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What's New About Gastroesophageal Reflux Disease in the Pediatric Population?

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Gastroesophageal reflux is a physiological phenomenon but becomes pathological if troublesome symptoms and/or complications occur. Gastroesophageal reflux disease (GERD) has different phenotypes ranging from non-erosive reflux disease (NERD), through reflux esophagitis and Barrett's esophagus (BE). It can present with either typical symptoms such as regurgitation and heartburn, or extra-esophageal symptoms such as cough and laryngitis. There has been an increasing trend in the prevalence of GERD over the last two decades in otherwise healthy children of all ages. Guidelines for the evaluation and management of GERD in pediatric age group have been developed recently from evidence-based medicine.¹ In most cases, diagnosis can be made from the history and physical examination. However, if the presentation is atypical or if response to empiric therapy is minimal, further evaluation is required.

■ Diagnosis

Newer modalities for diagnosis include wireless pH monitoring and impedance pH monitoring. A wireless capsule for pH measurement in the diagnosis of GERD is intended to be less uncomfortable, and facilitates activity during the measuring period, compared to the usual method with a naso-esophageal catheter. Ambulatory wireless pH monitoring has been studied in pediatric patients.² Use of a catheter-free, radio telemetric, esophageal pH-monitoring system in pediatric

clinical practice allows patients to follow a more normal physiological pattern of activities and causes less discomfort. The Bravo pH capsule was as accurate, safe and better tolerated than the conventional pH catheter in children 4 years of age and older in a study.³ Since additional extended observation is also feasible, results between 24 and 48 hours of monitoring were compared in a further report.⁴ There was no statistical difference between the pH-measurements or DeMeester scores during the first 24 hours compared with the 48-hour measurements. Individual variations were noted but had no clinical significance except in two patients, suggesting that use of pH-measurement for a period of 24 hours would be sufficient. The disadvantages of this technique are its invasiveness and that endoscopy is required.

Multichannel intraluminal impedance (MII) is a newer addition to the repertoire of tests available to evaluate GERD in children. MII has been used in 2 major areas. It can be helpful when aggressive treatment does not relieve symptoms and/or extra-esophageal symptoms are suspected. Its main advantage over traditional pH monitoring is its ability to detect both acid and nonacid gastroesophageal reflux (GER), to discern between liquid and gas GER, and to show the proximal extent of a GER episode.⁵ Compared to manometry, it detects the presence and direction of esophageal flow, duration of bolus presence, completeness of bolus clearance, and composition of a bolus. It may enhance our understanding of the pathophysiology of extra-esophageal symptoms of GERD.

Esophagogastroduodenoscopy (EGD) with biopsy is the most useful single test to conclusively exclude other upper gastrointestinal conditions. It is also helpful in evaluating patients not responding to pharmacotherapy. Severity of esophagitis can be assessed using various available classifications. In a recent study, Los Angeles (LA) classification was applied for the first time in a pediatric study.⁶ The number of mucosal eosinophils per high-powered field (hpf) is important to differentiate between eosinophilic (allergic) and reflux esophagitis and in excluding other pathologies. An important subtle finding on biopsies is also an increased diameter of intercellular spaces between squamous epithelial cells in the lower esophagus, which is usually detected by electron microscopy. Changes in this outcome measure can be used as a diagnostic marker for GERD. Dilated diameters were reported as a sensitive, specific, and objective indicator for diagnosis of GERD by routine light microscopy in a recent study.⁷

In epidemiologic studies, questionnaires are frequently employed.⁸

■ Management of GERD

Because of the development of many clinical, technological, and pharmacological advances, significant progress has been made in the management of pediatric GERD. Since infant GER is usually self-resolving, reassurance with conservative measures is sufficient. Both classes of acid antisecretory medications are increasingly being used for fussy and spitting infants. However, its indiscriminate use and abuse should be avoided.⁹ Clinical trials reveal that proton pump inhibitors (PPI) therapy is not an effective treatment for common infant GERD-associated symptoms.¹⁰⁻¹⁴ Evidence supporting safety of PPI use in infants is conflicting, and more large-scale, randomized, placebo-controlled trials are necessary to better establish the role of PPIs in infant GERD.

Lifestyle interventions are recommended for older children including avoidance of alcohol, tobacco and weight management of overweight or obese children.¹ Pharmacological intervention should be used in a “step-up” and “step-down” approach. Omeprazole, lansoprazole and esomeprazole use has been approved for 1 to 17-year olders by the Food and Drug Administration (FDA) and rabeprazole for 12 to 17-year olders.¹⁵⁻¹⁹ PPI

use may increase risk of *Clostridium difficile* infection.²⁰ The FDA has reviewed seven published studies, six of which reported an increased risk of fractures of the hip, wrist, and spine with the use of PPIs. Based on available data, it is not clear at this time if the use of PPIs is the cause of the increased risk of fractures seen in some studies. Most of the studies evaluated individuals over 50 years of age, and the increased risk of fracture was seen mainly in this age group. As a precaution, the FDA is reviewing the labels for both prescription and over-the-counter PPIs to include new safety information about the possible increased risk of the abovementioned fractures with the use of these medications. Rebound hypersecretion with use of PPIs has been reported in adults.²¹

It has also become obvious that besides medications and healing, one of the major goals of treatment must be assessment and restoration of quality of life of patients and caregivers.²²

■ Extraesophageal Symptoms and Pediatric GERD

A systematic review of articles in PubMed and EMBASE was conducted to investigate the prevalence of GERD in children with extraesophageal symptoms and the effect of GERD therapies. Data from pharmacotherapeutic trials were inconclusive and provided no support for a causal relationship between GERD and extraesophageal symptoms. This review suggests that possible associations exist between GERD and asthma, pneumonia, bronchiectasis, ALTE, laryngotracheitis, sinusitis and dental erosion, but causality or temporal association were not established.²³

In conclusion, Pediatric GERD is a chronic, heterogeneous disorder and its duration is an important factor in the development of esophageal complications. Childhood GERD is a risk factor for GERD in adolescence and adulthood.

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