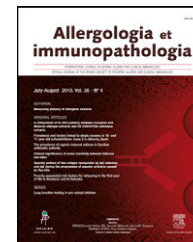




# Allergologia et immunopathologia

www.elsevier.es/ai



## EDITORIAL

### What can be expected from laryngoscopy in the study of laryngopharyngeal reflux?

In 1968, Cherry and Margulies provided the first description of a possible relationship between laryngeal disorders and gastro-oesophageal reflux disease (GERD), with the publication of three cases of laryngeal granulomas associated to reflux oesophagitis.<sup>1</sup> At present, GERD has become one of the most prevalent disorders, affecting an estimated 22% of the paediatric population,<sup>2</sup> although it is difficult to obtain reliable epidemiological data, due to the variability of the signs and symptoms, and the diagnostic difficulties involved.<sup>1</sup>

When reflux extends beyond the oesophagus, producing symptoms and tissue damage, the condition is referred to as laryngopharyngeal reflux (LPR). According to some authors, LPR and GERD are different disease conditions. The anatomical proximity between the larynx and oesophagus determines the development of airway disorders secondary to reflux. The larynx and trachea are very sensitive to acid from the stomach, and animal models have shown that acid exposure for 1 min a day during 8 days can turn a minor tracheal problem into subglottic stenosis.<sup>3</sup>

It has been suggested that over 40% of all children with GERD have associated respiratory symptoms.<sup>2</sup> The classical manifestations of GERD are heartburn, regurgitation and dyspepsia. The most frequent symptoms of LPR, in turn, comprise clearing of the throat; frequent coughing, globus; foreign body sensation; and hoarseness, among other manifestations, and the respiratory symptoms are often not associated to digestive manifestations.

The consequences of LPR are less predictable than those of GERD, and in the paediatric population include airway disorders, such as aspiration pneumonia, asthma attacks, bronchitis, apnoea, apparent life-threatening events (ALTE), chronic cough, stridor, croup, laryngitis, sinusitis, snoring, globus, dental erosions and recurrent otitis media. In some patients, a relationship has been established between GERD and chronic disorders such as cystic fibrosis and bronchopulmonary dysplasia.<sup>2,4,5</sup> It is important to mention that in a considerable number of cases GERD is a silent disease and

may give rise to inflammatory or neoplastic processes of the upper airway.<sup>6</sup>

It is not easy to demonstrate the cause-effect relationship between such signs or symptoms and GERD. Indeed, the existence of a relationship has not yet been firmly established, since some studies report a clear coexistence and possible association between the two conditions, few have demonstrated convincing causality.<sup>2,4-6</sup> The lack of consensus regarding GERD-LPR extends to different inter-dependent areas of knowledge: clinical manifestations, diagnostic tests, interpretation of the results, and treatment.<sup>7</sup>

There have been three main approaches to the study of the influence of LPR upon respiratory disease: the evaluation of suggestive symptoms, oesophageal pH monitoring, and laryngoscopy. The sensitivity and specificity of the diagnosis based only on the signs and symptoms is low, but improves in adults when using questionnaires such as the reflux symptom index (RSI), which have not been validated in children.<sup>7-9</sup> While studies based on the monitoring of oesophageal pH are currently regarded as the gold standard, they have many limitations – including differences in interpretation of the pharyngeal reflux episodes, a lack of consensus on the normality values, and variability in the diagnostic criteria used (definition of reflux, and the number and duration of its episodes). Likewise, alkaline and gas reflux are not adequately evaluated. The diagnostic roles of other techniques such as the oesophagogram, scintigraphy or impedanciometry have not been fully established.<sup>7</sup>

On the basis of the above, direct laryngoscopic evaluation of the laryngeal damage produced by GERD appears as an interesting exploratory option, although it also has important limitations. Several retrospective and prospective studies have described characteristic findings of the airways in paediatric patients with GERD or LPR. Such endoscopic data, often associated to chronic inflammation, include oedema and erythema of the arytenoid cartilages, the

inter-arytenoid zone and posterior glottic region, inter-arytenoid mucosal redundancy or pachyderma, laryngomalacia, and inflammatory changes of the vocal cords, subglottic stenosis or stricture, cobble stoning of the tracheal mucosa, and carinal flattening.

A survey of ear, nose and throat specialists found that 74% based the diagnosis of LPR mainly on the clinical signs and symptoms—particularly globus, clearing of the throat, and laryngeal erythema and oedema. However, these signs and symptoms represent the least specific markers of reflux.<sup>10</sup> Furthermore, such manifestations are more suspected when a flexible rather than a rigid laryngoscope is used – suggesting that the former is more sensitive but less specific in identifying laryngeal irritation. On the other hand, the symptoms and endoscopic findings are scantily correlated, and the lack of treatment response in patients with laryngitis associated to reflux could be due to the lack of specificity of the laryngeal signs in diagnosing LPR. Another problem in the diagnosis of LPR is the fact that laryngeal examination is subjective and is dependent upon the experience of the examiner in identifying the laryngeal signs. Likewise, inter- and intraobserver agreement over the laryngoscopic findings is poor, as evidenced by a study in which different ear, nose and throat specialists scored the laryngeal images of 120 patients.<sup>11</sup>

A recent meta-analysis has evaluated the correlation between the laryngoscopic findings in LPR and GERD among the paediatric population. An association has been found between six endoscopic findings of the airway and the presence of GERD. Specifically, arytenoid cartilage erythema and oedema were correlated to GERD with a relative risk (RR) of 2.46, i.e., children with arytenoid cartilage erythema and oedema are 2.5 times more likely to have GERD than the general population. Lingual tonsillar hypertrophy in turn presented an RR of 2.24, posterior glottic erythema and oedema exhibited an RR of 3.19, subglottic stenosis had an RR of 2.5, and tracheal oedema exhibited an RR of 1.86. The closest correlation was seen to correspond to the presence of nodules and oedema of the vocal cords (RR = 12.15).

The analysis also revealed the probability of suffering GERD with each of the endoscopic findings: patients with supraglottic and epiglottic collapse had a 67% probability of suffering GERD, versus 70% in those with erythema and oedema of the posterior glottic wall, 65% in those with subglottic stenosis, and 88% in the subjects with oedema and/or nodules of the vocal cords. The patients with four findings had a probability of over 70% of suffering GERD.<sup>2</sup>

In a retrospective review of children with respiratory symptoms and suspected reflux subjected to laryngoscopy and bronchoscopy, Carr concluded that these techniques can offer information with a strong positive predictive value referred to the presence of GERD. The combination of oedema of the posterior glottis, the arytenoid cartilages and vocal cords afforded the best sensitivity (75%) and specificity (67%). The combination of oedema of the posterior glottis and vocal cords in turn yielded a positive predictive value of 100%.<sup>3</sup>

Yellon et al. described a correlation between certain endoscopic findings of the airway and GERD, including laryngomalacia, subglottic stenosis and oedema and erythema of the posterior glottic region. Likewise, a correlation was

found between cough, stridor, asthma and croup, and the presence of GERD.<sup>2</sup>

In cases where the mentioned endoscopic findings are made, these correlations point to the need for aggressive management of the reflux, with a view to reducing the symptoms, airway findings and the possible requirement of surgical treatment of GERD.

In the current issue of *Allergologia et Immunopathologia*, the study by Ozmen et al. describes results similar to those found in the literature, and reflects the same problems referred to the correlation of airway signs and symptoms to LPR/GERD, the diagnosis of GERD, and the type of study design involved (retrospective, small sample size), etc.<sup>12</sup> Thus, although different options are available for diagnosing LPR, none of them are definitive. Consequently, a careful selection of study techniques is required after initial evaluation. Although there is still insufficient evidence, a combined approach based on suggestive clinical manifestations and laryngoscopy can be used in certain cases to indicate medical treatment. If the response proves insufficient, then other supporting techniques such as pH studies should be used. In any case, further studies with improved methodological designs are needed to definitively establish the causal relationship between LPR and the airway symptoms, and to define the role of laryngoscopy in the diagnostic algorithm of LPR.

## References

1. Santos VJ, Comes GT, Gonçalves TM, Carvalho Mde A, Weber SA. Prevalence of bronchopulmonary and otorhinolaryngologic symptoms in children under investigation for gastroesophageal reflux disease: retrospective analysis. *Braz J Otorhinolaryngol.* 2011;77:328–33.
2. May JG, Shah P, Lemonnier L, Bhatti G, Koscica J, Coticchia JM. Systematic review of endoscopic airway findings in children with gastroesophageal reflux disease. *Ann Otol Rhinol Laryngol.* 2011;120:116–22.
3. Carr MM, Nguyen A, Poje C, Pizzuto M, Nagy M, Brodsky L. Correlation of findings on direct laryngoscopy and bronchoscopy with presence of extraesophageal reflux disease. *Laryngoscope.* 2000;110:1560–2.
4. Michail S. Gastroesophageal reflux. *Pediatr Rev.* 2007;28:101–10.
5. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope.* 1991;101 Suppl. 53:1–78.
6. Wong RK, Hanson DG, Waring PJ, Shaw G. ENT manifestations of gastroesophageal reflux. *Am J Gastroenterol.* 2000;95 Suppl.:S15–22.
7. Stavroulaki P. Diagnostic and management problems of laryngopharyngeal reflux disease in children. *Int J Pediatr Otorhinolaryngol.* 2006;70:579–90.
8. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice.* 2002;16:274–7.
9. Bach KK, McGuirt Jr WF, Postma GN. Pediatric laryngopharyngeal reflux. *Ear Nose Throat J.* 2002;81 Suppl. 2:27–31.
10. Ahmed TF, Khandwala F, Abelson TI, Hicks DM, Richter JE, Milstein C, et al. Chronic laryngitis associated with gastroesophageal reflux: prospective assessment of

- differences in practice patterns between gastroenterologists and ENT physicians. *Am J Gastroenterol.* 2006;101:470–8.
11. Farrokhi F, Vaezi MF. Laryngeal disorders in patients with gastroesophageal reflux disease. *Minerva Gastroenterol Dietol.* 2007;53:181–7.
  12. Ozmen S, Demirceken F, Barut Y, Dibek Misirlioglu E. Role of laryngoscopy in children with respiratory complaints and suspected reflux. *Allergol Immunopathol (Madr).* 2012;40:204–9.

J. Figuerola Mulet\*, B. Osona Rodriguez de Torres  
*Hospital Universitari Son Espases, Servicio de Pediatría,  
Unidad de Neumología y Alergia Pediátrica, Palma de  
Mallorca, Spain*

\* Corresponding author.

*E-mail address:* [joan.figuerola@ssib.es](mailto:joan.figuerola@ssib.es) (J. Figuerola Mulet).