medications, including H_2 antagonists and PPIs. Surgical therapies include endoscopic and laparoscopic procedures and open surgeries.

There is moderately strong evidence that PPIs are superior to H_2 antagonists at relieving symptoms at four and eight weeks. Additional studies have found PPIs to be superior to H_2 antagonists at relieving symptoms for up to 12 months.[2]

Numerous randomized controlled trials have compared various PPIs. Esomeprazole (Nexium), 40 mg daily, is significantly better at relieving symptoms at four weeks than omeprazole (Prilosec), 20 mg daily. Limited evidence suggests that rabeprazole (Aciphex), 10 mg daily, is superior to esomeprazole, 40 mg daily, at four weeks, and that pantoprazole (Protonix), 20 mg daily, is superior to esomeprazole, 20 mg daily, at 24 weeks for symptom relief. However, it is likely that for PPIs, varying the dosage of one drug would achieve comparable effectiveness to another. Scheduled daily dosing of esomeprazole, 20 mg, provides better symptom control, improved quality of life, and improved endoscopic remission than on-demand dosing over six months. No other studies have shown clinically important differences in dosing regimens for individual PPIs. There also is no evidence to suggest that prescription PPIs are superior to over-the-counter PPIs. Clinically, these findings suggest that there is no single best choice of PPI or dosing regimen.[2]

Adverse effects with PPIs occur in less than 2 percent of patients and include diarrhea, nausea or vomiting, abdominal pain, dyspepsia, and headache. There is no difference in adverse effects among PPIs. Some studies have reported an association between PPI use and pneumonia and enteric infections, such as *Campylobacter* and *Clostridium difficile*.[3] Another potential serious complication of long-term PPI use is bone fracture.

Clinical Bottom Line: Managing Chronic GERD

Treatment with medication

Benefits

- PPIs were superior to histamine H_2 antagonists for esophagitis healing, patient satisfaction and compliance, and symptom remission. ●●○
- All of the commercially available PPIs appeared to be similarly effective for relieving symptoms and healing esophagitis for up to one year, although continuous therapy with a PPI appeared to be more effective than on-demand therapy for symptom control. ●●○
- Obesity, baseline symptoms, and severe baseline esophagitis were significantly associated with worse outcomes. Older age was associated with improved symptom control at six months. ●●○
- PPIs demonstrated no difference from placebo in resolving hoarseness, but inconsistently demonstrated some improvement in cough. ●○○
- Findings concerning the effectiveness of GERD treatment on asthma symptoms were inconsistent. ○○○

Adverse effects

- Potential adverse effects from PPI treatment included diarrhea, nausea or vomiting, abdominal pain, dyspepsia, headache, intestinal infection, pneumonia, and increased risk of bone fracture. ●○○

Surgical treatments

Benefits

- There was no significant difference in effectiveness between total and partial laparoscopic fundoplication, between laparoscopic fundoplication with and without division of short gastric vessels, or between open total and partial fundoplication. ●●○
- Older age, morbid obesity, female sex, presence of baseline symptoms or esophagitis, and a hiatal hernia of more than 3 cm at baseline were inconsistently associated with worse surgical outcomes. ●○○
- Evidence was inconclusive regarding the effectiveness of surgical treatment on extraesophageal manifestations of GERD.* ○○○

Adverse effects

- Serious adverse effects included bloating and dysphagia. Fundoplication was also associated with procedural complications such as postoperative infection and incisional hernia. ●○○

Endoscopic treatments

Benefits

- Evidence regarding the effectiveness of the endoscopic treatment Endocinch was mixed regarding improvement in symptoms, quality of life, and healing of esophagitis (●○○), and there was insufficient evidence to evaluate other endoscopic procedures (e.g., Stretta, EsophyX). ○○○
- With regard to how patient characteristics influenced treatment outcomes, lesser degrees of esophagitis were associated with a reduction in the need for PPIs after treatment. The patient's sex did not appear to influence outcomes. ●○○

Adverse effects

- Common adverse effects from endoscopic suturing included chest or abdominal pain, bleeding, dysphagia, and bloating. ●○○

Medical-surgical-endoscopic treatment comparisons

- Fundoplication is as effective as continued medical treatment in controlling GERD-related symptoms. In some studies, fundoplication was superior to medication.† ●●○
- Serious adverse effects could be more common with surgery than with medical treatment. ●○○
- Evidence was insufficient to determine whether prevention of long-term complications (such as Barrett esophagus and esophageal adenocarcinoma) is equivalent between medical and surgical treatments. ○○○
- Evidence was insufficient to compare endoscopic treatments with medication or surgery. ○○○

Strength of evidence scale

High: ●●● There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.

Moderate: ●●○ Findings are supported, but further research could change the conclusions.

Low: ●○○ There are very few studies, or existing studies are flawed.

Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

GERD = gastroesophageal reflux disease; PPI = proton pump inhibitor.

**—Extraesophageal manifestations of GERD include asthma, cough, and laryngeal symptoms.*

†—Out of seven evaluated studies, five included only patients whose symptoms were already well controlled by medication.

Adapted from the Agency for Healthcare Research and Quality, Effective Health Care Program. Managing chronic gastroesophageal reflux disease. Clinician summary. http://www.effectivehealthcare.ahrq.gov/ehc/products/165/757/gerd_clinician.pdf. Accessed June 15, 2012.

A recent meta-analysis comparing patients taking PPIs with patients not taking acid suppression therapy or taking acid suppression therapy other than PPIs showed an overall fracture odds ratio of 1.20 (95% confidence interval, 1.11 to 1.30), with the strongest evidence for spine fractures.[4]

Patients who have persistent symptoms of GERD despite adequate medical therapy, or who are intolerant of medical therapy, can

be considered for surgical options.[5] Surgical options have been shown to be superior to medical management.[1,6] Cost analyses have also suggested that surgery is a cost-effective approach.[6,7]

Laparoscopic fundoplication is considered the standard surgical procedure for medication-recalcitrant GERD.[8] There is no significant difference in effectiveness between total and partial laparoscopic fundoplication, between laparoscopic fundoplication with and without division of short gastric vessels, or between open total and partial fundoplication.[2] There are more limited data and conflicting evidence on the effectiveness of specific endoscopic techniques.

Patients undergoing surgical intervention had better long-term symptom relief than patients on medical therapy alone. The magnitude of this difference was difficult to estimate because of the large number of patients who dropped out of the long-term studies (33 to 58 percent).[2] Surgical patients generally were not able to discontinue medical therapy completely.

Short-term adverse outcomes were more common and more serious with surgery than with medication. The most common adverse outcomes in the first 30 days after surgery include splenic injury or splenectomy (less than 1 to 2.2 percent); gastrointestinal injury, including perforation (less than 1 to 3.4 percent); and infection or fever (less than 1 percent). The rate of conversion from laparoscopic to open procedures was 3.1 to 7.3 percent. The most common adverse outcomes in the first 30 days after endoscopic procedures were pain (0 to 83 percent), gastrointestinal injury (0 to 6.8 percent), bleeding (0 to 11 percent), and dysphagia (less than 1 to 24 percent). Up to 35 percent of patients may need additional surgery.[2] The decision to refer a patient for a surgical procedure must be made on an individual basis. Patients should be informed that surgery is associated with significant risks and that it may not eliminate the need for medical therapy.

Older age, morbid obesity, female sex, severe baseline symptoms, and esophagitis with a hiatal hernia of more than 3 cm were all associated with poorer surgical outcomes, although the strength of the evidence was weak. Obesity, baseline symptoms, and more severe baseline esophagitis are associated with worse outcomes in patients undergoing medical therapy.

The views expressed in this article are those of the authors and do not reflect the policy or position of the U.S. Army Medical Department, Department of the Army, Department of Defense, or the U.S. Government.

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