What is the Best Test for Pediatric Gastroesophageal Reflux Disease?

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BACKGROUND

Gastroesophageal reflux disease (GERD) in the pediatric population is associated with problems including esophagitis, irritability, Sandifer syndrome, Barrett esophagus, apnea, asthma, cough, dental erosions, dysphagia, laryngitis, pharyngitis, and aspiration. GERD may possibly associated with sinusitis, otitis media with effusion, laryngomalacia, and subglottic stenosis, but definitive evidence is lacking for these associations.1 The diagnosis of GERD in an irritable infant with clinical signs and symptoms of regurgitation, who has no other red flags, can have a trial of empiric medical therapy without further testing. The diagnosis of GERD is less clear in some children with the entities listed above, and a variety of tests for the diagnosis of GERD are available. These tests include: 1) A 24-hour pH probe (pHP); 2) Multichannel Esophageal Intralumenal Impedance Testing (MII); 3) upper gastrointestinal study (UGI); 4) Nuclear Medicine Gastric Emptying Scintigraphy (GES); 5) Esophagoscopy and Biopsy (EBx). Each of these tests for diagnosis of GERD in the pediatric population has advantages and limitations, and none of them are ideal for all patient situations. In this review, the advantages and disadvantages of each of these tests will be presented to assist the clinician in choosing the best test for each child with the suspected diagnosis of GERD.

LITERATURE REVIEW

Formerly considered the “gold-standard” for the diagnosis of GERD, the pH provides prolonged 24-hour testing with definitive evidence of acid reflux into the esophagus. If a multichannel pH is used, the acid refluxate may be measured at the lower and upper esophagus, as well as at the hypopharynx. The pH can also be used to assess the adequacy of acid suppressive therapy. In some patients, pH can establish the presence of a temporal association between signs and symptoms and acid reflux events. Disadvantages include the inability to diagnose nonacid reflux events, which are more frequent in smaller infants who are fed frequently.1,2 In some patients, upper airway symptoms can occur with brief episodes of reflux, whereas the reflux index may still be normal. The procedure itself is tedious with placement of the pH under fluoroscopy and requirement for hospitalization. Smaller children often are uncooperative and may pull out the probe. The new wireless pH may be helpful in such situations, but evidence for this is not yet available.

MII has several advantages. The impedance probe has seven sensors (electrodes) positioned along the length of the esophagus. The placement of the probe can be verified by manometry, endoscopy, or x-ray. MII measures the change in electrical resistance when a liquid, semi-solid, or gas bolus passes between the electrodes. The newer combined pH plus impedance probes (pHP-MII) is an excellent test to detect both acid and nonacid reflux. In addition, it can distinguish between air, liquid, or mixed contents, as well as swallowing versus reflux. The pH-MII can be used for children with ongoing symptoms while on acid reflux therapy. The pH-MII is superior to pH alone.1,2 Disadvantages are similar to the pH alone, with the need for hospitalization, difficult placement of the devices, and the possibility that toddlers may pull out the device. In addition, the interpretation is more tedious and has greater interobserver variability. The newer automated analysis has more reproducibility but still is being standardized.

UGI is very useful to detect functional and structural abnormalities such as tracheoesophageal fistula, achalasia, diverticulae, strictures, antral webs, annular pancreas, malrotation, etc. UGI can also help with the diagnosis of pyloric stenosis. It is not a useful test for diagnosis of GERD since it is a brief study and can also detect physiological reflux episodes.1,3 The consistency of barium is different from infant formulas, and often the child is upset during the study, which can further lead
to inaccurate conclusions. A barium study may also be helpful to detect a failed fundoplication.

GES is useful to detect GERD, aspiration, and especially delayed gastric emptying. It can detect both acid and nonacid reflux. Delayed gastric emptying can be associated with refractory GERD, and treatment with promotility agents, such as erythromycin, may be effective. At present, the role of GES for diagnosis and management of GERD is not well established. It may be useful for diagnosis in patients refractory to standard treatments.\(^{1,4}\) The pHP-MII, UGI, and GES all have the disadvantage of radiation exposure, although of varying degree.

Whereas EBx has the requirement for general anesthesia or sedation in children, it is a definitive test providing a histopathologic diagnosis of esophagitis, and it helps in the diagnosis of other conditions including eosinophilic esophagitis, Barrett Esophagus, infections, or Crohn’s disease. Ulcers, masses, strictures, and other structural abnormalities also can be detected and biopsied or treated. The endoscopic findings do not always correlate with histological esophagitis; therefore, three to five biopsies should be obtained since esophagitis can be patchy with normal mucosa dispersed between pathologic areas. Also, the absence of esophagitis does not rule out GERD.\(^{1,5}\) EBx can be added to any other procedures performed during general anesthesia, such as laryngoscopy, bronchoscopy, tonsillectomy, or tympanostomy tube placement. EBx does carry a small risk of esophageal perforation. EBx should not be performed in children with tenuous upper airway obstruction to avoid airway edema from the procedure. The advantages and disadvantages of the various tests for GERD in the pediatric population are summarized in the Table I.

**BEST PRACTICE**

The pHp was long considered the “gold standard” for diagnosis of GERD, but recent evidence indicates that pHp-MII is superior.\(^{1,2}\) Due to some limitations in the standardization of test results, pHp-MII is currently indicated for intractable patients and for correlation of symptoms with reflux episodes.\(^{2}\) Careful history and physical exam are essential to rule out red flags that mimic GERD before a trial of empiric therapy.\(^{1}\) Other entities can mimic or be associated with GERD that will not be detected by pHp-MII. Thus UGI, EBx, and GES have limited but specific roles for the diagnosis of GERD.

### Table I.
Advantages and Disadvantages of Tests for Gastroesophageal Reflux in the Pediatric Population.

<table>
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<tr>
<th>Test</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Medical Radiation Dose (mSv)</th>
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| pHp        | 1. Quantitative measure of esophageal acid exposure and acid clearance  
            2. Evaluation of efficacy of acid suppressive therapy  
            3. Can correlate symptoms with reflux events  
            4. Multiple probes may allow detection of pharyngeal reflux  | 1. Need for hospitalization  
            2. Reproducibility only 70%  
            3. Infants and toddlers may be uncooperative  
            4. Does not detect nonacid reflux events  | 0.02 |
| MII        | 1. Detects movement of liquids, solids, and gas in both directions  
            2. Allows detection of nonacid refluxate  
            3. Can detect height of refluxate  
            4. Can be used in infants with more frequent feeds or tube feeds  | 1. By itself does not detect acid reflux  
            2. Manual interpretation can be tedious and inconsistent  | None or up to 0.02 |
| pHp+MII    | 1. Can detect acid and nonacid reflux  
            2. Can correlate symptoms with reflux events  
            3. Assess adequacy of acid suppression  
            4. Has all advantages of MII  | 1. Norms have not been established  
            2. Day to day variability  
            3. Manual interpretation can be tedious and inconsistent  | None or up to 0.02 |
| UGI        | 1. Detects structural abnormality, failed fundoplication  | 1. High sensitivity but low specificity for GERD  
            2. Higher radiation exposure  | Up to 3 |
| GES        | 1. Detection of GERD, delayed gastric emptying, and aspiration  | 1. Normal standards are not well established  
            2. Radiation exposure  
            3. Uncooperative or vomiting leads to inaccurate results  | 0.06 |
| EBx        | 1. High specificity  
            2. Differentiate GERD from eosinophilic esophagitis, Barrett esophagus, webs, stricture  | 1. General anesthesia  
            2. Lower sensitivity  | None |

pHp = pH probe, MII = multichannel intraluminal impedance testing, UGI upper gastrointestinal study, GES = Nuclear medicine gastric emptying scintigraphy, EBx = Esophagoscopy and biopsy, GERD = gastroesophageal reflux disease.
and entities such as failed fundoplication, structural abnormalities of the esophagus, eosinophilic esophagitis, and delayed gastric emptying.

**LEVEL OF EVIDENCE**

Two of the references are large evidence-based medicine reviews (level 1a) that include randomized controlled trials, retrospective cohort studies, case series, and expert opinion studies. Three other references are included that are the following: an expert opinion review article (level 5), a retrospective case series (level 4), and a consensus panel with literature review (level 2a).  

**BIBLIOGRAPHY**