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Editorial

Multichannel intraluminal impedance associated with pH-metry in the study of gastroesophageal reflux disease

In the paper by de la Morena et al. (1) some of the contributions of multichannel intraluminal impedance associated with pH-metry (MII-pH) to the study of gastroesophageal reflux disease (GERD) are discussed, and MII-pH is ultimately considered the gold standard for GERD investigation. This editorial describes some limitations of this technique, which reduce its usefulness and advice "prudence" in assessing it.

In medicine, examination methods based on impedance measurement have been long in use to provide non-invasive monitoring for various organs. This technique is based on the measurement of changes in resistance to electricity between two electrodes, which emerge as a result of functional or structural modifications in the examined organ. In gastroenterology, initial applications included intestinal contraction monitoring (2) and gastric emptying investigation (3,4).

Initial esophageal pathophysiology studies with this technique were carried out by Silny more than fifteen years ago (5). Since then relevant advances have been made both in equipment development and record pattern recognition.

Current procedures use a thin (around 2 mm in diameter) catheter containing several ring-shaped electrode pairs, which are placed on the surface and collect information at various levels. The distance between electrodes in each pair is 2 cm, and the separation between electrode pairs varies according to esophageal length (children or adults). A weak electric current is applied to one electrode, and the resistance to the resulting electric flow towards the other electrode is recorded. Changes in intraesophageal impedance recorded by measuring electric conductivity (multichannel intraluminal impedance –MII) identify various intraluminal events, including the composition of esophageal contents (air, fluid, mixed) and their direction –anterograde transit of swallowed substances or retrograde passage of refluxed material.

The information provided by MII therefore complements manometry and pH-metry. That is why combination studies are usually performed with these techniques. When used in conjunction with manometry information on contractile activity and bolus progression within the esophagus is obtained. Combined with pH-metry it identifies reflux composition, distribution, and clearance, and tells fluid (regardless of pH), gaseous, and mixed refluxes apart (6).

An analysis of all these factors with data from pH-metry has led some authors to categorize up to 11 different types of reflux episodes (7), which are commonly narrowed down to three –acid (pH < 4), weakly acid (pH > 4 to < 7), and non-acid (with no changes in pH) reflux episodes.

The introduction of MII-pH evidently represents new possibilities in the study of GERD. It is the most accurate and detailed method for the detection of reflux of any

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type (8). However, MII studies still have significant limitations that should be considered regarding their indication and analysis.

As regards indications it must be pointed out that, while marked differences exist in absolute impedance value according to the presence of intraesophageal contents and their fluid or gaseous nature, what this technique assesses are changes from baseline, in such a manner that reference impedance is very low, with almost a flat baseline, in patients with histological esophageal mucosal changes (severe esophagitis, Barrett's esophagus) and/or severe motility disturbances interfering with esophageal transit or clearance, and hence resulting in esophageal fluid retention. This complicates MII-pH analyses and on occasion renders interpretation impossible (9).

On the other hand, MII-pH studies in untreated patients have shown that approximately one third of all reflux episodes are weakly acidic (10), and that these may also induce heartburn and regurgitation (11). However, weakly acid reflux in patients on no acid secretion inhibitors seems to be only responsible for a minority of symptoms (12). Therefore, the technique's impact and cost-benefit ratio have not proven truly favorable in this group of patients, where some studies suggests that MII-pH may identify a considerably higher number of patients with reflux-induced symptoms (7).

This technique is particularly indicated for GER detection and grading in: a) Patients on acid secretion inhibitors with persistent symptoms; b) Patients with symptoms primarily during the postprandial period and/or frequent meals, as is the case with newborns, infants, etc.; c) Patients with laryngeal-pharyngeal or respiratory symptoms (microaspiration) (13,14); and d) Patients with scarce or absent acid production (atrophic gastritis, gastrectomy). Regarding gastrectomy, its value remains to be demonstrated when bile reflux is suspected. Thus the few studies simultaneously performed with Bilitec® suggest that non-acid reflux (as defined with MII-pH) and bile reflux (as defined with spectrophotometry records using Bilitec®) are not equivalent, and therefore both diagnostic tests are required for a correct diagnosis (15).

As regards analysis limitations, the first question to consider is that automatic analysis software is insufficiently reliable and usually overestimates non-acid reflux events (16-18). It is therefore essential that an additional visual analysis be performed by experienced personnel in order to prevent false positive results, which inevitably entails a subjective component (19) and increased costs.

A strength of MII is the technique's higher ability to establish a potential association between symptoms and reflux. To establish such an association whether a reflux event is symptomatic or otherwise should be initially determined. Events considered symptomatic are those where symptoms occur within a given timeframe after reflux onset. It is here that an early challenge arises –what time interval is most adequate? While some authors consider 2 minutes (7,20) as most adequate, others suggest 5 minutes (21). Obviously, the longer the time lapses, the higher the possibilities that symptoms may be related to reflux events.

Finally, the best mathematical formula to ascertain a potential relationship between symptoms and reflux is not clear. Most commonly used formulas include: Symptom index (SI), symptom sensitivity index (SSI), and symptom association probability (SAP) (7,22). All of these have their advantages and disadvantages, and are therefore not ideal (22l). SI is most used; its main fault is its not taking the total number of reflux episodes into account. The greater the number of events considered reflux episodes, the higher the possibility that a symptom develops by chance

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within 2-5 minutes. Similarly, SSI does not take the number of symptom episodes into account, and a high number of symptom episodes is likely to result in a high index. The advantage of SAP is its taking all relevant factors into account; however, as a disadvantage, this parameter is difficult to estimate manually, and has an arbitrary statistical value according to some authors (22).

A primary contribution of MII-pH is no doubt its ability to demonstrate an absent relation between symptoms and reflux. This negative relationship aspect is much more relevant than at first thought, as in more than half of patients with persistent symptoms despite therapy reflux is seen to bear no responsibility (7,21), as is also the case with the patient reported by de la Morena et al. in this issue of *Revista Española de Enfermedades Digestivas* (1). In such a case, the final conclusion will not differ from that reached regarding conventional pH-metry, but demonstrating that symptoms bear no relation to reflux episodes regardless of pH will no doubt enhance certainty in considering a result really negative, and encourage the search for an alternative diagnosis as the cause of symptoms.

MII associated with manometry and/or pH-metry will certainly contribute to gain a deeper insight into esophageal pathophysiology, and to better diagnose our patients. We agree with Connor and Ritcher (22) in considering that the technique's current status allows to exclude reflux as a cause for symptoms with a high probability level, but also demands caution in assessing clinical significance and potential causality as determined by a positive score in the symptoms-reflux episodes relationship.

The fast spreading of this technique during the past few years will be a strong stimulus for criteria and definition unification among research teams, the establishment of normal values from extensive control groups, the performance of cost-benefit studies, the solving of record interpretation and analysis difficulties, and a definition of better indication profiles, thus putting this technique in its due place.

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