Diagnostic difficulties during combined multichannel intraluminal impedance and pH monitoring in patients with esophagitis or Barrett's esophagus

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Abstract

Gastroesophageal reflux disease (GERD) is one of the most common esophageal diseases in developed countries. It is widely believed that GERD symptoms are caused by acid refluxate within the esophagus, so ambulatory 24 hour pH-monitoring became the gold standard in detecting gastroesophageal reflux. Traditional ambulatory pH monitoring is unable to detect a gastroesophageal reflux with pH>4. The introduction of multichannel intraluminal impedance and pH (MII-pH) brought new possibilities in detecting GERD. In this technique impedance identifies reflux episode whereas pH sensor further characterizes it as either acid (pH<4) or non-acid (pH≥4). This is a great progress in diagnosing GERD but MII has also some imperfections related to pathological changes in the esophageal mucosa such as esophagitis or Barrett oesophagus, which are connecting with a very low baseline impedance values. Changes in the esophageal mucosa may also impair the esophageal motility and esophageal transit leading to some fluid retention in the esophagus. It should be stressed that very low impedance baseline creates a difficulty in interpreting the MII-pH study. In such a case it might be almost impossible to interpret the study as the interpreter does not see characteristic drop in impedance progressing either orally (reflux episode) or swallow but only almost flat impedance lines. Therefore, future studies are needed to further evaluate this problem.

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Gastroesophageal reflux disease (GERD) is one of the most common esophageal diseases in developed countries. It is a condition in which gastric contens reflux into the oesophgaus and provoke symptoms, complications and impairs quality of life. Typical GERD symptoms are: heartburn, regurgitation, pain in supraabdominal area, nausea or belching. Atypical symptoms, connecting with extraoesophageal manifestations of GERD are: reflux disease related asthma, chronic cough and laryngitis, but both typical and atypical GERD symptoms can impair quality of life. The pathogenesis of reflux disease is multifactorial, connecting also with insufficiency of antireflux barrier, especially lower oesophageal sphincter (LES) pressure abnormalities or LES transient relaxations (tLESR). It was commonly believed that symptoms attributed to GERD were caused by acid refluxate (pH<4) occurring in the esophagus. Therefore proton pump inhibitors (PPI) were considered the drugs of choice in the pharmacologic therapy of GERD [1-3].

Other factors contributing to the pathophysiology of reflux disease include hiatal hernia, impaired esophageal clearance, delayed gastric emptying and impaired mucosal defensive factors. It has been suggested that hiatal hernia is promoting LES dysfunctions. An impaired esophageal clearance is responsible for prolonged acid exposure of the esophageal mucosa and delayed gastric emptying results in gastric destension which may significantly increase the rate of tLESR corresponding with higher incidence of postprandial refluxes. Finally, the mucosal defensive factors play an important role against development of reflux disease by neutralizing the backdiffusion of hydrogen ion into the esophageal tissue [1,2].

Typical GERD symptoms occur every day in about 5-10% of population in the developed countries and once a week even in 20% of population. Incidence of GERD increases with the

age, social status, dietary habits, lifestyles and many other factors [1,2]. One of the most serious complications of GERD is esophagitis, with different severity, according to most common endoscopic graduation (most frequent in use is Los Angeles scale) and Barrett's esophagus. The widely accepted definition of Barrett`s esophagus, according to American College of Gastroenterology is: an oesophagus in which any portion of the normal squamous lining has been replaced by a metaplastic columnar epithelium which is visible macroscopically. In order to make a positive diagnosis of Barrett`s esophagus, a segment of columnar metaplasia of any length must be visible endoscopically above the oesophagogastric junction and confirmed or corroborated histologically. There is a need to specifically define the columnar metaplasia which carries a risk of malignant transformation and implications regarding surveillance [3].

The ambulatory 24 hour pH-monitoring became the gold standard in detecting gastroesophageal reflux, because it was widely believed that GERD symptoms were caused by acid refluxate within the esophagus, however, it was shown that there was a subset of patients who despite adequate gastric acid suppression still experienced GERD symptoms [4-7].

It has been suggested that symptoms occurring despite adequate gastric acid suppression might be caused by reflux with a pH greater than 4 [4]. Traditional ambulatory pH monitoring is unable to detect a gastroesophageal reflux with pH>4. However, some authors proposed esophageal pH≥7 as an indirect marker of alkaline reflux during ambulatory pH monitoring [5], but on the other hand several studies have shown that increased production of saliva or bicarbonate secreted by esophageal submucosal glands may increase esophageal pH in the absence of reflux and confound measurements [6-11]. Other authors claim that pH monitoring can still detect gastroesophageal reflux when esophageal pH remains above 4 but with accompanying definite fall greater than one pH unit [12].

The introduction of multichannel intraluminal impedance and pH brought new possibilities in detecting gastroesophageal reflux. Multichannel intraluminal impedance evaluates the direction of bolus movement and is determined by multiple impedance measuring segments placed within the esophagus. In this technique impedance identifies a reflux episode whereas pH sensor further characterizes it as either acid (pH<4) or non-acid (pH≥4). Reflux episode detected by impedance is defined as a retrograde bolus movement progressing from the most distal esophageal measuring site to at least the second distal esophageal measuring site. Swallow in turn is defined as an antegrade bolus movement progressing from the proximal esophageal measuring site to the distal esophageal measuring sites. In the absence of the bolus within the esophagus, the impedance is determined by the electrical conductivity of the esophageal lining [13].

Intraluminal impedance (expressed in Ohms) depends on changes in resistance to alternating current between two metal electrodes produced by the presence of bolus inside the esophageal lumen. Refluxed contents are characterized by high conductivity, which is the inverse of impedance what makes possible practical qualitative analysis of refluxate. For instance, the conductivity of air is almost zero and then impedance increases compared with baseline, whereas the conductivity of liquid is much higher and the impedance curve decreases remarkably. If we use the combination of impedance and traditional pH-metry we can detect both acid and non-acid liquid reflux episodes. From a clinical point of view, it might be useful for identifying the number and percent times of gas, acid and non-acid reflux episodes, it may improve the yield of symptom index, it may allow to evaluate the reasons for poor response of reflux symptoms to proton pomp inhibitors and to know the proximal extent of reflux events in patients with atypical symptoms [13-16].

Recent studies in adults and children suggested that combined multichannel intraluminal impedance and pH measurement has the potential to become the new "gold standard" for gastroesophageal reflux testing [17] and has the potential to become a useful clinical tool to assess ongoing reflux in patients on acid-supression therapy [18]. A recent multicenter study from the U.S. observed that among patients presenting with symptoms related to GERD despite gastric acid suppressive therapy, 37% of symptomatic patients had a positive symptom index with non-acid reflux whereas 11% of symptomatic patients had a positive symptom index with acid reflux [19]. These data were further supported by a recent multicenter study from Europe which observed that among symptomatic patients receiving PPI, 33% had a positive symptom index with non-acid reflux, 5% with acid reflux and another 5% with both acid and non-acid reflux [20]. In the group of symptomatic patients studied off PPI therapy, 10.8% had a positive symptom index with non-acid reflux, 32.4% with acid reflux and 13.% with both acid and non-acid reflux [20]. Therefore, it was shown that GERD symptoms might be caused by non-acid reflux in patients on or off PPI therapy [20].

This is a great progress in diagnosing GERD but MII has also some imperfections related to pathological changes in the esophageal mucosa such as esophagitis or Barrett`s esophagus. These changes are very likely to cause that baseline impedance values are very low and detection of the bolus movement in the esophagus is very difficult. In addition, changes in the esophageal mucosa may also impair the esophageal motility and esophageal transit leading to some fluid retention in the esophagus. A recent study by Domingues et al. [21] observed significantly lower postdeglutitive impedance values among GERD patients with mild-esophagitis than healthy controls indicating presence of bolus residues in the distal esophagus. Another study observed that patients with ineffective esophageal motility (IEM) had low baseline impedance values in the distal esophagus which were likely caused by some level of fluid retention within the esophagus and possibly inflamed esophageal mucosa [22]. In that study the distal baseline impedance values found in patients with IEM were comparable with those found in patients with achalasia or scleroderma [22]. The authors claimed that the low distal esophageal impedance values in patients with IEM may also reflect the inflammation within esophageal mucosa due to gastroesophageal reflux [22].

There are no further data regarding the difficulties of interpretation of MII-pH tracings in patients with very low impedance baseline which are very likely to occur in patients with abnormal esophageal mucosa (Barrett's esophagus or esophag-

titis). It should be stressed that very low impedance baseline creates a difficulty in interpreting the MII-pH study. In such case it might be almost impossible to interpret the study as the interpreter does not see characteristic drop in impedance progressing orally (reflux episode) but only almost flat impedance lines throughout the length of entire tracing.

During MII-pH monitoring the beginning of a reflux episode is defined as sequential 50% decrease in impedance baseline value beginning at the most distal recording site and reaching at least the second most distal recording site. The baseline impedance value used to determine a 50% decrease is the average impedance baseline in a 5-second interval preceding the reflux episode. The end of a reflux episode in turn is defined as sequential increase in impedance to at least 50% of baseline value. Therefore, in case of low impedance baseline values in the distal esophagus it is very difficult or almost impossible to notice the impedance detected reflux episodes.

Future studies are needed to further evaluate the use of MII-pH in patients with low values of impedance baseline.

Acknowledgments

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