

Use of special formula and food thickening, small meals and when needed use of medications.

Gastroesophageal Reflux

Pediatrics in Review 2007; 28:101-10

Sonia Michail, MD*

* Wright State University, Boonshoft School of Medicine, Dayton Children's Medical Center, Dayton, Ohio

Treatment

Management Strategies

The goal of treating children who have GERD is to eliminate symptoms, heal the esophagitis, and manage and prevent complications. In physiologic reflux, reassuring the family may be the only intervention necessary for this usually self-limited condition.

The rationale for empiric therapy in adults who have GERD is widely accepted. Empiric treatment trials with omeprazole have been reported for treating cough, heartburn, noncardiac chest pain, and dyspepsia in adult patients. In pediatric patients, the decision to proceed to empiric therapy has not been validated for any symptom presentation. However, when presenting symptoms are typical, the diagnosis can be based on the history, and additional diagnostic investigation is unlikely to affect the prognosis or management. If pharmacotherapy is warranted, most patients respond to treatment with acid suppression. Therefore, a therapeutic trial may be cost-effective. Currently, PPIs help many patients who have severe GERD.

A prompt diagnostic evaluation is indicated for patients presenting initially with unusual or serious complications, including emesis, failure to thrive, dysphagia, or severe respiratory complications. Diagnostic investigation is warranted when patients either do not respond to therapy or have an unusual course. No single test is appropriate for all patients suspected of having GERD. Which test to order depends on the clinical presentation and the questions the clinician would like to have answered.

Lifestyle changes can be helpful for children who have mild disease. Pharmacologic therapy is advocated for the child who has significant reflux disease, especially in the presence of complications. Because neurologically impaired children develop GERD more frequently and are more likely to develop GERD-related complications, management of these children may need to be more aggressive.

Reassurance and Lifestyle Changes

The natural history of physiologic reflux in most infants is resolution as lower esophageal sphincter function matures. Reassuring and educating the family about this disorder are keys for management. In an otherwise healthy infant, no testing or therapeutic intervention is necessary.

Infants who have GER do not benefit from changing formula protein. However, in a subset of infants who vomit due to milk protein intolerance, some authorities advocate a 2-week trial of hypoallergenic formula. Thickening the milk or formula with agents such as rice cereal does not improve GER index scores but can decrease the number of episodes of vomiting. Thickening the formula with thickening agents such as rice cereal increases the caloric density of the feedings, which may be beneficial in underweight infants who have reflux.

A number of pH probe studies have demonstrated a decrease in GERD episodes for infants placed in the prone position. However, the American Academy of Pediatrics advocates the supine position for infants to reduce the risk for sudden infant death syndrome (SIDS). Therefore, prone positioning during sleep is considered only when the risk of death due to GERD outweighs the potential increased risk of SIDS.

Mild symptoms of GERD in the absence of complications may be managed by lifestyle changes for older children and adolescents. Most of the evidence is extracted from adult studies. The recommendations include weight loss for obese patients and avoidance of tobacco and alcohol. Limited pediatric evidence suggests that avoiding caffeine, chocolate, and spicy foods that provoke symptoms is beneficial.

Pharmacologic Options

ANTACIDS. Antacids, which buffer the acidic contents of the stomach, can be used for short-term therapy and relief of symptoms. Aluminum-containing antacids should be prescribed with caution in infants due to potential development of adverse effects such as neurotoxicity, anemia, and osteopenia.

H2RAS. H2RAs inhibit histamine-2 receptors on the parietal cells. Cimetidine, famotidine, nizatidine, and ranitidine are examples of drugs in this family. A number of studies demonstrate efficacy of these drugs in treating esophagitis, but the healing rate of erosive esophagitis is 60% to 70%, which is less than the healing rate for PPIs. Table 4 provides doses and adverse effects of H2RAs.

Table 4. Pediatric and Adult Doses and Adverse Effects of Histamine-2 Receptor Antagonists

Drug	Pediatric Dose	Adult Dose	Adverse Effects
Cimetidine	40 mg/kg per day divided	400 mg QID or	Hypotension, gynecomastia, reduced hepatic metabolism of other drugs,

	TID	800 mg BID	neutropenia, agranulocytosis, and thrombocytopenia
Famotidine	1 mg/kg per day divided BID	20 to 40 mg BID	Headache, dizziness, constipation, diarrhea
Nizatidine	7 to 8 mg/kg per day divided BID/TID	150 mg BID	Headache, dizziness, constipation, diarrhea, nausea, anemia, urticaria
Ranitidine	7 to 8 mg/kg per day divided BID/TID	150 mg BID	Headache, dizziness, fatigue, irritability, rash, constipation, diarrhea, thrombocytopenia, elevated transaminases

PROKINETIC AGENTS. The primary underlying phenomenon contributing to GER is transient relaxation of the lower esophageal sphincter. Because prokinetic agents increase the tone of the sphincter, they could, theoretically, be effective drugs. However, studies have failed to demonstrate that prokinetic agents consistently reduce the frequency of reflux, suggesting that they do not affect the frequency of transient relaxations of the lower esophageal sphincter. Nevertheless, children can benefit from prokinetic therapy if gastric emptying is delayed, as evidenced by double-blind studies and randomized comparison studies for prokinetic agents such as cisapride, metoclopramide, and erythromycin.

SURFACE AGENTS. Sucralfate acts by adhering to peptic lesions, protecting the mucosal surface from the acidic or digestive enzyme effects. This agent has been shown to have similar efficacy as H₂RAs in the treatment of esophagitis. Because sucralfate contains aluminum, the potential adverse effects of aluminum, especially in infants, need to be considered.

Similarly, sodium alginate forms a surface gel that decreases the regurgitation of gastric contents into the esophagus and protects the esophageal mucosa. Efficacy studies have demonstrated conflicting results. The formulation used in most published studies is not available in the United States.

PPIs. PPIs deactivate the H⁺, K⁺ATPase pumps. Their efficacy is related to their ability to maintain higher gastric pH for a prolonged period of time and suppress the meal-induced acid secretion that did not occur with H₂R blockade. The use of PPIs is indicated when GERD is refractory to therapy with H₂RAs. The inhibition of acid secretion in the stomach is associated with lower gastric volumes, facilitating gastric emptying and decreasing the volume of refluxed material. Omeprazole and lansoprazole are the PPIs studied most frequently in children. The pharmacokinetic profiles of PPIs are similar to those in adults. However, because children have higher metabolic activities than adults, they need higher doses on a per-kilogram basis (Table 5). The effective dose of PPIs ranges from 0.5 to 3.3 mg/kg per day.

Table 5. Pediatric and Adult Doses and Adverse Effects of Proton Pump Inhibitors

Drug	Pediatric Dose	Adult Dose	Adverse effects
Omeprazole	1.0 mg/kg per day divided bid OR 10 mg QD if weight <20kg 20 mg if weight=20 kg	20 mg QD	Headache, diarrhea, abdominal pain, nausea, rash, vitamin B12 deficiency, constipation
Lansoprazole	15 mg QD (weight <30 kg) OR 30 mg QD (>30 kg)	15 to 30 mg QD	Headache, nausea, constipation, diarrhea, abdominal pain, proteinuria, hypotension, elevated transaminase
Esomeprazole	Not available	20 to 40 mg QD	Headache, diarrhea, nausea, abdominal pain, flatulence
Pantoprazole	Not available	40 mg QD	Headache, diarrhea, nausea, abdominal pain
Rabeprazole	Not available	20 mg QD	Headache, diarrhea, nausea, abdominal pain

Surgical Treatment

Antireflux surgery is indicated for children who have significant complications of GERD and have failed to respond to adequate medical therapy. Surgical treatment can be an attractive option because it can be curative, avoiding the need for long-term medication use, but the failure rates to control symptoms are high, and morbidity and occasionally death are reported in the literature. Complications related to antireflux surgery occur at higher proportions in neurologically impaired children, those who have repaired esophageal atresia, and children afflicted with chronic lung disease compared with otherwise normal children. Recognition of recurrent GERD after antireflux surgery requires a high degree of suspicion and the use of more than one test. Barium contrast studies are useful for identifying the fundoplication wrap or identifying a stricture. However, pH probe monitoring and endoscopy are required to determine the functional adequacy of the surgery in preventing acid reflux and esophagitis.