

THE INFLUENCE OF GASTRIC pH ON THE EVALUATION OF GASTROESOPHAGEAL REFLUX DURING PROLONGED ESOPHAGEAL pH MONITORING IN INFANCY

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Prolonged intraesophageal pH monitoring has become the preferred test to quantify acid gastroesophageal reflux (GER). We have performed this procedure concurrent with a regular feeding schedule as patients experienced symptoms in a similar environment. Hence, milk feedings tended to buffer gastric acidity, we attempted to investigate the influence of gastric pH on the evaluation of esophageal pH monitoring. Gastric and esophageal pH were simultaneously recorded by two separate pH electrodes for more than 20 hours in 81 infants (0~11 months) with GER symptoms. Radiological evaluations of GER and gastric emptying with barium and manometric studies were also performed in these infants. The results of this study indicate that: 1) Percentage of time with gastric pH < 4 increases with age in infancy. 2) Gastric pH is statistically not related to the evaluation of GER on esophageal pH monitoring. 3) Significantly delayed gastric emptying occurred in 15 out of the cases studied, however, gastric pH is not related to the delay. 4) In 36 cases that GER was negative on pH monitoring, GER was documented during radiological study in 20 cases, the abnormalities of lower esophageal sphincter (LES) pressure showed in 24 cases, and esophageal dysmotilities occurred in 18 cases on manometric study. These cases with abnormal findings were successfully treated followed by our treatment protocol for GER. In conclusion, prolonged esophageal pH monitoring with regular feeding is independent of the gastric acidity in infancy, and the method is useful to evaluate pathological GER. However, radiological and manometric studies, in addition to pH monitoring, should be required to evaluate the total gastroesophageal function.

Introduction

In recent years, long-term esophageal pH monitoring has become the preferred technique for the detection and the quantification of gastroesophageal reflux (GER)¹⁾. However, although it allows acid refluxes to be distinguished, it is less useful for identifying alkaline or mixed (acid mixed with alkaline material) refluxes. We performed the procedure concurrent with a regular feeding schedule as patients

experienced symptoms in a similar environment. It has been reported in young infants that intragastric pH may influence GER because formula feedings tend to buffer gastric acidity^{2)~5)}. We investigated the influence of gastric pH on the evaluation of GER on prolonged esophageal pH monitoring in this study.

Subjects and Methods

Subjects

Eighty one infants with GER symptoms such

as recurrent vomiting, apparent life-threatening events (ALTE), or wheezing (48, 18, and 15 cases, respectively), who had been referred to Tokyo Women's Medical College, Daini Hospital, between June 1991 and October 1994, were included in this study. Infants ranged in age from 6 days to 11 months.

Methods

Gastric and esophageal pH were continuously recorded for more than 20 hours using a flexible antimony pH probe with dual channel (two recording sites localized 7 cm from each other) placed 3 cm above and 4 cm below the manometric lower esophageal sphincter (LES) (ambulatory pH Liberty System and Digitrapper Mark II Gold, Synectics Medical, Sweden). Pathological GER on pH monitoring is defined as more than 5.15% of the time with esophageal pH less than 4.0. The value represents two standard deviations above the mean value from the normal controls (8 infants without GER symptoms, range 1~9 months, mean age 4.6 month: $2.85 \pm 1.15\%$) in our institute. Upper gastrointestinal series with barium were performed recording with video-film to obtain the grade of GER following by McCauley's

technique⁶). Anatomical abnormalities and strictures were also evaluated with the radiological examination, gastric emptying time at 30 and 60 minutes by intake of the barium equal to the amount of their general feeding. It was measured by holding them in a head-up position after barium intake. Manometric studies were also performed to evaluate LES function and esophageal motility such as peristaltic movement with wet swallow using a catheter with 3 pressure transducers (the length between sensors was 5 cm), Gaeltec Research, Goodman Co., Italy. The normal value of LES pressure is defined as 29.6 ± 12.0 mmHg for newborn babies, 26.0 ± 4.1 mmHg for infants taken from the normal controls (34 newborn babies and 10 infants without GER symptoms) in our institute (Table 1).

The treatment for GER followed by "the treatment protocol for GER" in our institute as shown in Table 2. In cases of positive GER on pH monitoring antacid agents is indicated, whereas, in the negative cases positional therapy only is taken. In cases of abnormalities of LES pressure or esophageal motility anticholinergics or prokinetics are indicated⁷).

Table 1 Evaluations of gastroesophageal reflux and esophageal motility

1) Esophageal pH monitoring
Criterion of significant GER ;
the percentage of the time with esophageal pH less than 4 is more than 5.15%
2) Upper gastrointestinal series with barium
Evaluation of GER (by McCauley's method)
grade 1) reflux into distal esophagus only
2) reflux extending above carina but not into cervical esophagus
3) reflux into cervical esophagus
4) free persistent reflux into cervical esophagus
5) reflux of barium with aspiration into the trachea or lungs
D) delayed reflux ; barium seen in esophagus on delayed films
Evaluation of anatomical abnormalities, strictures, and esophagospasms or pylorospasms
Gastric emptying time (holding in a head-up position) ;
Delayed time is defined as more than 1 hour.
3) Manometric study
Normal range of LES pressure ; < 1M 17.6~41.6 mmHg
< 12M 21.9~30.1 mmHg
Esophageal dysmotilities ; Non-peristaltic contractions
Simultaneous contractions
Inappropriate relaxations of LES

GER : gastroesophageal reflux, LES : lower esophageal sphincter.

Table 2 Treatment protocol for GER in our institute

GER studies			Treatment
24hr-pH monitoring	Upper GI with barium	Manometry	
GER(-)	GER(-)	normal LESp	A) positional therapy
	GER(+)	low LESp	B) antacids
GER(+)	esophagospasm pylorospasm delayed E. or G. emptying	high LESp	C) anticholinergics
		esophageal dysmotility	D) prokinetics

GER: gastroesophageal reflux, LESp: lower esophageal sphincter pressure.

A) head elevated position and/or dietary advice, B) antacids or alginic acids, C) atropine sulfate(6~10 $\mu\text{g}/\text{kg}/\text{dose}$ before every feeding), D) cisapride or domperidone(0.3~0.7, 1 mg/kg/day, respectively).

Statistical Analysis

Simple linear regression analysis was used to test for the association between the percentages of the time (% time) with gastric pH less than 4 ($\text{pH} < 4$) and age in the result of pH monitoring. A comparison of the two regression slopes between cases with positive and negative GER was also made, and differences with $p > 0.1$ were interpreted as insignificant.

Results

1. The trace of pH monitoring in a typical case of early infants with GER is shown in Fig. 1. Gastric pH was kept 5~6 for 1.5~2 hours

following every milk-feeding, and GER was documented during low gastric pH.

2. The relationship between age and %time with gastric $\text{pH} < 4$ during pH monitoring is shown in Fig. 2. The cases of positive and negative for GER are indicated as opened and closed circles, respectively. The single linear regression line could be made in each of the two groups. Regression line in the group GER (+) ($Y = 32.45 + 3.65X$) revealed as a dot line, and regression line in the group of GER (-) ($Y = 32.04 + 2.67X$) revealed as a solid line in Fig. 2.

These results suggest that %time with gas-

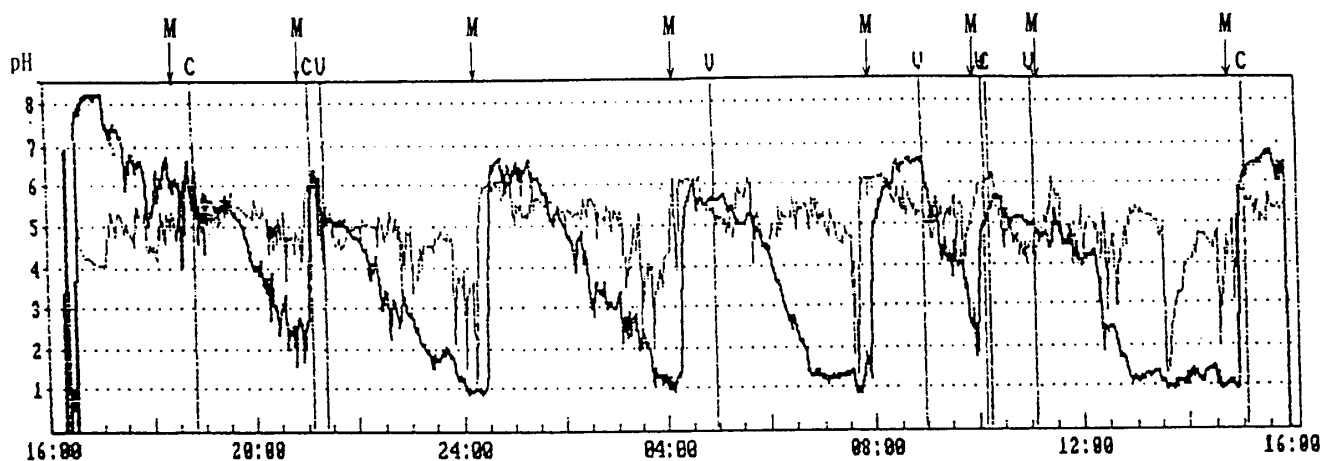


Fig. 1 A typical case of the infant with GER on esophageal and gastric pH monitoring. The gastric pH was kept 5~7 for 1.5~2 hours following every feeding, and GER demonstrated during low gastric pH. —: gastric pH, - - : esophageal pH, M: milk, V: vomiting, C: cough

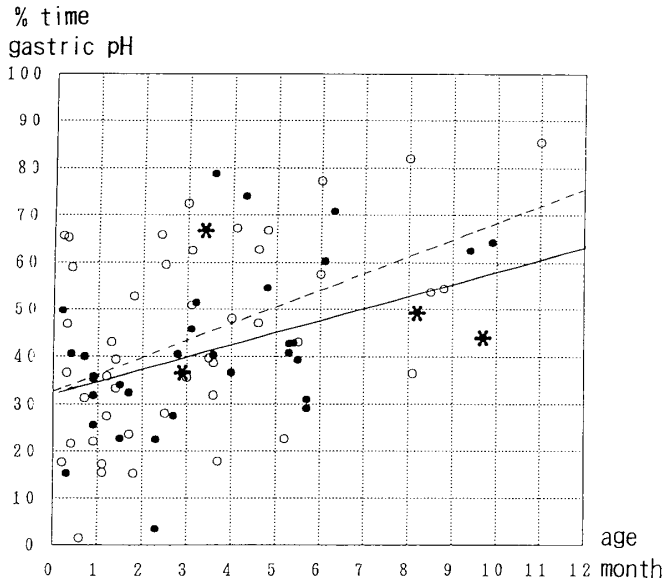


Fig. 2 The relationship between the change of gastric pH with age and GER on pH monitoring. The percentage of time with gastric pH < 4 increases with age in infancy, regardless of the result of GER. ○: GER(+)/pH monitoring, ●: GER(-)/pH monitoring, *: cases without abnormalities in all of the GER studies. ----: the regression line in the group of GER(+), —: the regression line in the group of GER(-).

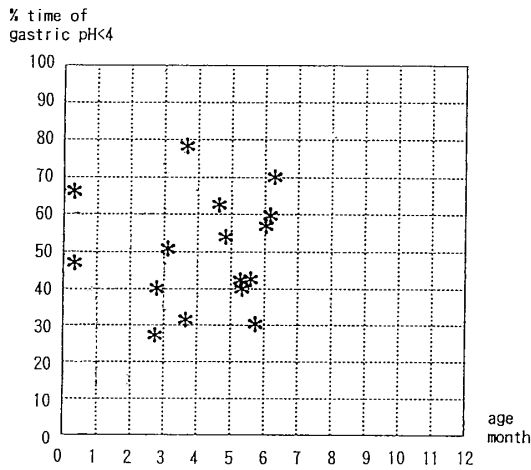


Fig. 3 The correlation between delayed gastric emptying and gastric pH
*: cases of delayed gastric emptying.

tric pH < 4 increases with age in infancy, regardless of positive or negative GER. In comparing the two regression slopes between positive and negative cases for GER, the difference was statistically insignificant ($p > 0.1$).

3. To investigate whether gastric emptying

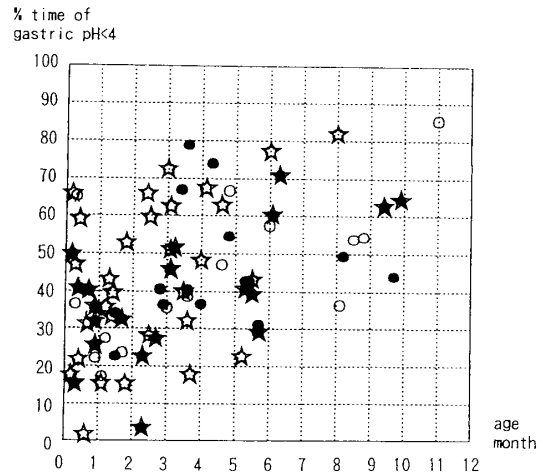


Fig. 4 The relationship among radiological GER, GER on pH monitoring, and gastric pH
○: GER(+)/pH monitoring, ●: GER(-)/pH monitoring, ☆: GER(-)/radiological and pH monitoring, ★: GER(+)/radiological and GER(-)/pH monitoring.

time was related to the gastric pH or not, a graph was made as shown in Fig. 3. Delayed gastric emptying occurred in 15 out of the 81 cases studied, however, %time with gastric pH < 4 was not related to the delay. While, delayed gastric emptying was documented in only 6 out of the 45 cases which was positive for GER on pH monitoring.

4. The relationship among radiological GER, GER on pH monitoring, and gastric pH showed in Fig. 4. Gastroesophageal reflux on radiological study with barium was documented in 51 out of the 81 cases regardless intragastric pH was high or low. In 36 cases that GER was negative on pH monitoring, GER was documented during radiological study in 20 cases. In manometric study abnormalities of LES pressure and esophageal motility occurred in 24 and 18 out of the 36 cases, respectively. These cases were successfully treated following by our treatment protocol for GER.

Discussion

It has been known that the elevated pH and a modest buffering capacity of milk temporarily neutralize gastric contents, and will possibly prevent the detection of reflux during pH

monitoring in young infants^{2)~5)}. In fact, gastric pH increases following every feeding as shown in Fig. 1. Therefore, in a typical case of early infants with GER, GER mainly detected with the presence of the low gastric pH after 1.5~2 hours of post feeding. It is an agreement that pathological GER is mostly noticed during the fasted or sleeping period³⁾⁴⁾. Several studies have confirmed that patients with proven esophagitis have more frequent reflux episodes and a higher percentage of time with a pH < 4 than do healthy controls^{8)~10)}. Agreement has been achieved that acid gastric content reflux into the esophagus constitutes major cause of reflux esophagitis during the patient's daily activities. Therefore, esophageal pH monitoring with regular feeding may be useful for finding the pathogenic factors in GER disease (GERD).

In our study, pH monitoring enabled us to document pathological GER in many younger infants with GER symptoms, in spite of low percentage of time with gastric pH < 4 during monitoring. Our results suggest that gastric pH may not be responsible for the evaluation of GER on esophageal pH monitoring with regular feeding. While delayed gastric emptying has been reported to be correlated to GERD¹¹⁾, some investigators have failed to show the correlation between gastric emptying and GER on pH monitoring in infants¹²⁾. Our radiological examination showed that there was no relationship between gastric pH and delayed gastric emptying. Although there were limitations of the method employed in this study, gastric pH might be determined by other factors such as secretory functions of gastric acid or hormones. The evaluation for GER with barium performed in our institute is useful to detect alkaline or mixed material reflux. In many cases of negative for GER on pH monitoring, there existed radiological evidence of GER or manometric documentation of esophageal dysmotility. It has been reported that manometric findings suspected esophageal dysmotility are more frequently present in

cases of severe GERD, and these abnormal manometric findings returned to be normal at the end to the therapy¹³⁾¹⁴⁾. We also documented that in infants with recurrent vomiting, the manometric finding of non-peristaltic contractions in the esophageal body and the incidence of inappropriate relaxations of LES significantly increased as compared with the control group¹⁵⁾. These results suggest that manometric study is valuable for the evaluation of pathogenic factors for GER. We conclude that the evaluation of acid GER on esophageal pH monitoring with regular feeding is independent of the gastric acidity in infancy, and the method is valuable to detect the pathogenic factors. However, for the total evaluation of gastroesophageal function radiological and manometric studies should be performed in infants with GER symptoms.

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乳児期の食道内 pH モニタリングの胃食道逆流症の 評価における胃内 pH の影響

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食道内 pH モニタリング (pH 検査) は, 現在, 胃食道逆流症 (GER) の評価法として最も信頼度が高いが, 乳児では哺乳による影響で胃内 pH が高い傾向にあり, GER の評価に影響を及ぼすといわれている。我々は GER 症状を有する乳児 81 例について, 日常生活と同じ授乳法で pH 検査を施行し GER も評価しているが, その際の胃内 pH の影響について検討した。これらの症例には消化管造影, 内圧検査も施行した。[結果]①胃内 pH < 4 の時間率は, 乳児期の月齢に従って上昇する。②日常生活と同じ授乳法で行った pH 検査の GER の評価は, 胃内 pH に影響されなかった。③胃排出能遅延は, 81 例中 15 例に認められたが, 胃内 pH との関連は認められなかった。④ pH 検査にて GER 陰性であった 36 例中 20 例は消化管造影による GER は陽性, 内圧検査にて下部食道括約筋 (LES) 圧の異常値は 24 例, 食道蠕動異常は 18 例に認めた。これらの症例には, 当科の GER の治療プロトコールに従って治療を行い, 全例, 症状は軽快した。[結論]乳児では, 哺乳により胃内 pH は変動するものの, 日常生活と同じ授乳法による pH 検査は, その GER の評価が, 胃内 pH < 4 の時間率に関係することなく, 乳児における GER の評価に有用であった。しかし GER の病態を把握するためには, pH 検査のみでなく, 内圧検査や放射線学的検査も行い, 胃食道機能の全体的な評価をすることが必要であると思われた。