ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Reason For Inconsistency Between pH Monitoring and Impedance in Detecting Acid Gastroesophageal Reflux: pH-Only Events

Gastro Özofageal Asit Reflünün Saptanmasında İmpedans ve pHmetre Tetkikleri Arasındaki Uyumsuzluk Nedeni: pH-Only Olayları

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Abstract

Introduction: Acid reflux events detected by pH and not identified by impedance are called 'pH only events'. We aimed to explain the incidence and the possible reasons of 'pH– only events'.

Materials and Methods: The automated multichannel intraluminal impedance (MII) analysis in 50 cases was investigated. Changes in impedance channels during pH-only acid reflux events were examined and grouped. 1. Events that fail to meet the impedance measurement criteria 2. Events with no change in impedance channels 3. Events that meet the impedance criteria, but do not have signs of reflux 4. Artifact 5. Positive deflection due to air.

Results: The number of acid reflux events detected in the MII records was 1475, the number of acid reflux events detected in the pH meter was 3093, and the number of pH-only acid reflux events was 1736. 56.1% of the acid reflux events were detected by pH meter not identified by MII. The most common reasons for this were events no changes in impedance channels (68%) and other reasons such as positive deflection due to air (14%), and events that could not meet impedance measurement criteria (10%). 8% of pH-only events that met MII criteria, but were not accepted as reflux by MII.

Conclusions: There was more than half of acid reflux events detected by pH meter but not identified by MII. The reason of this situation has been not clear. For the correct decision, it is important to evaluate MII recordings together with pH meter results rather than evaluating automatic analysis alone.

Keywords
Multichannel intraluminal impedance, acid gastroesophageal reflux, pH-only events

Öz

Giriş: İmpedansda saptanmayıp sadece pH metrede görülen pH'nın 4'ün altında olduğu olaylar 'pH-only' olayları olarak adlandırılmıştır. Biz çalışmamızda 'pH-only' olaylarının nedenlerini araştırmayı amaçladık.

Gereç ve Yöntem: 50 hastanın çok kanallı intraluminal impedans otomatik kayıtları incelendi. pHonly asit reflü olayları sırasında impedansa kanallarındaki değişiklikler incelendi ve önceden yapılmış olan araştırmalardan da yararlanılarak gruplandırıldı. 1) İmpedans ölçüm kriterlerini karşılayamayan olaylar 2) İmpedans kanallarında değişiklik olmayan olaylar 3) İmpedans kriterlerini karşılayan ancak reflü işareti olmayan olaylar 4) Artefakt 5) Hava nedeniyle pozitif defleksiyon.

Bulgular: İmpedansta saptanan asit reflü olaylarının sayısı 1475, pH metrede saptanan asit reflü olaylarının sayısı 3093, 'pH-only' olaylarının sayısı 1736 idi. pH metrede saptanan asit reflülerin %56.1'i impedans kayıtlarında saptanmadı. Bunun nedenleri arasında en sık impedans kanallarında değişiklik olmayan olaylar

Anahtar kelimeler
İmpedans, asit gastroözofageal reflü, pH-only olayları

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görülmüştür(%68), diğer sebepler ise hava nedeniyle pozitif defleksiyon(%14), impedans ölçüm kriterlerini karşılayamayan olaylardır(%10). %8 pH-only olayında ise reflü için impedans kriterlerini sağladığı halde reflü işareti olmayan durum saptandı.
Sonuç: İmpedans monitörizasyonu sonuçlarına göre pHmetreye göre 2 katından fazla sayıda asit reflü impedansda gösterilemiyor. pH-only olaylarının sebepleri ve klinik önemi halen net değildir. Bu nedenle impedans kayıtlarının otomatik analizlerinden çok pHmetre ile birlikte değerlendirilmesi önemlidir

Introduction

The pH meter, which can provide 24-hour monitoring of the pH in the esophageal lumen, has been considered as the gold standard in the diagnosis of gastroesophageal reflux disease for many years (1). Multichannel intraluminal impedance (MII) monitoring provides a more precise determination of reflux, as it allows the bolus movement to be shown simultaneously with the measurement of intraluminal pH. Besides acid reflux, MII recordings allow for observation of weak acid and alkaline reflux, the frequency of distal esophageal reflux exposure and the rise of reflux to the proximal.

The use of different criteria in the measurement of reflux causes inconsistencies in the measurement of number of acid reflux events and acid exposure by both the pH meter and MII tests (2). The acid reflux events that are detected by pH meter and not identified by MII are called pH-only events. In studies conducted with children, the frequency of pH-only events was reported to vary between 39-80% (2-5). Although pH-only events are not considered as reflux in the MII recordings, the clinical significance of these events is still unclear (3,6). In this study, we aimed to investigate the reasons behind pH-only events, while also revealing the difference between MII and pH meter in determining the number of acid reflux events.

Materials and Methods

Patient Selection

Uludag University Faculty of Medicine Ethics Committee approval was obtained (with the decision numbered 2014-2 / 14, dated January 21, 2014). Fifty patients aged 0-17 years that were admitted to the Department of Pediatric Surgery outpatient clinic of the Uludag University Faculty of Medicine with suspicion of gastroesophageal reflux disease and were scheduled to undergo MII monitoring from February 2014 to August 2015 were included in the study. After patients and parents were informed about the impedance measurement procedure and the study, the parents signed the informed consent and clinical research ethics committee informed consent forms. Two weeks before the procedure, patients were asked to discontinue the use of medications that could affect the outcome of the procedure such as antacids, H2 receptor antagonists, proton pump inhibitors, and prokinetic agents.

Catheter insertion

Before the MII catheter was placed, the impedance device and the catheter were calibrated in solutions with pH 7 and 1 (Reageon®). An infant or pediatric type 1.8-2 mm thick catheter with 6 impedance channels and 1 pH sensor was inserted transnasally into the esophagus. In the catheter, the impedance segments are placed 2 cm apart and the pH probe is at 2 cm, that is, it corresponds to the Z6 impedance channel (Catheter: pH Type (1pH, 7E) Unisensor ref: K6011 - EI - 0633) (Figure 1). The Strobel formula was used to identify an ideal catheter placement location, especially in younger patients, and the location of the catheter was confirmed by anteroposterior chest radiography in all patients. The other end of the catheter was connected to a data-recording device (MMS Ohmega Ambulatory Impedance and pH Recorder - Netherlands). Impedance signals were measured at 50 Hz, while pH signals were measured at 1 Hz.

During the follow-up, the patients were instructed to continue with their normal daily diets and activities, but avoid acidic foods. During the procedure, patients or their relatives were asked to record meal times in a diary using the clock on the impedance device. The patients were followed up in the clinic for 24 hours. After the processes were completed, the recorded data was transferred to a desktop computer and analyzed with the help of a special software program (MMS Investigation and Diagnostic Software®). Data were collected by conducting examinations on automatic analysis without manual analysis.

Examination of MII monitoring records:

Events with distal esophageal pH below 4 were determined. MII recordings were used to count acid reflux events and pH-only events one by one for each patient. Events during the meal periods were not included in the analysis. An acid reflux episode detected by MII was defined as a retrograde drop in impedance by more than 50% of baseline at least two consecutive impedance traces while pH was below 4 for at least 5 seconds. The pH-only event was accepted as an episode where the pH was below 4 for at least 5 seconds but was not detected in the impedance recordings. In other words, these were episodes with pH below 4 without evidence of retrograde bolus action.

Changes in impedance channels during pH-only acid reflux events were examined and grouped as follows based on the previous studies (4,7) (Figure 2).

1. Events that fail to meet the impedance measurement criteria (a decrease of more than 50% of the baseline impedance in only one channel or a decrease of less than 50% of the baseline impedance despite a decrease in at least two consecutive channels).

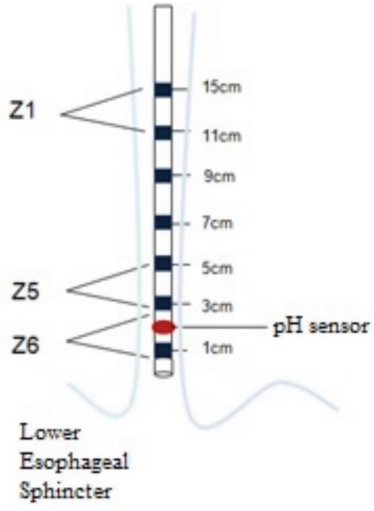

Figure 1. Placement of the pH sensor in the impedance catheter

2. Events with no change in impedance channels (low impedance during the procedure, event within 30 seconds after acid reflux, unexplained events).

3. Events that meet the impedance criteria, but do not have signs of reflux.

4. Artifact.

5. Positive deflection due to air.

Baseline impedance was determined by plotting a stable value area in the impedance channels within at least 10 seconds. In older children, we accepted the baseline impedance range as 2000-4000, which is close to the adult range, while in infants it was accepted as 1500-2000.

Statistical Analyses

Statistical analyses were done using IBM SPSS Statistics 22.0. While the results of numerical values were given as mean ± standard deviation (SD) and distribution (median; minimum-maximum), the nominal values were expressed as %. Wilcoxon sign rank test was used for comparison of dependent groups. A p value of <0.05 was considered statistically significant.

Results

Out of the 50 patients who underwent MII test, 35 were male (70%). The patients' mean age was 6±5 years (range: 4 years, 2 months - 17 years). The patients' mean MII monitoring recording time was 21.8 ± 1.4 hours.

In 50 patients, the number of acid reflux events detected in the MII records was 1475, the number of acid reflux events detected in the pH meter was 3093, and the number of pH-only acid reflux events observed only in the pH meter was 1736 (Table 1). According to MII monitoring results, acid reflux was detected 2.1 times more in pH meter recordings than in MII. Among acid reflux events detected in pH meter, 56.1% were not detected in MII recordings. Only one patient had equal reflux counts on pH meter and MII recordings,

Table 1. Numbers and distributions of acid reflux events detected in MII and pH meter

	pH meter	MII	pH-only event	p-value p<0.05
Mean acid reflux number (mean ± SD)	61.8 ±53.3	29.5 ±21.9	34.7 ±45.6	p<0.001
Distribution = Median (minimum-maximum)	50.5 (1-276)	27 (1-101)	21.5 (0-230)	p<0.001
Total number of acid reflux	3093	1475	1736	p<0.001

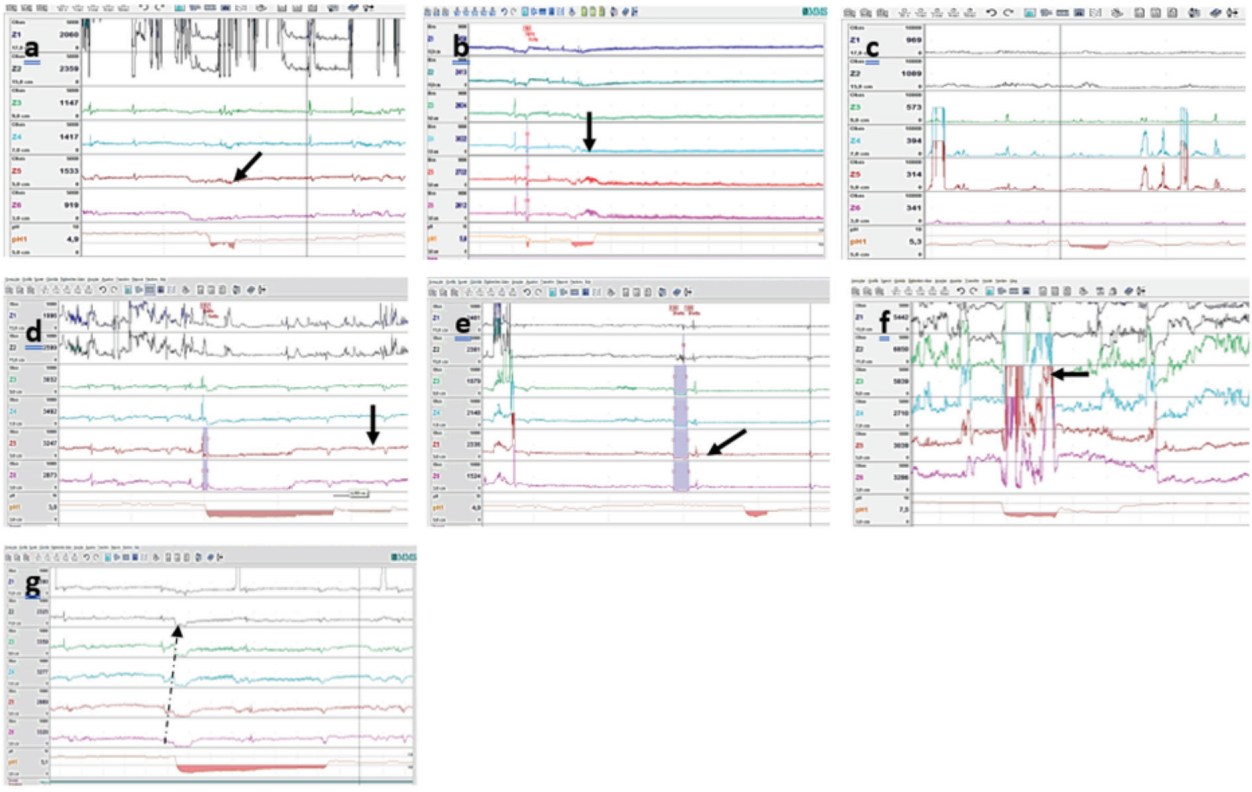

Figure 2. Examples of pH-only events (arrow)
a. Event with a decrease of more than 50% of the known baseline impedance in only one impedance channel
b. Event with a decrease in two or more impedance channels, but of less than 50% of the known baseline impedance
c. pH-only events occurring in case of low impedance during the study
d. pH-only event within 30 seconds of the previous reflux
e. pH-only event with no change in impedance channels even though pH was below 4 (unexplained event)
f. Positive deflection in impedance channels due to air
g. Events that meet the impedance criteria, are below pH 4, but without the sign of reflux

Table 2. Distribution and percentage of pH-only acid reflux causes

	Failure to meet the MII measurement criteria		Events with no change in impedance channels					
Causes of pH-only acid reflux	Events with a drop of >50% of basal impedance in one channel	Events with a decrease of < 50% of basal impedance	Low impedance throughout the study	Event within 30 seconds after acid reflux	Unexplained events	Events that meet the impedance criteria but have no signs of reflux	Positive deflection due to air	Artifact
Mean ± standard deviation	1.9 ±3.3	1.7±1.9	8.7±37.4	6.8±6.1	8±12.1	2.8±4.9	4.7±8.3	0.06±0.2
Distribution (minimum-maximum; median)	0-15; 1	0-7; 1	0-196; 0	0-23; 5	0-56; 3.5	0-24; 1	0-56; 3	0-1;0
Total number of pH-only events	94	84	437	342	400	141	235	3
Percentage	5%	5%	25%	20%	23%	8%	14%	0.3%

and the total number of acid reflux in this patient was 4. There were 70 events of re-reflux, which looked like one reflux event on the pH meter, but counted as more than one reflux events on the MII.

When the probable causes of 1736 acid reflux events not detected in the MII recordings, but detected in the pH meter were examined, the most frequent cause was the events with no change in impedance channel (68%) (Table 2). Among the events with no change in impedance channels, low impedance events were the most common throughout the study. Four patients had low impedance throughout the study, and 3 of these patients had high pH-only reflux numbers (in these four patients, the number of pH-only reflux-the number of events with no change in impedance channels due to low impedance throughout the study were 105-69; 230- 171; 212-196; 4-1, respectively).

Discussion

MII records provide information about acid reflux events detected by both MII and pH meter, non-acid reflux events detected only in MII, and pH-only events detected only by pH meter. Non-acid reflux is not seen in the pH meter and pH-only reflux is not seen in the MII. This shows that both techniques have some limitations in showing reflux events. Therefore, there is a need for studies comparing these two different reflux detection techniques with each other.

The acid reflux events that are detected by pH meter and not identified by MII are defined as pH-only events (8). Various mechanisms have been suggested for the causes of pH-only events such as failure to meet the scoring rules, short- column acid reflux that only reached the most distal canal, small volume acid reflux, residue of the previous reflux that was not completely cleared, catheter displacement to stomach due to shortening or contraction of the esophagus during swallowing, transient lower esophageal sphincter relaxation that allows small amounts of acid content to pass into distal esophagus during swallowing, technical artifact, catheter design, reflux esophagitis, and esophageal pathologies (7). In our study, 56.1% of acid reflux events detected in pH meter were not detected in MII recordings. The most common reasons for this were events no changes in impedance channels (68%) and other reasons such as positive deflection due to air (14%), and events that could not meet impedance measurement criteria (10%). In a similar study, Di Fiore et al. monitored infants for 12 hours with a different software device and reported that 59% of the reflux events detected in the pH meter were not detected in the MII recordings (4). Among those, 64% did not have any changes in the impedance channels, 13% did not meet the impedance scoring criteria, 12% had positive deflection due to air, and 11% had technical artifacts (4). Despite different software, timing and patient population, their rates are similar to ours.

The pH-only events with no change in impedance channels occurred most frequently in patients with low baseline impedance throughout the study (25%). Baseline impedance is relative and correlated with mucosal content and conductivity. Esophageal pathologies increase severe esophagitis and esophageal wall conductivity and result in low impedance throughout the procedure (9). In such cases, an already low impedance value makes it difficult to detect reflux in impedance (10). In our study, the baseline impedance of 4 patients was very low for their ages. The mean baseline impedance values of these four patients were 283, 443, 379, 787 ohms, respectively. 2 of these patients had esophagitis, one had esophagitis + esophageal atresia and one had a neurological disorder. In 3 of these patients, the number of pH-only reflux events was high. Therefore, although the number of patients was small, the percentage of cases where there was no change in impedance channels was relatively high, but even if these patients were excluded from the study, cases without changes in impedance channels were more common than other reasons.

There is no consensus on the time between two consecutive refluxes on a pH meter measurement. This time ranges from 5 seconds to 30 seconds (2). In our study, the incidence of pH-only events within 30 seconds of an acid reflux was 20% in the MII recordings. Studies have suggested that the situation where two consecutive reflux events were detected in the pH meter within 30 seconds, but only the first event was observed in the MII recordings and consecutive reflux was not detected within 30 seconds was due to the insufficient clearance of the previous acid reflux (4,11). In addition, pH-only rates did not change in the study of Wenzl et al., which was performed by manipulating the reflux detection criteria in MII recordings (2). The pH-only events in their study

constituted 39.3% of all events, while the probability of having reflux together with MII and pH meter was 56.7% (2). However, when the criteria for detecting reflux in the pH meter were changed, this rate was found to be 60.7% and no significant difference was observed.

In our study, the events where pH was below 4, but air-related positive deflection in the impedance channels that rendered determination of reflux impossible were at a level that cannot be underestimated. Belching or swallowing of air possibly affects acid exposure seen in the impedance recordings if the pH was below 4 during air deflection. Transient lower esophageal sphincter relaxation during belching and gastroesophageal reflux are thought to be related (12).

We could not explain 23% of events with pH below 4 that were not detected in the impedance recordings, as well as 8% of pH-only events that met the impedance criteria, but were not accepted as reflux by MII. Although the difference of visual and measurement sensitivity of the device is a possible cause, this situation, which we observed visually, may question the sensitivity of MII recordings.

Due to impedance catheter design, the location of the pH sensor in Z6 increases the incidence of detecting pH-only events compared to the design, where pH sensor is located in Z5. The pH sensor in Z6 corresponds to 2nd cm. Reflux events, reaching only 1 channel are defined as reflux in the pH meter since the pH sensor is in Z6, but they will not be considered as a reflux event in MII. Because reflux according to the MII criteria must reach at least 2 channels. For it to be considered a reflux, the event should have an average extension of 4-4.5 cm (5). In our study, the pH sensor was located in the Z6 and there was no question of skipping pH-only reflux events and 5% of our cases had a decrease of more than 50% of baseline impedance in only one channel. We think this situation is due to short extension of the acid reflux.

Some studies have found that 15% of the symptoms occur during pH-only events (6). Currently, the effect of pH-only events on symptoms and whether they should be included in impedance analysis is a matter of debate (5,6,11,13,14). In recent years, impedance has been seen to be superior to the pH meter, as it detects both acid reflux and non-acid reflux. However, pH-only events push the limits of impedance.

Corvaglia et al. reported that when pH-only events were added to the impedance record of preterm infants, an average of 53.2 more acid gastroesophageal reflux events was encountered and the esophagus was affected by an average of 11% more acid (5). In our study, we detected 2.1 times more acid reflux events in pH meter than in MII automatic recordings. The number of pH-only events found in the literature is substantial in children (2-5,15). The clinical significance and the reason for pH-only events are still unclear. For this reason, it is important to evaluate MII recordings together with pH meter results rather than evaluating automatic analyses alone.

Ethics

Ethics Committee Approval: All procedures performed on human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from parents of all patients prior to all procedures.

Conflict of Interest: No conflict of interest was declared by the authors.

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