LARYNGOPHARYNGEAL REFLUX AND ITS ROLE IN PEDIATRIC OTOLARYNGOLOGY

Wendy Mackey, APRN, CORLN
SOHN Congress Meeting
Washington, DC
September 2012

Definitions
- Laryngopharyngeal Reflux (LPR)
  - Retrograde movement of gastric contents beyond the esophagus
  - Refers to non-gastrointestinal manifestations of reflux disease
- Synonyms
  - Extraesophageal reflux (EER)
  - ‘atypical’ reflux
  - gastropharyngeal reflux
  - Reflux laryngitis
  - pharyngoesophageal reflux

Epidemiology
- GERD one of the most prevalent disease entities in the US
  - 20-30% adults, >75 million people in US with
  - US children prevalence - 22%
- Postulated that 40% of children with GERD have associated respiratory manifestations
  - Possible connection between GERD and airway abnormalities is controversial
  - Studies show coexistence and possible connection but few show convincing causality
- Patients with isolated LPR are not obese

Classic Symptoms of GERD
- Esophageal mucosa is much more tolerant of gastric contents including pepsin, bile and pancreatic enzymes than the mucosa of the upper and lower airway
- Esophagus can tolerate up to 50 episodes of GER daily without injury
- 3 laryngeal acid/pepsin exposures per week have shown induction of injury
- LPR is not always acidic, making it more difficult to diagnose

Symptoms of LPR
- Common symptoms
  - Frequent throat clearing
  - Cough
  - Globus
  - Hoarseness
  - Dysphagia
- Other symptoms
  - Postnasal drip
  - Nasal obstruction

Airway Symptoms
- Stridor
- Croup
- Laryngitis
- Hoarseness
- Asthma Exacerbation

DO NOT HAVE
- Esophagitis
- Heartburn

SOME CHILDREN HAVE NO SYMPTOMS
GERD and LPR are Different!!!!

- Unique but related disease entities
- Different risk factors
- Different symptoms
- Different pathophysiology
- Different Diagnostic criteria and modalities
- Different approach and response to therapy

GERD IS NOT LPR

**GERD**
- Heartburn and gastric upset
- Esophagitis
- No laryngitis (unless severe)
- No voice changes
- Abnormal LOWER esophageal sphincter
- Esophagus resistant to acid reflux
- Risk of esophageal adenocarcinoma
- No risk of Squamous Cell carcinoma of Larynx
- Heals with short course of PPI

**LPR**
- NO heartburn or gastric upset
- Rarely esophagitis
- Always posterior laryngitis
- Frequently voice changes
- Abnormal UPPER esophageal sphincter
- Larynx very sensitive to acid reflux
- Risk of esophageal adenocarcinoma
- Positive risk of Squamous Cell carcinoma of Larynx
- Requires prolonged use of PPIs

**History of LPR**

- GERD first described as a clinical entity in pediatrics in the 1950’s
  - incidence 1/4000 live births
- Cherry and Margulies (1968) - acid related laryngeal ulcerations and granulomas
- Subsequent studies suggested acid reflux as a contributing factor in various ENT diagnosis
- Landmark study - Koufman (1991)

Koufman (1991)

- 182 patients with laryngeal pathology
  (laryngeal carcinoma, stenosis, laryngitis, globus pharyngeus, dysphagia, chronic cough)
  - 62% abnormal acid reflux on dual pH probe testing
  - 43% symptoms of heartburn or regurgitation
  - most had laryngopharyngeal symptoms
  - Aggressive H2A therapy and behavioural mod x 6 months
  - 85% (n=123) had resolution of their EERD symptoms

**Diagnosis**

- * Symptoms
- * Laryngeal examination
  - (DL&B or fibroptic)
- Dual pH Probe Monitor

24 hr dual lumen pH probe

- Measure reflux events for 18-24 hrs
  - LPR episodes of reflux at proximal probe
  - GERD episodes of reflux acid exposure times at distal probe
- Results non conclusive
  - Measure only acid reflux
  - High false negative (up to 50%)
  - Limited consensus on interpretation

Endoscopic Airway Finding

• Commonly associated with LPR
  – Edema and erythema of the arytenoids
  – Redundancy of interarytenoid mucosa
  – Inflammatory changes of the vocal folds
  – Granulation tissue

• Also identified
  – Laryngeal edema
  – Subglottic stenosis
  – Cobblestoning of the tracheal mucosa
  – Blunting of the carina
  – Posterior Glottic edema


Determine correlation between findings at DL&B and presence of LPR

• 155 children - DL&B for airway symptoms due to suspicion of LPR
  – 0.3-11.7y, retrospective chart review

<table>
<thead>
<tr>
<th>Laryngeal anomalies (83%)</th>
<th>Tracheal anomalies (66%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior edema (60%)</td>
<td>– Tracheal cobblestoning (35%)</td>
</tr>
<tr>
<td>Arytenoid edema (90%)</td>
<td>– Blunting of carina (12.5%)</td>
</tr>
<tr>
<td>Large lingual tonsils (18%)</td>
<td>- Subglottic stenosis (11%)</td>
</tr>
<tr>
<td>Vocal fold edema (12%)</td>
<td>– Increased secretions (15%)</td>
</tr>
<tr>
<td>Vocal fold nodule (12%)</td>
<td>– General edema or erythema (5%)</td>
</tr>
<tr>
<td>Hypopharyngeal cobblestoning (3%)</td>
<td></td>
</tr>
</tbody>
</table>

Correlation of Findings at DL &B with GERD in Children

• 77 consecutive pts who underwent DL&B (prospective)
  – Age: 0.1-15.5 yrs -- 51 male 26 female 24 tracheostomy present
  – MR revealed history of positive GERD test

• Group Results:
  – GERD + group: 50/77 (65%) (1+ positive diagnostic test)
  – GERD - group: 21/77 (27%) (negative test, symptom free)
  – Indeterminate grp: 6/77 (8%) (equiv test, positive symptoms)


Upper GI Radiography


DL&B Findings GERD + Group

Laryngeal findings
• Large lingual tonsil (P<0.01)
• Posterior edema (P<0.001)
• Arytenoid edema (P<0.01)
• True vocal cord edema (P<0.001)

Cricotracheal findings
• General edema and erythema (P<0.001)
• Blunting of carina (P<0.01)

Severe arytenoid edema, postglottic edema or lingual tonsils pathognomonic of GERD (98%)

• However, only half of GERD+ diagnosis one of these findings
  • 17 GERD - no had one of these findings present, all minor score


Diagnosis

Response to Empiric Treatment
### Laryngeal symptoms in Children

**Bouchard et al pH study**

- Evaluate pH studies for ENT symptoms and their relationship to GER
  - 3,000 pH studies/16 years
  - 88 children referred for laryngeal symptoms
- Reasons for referral (n/mean age)/% positive pH probe
  - Stridor (n=31/8m) - 58%
  - Laryngomalacia (n=18/13m) - 61%
  - Laryngitis (n=16/50m) - 56%
  - Dysphonia (n=14/59m) - 14%
  - Laryngeal papillomatosis (n=8/62m) - 25%
  - Dysphagia (n=1)


### Follow-up of largest groups

- Stridor and GER- 83%
- Laryngomalacia and GER- 80%
- Laryngitis and GER- 86%

### Otolaryngologic Diseases Associated with EERD

- Hoarseness
- Laryngitis
- Chronic rhinitis
- Sinusitis
- Recurrent croup
- Subglottic stenosis

### Therapeutic Options

- Lifestyle modification
  - Diet
  - Mechanical methods
- Pharmacologic intervention
- Surgical intervention

### Classification

- Minor
  - Symptoms annoying, not socially and physically impairing
- Major
  - Symptoms impair way of life
- Life-threatening
  - Airway obstruction, severe pulmonary disease or malignancy
Medical Treatment

Dietary considerations
- Avoid acidic foods, caffeine, citrus, chocolate, smoke, alcohol
- Avoidance of trigger foods
- Thickening feeds
- Feeding schedule
- Positioning considerations
- Voice therapy

PPI - Basic Pharmacology

- Proton pump is a molecule in parietal cells: cells of the stomach which "pumps" acid into the stomach. It takes a non-acidic potassium ion out of the stomach and replaces it with an acidic hydrogen ion
- PPIs work within the parietal cell to decrease the production of HCl (hydrochloric acid) and target the final pathway of acid secretion
  - Inactived by gastric acid
  - 3 currently approved by the FDA in children
    - ranitidine (Zantac)
    - cimetidine (Tagamet, Tagamet HB)
    - famotidine (Pepcid, Pepcid AC, MS Pepcid AC)
- 4 agents are available:
  - Swallowed whole
  - no chewing, splitting, opening or crushing
  - Need to be fully absorbed into the blood stream before the first bite is taken
  - Daily vs twice daily dosing
    - preferred meal is dinnertime
  - unable to swallow tabs
  - no effect on gastric emptying
  - Absorbed in the proximal small bowel

PPI - Safety Profile

- Incidence of adverse effects < 5% (placebo)
  - most common headache, diarrhea, abdominal pain, nausea
- Long term use
  - Increased frequency of fractures, increased community-acquired pneumonia, development of gastric carcinoid tumors, decreased absorption of vitamin B12
- Contraindications
  - sensitivity
  - caution in patients with severe hepatic disease
- Drug Interactions

Dosage and Administration

- Inactivated by gastric acid
  - Swallowed whole
  - no chewing, splitting, opening or crushing
- Take 30-40 minutes prior to meals
  - Need to be fully absorbed into the blood stream before the first bite is taken
- Daily vs twice daily dosing
  - preferred meal is dinnertime
- Enteral feeding tube administration
- Unable to swallow tabs

H₂ Receptor Antagonists

- H₂ RA introduced in the late 1970s
- 4 agents are available:
  - ranitidine (Zantac, Zantac 25-75-150, Peptic Relief)
    - po (tablet, cap, effervescent, liquid), IM, IV
  - cimetidine (Tagamet, Tagamet HB)
    - po (tablet, liquid), IM, IV
  - famotidine (Pepcid, Pepcid AC, MS Pepcid AC)
    - po (tablet, liquid), IV
  - nizatidine (Axid, Axid AR)
    - po (tablet, liquid)
**H2RA- Basic Pharmacology**

- Inhibit the histamine pathway involved in gastric acid production
- Gastric pH begins to rise less than 30 minutes after dosing
- Duration of action up to 10 hours
- May be used in conjunction with PPI

**Prokinetic agents**

- Stimulate esophageal, gastric and intestinal motility
- Improves LES tone
- Particularly helpful when there are associated symptoms of nausea, bloating, and vomiting

**Operative Interventions**

- Fundoplication
  - Nissen fundoplication
  - Thal fundoplication

- Surgical Treatment
  - Approximately 15% of children with pathologic GERD require surgery
  - Indicated when medical management fails and complications of gastroesophageal reflux persist

**Prokinetic agents**

- **metoclopramide**
  - only promotility agent approved by the FDA

- **erythromycin**

- **bethanechol**

- **cisapride**
  - restricted in the US d/t potentially lethal cardiac arrhythmias
  - available by compassionate use parameters

**Treatment**

- Minor (symptoms annoying)
  - PPI daily or bid H2RA (bid PPI if treatment fails)
  - if asymptomatic at 6 months may taper down meds

- Major (symptoms impair way of life)
  - PPI bid
  - if no improvement in 2 months, double dose of PPI, add H2RA

- Life-threatening (airway obstruction, severe pulmonary disease, malignancy)
  - aggressive PPI
  - surgical intervention

**In Summary**

- EERD is a different entity from GERD
- There are numerous otolaryngologic diseases associated with EERD
- Treatment focuses on aggressive pharmacologic intervention with PPI
- The future….