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ORIGINAL ARTICLE

Findings of impedance pH-monitoring in patients with atypical gastroesophageal reflux symptoms

Mojgan Forootan[1], Maryam Ardeshiri[2], Nahid Etemadi[1], Nakisa Maghsoodi[1], Sara Poorsaadati[1]

[1] *Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2] *Shaheed Rajaei Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran*

ABSTRACT

Aim: This study was designed to investigate about findings of impedance pH-monitoring in patients with atypical symptoms of GERD.

Background: The routine treatment with proton pump inhibitors is not very effective in patients with atypical symptoms of Gastroesophageal Reflux Disease (GERD). It may be due to non-acid reflux, which cannot be monitored using common methods such as pH-metry. Therefore, in these patients combinational procedure of multi-channel intraluminal impedance and pH-monitoring has been suggested as a new approach.

Patients and methods: Sixty patients with atypical symptoms of GERD underwent combined impedance pH-monitoring. pH of reflux episodes, type of material refluxant, bolus clearing time, proximal extension and symptoms association probability (SAP) was recorded for each patient.

Results: Globus sensation was reported as the most common atypical symptom. 95% of patients experienced weakly acid reflux. Mixed and pure gas refluxates were more frequent than pure liquid reflux. Bolus clearing time was pathologic in 36.7% of cases and proximal extension was detected in 43 patients (71.7%). Of the 46 symptomatic patients, 33.3% had a positive SAP and 43.3% had a negative SAP.

Conclusion: The findings of current study showed that the combinational procedure of MII and pH monitoring could provide important information for resistant to treatment of patients' with atypical GERD symptoms.

Keywords: Gastroesophageal reflux disease, Impedance monitoring, pH-metry.

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Introduction

Gastroesophageal reflux disease (GERD) is a prevalent disease with ever-increasing incidence rate (1, 2). Burning the chest pain behind breast stone (also known as heartburn) and acid regurgitation are the typical symptoms of GERD (3). However, GERD has also atypical and unusual symptoms such as chronic cough, hoarseness and globus sensation due to the reflux of stomach contents into the esophagus with the prevalence of 11%, 23% and 14%, respectively(3-5).

The routine treatment with proton pump inhibitors (PPIs) with twice the standard dose or standard dose for 6-8 weeks in patients with atypical symptoms is not very effective (5). Patients with persistent symptoms unresponsive to PPIs are examined with pH-metry (4). The normal pH test means the normal esophagus for exposure

Received: 7 May 2013 *Accepted*: 17 July 2013
Reprint or Correspondence: Mojgan Forootan, MD.
Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences, Iran
E-mail: mfrootan2003@yahoo.com

to acid. However, a normal pH test following the treatment cannot explain, "why the patients are symptomatic despite the treatment" (2, 6). Thus, in patients with a normal test, the question arises whether the persistent symptoms could be due to non-acid reflux (NAR) which cannot be monitored using common methods such as pH-metry (5, 7, 8).

Therefore, in patients with persistent and atypical symptoms, a new diagnostic approach has been suggested based on the combinational procedure of multi-channel intraluminal impedance (MII) and pH monitoring (2, 9, 10). The proposed method is able to detect reflux by impedance and determine its acidity by pH-metry as well (1). This method has the ability to diagnose reflux episodes independent of the pH of the refluxate by changes produced by bolus presence in the esophagus and categorizes it as acid or non-acid. Using combined MII-pH in patients with ongoing symptoms on PPIs, in contrast with conventional pH, offers a more complete evaluation of the relationship between symptoms and gastroesophageal reflux(5).

Since there are no accurate studies on the effectiveness of this combinational diagnostic approach, several studies in western countries report the usefulness of MII-pH monitoring in GERD patients (6). The objective of the present study is to investigate about findings of MII in patients with atypical symptoms of GERD.

Patients and Methods

In this cross-sectional study, GERD was assessed using ambulatory 24-h impedance-pH measurements in 60 patients with atypical symptoms of GERD. These patients referred to the manometry ward of Taleghani hospital in Tehran, capital of Iran that is a referral center for gastroenterology diseases. Patients with refractory GERD (patients who were unresponsive to single or twice daily PPI treatment for at least one month) were included in this study. They all had atypical GERD symptoms. Atypical symptoms of GERD were considered as globus sensation, chronic cough and hoarseness. Exclusion criteria of this study were malignancy, age under 18 or higher than 80 years, any contraindication of catheter passing, any systemic disease, and PPI use in 14 past days, consumption of drugs that developed atypical symptoms of GERD and no consent to participation in the study.

Esophageal impedance-pH monitoring was performed using a digital ambulatory multi-channel intra-luminal impedance system (ΩMega, MMS, Enschede, The Netherlands). After at least 6 hours fasting; the pH recorder was calibrated using pH 4.0 and pH 7.0 buffer solutions for each patient. Then, under topical anesthesia the impedance pH catheter was passed transnasal and esophageal pH sensor was located 5cm above lower esophagus sphincter (LES). Intraluminal impedance was placed at 3, 5, 7, 9, 15 and 17cm above the LES. Patients were asked to maintain normal daily activities, sleep schedule and eat usual meals during the day. Also they were asked to record time of their meals, change in body position and the occurrence of any symptoms. Catheter was removed after 24 hours of recording data.

Reflux episodes were identified according to previously described criteria and categorized to three groups including acidic (pH<4), weakly acidic (pH 4-7), non-acid (pH>7) (11, 12). Liquid reflux was considered as a retrograde fifty percent decrease in impedance from baseline in at least two distal impedance sites (11). Gas reflux was identified as a rapid increase in impedance above 5000 Ω in at least two channels progressing distally to proximally (11). Mixed reflux (liquid–gas) was defined as gas reflux occurring simultaneously before or during a liquid reflux (11). Proximal migration of reflux episode was defined as extent of liquid reflux to impedance at 15 cm above the LES (6). Bolus clearance time

Table 1. Distribution of reflux events according to patients' position

	position					
	Normal N (%)	Upright N (%)	Supine N (%)	Upright/Total N (%)	Supine/Total N (%)	Upright/Supine/Total N (%)
Liquid	30(50)	0(0)	9(15)	6(10)	2(3.3)	13(21.7)
Gas	12(20)	1(1.7)	1(1.7)	8(13.3)	1(1.7)	37(61.7)
Mixed	6(10)	1(1.7)	1(1.7)	15(25)	2(3.3)	35(58.3)
Acid	31(51.7)	1(1.7)	8(13.3)	4(6.7)	2(3.3)	14(23.3)
Weakly acid	3(5)	0(0)	6(10)	12(20)	1(1.7)	38(63.3)
Non acid	45(75)	2(3.3)	0(0)	8(13.3)	0(0)	5(8.3)
BCT	38(63.3)	0(0)	11(18.3)	2(3.3)	3(5)	6(10)
Proximal extension	17(28.3)	0(0)	5(8.3)	1(1.7)	14(23.3)	23(38.3)

(BCT) of reflux at 5 cm above the LES was defined as the time from 50% impedance drop to 50% impedance recovery(6).

In the present study, pathologic MII was defined as occurrence of liquid reflux rather than 32 times/day or gas reflux >17times/day or mixed reflux >26 times/day. Also, BCT longer than 16 second/day or proximal extent rather than 17 times during 24 hours was considered as another component of pathologic MII. All reflux episodes were assessed in both upright and supine positions.

The symptom association probability (SAP) is a validate and simple method used to quantify the temporal relationships between symptoms and episodes of gastroesophageal reflux (13). It is assessed by 24-hour pH monitoring and can be calculated automatically by the MII system.

Data was presented as number and percentage. The computer software "SPSS.V.13" used for all calculations. $p<0.05$ was considered to be statistically significant.

Results

Of the 60 patients, 37 patients were male and 23 were female. The mean age of patients was 41.2±12.1. Globus sensation was reported as most common atypical symptom in individuals under study (40%, 24/60), followed by hoarseness (35%, 35/60) and chronic cough (25%, 15/60). Abnormal reflux parameters were detected by pH-metery in 66.7% of patients (40/60). 95% of patients (57/60) experienced weakly acid reflux. Also, acid reflux and non-acid reflux were recorded in 29 (48%) and 15 patients (25%), respectively. Mixed and pure gas refluxates were more frequent than pure liquid reflux, whereas almost 90% of the cases experienced mixed reflux, and pure gas reflux occurred at 80% of patients. BCT was pathologic in 36.7% of cases (22/60) and proximal extension was detected in 43 patients (71.7%). Of the 46 symptomatic patients, 20 (33.3%) had a positive SAP and 26 (43.3%) had a negative SAP. 10% of patients with positive SAP had acid, 45% weakly acid and 45% non-acid reflux events. Table 1 shows type of reflux, BCT and proximal extension according to patients' position.

Discussion

The results showed that the globus sensation was the common atypical symptom in patients. The majority of patients had mixed reflux with weakly acidity. In a study conducted by Devault (14), the hoarseness was the most common atypical symptom among patients (23.4%) and other symptoms such as globus sensation had less prevalence (14%).

In some studies, the most common atypical symptom was reported cough (1, 3, 4). The hoarseness and globus sensation were far from

coughing with similar ranges. The observed discrepancy in the prevalence of symptoms in these patients may be probably due to underlying cause of disease and the type of study design as well as the patients' referral to this center, which will vary the results.

Pathological BCT was found in 37% of cases. Accordingly, in cases with normal EGJ relaxation and morphology without pathological peristaltic contractions, normal BCT was observed. Therefore, the treatment of esophageal motor disorders may have a valuable role in improvement of atypical pathological BCT symptoms in gastroesophageal reflux (15). Given the most pathological BCT cases on the status of supine, the esophageal motor disorders are more likely in this situation. Moreover, the improvement of esophageal motor disorders may have a significant role in elimination of atypical symptoms of GERD in this group of patients.

In the present study, the most common refluxed material was mixed type and gas reflux was ranked second. Our results are consistent with the results of Ying L. Xiao et al (16, 17). In their study, the majority of patients had mixed reflux similar to the present study. However, the liquid reflux was found in 38% of cases (the second rank) and the gas reflux was observed only in 10% of cases.

The results of the present study showed that more than 90% of patients have reflux with low acid content. Acid and non-acid refluxes were put on the next ranks. These are not consistent with the results of other studies (5, 18). In a study conducted by Mainie et al, the non-acid reflux was the most common case (19). Further, research works with the same design and a larger sample size is needed for more accurate evaluation of these discrepancies.

In the SAP-negative patients, considering the normal values of pH in 67% cases, functional heartburn was diagnosed in 18 cases, while in the SAP-positive group, considering the normal range of pH, esophageal hypersensitivity was diagnosed in 8 patients. Perhaps the lower prevalence of acid might explain the less effect of PPI therapy on the improvement of atypical symptoms (5). Furthermore, in all three atypical symptoms, the refluxed material is weakly acid, which is the most common case in upright, supine and total situations. This perhaps indicates that life modification had no significant impact on improvement of these symptoms (6).

Small sample size and the lack of control group (healthy controls and patients with typical symptoms) are limitations that make it difficult to generalize the results.

Generally, it can be concluded that the combinational procedure of MII and pH monitoring could provide important information for resistant to treatment patients' with atypical GERD symptoms. These results could be used for treatment planning of patients with GERD. The treatment of weakly acid, gas reflux, functional heartburn, esophageal hypersensitivity and esophageal motility disorders may have a valuable role in improvement of the atypical symptoms. In patients with no proximal extension, the investigation of other causes of atypical symptoms is recommended (20). Studies for comparing the reflux patterns in patients with atypical symptoms in two groups of erosive and non-erosive esophagitis as well as multicenter case-control studies with larger sample size may reveal better reflux patterns in patients with atypical symptoms.

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