Gastroesophageal Reflux in Infants

Lindsey Albenberg, DO
Andrew Grossman, MD
The Children’s Hospital of Philadelphia

2013

Resident Education Series
Reviewed by Jyoti Ramakrishna, MD of the Professional Education Committee
Case

- 6 week old F presents to primary care clinic with vomiting
- Bottle feeding
- “Large amount” of nonbloody, nonbilious emesis following >50% of feeds
- Fussy following feeds, but consolable
- Weight gain excellent
- Baby is now fed Enfamil Gentlease (3rd formula) and parents are asking about medications
Objectives

• To briefly review the definitions, natural history, and mechanisms of GER and GERD

• To discuss the diagnosis of GERD in infants and the warning signs suggesting other more worrisome disorders

• To discuss the management options for physiologic GER and for GERD
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>GER</td>
<td>Passage of gastric contents into esophagus</td>
</tr>
<tr>
<td>GERD</td>
<td>Symptoms or complications that may occur when gastric contents reflux into esophagus or oropharynx</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>Passage of refluxed gastric contents into oral pharynx</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Expulsion of refluxed gastric contents from mouth</td>
</tr>
</tbody>
</table>
Mechanisms of GER in the Infant

- Angle of His underdeveloped
- Inadequate gastric accommodation
- Supine position + gravity = GER
GER Prevalence

  - Cross-sectional study of 19 pediatric practices in Chicago, IL
  - Survey parents of 948 pediatric patients (<13 months)
  - Excluded infants born prematurely, with chronic medical or developmental condition, or had been ill in the past two weeks
• Martin et al. *Pediatrics* 2002
  – Objective: To determine the natural history of infant “spilling” (regurgitation/vomiting) during the first two years of life
  – Prospective birth cohort was followed with daily symptom diaries during the first two years of life
    • Parents recorded whether their child vomited most feeds (50% or more) on a daily basis

Fig 2. Proportion (%) of children who spilled.
When to worry?

• GER becomes GERD when reflux of gastric contents causes troublesome symptoms and/or complications

• Physiologic GER can become GERD when:
  – Insufficient clearance and/or buffering of material refluxed into esophagus
  – Delayed gastric emptying
  – Anatomic abnormality (hiatal hernia)

• Signs & symptoms suggesting GERD
  – FTT (with feeding difficulty)
  – Irritability
  – Dysphagia
  – Odynophagia
  – Arching
Diagnosis of GERD

• Diagnosis is made clinically
  – Not easy!

• Symptoms and signs are nonspecific and unreliable
  – Individual symptoms in children generally are not highly predictive of findings of GERD by objective studies

• Major role of the history and physical is to exclude other more worrisome disorders that present with vomiting
Warning Signals In Vomiting Infant Requiring Further Investigation

- Bilious or continuous vomiting
- GI bleeding
- Onset of vomiting after 6 months of life
- Failure to thrive
- Diarrhea, constipation
- Fever
- Lethargy

- Hepatosplenomegaly
- Macro/microcephaly
- Bulging fontanelle
- Seizures
- Abdominal tenderness, distention
- Documented or suspected genetic/metabolic syndrome
Diagnosis of GERD

• Barium contrast radiography
  – Indication is detection of anatomic abnormalities
  – Neither sensitive nor specific for diagnosing GERD
    • Brief duration produces false-negatives
    • Frequent occurrence of non-pathological reflux during the examination produces false-positives
Pyloric stenosis

Malrotation
Diagnosis of GERD

• Esophageal pH monitoring
  – Gold standard
  – Measures the frequency and duration of acid reflux episodes (drop in esophageal pH < 4.0)
    • Measures reflux index (RI)
    • Other parameters: total number of episodes, number of episodes lasting > 5 minutes, patient position during episode, awake vs. asleep
Multiple Intraluminal Electrical Impedance Measurement

**Advantages**
- Detects nonacidic GER episodes
- 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
- Analysis of tracings time-consuming
- Portable device unavailable for outpatient studies
Impedance Measurement

http://www.nature.com/ajg/journal/v104/n2/fig_tab/ajg200823f2.html
Esophagogastroduodenoscopy (EGD)

**Advantages**
- Enables visualization and biopsy of esophageal epithelium
- Determines presence of esophagitis, other complications
- Discriminates between reflux and non-reflux esophagitis

**Limitations**
- Need for sedation or anesthesia
- Endoscopic grading systems not yet validated for pediatrics
- Poor correlation between endoscopic appearance and histopathology
- Generally not useful for extra-esophageal GERD
Esophageal Histology

Normal esophagus  GER  Eosinophilic esophagitis
Scintigraphy

**Limitations**
- Lack of standardized techniques
- Absence of age-specific normative data
- Period of observation limited to early postprandial period

**Advantages**
- Detects acidic and non-acidic GER
- Evaluates gastric emptying
- May demonstrate aspiration
Treatment: Reassurance

• The natural history of **physiologic** reflux in most infants is resolution as lower esophageal sphincter function matures

• Parental education, guidance, and support are always required
  – Usually sufficient to manage healthy, thriving infants with symptoms consistent with physiologic GER

• Often, the best approach is to sympathize with the family and present the natural history data
2009 Guidelines: Lifestyle Changes in Infants

- Avoid overfeeding
- Thicken formula (up to 1 tbsp per 1-2 oz)
- Avoid “carseat” positioning
- Upright positioning after feeds (less effective than thickening feeds)
- Consider 2-4 week trial of hypoallergenic formula
Treatment: Lifestyle Changes

- Hegar et al. *JPGN* 2008
  - Statistically significant natural decrease in regurgitation frequency in all 3 groups

  - 60 healthy, term infants, formula-fed with frequent regurgitation and/or vomiting
    - Standard formula thickened with 5g rice cereal per 100mL
    - Anti-regurgitation formula with bean gum
    - Standard formula
Treatment: Lifestyle Changes

• The bottom-line:
  – The use of AR formula and formula with added thickener may result in the reduction of regurgitation—but how much of this is related to natural history?
  – Reduced volume feedings may be useful—but necessary to monitor caloric intake/weight gain
Treatment: Pharmacologic Therapies

- Histamine-2 receptor antagonists
  - Decrease acid secretion by inhibiting histamine-2 receptors on parietal cells
  - Ranitidine has been shown, in infants, to reduce the time that gastric pH is <4
  - Pharmacokinetic studies in children show that gastric pH begins to increase within 30 minutes of administration and lasts for 6 hours (TID or QID dosing)
  - Drawbacks
    - Tachyphylaxis
    - Side effects in infants: irritability, head-banging, headaches
Treatment: Pharmacologic Therapies

• Proton Pump Inhibitors
  – Inhibit acid secretion by blocking Na-K-ATPase (the parietal cell proton pump)
  – Adult studies show that PPI’s produce higher and faster healing rates for esophagitis than H2RA’s
    • Maintain gastric pH at or above 4 for longer periods of time
    • Inhibit meal-induced acid secretion
    • Facilitate gastric emptying
    • Effect does not diminish with chronic use
  – No PPI has been approved for use in children younger than 1 year of age!
    • Few pharmacokinetic data for PPIs in infants
Is There Evidence to Support Increase in the Use of PPIs in Infants?

- Orenstein et al. *J Pediatr* 2009
  - Multicenter, randomized, double-blind, placebo-controlled evaluating lansoprazole versus placebo
  - 162 infants (1-12 months) with symptomatic GERD who remained symptomatic (crying, fussing, or irritability) following 1 week of conservative management
  - Similar efficacy for lansoprazole and placebo
  - Adverse events more common in lansoprazole group
PPI Safety Concerns

**Pediatrics**
- Acute gastroenteritis (OR 3.58)
- Community acquired pneumonia (OR 6.39)
- *Clostridium difficile* infection

**Adults**
- Pneumonia
- *Clostridium difficile* infection
- Bacterial gastroenteritis
- Hip fracture in elderly

Canani RB, *Pediatrics* 2006;117:e817-e820  
Yang YX, *JAMA* 2006;296:2947-2953

Available Prokinetic Agents Are Unproven or Ineffective

- Cisapride: Withdrawn
- Bethanechol: 1 randomized controlled trial (RCT)
- Erythromycin: no RCT
- Domperidone: available in Canada, no RCT
- Metoclopramide
  - Esophageal pH improvement in 1 of 6 RCT
  - Clinical improvement in 1 of 4 RCT
  - High incidence of adverse events (Black Box Warning)

No evidence based justification for routine use of these agents
Treatment: Surgical Therapy

- Most of literature on surgical therapy in children with GERD consists of retrospective case series.

- Anti-reflux surgery may be of benefit in children with confirmed GERD who have failed optimal medical therapy or who have life-threatening complications of GERD.

- It is important to provide families with appropriate education and a realistic understanding of potential complications.
Treatment: Surgical Therapy

• Complications following antireflux surgery may be due to:
  – Alterations in fundic capacity
  – Altered gastric accommodation
  – Altered sensory responses

• Complications may include:
  – Gas-bloat syndrome
  – Early satiety
  – Dumping syndrome
  – Post-operative retching
Summary Algorithm: Vomiting Infant -- Uncomplicated

• History and physical exam
  – Assess for warning signs/symptoms

• Parental education
  – Explain natural history
  – Feeding modification
  – ? 2 wk trial of hypoallergenic formula

• Medical therapy usually not necessary

• Further evaluation if symptoms don’t resolve by 18-24 months

Y Vandenplas and CD Rudolph et al, J Pediatr Gastroenterol Nutr 2009
Conclusions

• GER is common in infants
• GERD is relatively uncommon and is likely over diagnosed and over treated
• Pharmacologic and surgical therapies have potential risks which should be considered