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Editorial

Combined Multichannel Intraluminal Impedance and pH Monitoring for Patients With Suspected Laryngopharyngeal Reflux: Is It Ready to Use?

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Article: Combined dual channel impedance/pH-metry in patients with suspected laryngopharyngeal reflux **(J Neurogastroenterol Motil 2010;16:157-165)**

In the recently established Montréal definition, gastroesophageal reflux disease (GERD) can be classified into esophageal and extra-esophageal syndromes based on the clinical manifestations including symptomatology and structural damage.[1] Laryngopharyngeal reflux (LPR) is the most extensively investigated extra-esophageal syndromes with established associations. LPR is defined as the reflux of gastric content into larynx and pharynx. It may be manifested as laryngeal symptoms such as cough, sore throat, hoarseness, and globus as well as signs of laryngeal irritation on laryngoscopy.[2] However, the diagnosis of LPR is challenging. The laryngeal symptoms and signs of LPR are generally non-specific and a pathonomonic laryngoscopic sign is lacking. As a result, the role of GERD as cause of laryngeal symptoms and signs has been poorly defined. Despite the recommendation of high dose proton pump inhibitor (PPI) as empirical treatment for patients with suspected LPR, most placebo-controlled trials using laryngeal symptoms as outcome measures have failed to demonstrate any therapeutic benefit of PPIs.[3] Therefore, there is a need for a more accurate definition based on objective measurements.

Ambulatory dual channel esophageal pH monitoring, with pH probe positioned at both distal and proximal esophagus, has been utilized for investigation of suspected LPR in the past 2 decades. Unfortunately, most laryngeal symptoms are persistent rather than episodic in nature. Hence, it is difficult to discern the chronological relationship between reflux and symptoms. Moreover, the presence of abnormal acid reflux detected on pH monitoring is poorly predictive of the response to therapy.[4] In the past 10 years, esophageal pH monitoring has been superseded by multichannel intraluminal impedance and pH (MII-pH) monitoring, which becomes the preferred investigation for GERD patients, particularly with poor response to PPI. Combined MII-pH monitoring allows characterization of reflux episodes in liquid, gas or mixed forms and hence both acid and non-acidic reflux episodes can be detected.[5] It has at least 2 potential advantages over conventional pH monitoring. First, it allows more accurate evaluation of the chronological association between reflux episodes and laryngeal symptoms. Second, it helps determine the

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proximal extent of the refluxate. It has been reported that the proximal extent of reflux, rather than non-acidic reflux, is associated with globus symptom in patients with heartburn.[6]

In the current issue of the Journal, Lee et al. studied the diagnostic value of combined MII and dual channel pH monitoring in patients with laryngeal symptoms who were off-PPI. In this study, addition of MII to standard pH monitoring increased 2-fold of the diagnostic yield for detecting gastroesophageal reflux. It has also been observed that combined MII and dual channel pH monitoring has approximately 10% (49% vs. 38%) diagnostic gain over combined MII and single channel pH monitoring. Half of the patients with pathological GERD had non-acidic reflux.

This study evaluated consecutive patients in a prospective manner and all of them underwent MII-pH monitoring while they were not taking PPI. This study design avoids recruitment bias and allows more accurate evaluation of the genuine role of both acidic and non-acidic gastroesophageal reflux in the development of the laryngeal symptoms. The findings of this study further support the high diagnostic value of combined MII-pH monitoring for GERD in patients with laryngeal symptoms. While MII substantially increased the sensitivity of diagnosis of GERD, it is intriguing to note that there is still a role of adding proximal esophageal pH monitoring as an adjunct. This is probably because proximal pH monitoring allows more straightforward and therefore more sensitive detection of acidic reflux episodes, which may not be readily detected by impedance monitoring due to technical limitations such as reliability of software and experience of interpretation.

While combined MII-pH monitoring undoubtedly increases the sensitivity of detection of gastroesophageal reflux, there are still unresolved issues that have not been addressed in this study. First, the prior use of PPI among the study patients was not clearly defined and the relative proportions of PPI-naïve patients, PPI responders and PPI non-responders were unknown in this study. The relative merits of combined MII and dual pH monitoring for investigation of LPR in each subgroup of patients remain unclear. Second, the higher detection rate of gastroesophageal reflux has not been translated to higher predictive value of good response to anti-reflux treatment such as PPI or anti-reflux surgery. It is still unclear whether combined MII-pH monitoring enables better selection of patients for anti-reflux treatment. A randomized controlled trial is therefore necessary to determine the discriminative power of combined MII-pH monitoring in selection of treatment responders. Lastly, the role of weakly acidic reflux, which is defined as reflux episodes associated with pH drop of $>$ 1 in the pH range above 4, has not been evaluated. It is still unclear whether weakly acidic reflux plays different role in the development of LPR compared to non-acidic reflux.

In conclusion, further studies are still needed to clearly define the clinical application of combined MII-pH monitoring in patients with suspected LPR. The future directions of development and research of combined MII-pH monitoring in LPR should focus on minimization of artifacts, robust methodology of data interpretation, refined definitions of different forms of LPR and accurate selection of patients who will respond to anti-reflux treatment.

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