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Detection of Small Bolus Volumes Using Multiple Intraluminal Impedance in Preterm Infants

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ABSTRACT
Background: Multiple intraluminal impedance (MII) is a new technique that allows detection of reflux and swallows via changes in impedance caused by a liquid bolus inside the esophagus. The method is independent of pH. The authors studied the ability of this technique to detect the small bolus volumes potentially occurring in young infants.
Methods: Ten preterm infants (median gestational age at birth, 33 weeks; range, 25–36 weeks; age at study, 9 days; range, 2–39 days) underwent 10 instillations each of 0.1 mL to 0.5 mL saline while MII was recorded via a 2.4-mm nasogastric catheter. MII signals were analyzed for swallows, defined as a decrease in impedance starting within 1 minute. From the liquid instillation in the most proximal channel and extending downward, impedance changes during these induced swallows were compared with those occurring during spontaneous swallows.
Results: All 100 liquid instillations resulted in a typical impedance pattern, occurring after a median interval of 4.4 seconds (range, 1.8–8.9 seconds). The decrease in impedance was more pronounced than after spontaneous swallows (30% vs. 24%, $P < 0.03$) and extended downward more rapidly (12.3 cm/s vs. 5.8 cm/s, $P < 0.01$).
Conclusion: Bolus transport of small liquid volumes can be detected via MII. ***JPGN 36:381–384, 2003.*** **Key Words:** Gastroesophageal reflux—Multiple intraluminal impedance—Validation. © 2003 Lippincott Williams & Wilkins, Inc.

Diagnosis of gastroesophageal reflux (GER) has traditionally been performed using 24-hour esophageal pH monitoring. However, a disadvantage of this technique is that it does not allow for the detection of pH-neutral reflux, which may account for >75% of GER in infants (1–3). This potential problem can be avoided by using a new method for reflux detection, the multiple intraluminal impedance (MII) technique. This technique is based on the intraluminal measurement of electrical impedance between several closely arranged electrodes during a bolus passage. It allows the detection of fluid boluses that occur in an antegrade (swallows) and in a retrograde (GER) fashion and is increasingly used to diagnose disorders of gastrointestinal motility in pediatric and adult subjects (4,5).

Previous studies have shown that MII reliably detects large (5–15 mL) liquid boluses in adults and small (0.1–5 mL) air bubbles in vitro (6,7), but it is unknown whether it will also detect the small bolus volumes potentially found in young infants. In this study, we investigated whether small volumes of liquid, swallowed after being instilled into the pharynx, can be detected by MII.

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PATIENTS AND METHODS

Multiple intraluminal impedance was measured in 10 preterm infants (median gestational age at birth, 33 weeks [range, 25–36 weeks]; age at study, 9 days [range, 2–39 days]; weight at study, 1,698 g [range, 1,235–2,365 g]) while repeatedly instilling small volumes of prewarmed saline (37°C) into their oral cavity using a 1-mL syringe. Instillation volumes began with 0.1 mL and were increased in 0.1-mL increments up to 0.5 mL; each volume was given twice with a 3-minute pause between instillations. Infants were quietly awake in a 15° head-elevated supine position and had their heart rate and pulse oximeter saturation monitored throughout. The protocol called for termination of the study if an infant developed bradycardia or hypoxemia during the procedure. Infants were continuously observed, and any swallow visible after a fluid instillation was documented. If, after instillation, liquid flowed from the mouth, the procedure was discounted, and the fluid instillation was repeated. The MII equipment consisted of a specially designed impedance catheter with 9 metallic cylinders placed 1.5 cm apart from each other around an 8-French (2.4 mm) feeding tube, and a digital recording system (z-lab, Sandhill Scientific, Highlands Ranch, CO, U.S.A.). Catheters were introduced through a nostril into the esophagus and positioned so that the uppermost electrode remained visible inside the pharynx, allowing measurements of changes in impedance at the pharyngeal level. Recordings were electronically marked each time a liquid bolus was instilled. The investigator at bedside was blinded to the impedance measurements. The Ethics Committee at Hannover Medical School approved the protocol, and written informed parental consent was obtained.

Recordings were analyzed by one of the authors (C.W.) for the presence of swallows, defined as a decrease in impedance starting in the uppermost channel and extending downward within 1 minute after the liquid was instilled (Fig. 1) (8). The impedance changes occurring during a swallow were analyzed for the maximum decrease in impedance in relation to the preceding baseline, measured in the most proximal channel, and for the speed with which this decrease in impedance extended distally (Fig. 1). Baseline was defined as the mean of the impedance values measured 3, 4, 5, and 6 seconds before the onset of this decrease in impedance.

To further characterize these induced swallows, they were compared with swallows occurring spontaneously, i.e., when the infants had swallowed their saliva, and analyzed in the identical manner. These were defined as the first spontaneous swallow occurring during a 1-minute window before the next liquid instillation.

Data are presented as cumulative values and as medians and ranges of individual measurements. Correlations were calculated using the Spearman rank correlation test, and group comparisons were done using the Friedman analysis of variance (ANOVA) and Wilcoxon matched pairs test.

RESULTS

One hundred fluid instillations were performed. All resulted in an impedance pattern characteristic of swallowing. The decrease in impedance indicating a swallow started 4.4 seconds (median; range, 1.8–8.9 seconds) after the fluid had been instilled. Impedance decreased by 30% (median; range, 11–39%) from the preceding baseline. The average speed with which the decrease in impedance extended downward along the esophageal catheter was 12.3 cm/s (range, 6.2–13.3 cm/s).

Spontaneous swallows were found in 83 of 100 control windows and occurred significantly later than induced swallows (first spontaneous swallow occurred after a median of 20.8 seconds; range, 11.3–25.2 seconds;

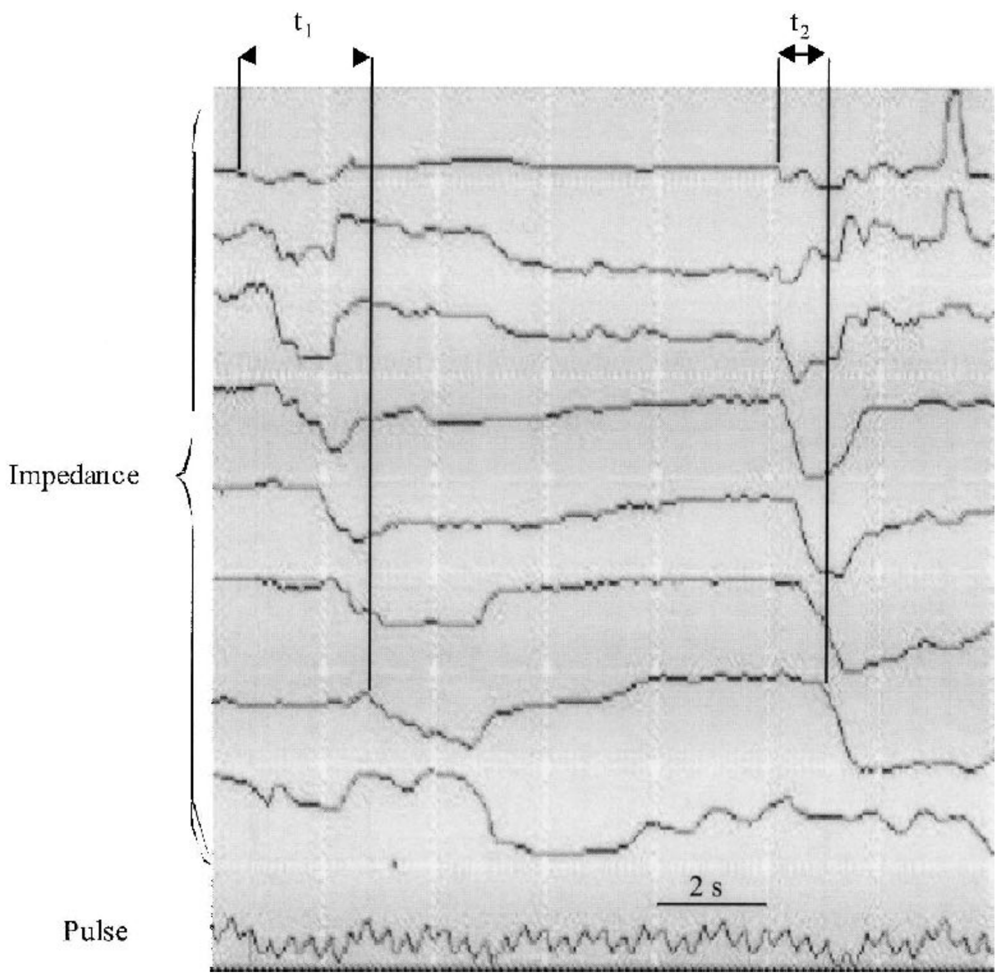

FIG. 1. Example of spontaneous swallow occurring immediately before an induced swallow. Note that the lowest electrode was placed inside the stomach. t_1, bolus transport time with induced swallow; t_2, same with spontaneous swallow.

$P < 0.01$). The decrease in impedance was less pronounced (median, 24%; range, 8–34%; $P < 0.03$) and extended downward only half as fast (median, 5.8 cm/s; range, 2.4–7.2 cm/s; $P < 0.01$) as with induced swallows (Fig. 1), but there was too much overlap between data measured during induced versus spontaneous swallows to reliably separate the two.

Analysis of the changes in impedance in relation to the volume instilled showed a trend toward more pronounced decreases in impedance with increasing volume, which extended downward more rapidly ($P < 0.05$, Table 1). However, there was no significant correlation between bolus size and either the extent of the decrease in impedance or the speed with which it moved downward ($r < 0.67$, $P > 0.05$).

DISCUSSION

All swallows, induced by instilling 0.1 mL to 0.5 mL saline into the oral cavity of preterm infants, resulted in a characteristic impedance pattern and thus could be identified using MII. They were associated with a larger decrease in impedance and a more rapid bolus transport than seen during spontaneous swallows. However, there was considerable overlap between induced and spontaneous swallow data. We speculate that the more pronounced decrease in impedance with induced swallows was not related to bolus volume but rather to the higher conductivity of saline compared with saliva (9).

This study was not designed to calculate the specificity or the positive predictive value of MII in detecting liquid boluses. Rather, we wanted to find out how sensitive this new technique is to the detection of small bolus volumes potentially associated with GER in preterm infants. In adults, reflux detection via MII can be verified using pH monitoring (10). This is not possible for infants, who have nonacidic gastric contents up to 90% of the time (11). Thus, we had to look for alternative methods to validate MII. Scintigraphy and barium radiography do not allow long-term observation and have side effects. Manometry requires catheters that are too large to be safely used in preterm infants, particularly if combined with an impedance catheter (12,13).

TABLE 1. *Extent of the fall in impedance baseline and of the speed with which these changes moved down the esophageal catheter during induced swallows of various volumes*

Volume	Fall in impedance from prior baseline (%): median (range)	Bolus speed (cm/s): median (range)
0.1 ml	27.1 (9.6–54.6)	6.6 (2.4–21.0)
0.2 ml	24.9 (6.4–50.0)	7.3 (3.6–21.0)
0.3 ml	28.1 (10.8–54.3)	12.4 (2.2–26.3)
0.4 ml	26.9 (7.7–49.9)	11.1 (2.8–26.3)
0.5 ml	30.0 (5.5–49.6)	11.1 (5.3–26.3)

The increases with volume in the extent of the fall in impedance and in bolus speed were significant ($P < 0.05$, Friedman Anova).

Thus, we hypothesized that except for the direction of the change in impedance and the number of channels involved, there should be no fundamental difference whether changes in impedance are induced by liquid that is flowing *down* the esophagus (swallows) or liquid that is flowing *up* the esophagus (GER). Therefore, we decided to test the sensitivity of MII to small bolus volumes via induced swallows. For safety reasons, namely avoidance of the laryngeal chemoreflex (14), we chose physiologic saline instead of milk, although it is unlikely that this affected impedance patterns substantially. A potential problem with our approach is that swallows also occur spontaneously. However, because of the consistently close temporal relationship between the fluid instillations and the subsequent decreases in impedance, we are confident that the changes in impedance observed did in fact reflect swallowing of the instilled liquid.

In vitro studies have already shown that air bubbles of 0.1 mL in a column of liquid can be detected by MII (7), yielding a significant correlation between air volume and the amplitude of impedance changes and bolus speed. Our in vivo results confirm the high sensitivity of this technique, demonstrating that liquid volumes of only 0.1 mL can be detected. Clinical questions not addressed by our study include 1) what is the typical refluxate volume in preterm infants, and 2) do nonacidic reflux volumes of 0.1 mL or 0.2 mL, which may flow up the esophagus and can now be detected using MII, have any clinical relevance? Nonacidic reflux is unlikely to damage the esophageal mucosa or to induce apnea in preterm infants (15). Hence, as with any new technique, further data must be collected to help distinguish between normal, abnormal, and pathologic GER in this age group when using MII.

Sensitivity might have been lower if older subjects, who have a larger esophageal diameter, had been studied, but then bolus volume would also likely have been larger. Including data on larger bolus volumes might have resulted in a better correlation between bolus volume and impedance changes, but this was not an aim of our study, which rather concentrated on sensitivity to small volumes. Finally, because of insufficient sample size, we could not establish reference values for the speed of propagation of dry or wet swallows. However, our data on the speed with which the bolus was propagated down the esophagus concur with those obtained using manometry (8,16), further confirming the validity of impedance in documenting esophageal motility.

In conclusion, this study has shown that liquid volumes as small as 0.1 mL result in a typical esophageal impedance pattern, suggesting that MII is highly sensitive for detecting GER.

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