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ORIGINAL ARTICLE

Multipoint measurement of intragastric pH in healthy preterm infants

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Background: The diagnostic use of 24 hour oesophageal pH monitoring in infants is controversial because of the impact of feed buffering of gastric acidity.

Aim: To re-evaluate the effect of feeding on gastric pH and reflux using multipoint pH measurements.

Subjects: Fifteen healthy premature infants fed every four hours.

Methods: Oesophageal pH and intragastric pH at 3, 6, and 9 cm below the lower oesophageal sphincter were simultaneously measured using a four channel pH probe for four hours after bolus feeding. Parameters of pH were compared for the different levels within the stomach. During reflux episodes, the nadir pH was compared with intragastric pH at all levels.

Results: The proximal stomach was more significantly buffered by feeding and slower to re-acidify postprandially than the mid and distal stomach (42.2% of the time at pH < 4 compared with 58.7% and 55.7% respectively). During 27 of 62 gastro-oesophageal reflux episodes, nadir oesophageal pH was lower than the pH of the proximal stomach but always equal to or higher than the pH of the distal stomach.

Conclusions: These data indicate that previous studies may have overestimated the effect of feeding on gastric acidity and reflux.

The use of 24 hour distal oesophageal pH monitoring as a diagnostic test for gastro-oesophageal reflux (GOR) disease in infants, particularly premature infants, is controversial, with little consensus among investigators on the appropriate normal/abnormal diagnostic criteria applicable in these patients. Studies of intragastric pH in premature infants have reported that the average percentage recording time that the gastric pH was below 4 was low, 24.5–42.4%,^{1, 2} and this has led to the derivation of "corrected" reflux indices (% time oesophageal pH < 4 when gastric pH < 4) for diagnosis of reflux. The utility of this approach has yet to be determined, but has led to a recommendation that oesophageal pH monitoring is deemed inappropriate in premature infants.³ It is also important to note in this context that a large study of 90 infants recently failed to find any effect of gastric buffering on reflux index.⁴ Therefore, the use of simultaneous gastric pH monitoring to correct for the effect of food buffering on gastric pH may be flawed. Furthermore, recent studies in preterm infants have used a gastric pH probe situated in the cardia. However, adult studies have previously shown that there are substantial regional differences in intragastric pH, with pH significantly less acidic in the cardia than in the body of the stomach.⁵

The aim of this study was therefore to use a novel pH feeding assembly to measure intragastric pH at multiple sites within the stomach to determine the extent to which gastric pH differs regionally within the stomach, and how these differences may influence oesophageal acidity during GOR episodes.

METHODS

Subjects

Intragastric pH monitoring studies were performed in 15 preterm infants from the special care baby unit at the Women's and Children's Hospital who were healthy for relative gestational age and were receiving full enteral bolus feeds at four hourly intervals. The protocol for this study had been approved by the research ethics committee of the hospital, and written informed consent was obtained from

the parents. The infants had a mean (SD) postmenstrual age of 36 (1) weeks (range 35–38) and a mean (SD) weight of 2614 (201) g (range 2330–3100). No infants had known gastrointestinal problems, feeding difficulties, or were receiving drugs that would interfere with normal gastrointestinal function. During the studies, the infants were fed 50–80 ml (22–30 ml/kg) of either non-fortified expressed breast milk (n = 13) or infant formula (n = 2).

Measurement techniques

Oesophageal and intragastric pH was measured simultaneously using a purpose built four channel antimony pH probe (2.2 mm outer diameter) with pH sensors located 0, 3, 6, and 12 cm from the probe tip and a port for feeding located at 3 cm (fig 1). In each infant, the probe was positioned with the most proximal pH sensor 3 cm above the lower oesophageal sphincter (LOS) and distal sensors 3, 6, and 9 cm below the LOS. The distance from the nares to the LOS was estimated using the established relation between body weight and LOS position.⁶ As the infants were healthy, positioning of the probe radiologically was deemed to be unacceptable. The Medtronic "Digitrapper" pH monitoring system (Medtronic, Stockholm, Sweden) was used to acquire the pH data, and analyses were performed using "Esophagram" program (Medtronic) and Acqknowledge v3.0 (Biopac Systems Inc, Goleta, California, USA).

Gastric half emptying time (GET_{1/2}) was measured using the [¹³C]octanoic acid breath test as previously described.⁷

Study protocol

At the beginning of the study, the infants were intubated with the pH probe and then positioned in the right lateral posture. After a 10 minute baseline pH recording, a bolus feed containing 100 µl [¹³C]octanoic acid was administered

Abbreviations: GOR, gastro-oesophageal reflux; LOS, lower oesophageal sphincter

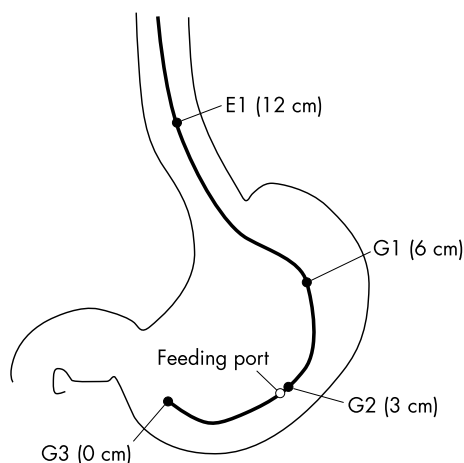


Figure 1 Schematic of the pH probe in situ. Sensors were located 12 cm (E1), 6 cm (G1), 3 cm (G2), and 0 cm (G3) from the tip. With the probe correctly positioned, E1 was located 3 cm above the lower oesophageal sphincter (LOS), and sensors G1, G2, and G3 were located 3, 6, and 9 cm below the LOS.

over a period of 10–15 minutes. Oesophageal and gastric pH was then continuously recorded for four hours from the start of feeding.

Analysis of pH recordings

The raw pH data (acquired at 1 Hz) were averaged over consecutive 10 minute epochs to assess the pattern of change in intragastric pH over the four hour study period and determine values for baseline pH (before feed), maximum pH (after feed), minimum pH (after feed), time taken to reach maximum pH, time taken to reach minimum pH, and time taken to reach to pH 4. Percentage time that pH < 4 was also calculated using automated analysis.

Acid GOR episodes were identified by falls in oesophageal pH of 1.0 pH unit or more over five seconds. GOR episodes with nadir pH > 4 were defined as “low acid” GOR, and episodes with nadir pH < 4 were defined as “acid” GOR. For

each GOR episode recorded, the pH of the refluxate (represented by the nadir pH of the reflux episode) was compared with the pH of gastric contents recorded at each of the three intragastric pH sensors. The reflux index (% time oesophageal pH < 4) was also determined by standard automated analysis.

Relations between intragastric pH, GOR, and $GET_{1/2}$ were also examined.

Statistical analysis

Mean (SE) data were compared using the paired *t* test. Relations between variables were assessed using simple regression analysis. Coefficient of variation was used to assess variability among patients.

RESULTS

Gavage feeding produced a characteristic pattern of gastric pH increase followed by re-acidification. This pattern was present at all levels within the stomach in all infants studied (fig 2). Significant regional variations in the pattern of feeding buffering and re-acidification were observed, the proximal stomach (gastric 1) being more significantly buffered by feeding and slower to acidify postprandially than the mid to distal stomach (gastric 2 and 3; table 1). Gastric 2 appeared to be most optimally positioned to record maximum acidity, as gastric 3, although the most distal sensor, tended to record higher pH values during the period two to four hours postprandially (fig 2, table 1). The mean (SE) % time pH < 4 calculated using automated analysis was 42.2 (4.4)%, 58.7 (3.7)%, and 55.7 (5.1)% for gastric sensors 1, 2, and 3 respectively. The mean % time pH < 4 taken across all sensors ranged from 30.9 to 67.5% (mean 52.7 (3.1)%; coefficient of variation (CV) 21.9%).

Reflux index (% time oesophageal pH < 4) ranged from 0 to 14.7% (mean (SE) 5.3 (1.4)%). A total of 62 GOR episodes were observed (mean (SE) 4.5 (0.6) per patient). Of these, 35 were low acid and 27 were acid.

Over time, the nadir pH during all GOR episodes decreased, and the magnitude of the pH fall during GOR episodes increased, leading to an increase in the proportion of acid versus low acid GOR episodes. During the period 0–2 hours

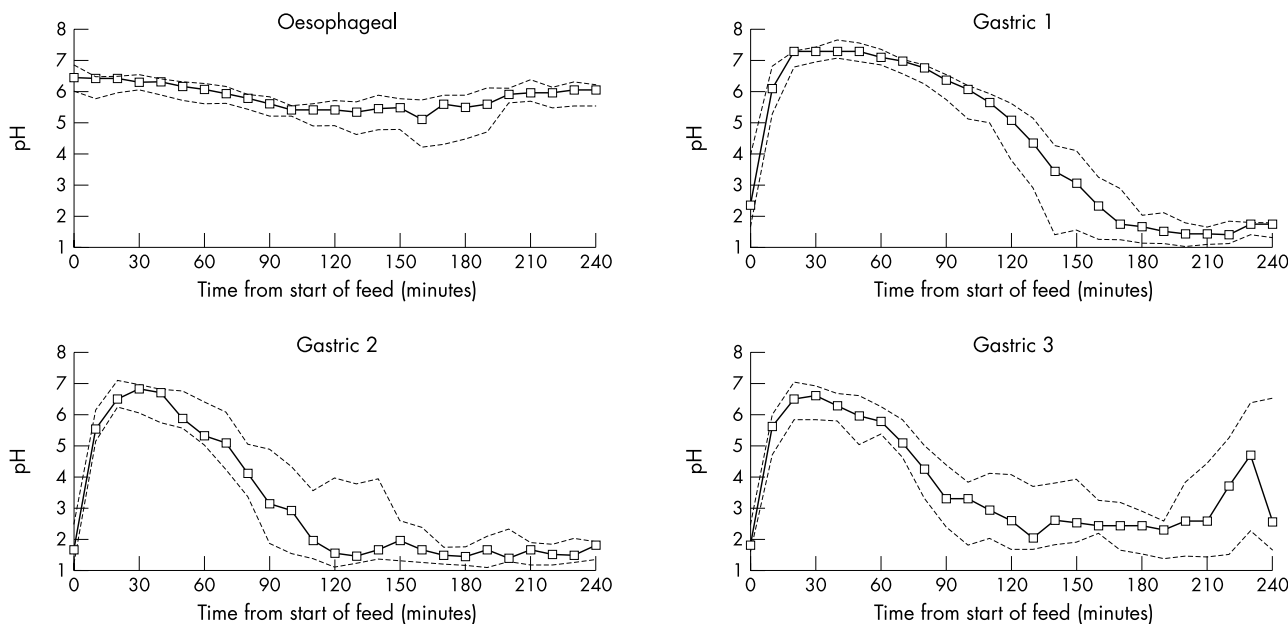


Figure 2 Median pH profiles recorded in the oesophagus and stomach at 3 cm (Gastric 1), 6 cm (Gastric 2), and 9 cm (Gastric 3) below the lower oesophageal sphincter in the 15 infants studied. Dotted lines represent the interquartile range.

Table 1 Spatial variation in parameters of intragastric acidity

Parameter	pH sensor		
	Gastric 1 (3 cm)	Gastric 2 (6 cm)	Gastric 3 (9 cm)
Baseline pH (before feed)	2.6 (0.4)	1.8 (0.2)	2.1 (0.3)
Maximum pH (after feed)	7.3 (0.2)	6.8 (0.1)*	6.6 (0.3)*
Minimum pH (after feed)	1.4 (0.2)	1.1 (0.1)	1.3 (0.1)
Time to reach maximum pH (min)	35 (3)	24 (2)**	29 (3)
Time to reach minimum pH (min)	197 (7)	161 (10)**	164 (12)*
Time to reach pH 4 (min)	136 (7)	91 (8)***	82 (9)**
Mean pH			
0–1 hours	6.9 (0.2)	6.0 (0.2)	5.7 (0.4)
1–2 hours	6.0 (0.2)	3.5 (0.4)***	3.7 (0.4)**
2–3 hours	2.8 (0.3)	2.0 (0.3)**	2.7 (0.3)†
3–4 hours	1.9 (0.3)	1.8 (0.3)	3.1 (0.5)*†

Data presented as mean (SE).
 *p < 0.05, **p < 0.005, ***p < 0.0005 compared with gastric 1.
 †p < 0.05 compared with gastric 2.

after feeding, 22 GOR episodes (consisting of 18% acid) were recorded with a mean (SE) nadir pH of 4.7 (0.2) and a mean (SE) pH fall of 1.3 (0.1) units. In comparison, during the period 2–4 hours, 40 episodes (consisting of 58% acid) were recorded with a mean (SE) nadir of 3.5 (0.2) (p < 0.05) and a mean (SE) pH fall of 2.1 (0.2) units (p < 0.05).

GOR nadir pH correlated with the mean gastric pH recorded across all three sensors (r = 0.650, p < 0.0001). When GOR nadir pH was compared with intragastric pH recorded by individual sensors, GOR nadir pH was always equal to or higher than the pH recorded by gastric 2 and 3, but GOR nadir pH often (n = 27; 45%) fell to levels below the pH recorded by gastric 1 (fig 3). Average GOR nadir pH was significantly lower than gastric pH recorded by gastric 1 during the period 2–3 hours postprandially (fig 4). The occurrence of GOR was often associated with rapid equalisation of pH across all sensors (fig 3). Such patterns of rapid pH change may suggest that expulsion of refluxate into the oesophageal body is sufficiently vigorous that it causes turbulence and mixing of contents between regions of varying acidity.

All infants had normal gastric emptying, with half gastric emptying times ranging from 32 to 70 min (mean (SE) 48 (4) min). Gastric emptying rate did not correlate significantly with any measured parameters of gastric acidity or acid GOR.

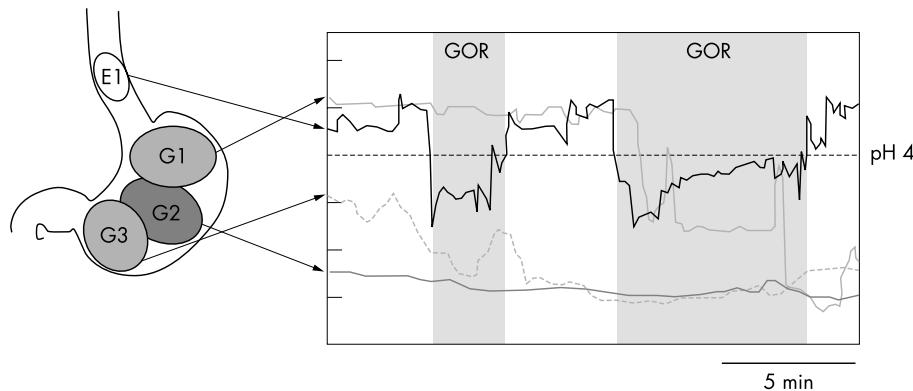


Figure 3 Example tracing of intragastric pH recorded at the time of gastro-oesophageal reflux (GOR). Two reflux episodes are shown (shaded regions). During the first episode, oesophageal pH falls to a nadir that is lower than the pH recorded in the proximal stomach (G1) but greater than that in the mid and distal stomach (G2 and G3), suggesting that refluxate is originating from the mid and/or distal stomach. During the second reflux episode, expulsion of refluxate is followed by acidification of the proximal stomach indicating mixing of gastric contents.

DISCUSSION

This study evaluated intragastric pH changes and acid reflux in response to feeding in a group of healthy premature infants with normal gastric emptying. Gastric pH measurements were simultaneously recorded at multiple sites within the stomach, and these recordings showed significant spatial and temporal differences in gastric acidity. During reflux episodes, the acidity of the refluxate is more closely related to the acidity of the distal stomach contents than the acidity of the contents of the cardia.

The major finding of this study is that the position of a pH sensor within the stomach is a critical factor affecting pH measurement. As shown previously in adults, gastric acidity is lower in the cardia than the distal stomach.⁵ Two previous studies, which measured gastric pH in symptomatic preterm and term infants, positioned one gastric pH sensor in the cardia approximately 2.5–3 cm below the LOS. These studies reported average values for gastric % time pH < 4 of 24.5–42.4%.^{1, 2} In our study, a sensor located in a similar position gave similar results (42.2%), but this sensor also overestimated the time required for gastric acidity to reach pH 4 by 36 min and underestimated the % time pH < 4 by 17%, compared with more distally located sensors. Our data suggest that the pH sensor was suboptimally positioned in previous studies, and this has led to an underestimation of gastric acidity and an overestimation of the impact of gastric pH buffering by feeds. In the patient group studied, the optimal location for the pH sensor appears to be 6 cm below the LOS for the 15 infants studied. At this location the gastric % time pH < 4 was 58.7%.

The previous studies also reported substantial variability among patients, the range of values for % time gastric pH < 4 being 1.7–98.8% (CV 68.4%)¹ and 0.6–69.1% (CV 70.6%).² In our study, the results were far less variable being 10.6–59.5% (CV 37.7%), 33.3–77.6% (CV 23.3%), and 15.3–97.7% (CV 34.5%) for 3, 6, and 9 cm below the LOS and 30.9–67.5% (CV 21.9%) for the mean taken across all sensors. The greater variability observed previously may be due to the studies being carried out over 24 hour in symptomatic rather than normal infants, meaning that the investigators were less able to control and standardise the feeding regimen.

Although these data suggest that the impact of feeding on gastric pH has been overestimated, it is clear that the way infants are fed reduces gastric acidity when compared with adults, where in the body of the stomach the median % time pH < 4 is about 88%.⁵ Feeding, however, also provides the stimulus for reflux to occur through gastric distension and stimulation of transient LOS relaxation and further

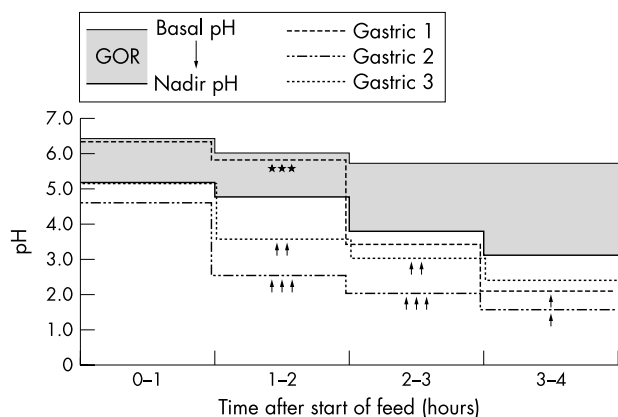


Figure 4 Comparison of the mean basal and nadir pH during gastro-oesophageal reflux (GOR) episodes with regional intragastric pH. *Gastric pH significantly higher than nadir pH (** $p < 0.005$); †gastric pH significantly lower than nadir pH († $p < 0.05$, †† $p < 0.005$, ††† $p < 0.0005$).

stimulation of gastric acid secretion. In our study, the correlation coefficient between reflux index and % time intragastric pH < 4 was 0.189 ($p = 0.530$), suggesting that a reduction in the % time pH < 4 will not necessarily equate to a reduction in the reflux index per se.

Of the acid reflux episodes detected using our criteria (fall of 1 pH unit), 55% were acid and 45% were low acid. The nadir pH recorded during reflux correlated significantly with the average pH across all sensors, but on 45% of occasions the nadir pH fell to a level that was lower than the pH recorded 3 cm below the LOS. This type of event occurred predominantly in the first two hours after feeding. Such events are nevertheless interesting as they indicate that the gastric contents, which ultimately become refluxate, originate at a level that is below the cardia. Our multiple point measurements show that in these infants, who are receiving

liquid feeds, gastric pH is clearly stratified and that expulsion of gastric contents during a reflux episode results in turbulent mixing as gastric content is expelled as shown in fig 3.

In conclusion, this study readdresses the issue of feed buffering and gastric acidity in the neonate. Our data indicate that previous studies may have underestimated the level of gastric acidity because of suboptimal positioning of the pH sensor within the stomach. We therefore recommend a dual sensor spacing of 8–9 cm rather than 5 cm to allow more optimal positioning of a sensor in each of the distal oesophagus and stomach. Recent commentary on the suitability of oesophageal pH monitoring, based on these previous reports,³ needs to be treated with caution in the light of our findings.

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REFERENCES

- 1 Washington N, Spensley PJ, Smith CA, *et al*. Dual pH probe monitoring versus single pH probe monitoring in infants on milk feeds: the impact on diagnosis. *Arch Dis Child* 1999;**81**:309–12.
- 2 Mitchell DJ, McClure BG, Tubman TRJ. Simultaneous monitoring of gastric and oesophageal pH reveals limitations of conventional oesophageal pH monitoring in milk fed infants. *Arch Dis Child* 2001;**84**:273–6.
- 3 Grant L, Cochran D. Can pH monitoring reliably detect gastro-oesophageal reflux in preterm infants? *Arch Dis Child Fetal Neonatal Ed* 2001;**85**:F155–8.
- 4 Hegar B, Vandemaele K, Arana A, *et al*. Oesophageal pH monitoring in infants: elimination of gastric buffering does not modify reflux index. *J Gastroenterol Hepatol* 2000;**15**:902–5.
- 5 Katzka DA, Gideon RM, Castell DO. Normal patterns of acid exposure at the gastric cardia: a functional midpoint between the esophagus and stomach. *Am J Gastroenterol* 1998;**93**:1236–42.
- 6 Omari T, Benninga M, Haslam R, *et al*. Lower esophageal sphincter position in premature infants cannot be correctly estimated with current formulas. *J Pediatr* 1999;**135**:522–5.
- 7 Barnett C, Snel A, Omari T, *et al*. Reproducibility of the ¹³C-octanoic acid breath test for assessment of gastric emptying in healthy preterm infants. *J Pediatr Gastroenterol Nutr* 1999;**29**:26–30.