TITLE: Manifestation and Diagnosis of Pediatric Laryngopharyngeal Reflux
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Introduction:

Gastroesophageal reflux (GER) is a common physiologic condition in children; larygopharyngeal reflux (LPR) has gained increasing recognition over the past few years as a distinct pediatric condition. The former refers to retrograde flow gastric content into the esophagus, while the refluxate passes through the upper esophageal sphincter to reach the pharynx in the latter condition.

Clinical Manifestation:

Although the prevalence of LPR in children is not known, it is estimated that up to 10% of adult patients present to otolaryngologists with symptoms related to reflux. It occurs more commonly in the upright position and during daytime. Unlike GER, esophageal motility is thought to be normal in LPR. Laryngeal and pharyngeal symptoms are more common in LPR than GER, which tends to present with heartburn and/or abdominal complaints. Symptoms of LPR are non-specific, thus making accurate diagnosis difficult. Infants may present with vomiting, regurgitation, failure to thrive, irritability, chronic respiratory disorder; while children may present with dysphagia, globus sensation, otalgia, dental pain, nasal congestion, chronic cough.

Reflux has been implicated in a number of otolaryngologic conditions, including:

Chronic rhinosinusitis:

Phipps et al. reported a higher incidence of GER in patients with sinusitis and their symptomatic improvement after acid suppressive therapy. Bothwell et al. reviewed the records of 28 patients who met the criteria for endoscopic sinus surgery and 25 of them (89%) showed improvement and avoided surgery after GER treatment. Though it is possible that refluxate might reach the nasopharynx and cause inflammatory changes, there is no prospective controlled trial to support that reflux contributes to sinusitis.

Otitis media:

A recent prospective non-randomized study by Crapko et al. demonstrated that pepsin is present in 60% of middle ear effusion samples of children who underwent myringotomy for chronic otitis media with effusion (OME). A possible mechanism is reflux-induced nasopharyngeal inflammation and Eustachian tube dysfunction. Further investigation is underway to establish the relationship between LPR and otitis media in children.

Chronic cough:

Holinger and Sanders retrospectively studied 72 infants and children who had cough for at least 1 month and found that GER was present in 15% of the cases. However, there is no prospective data to date on the causal relationship between LPR and chronic cough.

Asthma:

Several studies have tried to demonstrate the relationship between asthma and GER. Debley et al. performed a cross-sectional study of 2397 adolescents and found that GER was eight times more prevalent in the asthma group than non-asthma group. The study also showed that morbidity associated with asthma, such as the number of visits to ER and clinic, is higher among those with GER. Reflux-induced bronchospasm and reduction of peak flow are possible mechanisms to explain the association.

Reflux-induced stridor:

In contrast to laryngomalacia, reflux-induced stridor is intermittent and not affected by change in position. Stridor might be a result of acid-induced laryngospasm or rapid breathing associated with esophageal irritation. Bouchard et al. reported 61 of 105 (58%) children presented with stridor and pH study-proven GERD; 83% of those improved with acid suppressive therapy. Flexible laryngoscopy is recommended to distinguish this condition from laryngomalacia.

Laryngomalacia:

Laryngomalacia is the most common cause of stridor in infants, who present with inspiratory stridor that worsens with crying or supine position. The prolapse of supraglottic structures during inspiration is thought to create negative pressure that induces upward flow of refluxate into the larynx. Incidence of GER in laryngomalacia has been reported to range from 50-80%. Direct laryngoscopy and bronchoscopy may be indicated in prolonged symptomatic cases because the incidence of a second synchronous lesion is reported to be 15-30%.

Subglottic stenosis:

Evidence linking reflux and subglottic stenosis is limited to animal studies and uncontrolled human studies. Numerous animal studies were able to demonstrate acid could induce ulceration, basilar hyperplasia, and edema of the subglottic mucosa. Yellon et al. reported that 80% of 26 children who underwent laryngotracheal reconstruction were diagnosed of GER either by barium esophagram, pH monitoring, nuclear scintiscan, or esophageal biopsy.

Diagnosis:

Because of its intermittent pattern, the diagnosis of LPR in children is often difficult. Given the limitations of the diagnostic tests discussed below, it remains controversial which test is optimal for detecting LPR.

Barium esophagram:

It is used frequently to diagnose associated anatomical anomalies such as web and stricture. However, its poor sensitivity (20-60%) as a result of short sampling time makes it less useful for diagnosing LPR.

Nuclear scintigraphy:

It has the advantage of detecting aspiration, non-acidic reflux episodes, and gastric emptying. Like barium esophagram, it only has a short sampling time and sensitivity is low (15-59 %). In addition, the correlation of scintigraphy with pH monitoring is poor.

Direct Laryngoscopy and bronchoscopy (DLB):

There is limited data evaluating DLB as a diagnostic tool in pediatric LPR. Carr et al. reported a prospective uncontrolled trial on 77 children who underwent DLB for complete airway evaluation. Endoscopic examination was graded based on laryngeal (eg. post-glottic edema, arytenoid edema) and cricotracheal (eg. cobblestoning, blunting of carina) findings. Those diagnosed with GERD were found to have significantly higher scores than those without GERD.

The subjective nature of DLB in diagnosing LPR was evaluated in Branski's prospective randomized trial. 120 adult stroboscopic findings were graded by 5 otolaryngologists based on criteria such as edema, erythema, and pachydermia of the larynx. The study found that both inter-rater and intra-rater reliability were poor especially in arytenoids measurements. In another study, McMurray et al. also found a poor correlation between laryngoscopic findings and pH probe.

24-hour pH monitoring:

Considered the gold standard for diagnosing GER, it is one of the most commonly used techniques to document LPR. The double probe (pharyngeal, esophageal) design allows for simultaneous detection of pH change in both the hypopharynx and esophagus. Manometry has been used in the past to confirm positioning of the distal probe, which is usually 3-5 cm above the lower esophageal sphincter. Ulualp et al. recently reported a new technique using flexible laryngoscopy to guide the placement of the dual-probe.

The criteria for what constitutes a reflux episode are not standardized but usually require 1) a decrease in pH below 4 and 2) pharyngeal event following an esophageal event. The total amount of time of acid exposure in 24 hours has also been suggested as a useful criterion.

There are several limitations regarding the use of pH monitoring for LPR. It is invasive, time consuming, and generally not well tolerated by children. Brief, non-acidic, and gaseous reflux episodes might be missed by this technique. In addition, the criteria for a significant LPR

episode are not well defined and vary among studies. Furthermore, pharyngeal reflux events do not correlate well with symptoms of laryngitis, as Joniau et al. pointed out in an adult study.

Multichannel Intraluminal Impedance (MII) Monitoring:

This technique measures the change in impedance between two electrodes during the passage of food bolus. Impedance, a measure of electrical resistance, decreases as bolus passes through measuring segments. It has the advantage of measuring the direction and speed of bolus, as well as detecting non-acidic and gaseous reflux episodes. Although there is no study to date using MII to diagnose pediatric LPR, preliminary results on GER are encouraging. Rosen et al. compared MII and pH monitoring in 50 children and found that sensitivity of MII (80%) is significantly higher than pH monitoring (47%) in the group treated with proton pump inhibitor.

Conclusions:

Manifestation and diagnosis of pediatric laryngopharyngeal reflux remain controversial. Despite increasing effort to establish an association between reflux and otolaryngological manifestations, conclusive evidence is lacking. In addition, well-designed controlled studies are needed to evaluate the optimal diagnostic tool for pediatric LPR.

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