Evaluation of Gastroesophageal Reflux Events in Children Using Multichannel Intraluminal Electrical Impedance

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The majority of gastroesophageal reflux (GER) episodes in infants and children are nonacidic (pH >4). However, extraesophageal symptoms (e.g., breathing irregularities, apnea, aspiration) apparently can be caused by both acidic (pH <4) and nonacidic reflux. The standard diagnostic tool for suspected GER is pH monitoring. However, physicians should be aware of the limitations of pH monitoring in the pediatric population, because most reflux episodes in this age group are undetectable by this method. In contrast, the pH-independent multiple intraluminal electrical impedance technique (IMP) allows all bolus movements in the esophagus to be detected. Data can be analyzed for bolus composition and reflux height, duration, and clearance. Combining IMP with pH monitoring on a single catheter has proved to be a valuable tool for diagnosing GER and associated symptoms in infants and children. *Am J Med.* 2003; 115(3A):161S–165S. © 2003 by Excerpta Medica, Inc.

The most widely accepted tool for the diagnosis of gastroesophageal reflux (GER) is pH monitoring.[1,2] However, this method only provides pH values; it does not actually document reflux. The parameters that define reflux episodes by pH monitoring must be derived empirically.

Presumably, reflux-associated supraesophageal symptoms in infants and children include serious events, such as oxygen desaturation, episodes of apnea, recurrent aspiration, and apparently life-threatening events, as well as symptoms such as bronchitis, irritability, and sleep disturbances.[3,4] These situations can apparently be induced by both acidic (pH <4) and nonacidic (pH >4) GER.[5] However, pH monitoring is only able to detect acidic and alkaline (pH >7.5) GER, resulting in a method-inherent diagnostic gap. Many instances of reflux are likely to occur in the physiologic esophageal pH range (pH 5–7) and are therefore not detected during pH monitoring.

During postprandial periods, a neutralization of gastric contents of variable duration occurs that is affected by several factors, including the patient's age, the frequency of feedings, and, especially, the composition and volume of the feeding.[6] These phases last from 1 to 2 hours after each formula feeding in an infant, representing about half of the total measuring time. A comparable situation is encountered with antacid treatment. GER during these intervals is concealed from pH monitoring. Additionally, pH monitoring might not even be reliable in detecting acidic GER because of indirect GER detection by interpreting pH values as reflux events using software algorithms. Based on these assumptions, there is an urgent need for a pH-independent long-term identification technique for GER.[7,8]

TECHNIQUE

The multiple intraluminal electrical impedance technique (IMP) is a new method for the pH-independent detection of GER based on the registration of gastrointestinal motility.[9–13] The principle of IMP is a change of electrical impedance during the passage of a bolus through a measuring segment (i.e., between 2 adjacent electrodes).[14] The use of multiple segments along a catheter placed in the esophagus allows analysis of the direc-

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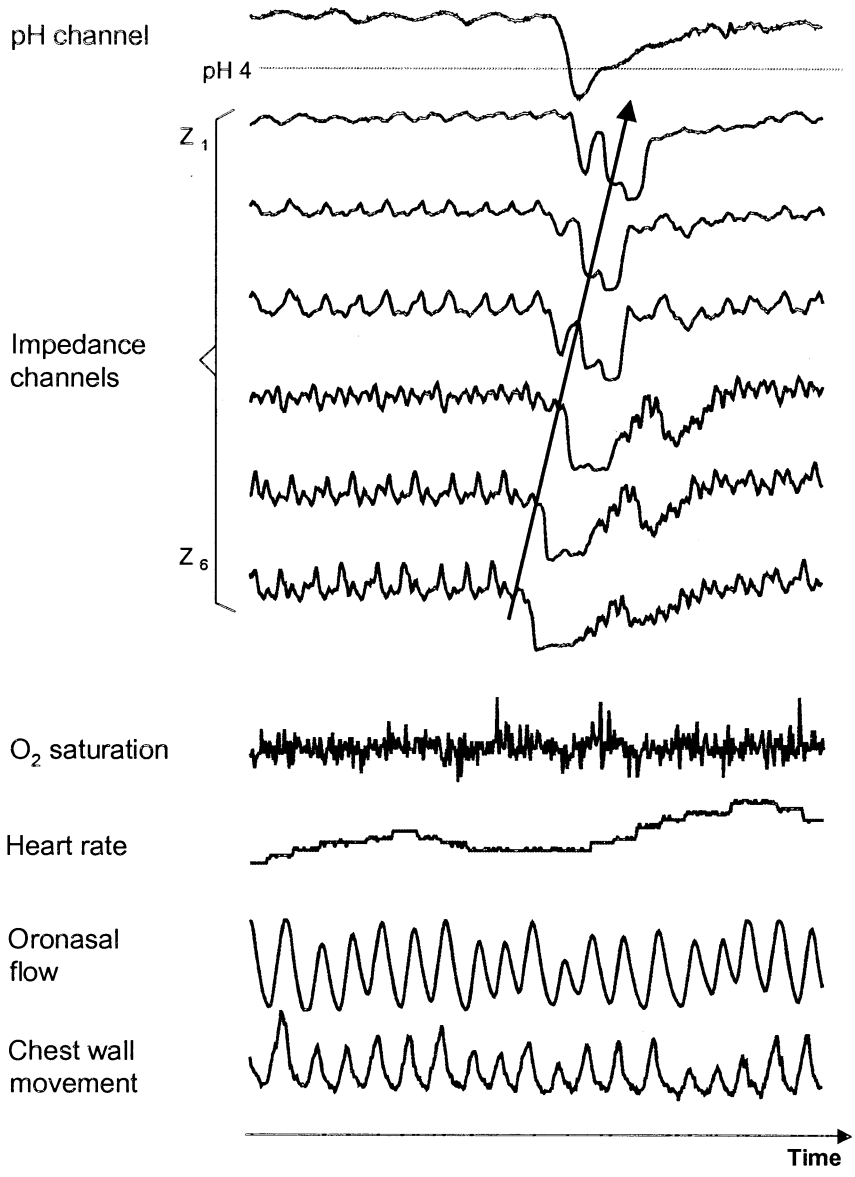

Figure 1. Original tracing of acidic gastroesophageal reflux during undisturbed oronasal airflow and chest wall movement in a 48-day-old boy. Note the retrograde esophageal bolus passage with sequential decrease of impedance (Z) over time (impedance channel Z_1, proximal; channel Z_6, distal) and pH <4. pH sensor situated at the level of channel 5. Bolus passage, from distal to proximal, is indicated (*arrow*).

tion of the bolus transport. Thus, anterograde and retrograde bolus movements can be distinguished. In infants, a catheter with a pH-sensitive antimony electrode and 7 integrated impedance electrodes (Helmholtz-Institut für Biomedizinische Technik, Aachen, Germany), representing 6 measuring channels, is used.[15] The total measuring length reaches from the cardia (channel 6) to the pharynx (channel 1), with the pH sensor situated at the level of channel 5, approximately 3 cm above the gastroesophageal junction. Impedance and pH signals are sampled at a rate of 50 Hz per channel, compared with 0.25 Hz in conventional pH monitoring.

COMPARISON OF INTRALUMINAL IMPEDANCE WITH pH MONITORING

Combined intraesophageal IMP and pH monitoring were performed in 50 infants who were being evaluated for GER.[16] Impedance tracings were analyzed for the unique pattern of retrograde bolus movement. Impedance values decrease in all channels reached by the refluxate. Change in impedance values begins in the distal channel and proceeds to more proximal channels, indicating a retrograde flow of gastric contents and representing an episode of GER. Software was developed to com-

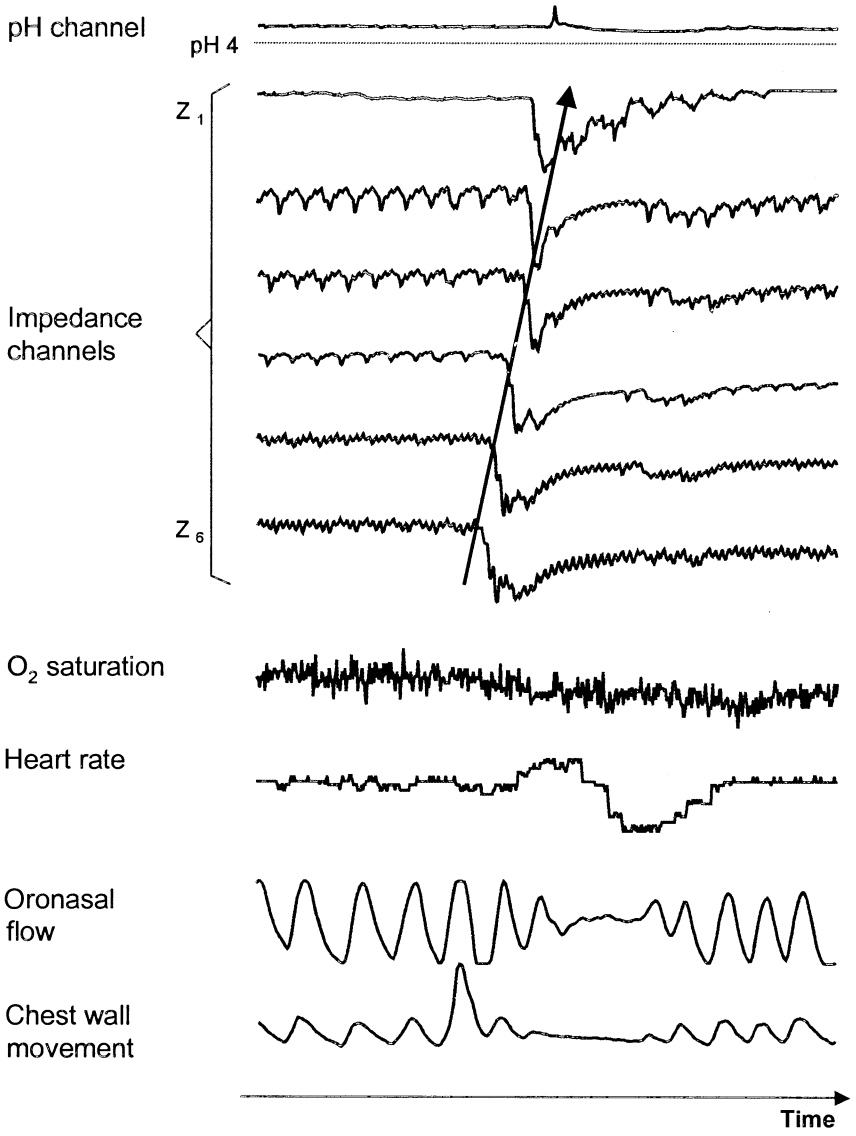

Figure 2. Original tracing of nonacidic gastroesophageal reflux and central apnea in a 37-day-old boy. Note the retrograde esophageal bolus passage with sequential decrease of impedance (Z) over time (impedance channel Z_1, proximal; channel Z_6, distal) and pH remaining >4. pH sensor situated at the level of channel 5. Bolus passage, from distal to proximal, is indicated (*arrow*).

pare all parameters of the algorithm systematically to analyze pH monitoring data; these parameters include sampling rate, threshold pH level below which reflux was defined, minimal duration necessary to define a reflux episode, and latency time between separate episodes. IMP detected 1,887 episodes of bolus reflux; 282 (15%) of these episodes were associated with a pH <4. The sensitivity of pH monitoring for acidic GER detection was 54% using a standard algorithm, with a positive predictive value of 57%. Independent and combined variation of all algorithm parameters in >1,000 software analyses did not lead to a significant increase of sensitivity and positive prediction. The most frequent reason for false-negative GER detection by pH monitoring was acidic reflux episodes of too short a duration; the most frequent reasons for false-positive detection were misinterpretation of pH drops during deglutition and misinterpretation of oscillation around the pH cutoff due to a low sampling rate.

Overall sensitivity of pH monitoring for the detection of retrograde bolus reflux was only 8%. Although pH monitoring is an inadequate technique for detecting GER, this can be accomplished elegantly using IMP. By combining the 2 methods, it is possible to achieve a more complete picture of bolus movement in the esophagus.[16]

GASTROESOPHAGEAL REFLUX DETECTION AND ASSOCIATED SYMPTOMS

Infants with a history of apnea, aspiration, or breathing irregularities were investigated simultaneously by combined intraesophageal IMP, pH monitoring, and overnight polysomnography.[17] Polygraphic recording included, among other parameters, transcutaneous oxygen saturation (SO_2), heart rate, oronasal flow, and chest wall movement. Documentation during each episode of GER included the minimal pH value, the maximal height reached by the refluxate in the esophagus, and the duration of GER (i.e., bolus clearance). In 22 patients, IMP detected 364 GER episodes with the unique pattern of retrograde bolus movement. Only 12% of these episodes had a pH <4 and therefore were potentially recognizable by pH monitoring (**Figure 1**). Of the total GER episodes, 312 (86%) were associated with breathing abnormalities; again, only 12% had a pH <4. In all, 128 of the GER episodes with breathing irregularities were accompanied by a decrease of SO_2 of $<90\%$. Another 19 GER episodes were associated with an SO_2 decrease of $>10\%$ compared with baseline; only 3 of these had a pH <4, while the remaining 16 reflux episodes were recognized by IMP only.[17] With the aid of software (ALICE II; Apreco, Bad Ems, Germany) preselection, 165 apneas were visually validated. Of these, 49 apneas (30%) were accompanied by GER (**Figure 2**). In all, 38 of these GER cases were recorded exclusively with IMP; only 11 (22%) reflux episodes were also recognized by pH monitoring. There was a significant correlation between GER and the amount of time that patients were apneic.[18] Compared with shorter episodes, reflux episodes lasting >30 seconds were more often associated with apnea. Most cases of GER (71%) reached the pharynx (impedance channel 1).

CONCLUSIONS

Numerous infants and children have been examined using IMP in Aachen, Germany. There have been no untoward side effects and only a few discontinuations due to technical reasons. Our results suggest that IMP for the registration and evaluation of GER provides important information that can supplement pH monitoring data in this population.[19] This new method is especially useful in phases of gastric hypoacidity, which is common in the postprandial period, or during acid-suppressive therapy. By itself, pH monitoring is unable to detect the majority of these reflux episodes; indeed, it misses about half of the cases of acidic (pH <4) GER.

Use of pH-independent IMP is also a reliable tool for evaluating GER-associated symptoms that are not associated with acidic reflux. Additionally, information about the height reached by the refluxate in the esophagus and about the clearance process of GER can be obtained and analyzed via this method.[20]

However, because GER without other symptoms appears to be a physiologic phenomenon in infants, normal values remain to be defined. The manual and visual evaluation of the high-resolution recordings is still a time-consuming procedure. With the development of automated analysis,[21,22] IMP may become the new standard tool for detection of GER in infants and children. International technical and clinical collaboration must be sought to further evaluate this promising tool, without repeating the misinterpretations of pH recording that have now become apparent.[23,24]

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