Pressure events surrounding oesophageal acid reflux episodes and acid clearance in ambulant healthy volunteers

C P Barham, D C Gotley, R Miller, A Mills, D Alderson

Abstract
Previous studies of the mechanisms that precipitate acid reflux episodes and acid clearance have used unphysiological, short term hospital based data. A new 24 hour pH and motility recording system combined with computerised data analysis have been used to study naturally occurring acid reflux episodes in healthy ambulant volunteers. A variety of events that produced recognisable transdiaphragmatic pressure patterns were associated with acid reflux episodes (particularly belching). Peristaltic waves were the predominant contractions leading to oesophageal acid clearance and were the commonest contraction type during reflux episodes. Peristaltic wave parameters (amplitude, velocity, frequency, and percentage proportion) varied during different periods of the 24 hour recording. This study has produced new information about 24 hour oesophageal function and naturally occurring acid reflux which will provide a basis for comparison with patients with gastro-oesophageal reflux disease.

Figure 1: Examples of some of the pressure events precipitating acid reflux episodes in ambulant subjects. Arrows indicate the onset of a reflux episode and its associated pressure event.
clearly not physiological and, like inpatient pH studies compared with 24 hour recordings, the results may not represent naturally occurring reflux episodes in ambulant, outpatient subjects. The recent development of solid state recording systems has led to ambulatory studies. Most studies have not examined events surrounding reflux episodes, however, and have been limited by small memory capacity. too few pressure transducers, or difficulties in analysing the enormous amounts of data generated from long term measurements.

In order to study the mechanisms precipitating acid reflux episodes and examine acid clearance in control subjects, a unique 24 hour recording system has been developed which incorporates oesophageal pH measurement and simultaneous oesophageal body, LOS, and intragastric pressure recordings combined with computerised waveform analysis.

Methods

COMBINED OESOPHAGEAL MANOMETRY AND PH RECORDING SYSTEM

Recordings were obtained using two connected catheters—one for measuring pH, located 5 cm above the manometrically determined LOS (Synectics, UK, Oxford), and the other measuring pressures at several sites. The manometry catheter contains five solid state intraluminal pressure transducers (CTO-5/Sphinctometer, Gaeltec, Isle of Skye, Scotland). Three of these transducers are located in the oesophageal body (5 cm apart and radially offset by 1200), the lowest being level with the pH probe. A fourth transducer (starting 5 cm below the lowest oesophageal body transducer) consists of the 'sphinctometer'. Its design and performance has been described in detail elsewhere, but it essentially consists of a 6.3 cm long oil filled silastic chamber connected to a strain gauge. It records an integrated output of the pressure and length components of LOS function. Its length allows up and down movement of the LOS while still retaining sphincter contact. The fifth transducer lies 5 cm below the sphinctometer and is positioned in the stomach.

The recording unit (7-MPR, Gaeltec, Isle of Skye) allows 24 hour recordings from up to seven data channels because incoming pressure signals are processed so that rapidly changing pressure data are retained while few data points are stored when little pressure activity is occurring (for example, while sleeping). This data compression allows a full patient record to be stored on one 0.79 megabyte floppy disc.

Data is off loaded onto a 410/1 Acorn Archimedes computer (32 bit, 4 megabyte RAM; Acorn Computers, Cambridge). The automated analysis program scans the patient recording for pressure rises greater than 20 mmHg above the baseline for each pressure transducer.

Swallow waves are classified as peristaltic (when contractions recorded in the oesophageal body show a continuous progression down the oesophagus in all three transducers), non-propagated (if a distal oesophageal contraction fails to follow a propagated wave from the proximal two transducers), simultaneous (contractions in all three transducers at the same time), and segmental (isolated contractions in any of the three oesophageal transducers). All other patterns of contraction are grouped as complex waves. A table of the different types of waves and parameters describing those waves (for example, wave amplitude, velocity, and duration) is generated.

The oesophageal pH channel is scanned to identify and record pH fluctuations. A reflux episode begins when the pH falls below 4.0 and ends when the pH rises above 5.0.

STUDY PROTOCOL

Eighteen healthy volunteers (12 men and six women) with a median age of 48 years (range 16–73) underwent long term ambulatory pH and motility recordings. Volunteers were excluded if they experienced heartburn more than once a fortnight, complained of dysphagia, or suffered from epigastric pain. Surgery on the upper gastrointestinal tract, medication known to affect oesophageal motility, and pre-existing medical conditions were also excluding factors.

The pH and pressure catheters were calibrated, tied together, and passed through the nose (anaesthetised with 1% lignocaine spray, Astra Pharmaceuticals, Hertfordshire) into the stomach. A standard motility test was carried out, with the patient in a sitting position, by slowly withdrawing the catheter in 1 cm increments to establish the position and resting pressure of the LOS. Catheters were then secured so that the pH and lowest oesophageal pressure transducer were 5 cm above the previously determined LOS. A series of 10 wet swallows were then carried out using 4 cm³ aliquots of water, at room temperature, administered through a syringe at 30 second intervals. For the 24 hour study, patients were instructed to carry out normal daily activities; record meals, drinks, position, activities, and symptoms on a diary sheet; and to use the event button. At the completion of the recording, the data were

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**TABLE I** pH data from 18 volunteers—day and night comparisons (values are median and interquartile range).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Day</th>
<th>Night</th>
</tr>
</thead>
<tbody>
<tr>
<td>% pH &lt;4</td>
<td>0.9 (0.2–1.6)</td>
<td>1.35 (0.3–2.6)</td>
<td>0 (0–0.1)</td>
</tr>
<tr>
<td>No of episodes</td>
<td>191</td>
<td>174</td>
<td>17</td>
</tr>
<tr>
<td>Median per patient</td>
<td>10 (5–18)</td>
<td>8.5 (4–17)</td>
<td>0 (0–2)</td>
</tr>
</tbody>
</table>

**TABLE II** pH data from 18 volunteers with reflux episodes divided into short, intermediate, and long duration (values median and interquartile range).

<table>
<thead>
<tr>
<th></th>
<th>% of total</th>
<th>Median/ patient</th>
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<tr>
<td>Short episodes 0–5 min</td>
<td>86%</td>
<td>8.5 (4–13)</td>
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<td>Intermediate episodes 5–15 min</td>
<td>11%</td>
<td>0.5 (0–2)</td>
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<tr>
<td>Long episodes &gt;15 min</td>
<td>3%</td>
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**TABLE III** Mechanisms of all gastro-oesophageal reflux episodes in the 18 volunteers and the total percentages.

<table>
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<th>Belching</th>
<th>Motor</th>
<th>Stress</th>
<th>Unclear</th>
<th>Spontaneous</th>
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<tr>
<td>No</td>
<td>131</td>
<td>10</td>
<td>14</td>
<td>25</td>
<td>11</td>
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</tr>
<tr>
<td>Percentage</td>
<td>68.6</td>
<td>5.2</td>
<td>7.3</td>
<td>13.1</td>
<td>5.8</td>
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pressures measured during ambulatory recordings and compared with those obtained in outpatients. The results of these recordings have been presented elsewhere (refs 8, 10–12).

Ambulatory recording was begun Monday in the afternoon, with patients being instructed to keep a diary of all meals, drinks, and symptoms. The patient was then instructed to swallow 4 cm³ of water at 30 min intervals and to mark the time on the sheet; and to use the event button. At the completion of the recording, the data were

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**TABLE III** Mechanisms of all gastro-oesophageal reflux episodes in the 18 volunteers and the total percentages.

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**TABLE IV** pH data from 18 volunteers with reflux episodes divided into short, intermediate, and long duration (values median and interquartile range).

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Figure 2: Clearance parameters for acid reflux episodes occurring during the 24 hour period and for the daytime period.

Figure 3: Different categories of contraction waves occurring during the 24 hour recording.

off loaded onto the computer for automated analysis.

**DATA ANALYSIS**

**pH data**

Standard measurements of pH data were carried out (% time pH<4, number of reflux episodes, number of episodes lasting more than 5 minutes).

**Mechanisms of gastro-oesophageal reflux**

Various events such as coughing, sneezing, belching, and straining produce characteristic, recognisable pressure patterns on the manometry tracings (Fig 1). It was noted that acid reflux episodes often followed these pressure changes. Consequently, all acid reflux episodes were studied to determine their precipitating pressure event. LOS behaviour at the moment of acid reflux was assessed using the sphinctometer. Reflux episodes were classified as spontaneous (if no pressure activity preceded the pH fall), belch related (if caused by belching), stress induced (if caused by activities such as coughing, sneezing, straining, hiccuping), motor related (if preceded in the 15 seconds before a pH fall by an oesophageal body contraction, peristaltic or otherwise), or 'unclear' (if two or more of the above occurred so that the precipitating cause of the reflux episode could not be confidently determined) (Fig 1).

**Acid clearance**

As peristaltic contractions are the major factor in clearing refluxed acid, the following parameters were studied for each acid reflux episode: duration of the reflux episode, time (seconds) to the first peristaltic contraction, time (seconds) between peristaltic contractions, and the proportion of the different types of oesophageal contractions occurring during the reflux episode. In addition, the effectiveness of a contraction to clear acid was correlated to the contraction amplitude.

**Oesophageal motility**

Motility was assessed during four different periods over the 24 hours – digestive, post-digestive (2 hours after eating), interdigestive, and nocturnal. Ambulatory motility during these periods was compared with the standard pull through study. Contraction waves were classified as described above and the amplitude, duration, and velocity of peristaltic waves recorded. The frequency of the different oesophageal contractions was also noted.

**STATISTICS**

It was assumed that data were not normally distributed and these are expressed as medians and interquartile ranges (IQ). The Wilcoxon signed rank and Spearman rank correlation tests were employed as appropriate.
Results

PH DATA

The median percentage of the recording time that the oesophageal pH remained below 4, the total number of acid reflux episodes, and the median number of episodes per patient are shown in Table I. In common with other studies of long term pH monitoring, most episodes occurred during the daytime (91%). Altogether 166 (87%) episodes lasted less than 5 minutes with only 25 (13%) lasting longer than 5 minutes (Table II). Reflux episodes occurring during the diary marked night time periods, generally occurred before sleep or during temporary arousals from sleep (deep sleep is recognisable from the regular rhythmic pressure changes caused by deep breathing).

MECHANISMS OF GASTRO-OESOPHAGEAL REFLUX

Belching accounted for 69% of all acid reflux episodes. Most episodes in the 'unclear' category had belching as one of the two or more simultaneously occurring mechanisms that made a simple classification impossible. The other mechanisms precipitating acid reflux episodes occurred but were much less important when compared with belching (Table III).

Sphincter behaviour over the 24 hour recording was monitored by the sphinctometer. Of the 191 acid reflux episodes in the control subjects, a sphinctometer reading was available in 161 (84.3%). In one subject (with 23 reflux episodes), the sphinctometer malfunctioned near the beginning of the recording and in a further two subjects (with seven reflux episodes between them) half way through the recording. Of the reflux episodes available for study, 62.7% were associated with a visible LOS relaxation. In 32.3% either no sphincter pressure change could be determined or the sphincter pressure change was hidden by other pressure changes such as coughing, straining, or deep breathing.

OESOPHAGEAL ACID CLEARANCE

The median number of oesophageal contractions per reflux episode was 2.9 (IQ range 2.5–3.8). The number of peristaltic contractions per reflux episode was 1.7 (IQ range 1.6–2.6). Peristaltic waves comprised 83% of the first or second oesophageal contraction (IQ range 70–94%) after the onset of the reflux episode. Figure 2 illustrates the median duration of reflux episodes, the time interval (in seconds) between peristaltic clearance contractions, the time to the first oesophageal peristaltic contraction after the onset of the reflux episode, and the percentage of peristaltic waves occurring during a reflux episode. Results are given for all reflux episodes occurring during 24 hours and also for day time reflux episodes only. There were few nocturnal reflux episodes that no clearance analysis has been attempted for that period.

There was no correlation between pH rise and distal peristaltic wave amplitude (for the first peristaltic contraction after the onset of the reflux episode). This was true if all control subjects results were grouped (correlation coefficient r=0.13, 95% confidence interval 0.02, 0.27) or if individual subject results were treated separately.

OESOPHAGEAL MOTILITY

Figure 3 illustrates the proportions of the different type of contractions that occurred in the four time periods. Peristaltic contractions predominate during eating and are significantly more frequent at this time than during any other recording period. Segmental contractions

Figure 4: Characteristics of peristaltic waves during different periods of the 24 hour study.
account for about one third of pressure sequences in all recording periods. Peristaltic wave intervals (the time interval between peristaltic contractions; Figure 4) are shortest during eating, longest at night, and intermediate in duration during the postdigestive and interdigestive periods.

Figure 4 illustrates other parameters describing peristaltic contractions during the four recording periods. Peristaltic wave amplitudes increased as the wave moved down the oesophagus, and were greater during eating than at all other time periods. Peristaltic wave velocity increased as the contraction wave moved down the oesophagus. This velocity in both the upper (P5→P4) and lower (P4→P3) oesophagus was slower during eating than at other time periods. There was no pressure parameter that was statistically different between the postdigestive and interdigestive periods.

Standard motility testing showed a median LOS pressure of 17 mmHg (IQ 12–22). The median percentage of peristaltic contractions out of the 10 wet swallows was 100% (IQ 85–100). Comparison of 24 hour motility patterns with standard pull through manometry showed that each of the different peristaltic contraction variables (amplitude, duration, area, and velocity) had a different period when they were in closest agreement. The percentage of peristaltic contractions occurring during standard pull through manometry was 100% while the proportions in the different 24 hour recording periods were significantly less (Fig 5).

Discussion

Ambulatory pH and motility recordings allow the assessment of naturally occurring acid reflux episodes and show how acid is cleared under physiological conditions. This is better than previous assessments where acid reflux episodes have been precipitated artificially by abdominal compression, straight leg raising, distending the stomach with balloons or carbon dioxide, or infusing the oesophagus with hydrochloric acid. Progress in our understanding of the pathogenesis of gastro-oesophageal reflux disease requires knowledge of the mechanisms and clearance ability of control subjects under these ambulant conditions.

The pH results were in keeping with the many other studies of long term pH monitoring showing that in control subjects, acid reflux episodes are few in number, short lived, and rare even at night.4

Previous studies in supine immobile subjects have shown that acid reflux episodes in control subjects are caused by transient LOS relaxations.5 It was apparent in this study that most acid reflux episodes in ambulant subjects were associated with the clearly recognisable pressure patterns produced by the activities shown in Figure 1. The single most important cause of acid reflux in control subjects was belching. The actual number of reflux episodes produced by belching may be higher than 69% as most of the ‘unclear’ group had belching as one of the two or more simultaneous occurring mechanisms that confused the classification. Belching produces two types of pressure patterns. Forceful belching produces positive pressure rises on both sides of the diaphragm, but because of the smaller pressures involved, it can be clearly differentiated from other stress related causes (coughing, sneezing, and straining). The other type of belching is the common cavity type (Fig 1 section 2) where a plateau pressure rise is produced in the body of the oesophagus. This is caused by gas (or gas and acid) from the stomach distending the oesophagus and leading to the pressure rise. The number of the oesophageal pressure transducers showing the plateau pressure rise depends on how high up the oesophagus the refluxed gas rises. A secondary peristaltic contraction is not uncommon after this type of event and is probably a reflex to oesophageal distension. Acid reflux caused by belching must occur by the inadvertent reflux of acid accompanying gaseous reflux. This may be the explanation of the common finding of acid reflux episodes postprandially when gas has been ingested with the meal and when the stomach is full of food and acid. This also probably explains the phenomenon of transient LOS relaxation. Other studies have shown that these sphincter relaxations are the major cause of acid reflux in control subjects, in addition 86% of belches (gas gastro-oesophageal reflux) are associated with transient sphincter relaxations.16 It seems therefore that transient LOS relaxations are the physiological mechanism to allow the venting of ingested gas, and that in control subjects most acid reflux episodes occur during this physiological event.

Ambulatory LOS pressure measurement is problematic because of the conflicting pressure changes that occur in and around a dynamic LOS. As part of the sphinctometer lies in the chest (negative pressure) and part in the stomach (positive pressure) its output is susceptible to the pressure changes occurring in these areas away from the LOS. In supine immobile subjects these pressure influences are minimal. In ambulant subjects, however, because of movement, variations in breathing patterns, and muscular activity, transdiaphragmatic pressures can have an important effect on the sphinctometer and may mask subtle pressure changes occurring in the LOS. This may be why sphincter relaxations were not demonstrable in 32–3% of reflux episodes.
The importance of peristaltic contractions in clearing refluxed acid has been shown by previous authors. In ambulant subjects, a stepwise clearance of acid after peristaltic contractions could be seen during reflux episodes. A peristaltic wave interval of one contraction every 65 seconds lies between the peristaltic rate for the digestive and post digestive periods. This may suggest an increased peristaltic contraction rate because of the presence of refluxed acid in the oesophagus. It has been suggested that sensory receptors in the oesophagus can detect the presence of refluxed acid, thus initiating peristaltic clearance contractions. In reflux episodes lasting longer than 5 minutes it was common for a new reflux episode to occur before complete clearance of the preceding reflux episode. There was no relationship between the magnitude of the pH rise and the distal peristaltic wave amplitude. This is probably because acid clearance depends on several factors. Previous studies have shown that a peristaltic wave amplitude of at least 20 mmHg is required for effective volume clearance but this is not necessarily the same as acid neutralisation. Despite most of an acid load being cleared on the first peristaltic wave several further swallows are often required before pH is neutralised. This is because of a film of acid lining the oesophagus that requires swallowed saliva to neutralise. While amplitude of peristaltic contractions may be important in effective volume clearance it may not be as important to acid neutralisation.

The results from these 24 hour motility recordings are broadly similar to other recent reports. Peristaltic waves are more common during meals and the amplitude of peristaltic contractions increases while wave velocity decreases. As would be expected, peristaltic wave frequency is greatest during eating, least during sleeping, and intermediate during other periods. It is surprising that the different peristaltic wave parameters (amplitude, duration, velocity etc) from the standard pull through study as a group did not correlate with a single 24 hour recording period. If any 24 hour time periods were to be approximated to the standard pull through study these would be the non-eating and non-sleeping periods. Unless, however, specific importance is given to a particular peristaltic contraction variable (for example, amplitude) it seems that standard pull through manometry does not provide accurate information about peristaltic wave behaviour over a 24 hour period. This would also apply to the percentage of peristaltic contractions (Fig 5) where almost all standard pull through contractions are peristaltic while the percentage during a 24 hour study are significantly less during all time periods. This may reflect the fact that the standard pull through study uses small quantities of water which may produce different results from eating solid food.

This study has given new information on the precipitating causes of acid reflux in control subjects and has shown acid clearing mechanisms in ambulant subjects. Further work is needed on patients with gastro-oesophageal reflux disease to increase our understanding of the pathophysiology of this common condition.

The authors gratefully acknowledge the financial assistance given for this work by the MRC and the British Digestive Foundation.
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Gut 1993 34: 444-449
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