Alimentary tract and pancreas

Motor activity of the distal oesophagus and gastro-oesophageal reflux

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SUMMARY The relationship between intraoesophageal pH value and motor activity of the lower oesophageal body and sphincter was investigated by simultaneous evaluation of intraluminal pressure and pH in 13 patients complaining of heartburn and regurgitation. One hundred and thirty one episodes of gastro-oesophageal reflux were recorded. One hundred and eighteen (90.1%) were preceded by a swallow (one to 12 seconds), 13 reflux episodes (9.9%) were not preceded by a swallow. Gastro-oesophageal refluxes preceded by swallow were accompanied by an equal number of normal and abnormal primary peristaltic sequences and, while recording at level of the lower oesophageal sphincter, occurred during inhibition of the sphincter. Frequency of abnormal primary peristalsis increased ($p < 0.01$) during periods of low intraluminal pH (< 5.0). An increase of at least 0.5 U in intraluminal pH occurred with 45.2% of normal primary peristalsis, 29.3% of abnormal primary peristalsis, 4.3% of secondary peristalsis, 3.5% of non-peristaltic contractions. The results of this study indicate that in patients with symptoms of reflux oesophagitis, gastro-oesophageal reflux appears to be related to swallow-induced lower oesophageal sphincter inhibition and not related to abnormal motor activity of the distal oesophageal body where an increased frequency of abnormal primary peristalsis appears to occur during low intraluminal pH and primary peristalsis appears to be the most important mechanism of oesophageal clearing.

It is commonly reported that reflux of gastric contents into the oesophagus occurs whenever gastro-oesophageal pressure gradient exceeds lower oesophageal sphincter resting tone. In any given patient, however, resting pressure values recorded at this level are not strictly related to the presence or absence of gastro-oesophageal reflux.^{1 2} Therefore, slow fluctuation or a sudden fall in pressure, secondary to spontaneous or swallow induced phasic lower oesophageal sphincter motor activity, may facilitate gastro-oesophageal reflux. Dent *et al*² have recently suggested that gastro-oesophageal reflux, which may occur physiologically, is mainly connected to lower oesophageal sphincter spontaneous critical pressure drop, in healthy subjects at least. The aims of this study performed in patients with symptoms of reflux oesophagitis were the following: (1) to evaluate the relationship between gastro-oesophageal reflux and lower oesophageal

sphincter resting and phasic motor activity, to identify whether pressure variations facilitate reflux episodes and if so, their type; (2) to evaluate the relationship between gastro-oesophageal reflux and motor activity of the distal oesophagus in the attempt to analyse (a) whether deranged motor behaviour facilitates reflux episodes, (b) whether a low intraluminal pH affects oesophageal motor activity. In addition, the clearing mechanism of the oesophagus following a reflux episode was also assessed.

Methods

PATIENTS

Thirteen patients, 10 men and three women, mean age 44.8 ± 19 years (mean $\pm$ SD; range 16-74 years) complaining of heartburn and/or acid regurgitation (range two months to 36 years) were investigated. Upper gastrointestinal endoscopy performed in nine patients showed erosion and hyperaemia of the distal third of the oesophagus in three and five patients, respectively. Three water filled polyvinyl

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catheters, 1 mm in diameter, were used to transmit intraluminal pressures to Statham pD23 external transducers. The catheters had side openings 1.2 mm in diameter placed to measure the intraluminal pressures at three distinct points 3 cm apart. The pressure recording tubes were perfused with distilled water at a constant rate of 0.75 ml/min using a Braun syringe pump. Sudden occlusion of a side opening resulted in a pressure rise of 100 cm H₂O/sec. A Beckman intraluminal pH glass electrode No 39042 was used to measure oesophageal pH. A reference electrode Beckman No 39168 was kept immersed with two fingers in KCl saturated solution. The glass electrode was calibrated in standard buffer solutions at pH 4 and 7 before each examination. Swallowing was recorded by a pneumograph located around the patient's neck. Intraluminal pressures, pH variations, and swallowing were simultaneously recorded on multi-channel polygraph.

DESIGN OF THE STUDY

Studies were performed on patients at rest in the supine position after overnight fasting. The manometric and intraluminal pH catheters were passed through the nose into the gastric fundus and 200 ml HCl 0.1N were instilled into the stomach in order to easily perform the investigation on outpatients population. The manometric catheters were then withdrawn by 0.5 cm station pull through technique. In each subject the manometric catheters were located at random for two consecutive 20 minute periods with the distal side opening at lower oesophageal sphincter level and at 7 cm proximal to the lower oesophageal sphincter. The pH glass electrode was positioned 5 cm proximal to the lower oesophageal sphincter for the entire 40 minute period. Swallowing was not stimulated with water and no acid was infused in order to stimulate motor activity.

DATA ANALYSIS

At the beginning of each study period manometric configuration of swallowing in any single patient was identified: only phasic variations which were constantly caused by swallowing on command and followed by regular peristaltic sequence in the oesophageal body was considered as an act of swallowing. A sudden drop in intraoesophageal pH value of at least 1.0 unit below 5.0 was considered proof of gastro-oesophageal reflux. The time interval between each episode of gastro-oesophageal reflux and the preceding swallow was timed. Lower oesophageal sphincter pressure was recorded as cm H₂O and the mean gastric fundus pressure was taken as zero reference. The highest

mid-inspiratory pressure recorded from one of the three manometric orifices was considered the lower oesophageal sphincter pressure. Oesophageal motor activity was classified as primary peristalsis, secondary peristalsis, and non-peristaltic motor activity.

Oesophageal peristalsis was considered primary when preceded by swallowing. Primary peristalsis was considered abnormal when, after swallowing, no intraoesophageal pressure variations occurred or when sequential motor contractions did not reach the distal recording side opening(s) or when motor contractions were not sequential. Oesophageal peristalsis was considered secondary when sequential monophasic pressure waves were not preceded by swallowing. Motor activity was considered non-peristaltic when pressure waves occurred spontaneously with no sequential order. Non-peristaltic motor activity was represented by single or isolated, synchronous and repetitive pressure waves. Oesophageal motor activity in the presence of low (pH <5) intraluminal pH was separately evaluated from that occurring when intraluminal pH (≥5) was normal. Oesophageal clearing efficacy was measured in terms of the capacity of different types of motor activity to raise intraluminal pH by at least 0.5 unit.

Results

A total of 1016 swallows (78.1 ± 37.7 ; mean $\pm$ SD) and 131 episodes of gastro-oesophageal reflux (10.1 ± 12.8) were recorded; 114 (87.0%) (8.8 ± 12.5) reflux episodes were preceded by a single swallow (Fig. 1), four (3.1%) by repetitive acts of swallowing, and 13 (9.9%), recorded in four of the 13 patients, were not preceded by swallowing (Fig. 2). The mean lower oesophageal sphincter resting pressure in patients who showed reflux episodes which were not preceded by swallowing (11.9 ± 6.7 cm H₂O) did not significantly differ from those in which all reflux episodes were preceded by swallowing (13.9 ± 9.5 cm H₂O).

Intraoesophageal pH value was equal or above 5.0 U for 19 minutes 8 seconds $\pm$ 13 minutes 9 seconds and below 5.0 U for 17 minutes 55 seconds $\pm$ 15 minutes 29 seconds. Frequency of swallowing did not differ during the study periods when intraoesophageal pH was above 5.0 U (1.9 swallows/min) and below 5.0 U (1.8 swallows/min). The frequency and duration of gastro-oesophageal reflux, preceded or not preceded by swallowing, were not influenced by the position of the catheter – that is, placed through the lower oesophageal sphincter or at least 7 cm proximal to the lower oesophageal sphincter (Table 1).

Fig. 1 Intraoesophageal pressure and pH recording. From top to bottom, recording of: swallowing; (a) oesophageal body 6 cm proximal to LOS; (b) oesophageal body 3 cm proximal to LOS; (c) LOS; intraluminal pH 5 cm proximal to LOS. Four single acts of swallowing are followed by gastro-oesophageal refluxes. Calibration in cm H₂O.

Fig. 2 Intraoesophageal pressure and pH recording. From top to bottom, recording of: swallowing; (a) oesophageal body 13 cm proximal to LOS; (b) oesophageal body 10 cm proximal to LOS; (c) oesophageal body 7 cm proximal to LOS; intraluminal pH 5 cm proximal to LOS. Gastro-oesophageal reflux not preceded by swallowing. Calibration in cm H₂O.

Table 1 Gastro-oesophageal reflux: number and duration of episodes

Position of catheter	Study period (min/sec)	Episodes of GOR preceded by deglutition	Episodes of GOR not preceded by deglutition	Total GOR (no)	GOR:duration (M $\pm$ SD) sec
Through the LOS	240/30	45	7	52	52.3 $\pm$ 59.7
Proximal to LOS	252/30	73	6	79	49.4 $\pm$ 83.3

GOR = gastro-oesophageal reflux.

Reflux episodes preceded by deglutition followed swallowing by mean time interval of 4.5 ± 2.2 seconds (range 0–12 seconds); 111 (94.1%) occurred within 0–8 seconds and seven (5.9%), recorded in five patients, occurred within 9–12 seconds. The mean duration of reflux episodes was 51 ± 75 seconds (range one second to 8 minutes 22 seconds), the duration of 32 reflux episodes (24.4%) was equal or less than 5 seconds. Fifty two reflux episodes were recorded when the distal side opening of the manometric catheter was placed at the level of the lower oesophageal sphincter, 45 of these occurring in eight patients, were preceded by swallowing within an interval of 4.4 ± 2.2 seconds (range 0–11 seconds). Accurate measurement of lower oesophageal sphincter pressure was possible in four patients who showed 21 reflux episodes preceded by swallowing. These all occurred during sphincter inhibition induced by deglutition reflex (Fig. 3). The interval measured between sphincter pressure drop and occurrence of gastro-oesophageal reflux was 2.4 ± 1.9 seconds (range 0–8 seconds). In the remaining four patients, the absence of a high pressure zone and/or the pressure variability, possibly due to catheter-lower oesophageal sphincter spatial variations, did not allow accurate lower oesophageal sphincter pressure measurements. The interval between swallowing and the lower oesophageal sphincter pressure drop (Table 2), as well as the degree of inhibition, did not significantly differ in the study periods in which intraoesophageal pH ≥ 5.0 U, pH < 5.0 U or during occurrence of reflux episodes. Duration of lower oesophageal sphincter pressure inhibition could not be correctly evaluated because the frequent

presence of spontaneous and swallow induced oesophageal motor activity interfered with lower oesophageal sphincter reflex inhibition. Of the seven remaining episodes of reflux not preceded by swallowing, one occurred during spontaneous inhibition of the sphincter (Fig. 4) and six were observed in a patient in whom sphincter pressure was too low to detect inhibition.

Although individual variability in oesophageal motor behaviour was seen, the most frequent

Fig. 3 Intraoesophageal pressure and pH recording. From top to bottom, recording of: swallowing; (a) oesophageal body 6 cm proximal to LOS; (b) oesophageal body 3 cm proximal to LOS; (c) LOS; intraluminal pH 5 cm proximal to LOS. Episode of gastro-oesophageal reflux after swallowing and during LOS inhibition. Calibration in cm H₂O.

Table 2 Time interval (seconds) between swallowing and fall in lower oesophageal sphincter pressure

pH ≥ 5	During occurrence of GOR	pH < 5
2.1 $\pm$ 1.4	2.5 $\pm$ 1.2	2.5 $\pm$ 1.3

M $\pm$ SD.

GOR = gastro-oesophageal reflux.

Fig. 4 Intraoesophageal pressure and pH recording. From top to bottom, recording of: swallowing; (a) oesophageal body 6 cm proximal to LOS; (b) oesophageal body 3 cm proximal to LOS; (c) LOS; intraluminal pH 5 cm proximal to LOS. Gastro-oesophageal reflux during LOS inhibition not preceded by swallowing and coincident with synchronous contractions of distal oesophageal body. Calibration in cm H₂O.

pattern of motor activity was abnormal primary peristalsis (44.6%), followed by non-peristaltic motor activity (29.1%), normal primary peristalsis (23.4%), and secondary peristalsis (2.8%). Episodes of gastro-oesophageal reflux preceded by swallowing were accompanied by an equal number (57) of normal and abnormal primary peristalsis. Episodes of gastro-oesophageal reflux with a duration of 5 seconds or less, as compared with those of longer duration, however, were more frequently preceded by normal primary peristalsis ($\chi^2=3.6$; $p<0.1$) (Table 3). In 13 episodes of gastro-oesophageal reflux not preceded by swallowing, oesophageal motor activity was not evident in three cases; gastro-oesophageal reflux was preceded by non-peristaltic motor activity in one and by secondary peristalsis in nine episodes recorded in the same patient. The frequency in abnormal primary peristalsis increased while that of normal primary peristalsis decreased in study periods in which intraoesophageal pH <5.0 U (respectively 77.6% and 22.4%) as compared with study periods in which intraoesophageal pH ≥ 5.0 U (respectively 58.8% and 41.2%; $\chi^2=7.3$; $p<0.01$).

Table 3 Primary peristalsis and duration of GOR episodes

	Duration of GOR episodes	
	≤ 5 sec	> 5 sec
Normal primary peristalsis	21 (65.6%)	36 (43.9%)
Abnormal primary peristalsis	11 (34.4%)	46 (56.1%)

$\chi^2=3.64$; $p<0.1$.
GOR = gastro-oesophageal reflux.

The incidence of non-peristaltic motor activity did not differ in study periods in which intraoesophageal pH ≥ 5.0 U and <5.0 U (respectively 29.6% and 33.9%).

As compared with periods in which intraoesophageal pH value was greater than 5.0 U, the first oesophageal motor pattern recorded immediately after gastro-oesophageal reflux differed in a lower incidence of swallow induced motor activity and an increased incidence of non-peristaltic contractions and secondary peristalsis. The low frequency of secondary peristalsis did not allow statistical evaluation of this type of motor activity (Table 4).

An increment in pH values of at least 0.5 U was observed in 45.2% of cases with normal primary peristalsis, in 29.3% of abnormal primary peristalsis, in 4.3% of secondary peristalsis, and in 3.5% of non-peristaltic motor activity.

Discussion

In these experimental conditions more than 90% of gastro-oesophageal reflux episodes detected during lower oesophageal sphincter pressure recordings occurred during swallow-induced lower oesophageal sphincter relaxations.

This result suggests that in patients with reflux oesophagitis symptoms, gastro-oesophageal reflux is principally caused by sphincter pressure phasic

Table 4 Motor activity (%) at different intraoesophageal pH

	pH ≥ 5.0 U	pH < 5.0 U	Immediately following GOR
Normal primary peristalsis	28.4	14.0	13.8
Abnormal primary peristalsis	40.5	48.6	44.8
Non-peristaltic motor activity	29.6	33.9	34.5
Secondary peristalsis	1.5	3.5	6.9

GOR = gastro-oesophageal reflux.

inhibition and less frequently to low resting pressure.

The position of catheter through the sphincter did not appear to facilitate gastro-oesophageal reflux as no statistical difference in the episodes was found when periods with and without lower oesophageal sphincter placed catheters were compared. Furthermore, the constant and strict time relationship between more than 90% of gastro-oesophageal reflux episodes and swallowing suggests that even all the other reflux episodes preceded by swallowing occurred during lower oesophageal sphincter inhibition.

Radiological evidence of swallow-induced gastro-oesophageal reflux has been reported in normal subjects,³ in patients with hiatus hernia,⁴ and in experimental animals with surgically created hiatus hernia.⁵ Dent *et al*² reported more recently that in healthy subjects gastro-oesophageal reflux occurs in association with phasic transient relaxations of lower oesophageal sphincter with an otherwise normal resting pressure. Their results show that 85% of reflux episodes occurred during spontaneous lower oesophageal sphincter relaxations. In the present study 90% of gastro-oesophageal refluxes were related to swallow-induced motor activity. In adult oesophagitis patients also¹ the majority of reflux episodes have been connected to spontaneous phasic lower oesophageal sphincter relaxation. A somewhat increased frequency (45%) of swallow related episodes of gastro-oesophageal reflux were reported in both normal and refluxers' children by Dent *et al*⁶ and Werlin *et al*.⁷ Although simple ways of reconciling the differences reported in the frequency of gastro-oesophageal reflux and spontaneous or swallow-induced lower oesophageal sphincter relaxations are not available, it would appear that reflux episodes are mainly linked to transient lower oesophageal sphincter pressure inhibition rather than to low resting sphincter pressure.

Absent or abnormal peristaltic motor activity in the distal oesophagus has been advocated as a possible mechanism in the facilitation of gastro-oesophageal reflux after swallowing⁴ or during spontaneous lower oesophageal sphincter relaxation.² In the present study swallow-induced gastro-oesophageal reflux was associated with an equal number of normal and abnormal cases of primary peristalsis in the distal oesophagus. Thus, reflux would appear to be essentially related to transient swallow-induced lower oesophageal sphincter relaxation. Intraoesophageal infusion of acid solution⁸ or the ingestion of acidified barium^{9,10} have been shown to induce changes in oesophageal motor activity. Dent *et al*² could not detect any

significant variations in the rate of primary peristalsis and spontaneous contractions in healthy subjects when periods of normal and low (pH <4) introesophageal pH values were compared. In our study no difference was found in the rate of primary and spontaneous motor activity in periods in which intraluminal pH was normal and low (pH <5). The normal/abnormal primary peristalsis ratio significantly decreased, however, during periods of low intraluminal pH (<5). Acid gastro-oesophageal reflux may therefore affect the normal peristaltic progression in the distal oesophagus.

Primary peristalsis seems to be the most important mechanism involved in clearing refluxed acid as it is by far the most frequent motor event and as a higher frequency in this type of activity induced a 0.5 U increment in intraoesophageal pH value. The lower clearing rate of abnormal primary peristalsis suggests that the clearing mechanism is influenced by normal motor activity. Even lower clearing rates of secondary peristalsis indicate that saliva may be an important factor in buffering refluxed intraoesophageal acid. No definite conclusions on the clearing mechanism can be drawn from this study, however, as no data on the amount of saliva swallowed, and on the volume of refluxed gastric contents are available.

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