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Performance and Optimal Technique for Pharyngeal Impedance Recording: A Simulated Pharyngeal Reflux Study

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BACKGROUND AND AIMS: Detection rate, influence of recording site, and subject posture for impedance monitoring of pharyngeal reflux of gastric contents remain unknown. We evaluated the ability of the impedance sensor for detection of various volumes of intrapharyngeal infusate at two sites and in two subject positions.

METHODS: Nineteen healthy subjects were studied using concurrent videoendoscopic, manometric, impedance, and pH recording.

RESULTS: Detection rate of simulated pharyngeal reflux events ranged between 87% and 100% for 1–4 mL. Detection rate for 0.1–1 mL volumes in the upright position was significantly higher (78–85%) when the impedance sensor was located at the proximal margin of the upper esophageal sphincter (UES) compared to 2 cm proximally (38–68%) ($P < 0.001$). With the sensor at 2 cm above the UES, the average detection rate for all volumes in the upright position was significantly less ($P < 0.001$) compared to the supine position (48% *vs* 84%). There was substantial variability in the magnitude of impedance changes induced by different infusates.

CONCLUSIONS: Impedance sensors can detect as small a volume as 0.1 mL and combined with a pH sensor can detect acidic and nonacidic liquid and mist reflux events. Sensor placement at the proximal margin of the UES yields the highest detection rate irrespective of subject posture compared to placement 2 cm proximally. Depending on the volume of refluxate and location of the impedance sensor, a substantial minority of simulated reflux events can be missed.

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INTRODUCTION

Despite considerable clinical interest, the pathophysiology of supraesophageal complications of reflux disease such as those involving the larynx (1–3), pharynx (1), and sinuses (4, 5) remains poorly understood. Adding to this difficulty is the fact that despite the availability of strong acid suppressive agents such as proton pump inhibitors, the response of patients with supraesophageal symptoms attributable to pharyngeal reflux of gastric content remains unpredictable, and in fact, placebo-controlled trials report suboptimal results (6, 7). In addition, although the role of pharyngeal reflux of gastric acid in the pathogenesis of these disorders has been extensively studied by concurrent pharyngoesophageal pH monitoring, the sensitivity and specificity of this test for correct stratification of patients remain clinically unacceptable (3, 8, 9). As a result of these aforementioned observations, a role for pharyngeal reflux of gastric contents irrespective of its acidity in the pathogenesis of supraesophageal complications of reflux disease has been suggested (10, 11). Given the fact that, contrary to the esophagus, the aerodigestive tract and airway are not normally exposed to enzyme-laden gastric and duodenal secretions, this notion seems meritorious. However, a reliable method of recording these events has not been available. Bile and pH monitoring systems and their interpretation techniques, although specific for the presence of the intended compound, are also limited in identification of refluxates that do not contain enough acid or bile or are not in fluid form. With the recent availability of impedance measuring devices and their successful use in the evaluation of esophageal reflux of nonacidic gastric contents, several attempts (3, 4, 11, 12) have been made to record pharyngeal reflux of nonacidic gastric contents in the pharynx using this technique. Despite these attempts, the performance characteristics of this new modality in detecting refluxate with various physical and chemical properties (*e.g.*, acidic and nonacidic gas, fluid, mixed gas and fluid), as well as the influence of the recording position within the pharynx and volume of the refluxate on its performance have not been systematically evaluated.

The aims of the present study, therefore, were to: (a) evaluate the ability of the impedance sensor to detect various volumes of intrapharyngeal liquid, gas, and mixed liquid/gas with acid and nonacid pH; (b) define the impedance signature of such events; and (c) determine and compare the ability of the impedance sensor in detection of minute volumes of simulated reflux events at two intrapharyngeal levels with respect to the upper esophageal sphincter (UES) in supine and upright positions.

METHODS

We studied a total of 19 subjects. The study was approved by the Human Research Review Committee of the Medical College of Wisconsin and volunteers gave written informed consent before their studies. Volunteers fasted for at least 6 h prior to their study.

Studies were performed in two stages. In stage 1, we studied 8 healthy volunteers to determine the ability of the impedance sensor to detect various volumes of intrapharyngeal liquid, gas, as well as acid and nonacid mists and define the impedance signature of such events. In stage 2, we studied an additional 11 subjects to determine the ability of the impedance sensor to detect minute volumes of simulated reflux events at two intrapharyngeal levels with respect to the UES high-pressure zone in the supine and upright positions.

We used a concurrent videoendoscopic, manometric, impedance, and pH recording technique for both stages. Manometry was used to precisely position the recording devices in the pharynx in reference to the UES. Videoendoscopy was used to visually observe and record the simulated reflux events and the contact of refluxate with the recording sensors. Impedance sensors were used to detect simulated refluxate and ascertain their physical properties, *i.e.*, liquid, gas, or mixed liquid and gas, and pH recording sensors were used to document the acidic properties of the simulated refluxuate. To facilitate visual documentation of infusate contact with the recording devices, the injected fluids were colored by the addition of food dye. The location of the upper and lower esophageal sphincters (LES) were determined with the help of a perfused double lumen polyvinyl catheter attached to the UPS 2020 Motility System (Medical Measurement Systems, USA, Inc., Dover, NH). The same catheter was also used for infusion of colored normal saline 0.1N HCl and air.

Impedance was recorded with the bifurcated type combined impedance and pH probe (model PRZ-062B00002, Sandhill Scientific Inc., Highland Ranch, CO) that consists of two 2.1-mm diameter polyvinyl probes; one for recording from the pharynx and the proximal esophagus, and the other for recording from the distal esophagus. The probe for the pharynx and proximal esophagus had two impedance sensors 9 cm apart and a pH sensor, a tiny knob affixed at the center of the pharyngeal impedance sensor to be positioned in relation to the UES, in this study 2 cm above or at the proximal margin of the manometrically determined UES. The probe for the distal esophagus had four impedance sensors that were positioned 9, 7, 5, and 3 cm from the proximal margin of the manometrically determined LES and a pH sensor affixed at the center of the third impedance sensor, *i.e.*, 5 cm above the LES. For both probes, each impedance sensor was comprised of a pair of 4 mm cylindrical electrodes placed 1.6 cm apart from their centers. Data sampling frequency for both impedance and pH sensors was 50 Hz. The above-mentioned locations of the impedance sensors are measurements from their centers in relation to the proximal margin of the manometrically determined UES or LES, respectively.

To prevent inadvertent aspiration of the infusate, subjects were asked to perform a Valsalva maneuver immediately prior to the start of infusion and maintain the position until they were asked to swallow. During the Valsalva maneuver, the introitus to the trachea is closed by adduction of the vocal cords and approximation of the adducted arytenoids to the base of the epiglottis providing two superimposing tiers of closure to the introitus of the trachea.

In stage 1, we studied 8 volunteers (age 33 $\pm$ 9 yr, 6 men). After determining the locations of the lower and upper esophageal sphincters, the combined impedance and pH monitoring assembly was passed transnasally. The probe used for pharyngeal and proximal esophageal pH and impedance recording was positioned such that the pharyngeal pH sensor and center of the impedance couplets were resting 2 cm above the manometrically determined proximal margin of the UES. With this arrangement, the proximal esophageal impedance sensor was located 9 cm distally, approximately 3–4 cm below the UES. The injection port on the polyvinyl catheter was positioned 2 cm above the UES proximal margin. The endoscope (laryngoscope) was passed transnasally and positioned in the pharynx such that a clear view of the injection port and the impedance sensor and its surroundings were continuously observed. Videoendoscopic images were videotaped at 30 frames/60 fields per second. All recording modalities were synchronized using a timer (Thalner Labs, Inc., Ann Arbor, MI).

Once the setup was complete and the recording assembly was in place, we tested intrapharyngeal injections of 1, 2, 3, and 4 mL of colored normal saline at rest and during Valsalva maneuver, as well as 10 and 20 mL room air, and mixed saline/air in the supine position. Subjects were then requested to sit upright and the polyvinyl catheter was repositioned so that the infusion port was located at the mid-esophagus. The combined impedance and pH monitoring assembly remained in the same position in the pharynx. We tested esophageal belch, neutral mist, and acidic belches. Esophageal belches were induced by injections of 30–60 mL of air into the esophagus. Neutral mist belches were induced by injecting 50–60 mL of air into the esophagus following esophageal perfusion of 30 mL of normal saline. Acidic belches were induced by injecting 50–60 mL of air into the mid-esophagus following esophageal infusion of 30 mL of 0.1 N HCl (acidic mist). A total of 55 colored saline injections, 57 air, 17 neutral mist, 38 acid belch, and 40 nonacid belch events were analyzed in 8 healthy volunteers during phase 1 of the study. We repeated each event three times when subjects were able to continue. Events were discarded when subjects swallowed during the event and when there was no steady pre-event impedance baseline.

In stage 2, we studied 11 subjects (age 33 ± 11 yr, 7 men), using a similar experimental setup. For this stage, the impedance recording was done at two sites within the pharynx: (a) at the proximal margin of the UES and (b) 2 cm above the manometrically determined UES high-pressure zone. We tested simulated intrapharyngeal reflux of minute volumes by injecting 0.1, 0.2, 0.3, 0.4, 0.5, 0.7, and 1 mL of colored normal saline at two levels in reference to the proximal margin of the UES, *i.e.*, 2 cm proximal to the UES high-pressure zone as well as at the point where the UES high-pressure joins the pharyngeal atmospheric pressure. Each volume of injection was tested ×3 in supine and upright positions to simulate minute amounts of refluxate as well as to address the influence of the recording site on detection of reflux events.

The criterion for a positive event was arbitrarily chosen as minute quantities of the infusates were tested as simulated pharyngeal refluxes. In that, change of 100 mΩ from the average pre-event baseline impedance within 10 s of the beginning of infusion in case of simulated pharyngeal liquid and gas refluxes and within 15 s of air injection for mist events was considered a positive event.

Statistical Analysis

Descriptive and comparative statistical analyses were performed using a computerized statistical software system (Sigmastat, Systat Software, Inc., Richmond, CA). Where appropriate, average data are presented as mean ± standard error of mean (SEM). Detection rate comparisons were made using χ^2 proportion comparison methods (13). Comparison of average data was done using Student's *t*-test.

RESULTS

All subjects tolerated the procedure well and completed the study.

Phase 1: Impedance performance during simulated reflux events of large volumes:

Detection rate of the simulated pharyngeal reflux ranged between 87% and 100% for 1–4 mL of liquid infusate (Table 1). Detection rate for acidic and nonacidic esophageal belch was lower and ranged between 65% and 71%. While esophageal neutral gas ventilation as a consequence of belching resulted in impedance changes in 65% of instances and induced abrupt change in impedance, the intrapharyngeal gas infusion resulted in impedance changes in 30% of the instances and resulted in a gradual change in pharyngeal impedance (Fig. 1). Of 71% detected esophageal acid mist-belch events, pharyngeal impedance was decreased in 63% (1,809 ± 511 Ω), increased in 29% (1,750 ± 247 Ω), and was biphasic in 8% of instances.

Liquid infusate induced a brief increase in impedance followed by a profound decrease. This decrease in pharyngeal impedance was gradually restored even before swallowing (Fig. 2). For neutral mist of pharyngeal origin, after infusion of colored normal saline, we performed intrapharyngeal infusion of 30–50 mL of room air. This resulted in a shallow followed by a sharp increase in impedance (Fig. 3). Pharyngeal impedance returned to baseline after a command swallow.

Phase 2: Effect of sensor position on impedance performance during simulated reflux events of minute volumes:

In the upright position, the detection rate for all tested volumes was significantly higher (78–85%) when the impedance sensor was located at the proximal margin of the UES compared to when it was located 2 cm above the UES high-pressure zone (38–68%) ($P < 0.001$) (Fig. 4A). The lower rate of detection with the sensor at 2 cm above the UES was more profound for volumes of 0.1–0.5 mL. In the supine position (Fig. 4B), the detection rate for both sensor positions was similar and ranged between 62% and 92%. The worst rate was observed for 0.1 mL infusate.

In addition, with the sensor at 2 cm above the UES, the average detection rate for all volumes in the upright position was significantly less ($P < 0.001$) compared to that of the supine position (48% *vs* 84%). In contrast, there was no difference in the detection rate between the upright and supine positions when the impedance sensor was positioned at the proximal margin of the UES high-pressure zone.

The magnitude of the impedance change for volumes of 0.1 to 1.0 mL intrapharyngeal infusion of normal saline is shown in Figure 5. There was substantial variability in the impedance changes induced by different infusates. In general, larger volumes induced more impedance changes compared to smaller volumes, but because of substantial variability those differences did not reach statistical significance.

Table 1. Detection Rate of Simulated Pharyngeal Reflux

	Simulated Liquid Reflux				Esophageal Belch		Pharyngeal	
Impedance Performance	1 mL	2 mL	3 mL	4 mL	Acid	Nonacid	Gas	Mist
Detected (%)	92 (↓)	87 (↓)	100 (↓)	100 (↓)	71 (↓↑)	65 (↑↓)	30 (↓↑)	100 (↓↑)
Impedance change	2,530 ± 593	2,102 ± 382	2,102 ± 394	2,986 ± 685	1,809 ± 511	1,830 ± 828	808 ± 121	4,042 ± 598

Detection rate of simulated liquid and gaseous pharyngeal reflux events by impedance sensor located 2 cm proximal to the upper margin of the UES high-pressure zone. Arrows indicate direction of impedance change.

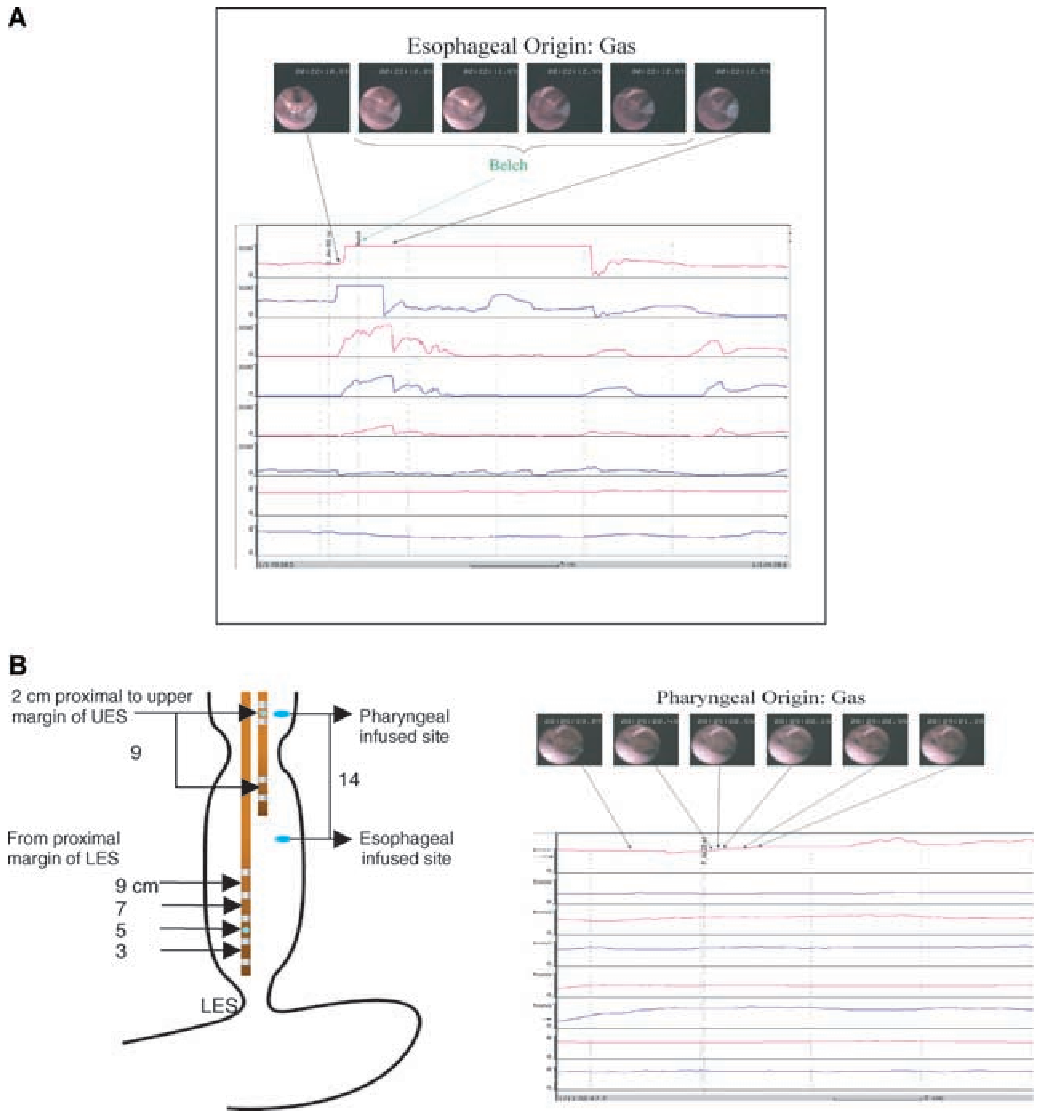

Figure 1. Examples of impedance changes associated with pharyngeal ventilation of neutral gas (room air) during esophageal belching (*A*) and direct infusion of room air into the pharynx (*B*). Although in both events impedance change occurred by intrapharyngeal entry of neutral gas, the changes induced by belching were abrupt and reached the maximum recording capacity of the sensor, while infusion of air induced modest changes. This difference suggests the possible effect of change in pharyngeal cavity configuration during belching on the magnitude of impedance change. As seen on the videoendoscopic recordings, belching was accompanied by vocal cord closure, anterior movement of the glottis, and UES opening resulting in changes in the pharyngeal cavity, while intrapharyngeal injection of air did not induce any visible change in pharyngeal cavity configuration.

DISCUSSION

In this study, we determined the capability of the impedance sensor in the detection of various volumes of the simulated reflux events at two different sites within the pharynx. Study findings indicate that the closer the location of the impedance sensor is to the entry point of the refluxate in the pharynx, the higher the impedance detection rate. In that, when the infusate was delivered at the proximal margin of the UES with the sensor located in the same vicinity, the detection rate was significantly higher than if the sensor was placed 2 cm proximally. This effect, however, seems to be limited to the upright and not the supine position. Study findings indicate that sensor position does not affect the detection rate in the recumbent position. Considering the fact that the proximal margin of the UES under normal conditions is the point of entry of the refluxate into the pharynx, the findings of this study suggest consideration of placing the pharyngeal impedance sensor as close to the UES margin as possible for achieving a maximum detection rate in the upright position.

Study findings also indicate that the impedance sensor is capable of detecting as small a volume as 0.1 mL, however, this volume was only detected by the sensor about 65% of the time when the sensor and infusion entry point were adjacent, most probably due to the inability of this minute volume to reach the sensor. This finding also supports the concept of

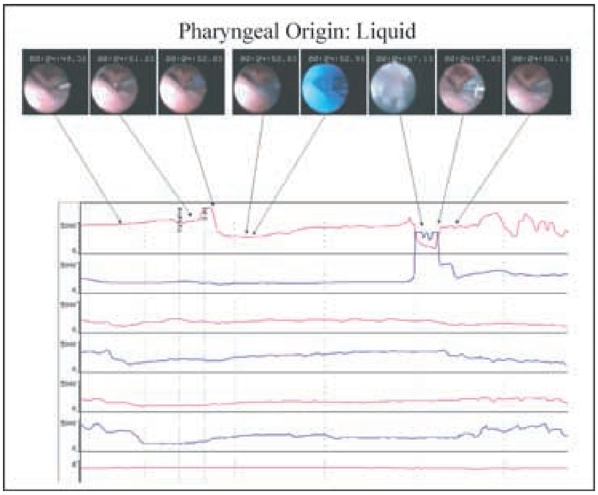

Figure 2. An example of pharyngeal impedance changes in response to intrapharyngeal injection of 3 mL of colored normal saline. Infusion of 3 mL of colored saline following a Valsalva maneuver (to prevent aspiration) induced a brief increase in impedance followed by more than a 50% decrease in impedance. Pharyngeal impedance was restored spontaneously. A command swallow is shown on the right. The reason for spontaneous recovery of impedance is not clear, however, pooling of the infused saline away from the sensor due to gravity is a possibility.

placing the impedance sensor at the margin of the UES high-pressure zone to reduce the miss rate.

Pharyngeal impedance recording in healthy controls as well as patients with esophageal and supraesophageal complications of gastroesophageal reflux disease (GERD) has been reported previously (12). In that study, a scant number of reflux events in the pharynx were detected, which were comprised of acidic fluid, nonacidic fluid, mist and mixed fluid, and gas reflux events. Considering the effect of the intrapharyngeal location of the impedance sensor on the detection rate of simulated reflux events described above, the position of the impedance sensor at 2 cm above the UES in that study can potentially explain the reason for the lower than expected recorded pharyngeal reflux events.

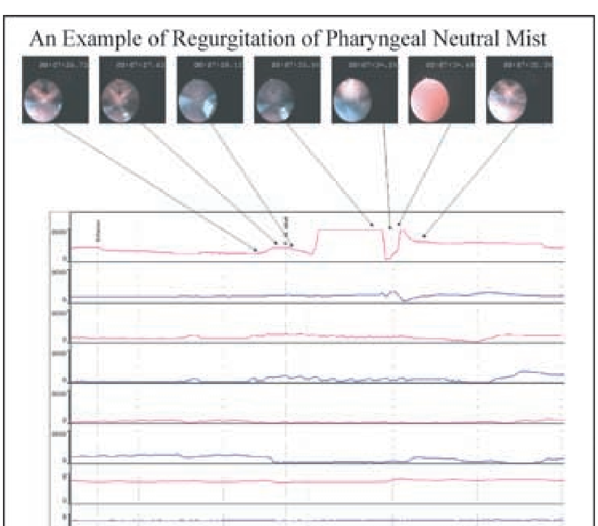

Figure 3. An example of registration of pharyngeal neutral mist by impedance sensor located 2 cm above the upper margin of the UES. Development of neutral mist in the pharynx resulted in a shallow increase followed by a sharp increase in impedance. Pharyngeal impedance was returned to baseline by a command swallow. Onset of infusion of normal saline is marked by a dashed line seen on the left. PN mist = pharyngeal neutral mist; SW = command swallow.

A

B

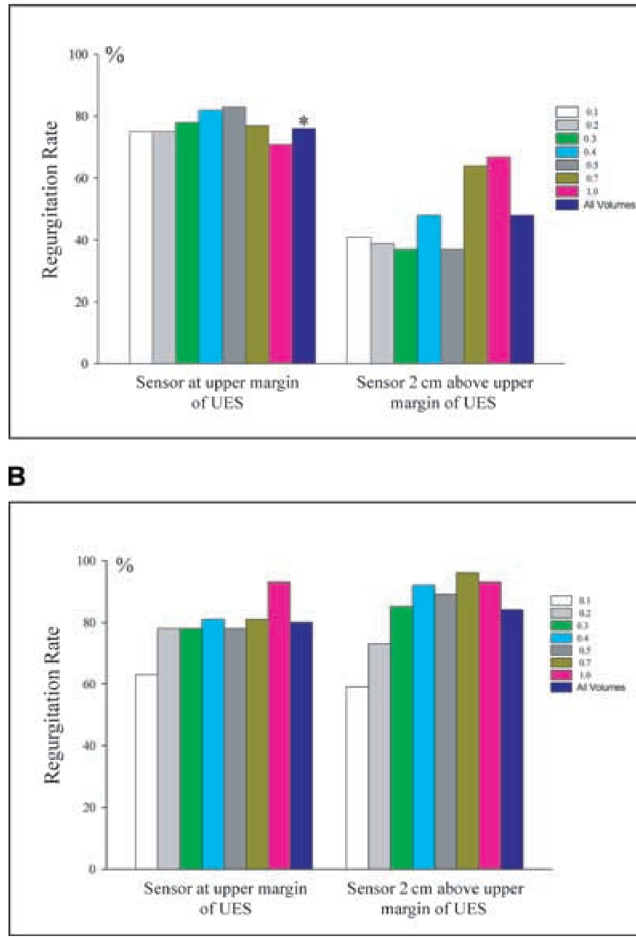

Figure 4. The effect of sensor position and volume of infusate on impedance registration rate in the upright (*A*) and supine (*B*) positions. For all volumes, detection rate in the upright position was significantly higher when the impedance sensor was located at the UES upper margin adjacent to the injection port compared to when it was located 2 cm proximal to the UES margin and injection port ($P < 0.001$). In the supine position, the location of the impedance sensor did not significantly influence the detection rate. Moreover, the detection rate in the supine position was significantly higher compared to the upright position when the sensor was 2 cm away from the injection port. In contrast, when the sensor was located at the upper margin of the UES adjacent to the infusion port, there was no significant difference in the detection rate between the upright and supine positions. Values for infusate are color coded and shown in millimeters on the right.

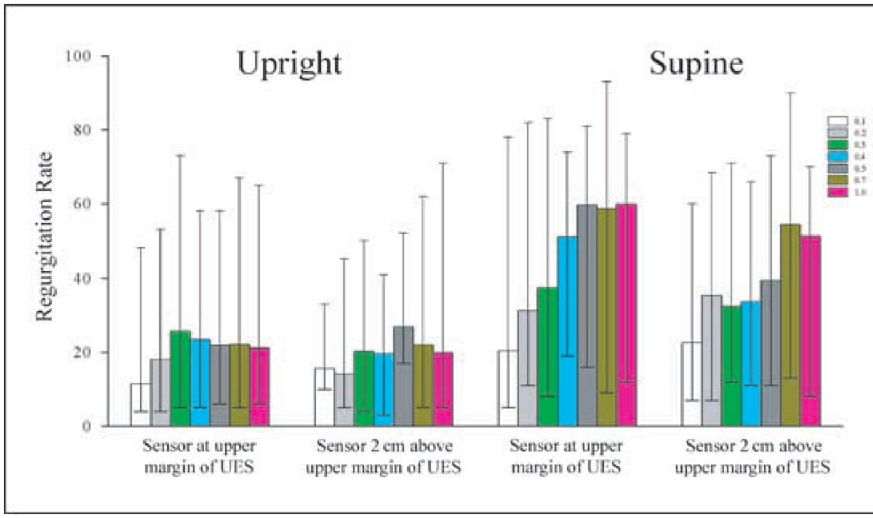

Figure 5. Median and range of the impedance drop associated with different volumes of infusate for two sensor locations in the upright and supine positions. There was significant variability in the magnitude of the impedance decrease in response to intrapharyngeal infusion of minute volumes of colored normal saline. Although, in general, the magnitude of the impedance drop due to intrapharyngeal infusion of 0.1 to 1.0 mL of colored normal saline in the upright position seemed to be less than that for both sensor locations, the differences did not reach statistical significance.

The fact that, depending on the infusate volume and distance between the infusate entry point and impedance sensor, up to 60% of the minute simulated pharyngeal reflux events were missed in this study should reiterate the notion that this technology and the pH recording technology are unable to record all of the pharyngeal reflux events. If, indeed, this simulated study is any representation of the possible scenarios in clinical practice, these recording devices can grossly underestimate the occurrence of pharyngeal reflux events.

The experimental design in the present study allowed us not only to simulate fluid reflux events, but also to simulate acidic and nonacidic gaseous/mist reflux episodes. For nonacidic gaseous reflux, we rapidly injected 50 mL of air into the esophagus causing belching with its resultant gas ventilation into the pharynx. For acidic mist, we infused 0.1 N HCl into the esophagus before inducing belching. This resulted in ventilation of acid mist and its low pH was documented by the pH-recording site incorporated on the impedance probe at the middle of the distance between impedance couplets. Study findings indicate that combined impedance and pH sensors are capable of recording acidic and nonacidic liquid and mist/gaseous reflux events.

The findings of the present study indicate a different pattern of impedance change between neutral gas vented from the esophagus and that infused into the pharynx. While for the former, impedance change is abrupt and substantial, for the latter, changes are gradual and relatively small. This finding suggests the existence of an additional mechanism for belch-induced pharyngeal impedance changes than that of mere gas entry into the pharynx. Among these, the change in configuration of the pharyngeal cavity due to belching, which can result in separation of the sensor from the pharyngeal wall, needs to be considered. It needs to be remembered that in this study different volumes of infusate were used to simulate contact of refluxate of different volumes with the impedance sensor and assess its sensitivity. These infusions only simulate certain volumes of reflux events. The biomechanics of reflux events, which in addition to volume includes intrabolus pressure, pressure gradient, and velocity, etc., are not simulated here, because the purpose of this study was not to model reflux events.

Identification of naturally occurring pharyngeal reflux events in the clinical setting can pose a significant difficulty if a single detecting sensor, either pH or impedance, is used because of the inability of a single sensor to determine the direction of the flow. For this reason, earlier studies (2–4) have used double or triple sensors spanning the esophagus and pharynx to ascertain the retrograde nature of the recorded events. In the present study, the above-mentioned difficulty was overcome by direct observation of the simulated reflux events using transnasal pharyngo-laryngoscopy.

In general, the documentation of pharyngeal reflux of gastric contents by available pH and impedance monitoring systems has not provided an acceptable diagnostic yield (4, 12). The reasons for this shortcoming, we believe, include in part the lack of knowledge about the best sensor position, influence of posture on contact of refluxate with the sensor, incomplete characterization of physical and chemical properties of injurious refluxate, etc. The present study addresses some of these issues, and the obtained information can help modify the current recording techniques to achieve better sensitivity and specificity and symptom association in patients with reflux-attributed supraesophageal symptoms.

In summary: (a) impedance sensors can detect as small a volume as 0.1 mL, and combined with a pH sensor can detect acidic and nonacidic liquid, mist or combined liquid, and mist reflux events; (b) placement of the impedance sensor at the proximal margin of the UES yields the highest detection rate compared to probe placement 2 cm proximally; and (c) depending on the volume of refluxate and location of the impedance sensor, a substantial minority of simulated reflux events can be missed. This issue should be taken into consideration before dismissing the occurrence of pharyngeal reflux of gastric contents in patients with supraesophageal symptoms of GERD.

ACKNOWLEDGMENT

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STUDY HIGHLIGHTS

What Is Current Knowledge

- Multichannel intraluminal impedance (MII) can record pharyngeal reflux.
- Performance characteristics of an MII device in the pharynx are unknown.

What Is New Here

- Defines optimal recording site and influence of subject posture on pharyngeal impedance recording.
- Defines the performance characteristics of MII device in recording pharyngeal reflux events.

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CONFLICT OF INTEREST

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