Multichannel Intraluminal Impedance and pH-Metry for Investigation of Symptomatic Gastroesophageal Reflux Disease

J. Weigt K. Mönkemüller U. Peitz P. Malfertheiner

Department of Gastroenterology, Hepatology and Infectious Diseases, Otto von Guericke University Magdeburg, Magdeburg, Germany

Key Words

Multichannel intraluminal impedance • MII-pH • Impedance • Reflux monitoring • Nonacid reflux • Reflux disease questionnaire • Gastroesophageal reflux disease

Abstract

Background: Combined multichannel intraluminal impedance and pH-metry (MII-pH) is a technique that enables monitoring of gastroesophageal reflux independent of its acidity. **Aim:** To investigate the utility of MII-pH in the clinical investigation of patients with gastroesophageal reflux disease (GERD) symptoms. **Methods:** 32 consecutive patients underwent 24-hour ambulatory MII-pH. 16 patients were on PPI (PPI⁺) therapy and 16 were taking no acid-suppressive medication (PPI⁻). We investigated the pattern of reflux by means of acid and nonacid reflux and the relation to typical and atypical symptoms. In addition, we investigated the symptom association by using the symptom index. **Results:** Symptom-related acid reflux was higher in the PPI⁺ group (33 vs. 25%) and symptom-related nonacid reflux was higher in the PPI⁻ group (36 vs. 21%). The association between type of symptoms and the association to reflux is highly significant ($p < 0.001$) in the PPI⁻ group. In this group the association of acid reflux is more likely to correlate with typical symptoms and the association of nonacid reflux is more like-

ly to be associated with atypical symptoms. **Conclusions:** These data show that nonacid reflux can be associated with symptoms in patients with GERD symptoms. The diagnostic value of MII-pH is independent of PPI therapy.

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Introduction

Combined multichannel intraluminal impedance and pH-metry (MII-pH) is a technique that enables monitoring of gastroesophageal reflux independent of its acidity, and therefore is suitable for investigation of symptomatic patients on and off PPI therapy [1]. MII-pH detects the presence of a bolus by means of changes in the conduction between electrodes placed in the esophagus [2]. Bolus contents as liquids and mixed contents have a low impedance, whereas gas contents have a higher impedance than the threshold in the esophagus. By using several pairs of electrodes, the detection of bolus movement is possible. The reflux is categorized as acid or nonacid by combination with pH-metry. A retrograde bolus movement with simultaneous decrease in esophageal pH would be categorized as an acid reflux. Without the pH fall the reflux episode would be a nonacid one [3]. The basic principles of this method are illustrated in figure 1.

Fig. 1. Basic technical issues of MII-pH. **a** Configuration of electrodes on the catheter. The pH electrode at 5 cm helps to classify the reflux as acid or nonacid. **b** Typical appearance of a wet swallow. The fall in intraluminal impedance is first detected orally and then propagates distally through the esophagus body towards the stomach (arrow). The initial increase of impedance [R] is due to swallowed air that encircles the bolus. **c** A reflux episode is plotted. The fall in intraluminal impedance is first detected in the very distal channel and then propagates orally. After reaching its maximum proximal extent, the bolus (refluxate) moves back (arrows) towards the stomach.

Recent studies showed that symptoms in patients with acid-suppressive therapy are often associated with non-acid reflux [4].

Aims

To investigate the utility of MII-pH in the clinical investigation of patients with symptoms of gastroesophageal reflux disease (GERD) and to compare patients taking PPI with patients without acid-suppressive medication.

Patients and Methods

Patients with GERD symptoms were investigated. Symptoms were defined as typical (heartburn, regurgitation and chest pain) and atypical (upper abdominal pain, coughing, sore throat, globus, pressure, burning of the tongue). PPI therapy was not stopped during the investigation. Patients presented after an overnight fasting period. Before MII-pH monitoring we performed esophageal manometry in each patient to rule out motility disorders and to label the distance between the lower esophageal sphincter (LES) and the nostril for defining the depth of insertion of the MII-pH probe. Immediately after the manometry the impedance catheter (Sandhill Scientific Inc.) was inserted. The pH electrode was placed 5 cm above the LES and the impedance channels were

located at 3, 5, 7, 9, 15 and 17 cm above the LES. Data were sampled stored in a portable recorder (Sleuth®, Sandhill Scientific Inc.). The patients were advised on the use of the recorder and instructed to keep a detailed diary report in addition to the electronic data sheet recording documenting body position, meal intake, medication and symptoms. The MII-pH recording lasted over a period of 24 h.

The data were analyzed using the BioView Analysis® program software tool from Sandhill Scientific Inc. In addition, all records were also analyzed manually to obtain the highest detection rate of reflux episodes. Meal periods were excluded from the analysis. The analysis of symptoms was made by relationship to reflux, either acid- or nonacid-related, all reflux-related and not related to any kind of reflux. We also used the symptom index (SI) as a classification of overall association of reflux symptoms. SI is defined as the percentage of symptom-associated reflux from all detected reflux episodes. A SI $\geq 50\%$ was defined as positive (SI+).

All patients were asked to perform the Reflux Disease Questionnaire (RDQ; German version) [5] on the day of MII-pH performance. This short questionnaire contains 12 items regarding heartburn and regurgitation as well as dyspepsia symptoms. A good correlation of RDQ score and presence of GERD has been shown [5].

Statistical Analysis

Data were analyzed using Microcal Origin® statistical software. For comparison of the symptoms and their association to reflux, the χ^2 test was used. $p < 0.05$ was considered to be significant.

Table 1. Findings and results of MII-pH in patients on PPI therapy (PPI⁺) and without PPI medication (PPI⁻)

	PPI ⁺	PPI ⁻
Mean acid exposure pH <4, %	7.35 ± 11.37	11.39 ± 17.92
Composite score >14.9 ¹	5/16	6/16
Mean acid clearance time, s	96.9 ± 92.6	118.3 ± 126.4
Mean bolus clearance time, s	15 ± 6	12.2 ± 4.6
Mean acid reflux episodes	40.3 ± 45.7	49.4 ± 60.3
Mean nonacid reflux episodes	84 ± 76.8	50.7 ± 35.4
Reported symptoms	560	698
Symptom correlation to acid reflux	33%	25%
Symptom correlation to nonacid reflux	21%	36%
Symptom index positive for atypical symptoms	63.2% (12/19)	33.3% (7/21)
Symptom index positive for typical symptoms	36.8% (7/19)	66.6% (14/21)

¹ Clinical definition of GERD.

Results

We investigated 32 patients (16 male, 16 female) with symptoms of reflux disease. Mean age was 53.5 years (range 19–74). 16 patients were on PPI therapy (PPI⁺) and 16 patients were not taking any acid-suppressive medication (PPI⁻). Detailed results of the MII-pH recordings are summarized in table 1. The mean study duration was 22 h 57 min (range from 17 h 02 min to 44 h 23 min).

A total of 3,591 reflux episodes were recorded. Reflux was more common in the upright position (3,014 episodes) than in the recumbent position (577 episodes). A total of 1,258 symptoms were reported (560 in the PPI⁺ group and 698 in the PPI group). While the overall relation of symptoms to reflux was comparable in both groups, the relation of symptoms to acid reflux was higher in the PPI⁺ group (33 vs. 25%) and the relation of symptoms to nonacid reflux was higher in the PPI⁻ group (36 vs. 21%). Regarding reflux acidity, there was more acid reflux in patients off PPI (49.4 episodes) than on PPI (40.3 episodes). Nonacid reflux is more common in patients taking PPI medication (mean 84 episodes) than without PPI (mean 50.7 episodes). A part of 67% of all reflux episodes in the PPI group had a nonacid content, while in the off PPI group the fraction of nonacid reflux was 51%. The number of reflux episodes that reach up to 15 cm above the LES were similar in both groups (on PPI 37; off PPI 33).

Discriminating the two groups of patients, there was no association between the type of symptom and the association to reflux in the PPI⁺ group. In the patients taking no PPI, the association between type of symptom and the association to reflux was highly significant ($p < 0.001$).

In the PPI⁻ group the association to reflux is more likely to show typical symptoms, whereas atypical symptoms are less associated to reflux. In the PPI⁺ group a positive SI was found more often in combination with atypical symptoms (13 times) than with typical symptoms (6 times). SI was more often positive regarding nonacid reflux (12 times) than acid reflux (4 times). In the PPI⁻ group a positive SI was found mostly in combination with typical symptoms (13 times; atypical 7 times). Regarding the acidity of reflux there was no difference.

Analysis whether the typical or atypical symptoms are associated to reflux (positive or negative SI) show that most reported symptoms have a positive SI (40 positive; 26 negative). In addition, there is a difference between typical SI⁺ and atypical SI⁺. On PPI the atypical SI⁺ rate is higher (12/19) than the typical SI⁺ rate (7/19). Off PPI a reverse ratio shows with an atypical SI⁺ rate of 7/21 and a typical SI⁺ rate of 14/21 (table 1).

Questionnaires

Of the 32 questionnaires, 6 were not filled out completely. They were excluded from further analysis (PPI⁺ = 2; PPI⁻ = 4). There were no statistical differences in RDQ score between the PPI⁺ and PPI⁻ group. This was also for analysis of subgroups, made with regard to either positive or negative SI to either typical or atypical symptoms. The mean RDQ score in the PPI⁺ group was 17.8 ± 10.4 (0–33) and in the PPI⁻ group 20.1 ± 9.7 (0–34). The patients with the lowest RDQ score (0 respectively in both groups) both did not have a pathologic DeMeester score and both had a negative SI.

Discussion

MII-pH appears to be a useful tool to investigate patients with symptoms of GERD on and off PPI therapy. These data show the important role of nonacid reflux in patients with GERD symptoms. We found that the discrimination between typical and atypical symptoms and their association to reflux was higher in patients taking no PPI medication. Nonacid reflux was mostly associated with atypical symptoms and acid reflux was more frequently associated to typical symptoms. Our results are in agreement with the data from a recent multicenter trial [1]. The data of this trial underline the association of atypical symptoms to nonacid reflux.

Patients without a pathologic DeMeester score would usually be categorized as 'no reflux disease'. Our data show that even in these patients there was correlation of symptoms to either acid or nonacid reflux. That underlines the use of MII-pH in patients that were uninvestigated before.

There are limitations to MII-pH. Normal values for all parameters acquired during MII-pH are not established. There are significant interindividual differences in nonacid reflux that depend on the individual him/herself. Eating and drinking behavior may have a certain influence on reflux and surely on reflux content. The likelihood of symptom association to reflux episodes is not well expressed with the SI. There are other modalities like the symptom association probability (SAP), which should

minimize these limitations [6]. Recent investigations found restrictions also for the SAP if patients report rarely or too frequent about their symptoms [7].

The exact composition of nonacid reflux contents cannot be investigated. MII-pH can only determine whether the reflux contents are liquid, gas or solid. Other modalities like the Bilitec system are able to detect bile reflux [6, 7], therefore we believe that a combination of MII-pH and Bilitec would be useful to further investigate the type of gastric refluxates in the esophagus.

Although PPI therapy clearly decreases the esophageal acid exposure, it is already known that PPI therapy has no impact on reflux frequency [8]. In our study the impact on PPI on reflux frequency could not be studied due to study design. There was no difference in RDQ score between patients taking PPI and those without acid-suppressive medication. The RDQ score was independent of acid and nonacid reflux and its correlation to symptoms (SI). In the evaluation of the original RDQ, the presence of nonacid reflux causing symptoms was not considered. The results of this study support the feasibility of the RDQ to acquire information about symptomatic reflux independent of its acidity.

Summarizing, MII-pH is a useful tool to investigate patients with symptoms of GERD on and off PPI therapy. Furthermore, MII-pH provides the opportunity to investigate additional mechanisms of GERD that can potentially lead to new strategies for treatment.

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