Gastroesophageal Reflux in Children

To Treat or not to Treat?

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Guidelines
October 2009

• Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of NASPGHAN and ESPGHAN
  (European and North American Pediatric Gastroenterology, Hepatology and Nutrition)
  • Journal of Pediatric Gastroenterology and Nutrition 49:498–547
  • www.jpgn.org / www.NASPGHAN.org

GER vs. GERD

GER
- Normal physiologic process occurring several times per day in healthy infants, children, and adults
- Passage of gastric contents into the esophagus with or without regurgitation and vomiting
- Most episodes in healthy individuals last <3 minutes
- Frequently occur in the postprandial period, and cause few or no symptoms

GERD
- Reflux of gastric contents causes troublesome symptoms and/or complications

Who has reflux?

• Everyone reflexes!
  - Most asymptomatic
  - Most rapidly cleared

• Extraesophageal manifestations of GERD
  - Dental erosions
  - Hoarseness
  - OM/Sinusitis
  - Wheezing/Asthma
  - Chronic cough/chronic sore throat
  - Apnea/Bradycardia

Anatomy of reflux barrier

Pathophysiology of reflux

• LES – tonically contracted
  - Relaxes with deglutition
  - Crus of the diaphragm contracts with inspiration counterracting negative thoracic esophageal pressure
  - Angle of His
  - Underdeveloped in infants

• Mechanisms of GER
  - Transient LES relaxation
  - Intra-abdominal pressure
  - Reduced esophageal capacitance
  - Gastric compliance
  - Delayed gastric emptying

• Mechanisms of Airway Complications
  - Vagal reflexes
  - Impaired airway protection
GERD presentation in children

- Recurrent vomiting in infant
- ± poor weight gain
- ± irritability
- Recurrent vomiting in older child
- Heartburn in child/adolescent
- Dysphagia or feeding refusal
- Recurrent pneumonia
- Upper airway symptoms

- ALTE / Apnea
- Esophagitis
- Asthma

Diagnostic approach

- History and PE is sufficient for diagnosis in infants, children and adults
- Empiric therapy
- Important to exclude other causes

Differential Diagnosis of Vomiting in Infants and Children

GI Obstruction
- Pyloric stenosis
- Malrotation
- Intermittent intussusception

GI Disorders
- Achalasia
- Gastroplexy
- Gastroenteritis

Metabolic/Endocrine
- Selective insulin resistance
- Unusual cyclic defects

Toxic
- Lead

Allergic
- Dietary protein intolerance

Prevalence of Regurgitation in Infants


Testing for GERD

- Quantification and detection of reflux
  - pH
  - Impedance
  - (Scintigraphy)
  - (Fluoroscopy, radiography)

- Determine extent of inflammation
- Endoscopy with biopsies
- Visual appearance of esophagus is not sufficient

Esophageal pH Monitoring

- Advantages
  - Detects episodes of reflux
  - Determines temporal association between acid GER and symptoms
  - Determines effectiveness of esophageal clearance mechanisms
  - Assesses adequacy of H2RA or PPI dosage
  - Determines if patient is at increased risk for airway complications from GER

- Limitations
  - Cannot detect nonacidic reflux
  - Postprandial
  - Cannot detect GER complications associated with "normal" range of GER
  - ALTE

Adapted from Rudolph et al., J Pediatr Gastroenterol Nutr 2001;32:S1
**Impedance-pH Monitoring**
- Impedance allows detection of all bolus movement in the esophagus
- Identify direction of bolus
- Reflux is detected by impedance with retrograde bolus movement
- Combined with pH sensors

**Impedance pH Monitoring**
- Advantages
  - Detects nonacidic GER episodes
  - Postprandial reflux
  - Reflux on acid suppression
  - Detects brief (<15 s) acidic GER episodes
  - Useful for studying respiratory symptoms and GER in infants
- Limitations
  - Normal values in pediatric age groups not yet defined

**Bravo pH Monitoring**
- Detachable pH probe
- 24-48 hours of pH monitoring
  - Wirelessly transmitted to the receiver
- Self detaches and passes out of the GI track in 4-10 days
- Not used in smaller children

**Physiologic Gastroesophageal Reflux (Mean upper limit of normal)**

<table>
<thead>
<tr>
<th></th>
<th>Infants (N=509)</th>
<th>Children (N=48)</th>
<th>Adults (N=432)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of daily reflux episodes</td>
<td>73</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>No. of reflux episodes &gt; 5 min</td>
<td>9.7</td>
<td>6.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Reflux Index (% of time pH &lt; 4)</td>
<td>11.7%</td>
<td>5.4%</td>
<td>6%</td>
</tr>
</tbody>
</table>

*Rudolph et al, J Pediatr Gastroenterol Nutr 2001;32:S1*

**Upper GI Radiography**
- Advantage
  - Useful for detecting anatomic abnormalities
- Limitation
  - Cannot discriminate between physiologic and nonphysiologic GER episodes
  - "Snap shot"

**Upper GI Radiography**
- Pyloric stenosis
- Malrotation
**Scintigraphy**

- **Advantages**
  - Detects movement of any gastric contents
  - Evaluate gastric emptying
  - Evaluate for aspiration

- **Limitations**
  - Time period limited to postprandial interval
  - Solid meal
  - Lack of normative data or standardized techniques

**Esophagogastroduodenoscopy (EGD)**

- **Advantages**
  - Enables visualization and biopsy of esophageal epithelium (+/- eosinophils)
  - Determines presence of esophagitis, other complications
  - Discriminates between reflux and non-reflux esophagitis
  - Histologic findings correlate with acid exposure (Winkel et al., 1982)

- **Limitations**
  - Need for sedation or anesthesia
  - Endoscopic grading systems not yet validated for pediatrics
  - Poor correlation between endoscopic appearance and histopathology

**Differential Diagnosis of Esophagitis**

- Gastroesophageal reflux
- Food allergy or intolerance
- Primary eosinophilic esophagitis
- Drug induced
- Infection
  - *Candida*
  - Herpes simplex
  - Cytomegalovirus

**Treatment / Management**

- Non-pharmacological therapy:
  - Life-style changes
  - Positioning
  - Feeding (volume, consistency)
  - Thickening of liquid feeds
- Pharmacological therapy:
  - Antacids
  - Acid suppression
  - Prokinetic agents
  - Surgery

**Non-pharmacological Treatment Options in Infants**

- Reassurance
- Parental education
  - Warning signs
  - Feeding techniques
  - Quantity
  - Age appropriate feeds
Non-pharmacological Treatment

- Positioning:
  - Prone position is associated with less acid exposure when compared to supine. (Meyers et al, 1982; Vandenplas et al, 1985; Tobin et al, 1997)
  - Potential advantage of prone positioning needs to be balanced against the proven risk of SIDS in infants sleeping prone. (Oyen et al, 1997; Skagberg et al, 1998)
  - In most cases, prone positioning is not recommended.

![Prone Positioning and GER](image)

<table>
<thead>
<tr>
<th>Sleep Position</th>
<th>GER Index</th>
<th>SIDS Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td>15.3</td>
<td>0.05*</td>
</tr>
<tr>
<td>Left side</td>
<td>7.7</td>
<td>0.05*</td>
</tr>
<tr>
<td>Right side</td>
<td>12.0</td>
<td>0.05*</td>
</tr>
<tr>
<td>Prone</td>
<td>6.7</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Reflex Index (%) time pH <4

Effect of Sleep Position on GER in Infants and SIDS Mortality

- Formula Changes:
  - In most cases of infantile reflux, formula plays no role
    - Trial of thickened formula or commercial anti-regurgitation formula may decrease vomiting
    - Thickening can be associated with increased coughing
  - In a subset of infants, milk protein or soy protein allergies may cause symptoms of irritability and GERD
    - Consider trial of hypoallergenic formula for 2-4 weeks

![Effect of Thickening Milk Formula Feedings With Rice Cereal](image)

- Use of acid suppression

![Effect of pH on Viscosity](image)
Formula thickening

- In general brand of infant rice formula is not important except when hydrolyzed formula is used
- Nipple change or modification
- Additional 14 cal/tablespoon

Non-pharmacological Treatment

- Older children/adolescents
  - Avoid large meals
  - Do not lie down immediately after eating
  - Weight loss in obese children/adults
  - Avoid caffeine, chocolate, and spicy foods that provoke symptoms
  - Eliminate exposure to tobacco smoke

Pharmacotherapy

- Antacids
- Histamine-2 receptor antagonists
- Proton pump inhibitors
- Prokinetic agents
- Surface agents

Goals of Pharmacotherapy

- Control symptoms
- Promote healing
- Prevent complications
- Improve health-related quality of life
- Avoid adverse effects of treatment

Pharmacological Treatment

- Antacids:
  - Directly buffer gastric acid – Fast acting
  - Antacids are effective when given PRN symptoms
  - Chronic use is not recommended
    - Aluminum hydroxide - increased plasma aluminum
    - Osteopenia, Rickets, anemia, neurotoxicity
    - Calcium Carbonate
      - Milk-alkali syndrome: hypercalcaemia, alkalosis and renal failure

- Surface protectants

  - Sucralfate – combination of sucrose, sulfate and aluminum (Carafate)
    - Forms a gel in acidic environment coating exposed mucosa of peptic ulcers
    - Potential aluminum toxicity in infants
  - Alginate – insoluble salt of alginic acid (seaweed) (Gavascon)
    - Creates “foam” “raft” barrier when in contact with acid
Inhibition of Acid Secretion in Gastric Parietal Cell

Adapted from Sanders SW, Clin Therapeutics 18, 2-34. Copyright 1996 by Excerpta Medica Inc.

Pharmacological Treatment

- Selection of acid-reducing therapy
  - Step Up vs. Step Down
  - Optimal timing of administration to achieve peak plasma concentrations prior to a meal time
  - Formulation
    - Tablets, dissolvable/chewable tablets, suspension, capsules with granules

Available Prokinetic Agents Are Unproven or Ineffective

- Insufficient evidence to determine effectiveness:
  - Bethanechol
  - Erythromycin
  - Domperidone
  - Metoclopramide
    - Esophageal pH improvement in 1 of 6 RCT
    - Clinical improvement in 1 of 4 RCT
    - High incidence of adverse events
    - Black box warning
  - Withdrawn from the US market
    - Cisapride
    - Tegaserod

Reasons to consider surgical interventions

- Failure of medical management
- Symptom relief
- Prevent the long term esophageal damage
  - Barrett’s lesions
  - Long term risk of cancer
  - Eliminate long term use of medications
  - Prevent extraesophageal manifestations of GERD
    - Recurrent pneumonia
    - Aspiration

Surgical vs. Pharmacological intervention

- Symptom relief
  - Numerous studies now document short-term symptom relief using either therapy
- Prevention of long-term esophageal damage
  - No statistical difference in healing erosive esophagitis
- Prevention of Barrett’s and cancer
  - No statistical difference in 10-13 year follow-up
- Prevent long-term use of medication
  - Most patients have resumed antireflux medication within five years of surgery
- Selected patient population will require surgical interventions in addition to pharmacological management

Summary

- GER is common in healthy infants and usually resolves by 18 months of age
- Pediatric GER can present with variable symptoms
- Approach to diagnosis and treatment depends on presenting symptoms and signs
- Currently available tests often do not conclusively demonstrate a relationship between GER and specific symptoms
- Good history and clinical judgment are important for optimal evaluation and management