



Treatment of Gastroesophageal Reflux Disease in Children

Elizabeth A. Berg, MD,* Julie Khlevner, MD*

*Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Columbia University Irving Medical Center, New York, NY

Gastroesophageal reflux (GER) is the physiologic process of gastric contents transferring upward, past the lower esophageal sphincter (LES), and into the esophagus. GER occurs naturally in more than 25% of infants, peaks at approximately 3 to 4 months of age, and usually self-resolves with time without pathologic consequences. When reflux symptoms become severe or complications such as esophagitis, refusal to eat, or weight loss develop, GER progresses to gastroesophageal reflux disease (GERD). Intractable GERD occurs when symptoms or complications of GERD persist despite optimal medical treatment. The prevalence of GERD is less than 5% in early school-aged children and approximately 10% in children older than 10 years.

GERD is an umbrella term for a spectrum of manifestations that can be classified into categories based on symptoms, endoscopic findings, reflux monitoring, and underlying pathophysiology. The 4 major subtypes of GERD are 1) erosive reflux disease, 2) nonerosive esophageal reflux disease, 3) reflux hypersensitivity, and 4) functional heartburn. Functional heartburn is the most prevalent phenotype in children. Identifying a patient's distinct GERD phenotype aids in selection of more effective treatment. GERD management should be based on the best available evidence, consistent with practice guidelines from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN).

Nutritional management is the mainstay of nonpharmacologic treatment of GER in infants younger than 1 year. The initial approach involves avoiding overfeeding, thickening feeds, or switching to an extensively hydrolyzed formula. Thickening standard formula with cereal, cornstarch, locust bean gum, and other agents has effectively reduced regurgitation, vomiting, and agitation and has led to better weight gain. Given the overlap in symptoms of GER and milk protein allergy, using a hydrolyzed formula or eliminating cow milk from the maternal diet for breastfed infants is often effective in improving GER. Amino acid–based formulas are recommended only for intractable GERD. Such formulas and overall cow milk protein restriction have been associated with increased risk of disordered eating in children. Furthermore, long-term milk avoidance beyond 1 year of age requires nutritional guidance. Any formula change should include a minimum 2-week trial to allow time to assess response. Unlike the case with infants, dietary and lifestyle modifications for children and adolescents are mostly based on adult recommendations rather than on high-quality evidence in the pediatric age group.

AUTHOR DISCLOSURE Drs Berg and Khlevner have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). Rosen R, Vandenplas Y, Singendonk M, et al. *J Pediatr Gastroenterol Nutr.* 2018;66(3):516–554

How to Care for Patients with EA-TEF: The Known and Unknown. Mousa H, Krishnan U, Hassan M, et al. *Curr Gastroenterol Rep.* 2017; 19(12):65

European Society for Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children with Neurological Impairment. Romano C, van Wynckel M, Hulst J, et al. *J Pediatr Gastroenterol Nutr.* 2017;65(2):242–264

Pharmacologic management options include acid blockade, mucosal protectants, and prokinetics. Acid blockade can be achieved with a proton pump inhibitor (PPI) or histamine receptor antagonist (H₂RA). PPIs support esophageal healing and prevent complications, including ulcers and gastrointestinal bleeding. For children older than 1 year, PPIs are effective in managing reflux symptoms and treating esophagitis. However, PPIs and H₂RAs should be used only in the first year of life with the presence of esophagitis. In children, PPIs confer increased risk of upper respiratory and *Clostridium difficile* infections, as well as risk of drug-drug interactions with other medications metabolized by cytochrome P₄₅₀. In addition, infants treated with a PPI, either alone or combined with an H₂RA, seem to have an increased risk of fractures during childhood. No strong evidence suggests a difference between PPIs and H₂RAs in symptom control of reflux; therefore, in the absence of erosive esophagitis, the choice of agent can be based on practical factors, including cost and availability.

Mucosal protectants include sucralfate and alginates. Alginates contain salts that neutralize acid and are typically used for on-demand relief of heartburn. They are not recommended for treatment of GER in infants and children because of limited evidence of their efficacy over benign treatments such as formula thickeners and uncertainty about the safety of the aluminum and calcium salts in alginates.

Prokinetic agents are not recommended as first-line therapy because of their more worrisome adverse effect profiles compared with acid blockers and mucosal protectants. However, for patients who do not respond to other treatments, they can be useful. Baclofen, a γ -amino-butyric acid B receptor agonist, can reduce transient lower esophageal sphincter relaxation, which allows increased gastric emptying. Prokinetic agents, including erythromycin, cisapride, bethanechol, domperidone, and metoclopramide, are not recommended for the treatment of GERD in children.

Surgical or endoscopic techniques are occasionally used for children with complications associated with refractory GERD. Nissen fundoplication, a technique in which the gastric fundus is wrapped around the lower esophagus to prevent refluxate from entering the esophagus, has low evidence of efficacy but is still performed in some centers. Transpyloric tube feeding has been shown to be as effective as fundoplication in children with neurologic disabilities. Endoscopic therapies, including radiofrequency ablation and endoluminal plication, have been used in a small number of patients but lack sufficient evidence to be recommended as treatment for GERD.

Special populations of children have unique treatment needs. Esophageal atresia/tracheoesophageal fistula (EA/TEF)

is a complex congenital anomaly with an estimated incidence of 1 in every 2,500 to 4,000 live births. The condition carries lifelong health implications and morbidities. GERD is the most common long-term complication of EA/TEF, affecting up to 58% of children with the anomaly. Despite the lack of controlled studies on the benefit of acid suppression, the ESPGHAN-NASPGHAN Working Group recommends that all infants with repaired EA/TEF stay on a PPI for the first 12 months after birth or longer because of the high prevalence of GERD and its complications in these children. The risk-to-benefit ratio of long-term PPI treatment for these patients should be reassessed regularly.

Children with neurologic impairments have reported an incidence of GERD as high as 70%. Among the many mechanisms that may contribute to GERD in these patients are decreased lower esophageal sphincter tone, delayed gastric emptying, impaired esophageal motility, scoliosis, and medications. The ESPGHAN Working Group recommends that, with careful monitoring, these at-risk children be given a trial of PPIs, as well as modification of their diet by thickening of formula and using whey-based formulas to ameliorate GERD. Prokinetic agents are not recommended because of their questionable efficacy and substantial risk for adverse effects.

Antireflux surgery, including Nissen fundoplication, can be considered for neurologically impaired children with a significant risk of GERD-related complications. As an alternative, the NASPGHAN-ESPGHAN Working Group suggests that transpyloric/jejunal feedings are an option for infants and children with refractory GERD. At an extreme, total esophagogastric disconnection can be offered as a last resort for neurologically impaired children with a failed fundoplication.

Future management options for GERD will aim to control symptoms for patients who do not achieve relief or healing or who develop complications with the previously mentioned measures. Potassium-competitive acid blockers are newer agents, have fast onset of action, and are approved in Asia for adults who are not responsive to PPIs. Newer prokinetic agents, including prucalopride, show promise by increasing gastric emptying and decreasing acid exposure time in otherwise healthy adults with GERD. For these and other pharmacologic options to become useful in children, studies are needed to determine their risks and benefits in the pediatric population.

COMMENTS: GER is a prime example, and unfortunately not the only one, of treating a physiologic process as though it were a disease. Over the years, how many doses of an H₂ blocker or PPI have been given to apparently thriving infants

who worried their parents by spitting up? Now that the distinction between reflux and reflux disease has been well established, we at least have the criteria (poor weight gain, resistance to feeding, associated irritability) with which to try to reassure anxious parents.

But in a broader context, the overuse of antireflux medications is emblematic of a tendency to overly depend

on pharmacy. How many courses of amoxicillin have been prescribed for viral infections? How often are stimulant medications the first recourse in place of behavioral interventions? Pick your own examples—there are far too many.

—Henry M. Adam, MD
Associate Editor, *In Brief*

ANSWER KEY FOR JANUARY 2021 PEDIATRICS IN REVIEW

Pediatric Ingestions: New High-Risk Household Hazards: 1. C; 2. B; 3. D; 4. E; 5. B.

Iron Deficiency: Implications Before Anemia: 1. E; 2. A; 3. C; 4. B; 5. A.

Review of Scabies Infestation and Selected Common Cutaneous Infections: 1. E; 2. B; 3. D 4. C; 5. C.

Treatment of Gastroesophageal Reflux Disease in Children

Elizabeth A. Berg and Julie Khlevner

Pediatrics in Review 2021;42;51

DOI: 10.1542/pir.2020-001602

Updated Information & Services

including high resolution figures, can be found at:
<http://pedsinreview.aappublications.org/content/42/1/51>

Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):
Gastroenterology
http://classic.pedsinreview.aappublications.org/cgi/collection/gastroenterology_sub

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
<https://shop.aap.org/licensing-permissions/>

Reprints

Information about ordering reprints can be found online:
<http://classic.pedsinreview.aappublications.org/content/reprints>



Treatment of Gastroesophageal Reflux Disease in Children

Elizabeth A. Berg and Julie Khlevner

Pediatrics in Review 2021;42;51

DOI: 10.1542/pir.2020-001602

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pedsinreview.aappublications.org/content/42/1/51>

Pediatrics in Review is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1979. Pediatrics in Review is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2021 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0191-9601.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

