Relationship between spontaneous non-propagating pressure activity in the oesophagus and acid gastro-oesophageal reflux in pathological and non-pathological refluxers

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SUMMARY To evaluate the oesophageal motor activity preceding episodes of reflux, 10 pathological and 10 non-pathological refluxers and 26 normal subjects were investigated. The pressure events in spontaneous short periods of pressure activity (≤ 60 sec) and in long activity periods were registered. The last contraction before reflux was more frequently found non-propagating than the last contraction of pressure periods not followed by reflux ($p < 0.01$). The interval from the last contraction to reflux was shortest, if the contraction terminated in, or confined to the upper part of the oesophagus ($p < 0.001$). Increased proportion of reflux episodes were preceded by an upper segmentary contraction ($p < 0.05$) and a short activity period ($p < 0.02$) in patients with pathological reflux in comparison with non-pathological refluxers. Spontaneously occurring sphincter relaxations might be triggered by preceding non-propagated contractile activity. The relative number of reflux episodes preceded by non-propagated pressure activity seems to be increased in patients with frequent episodes of acid reflux, compared with patients with infrequent episodes, or with normal subjects.

Episodes of acid gastro-oesophageal reflux have been shown to occur spontaneously in normal volunteers and in patients with duodenal ulcer.^{1,2} Duodenal ulcer patients have an increased reflux frequency and delayed acid clearance as compared with normal subjects.¹ In asymptomatic subjects as well as in patients with reflux disease spontaneous episodes of acid reflux occur predominantly by the mechanism of inappropriate gastro-oesophageal sphincter relaxations.^{1,5} Episodes of acid reflux are frequently preceded within a short time by spontaneous oesophageal pressure activity.^{1,6}

The aim of the present investigation was to evaluate the quality of spontaneous oesophageal motor activity preceding acid gastro-oesophageal reflux episodes in a patient group with a known generally increased reflux tendency, but without oesophagitis.

Methods

STUDY POPULATION

The material consisted of 20 duodenal ulcer patients, who within a month of the primary diagnosis underwent 12 hours of simultaneous monitoring of pH and pressure activity in the oesophagus. They were drawn from a population of duodenal ulcer patients referred for evaluation of acid gastro-oesophageal reflux. Patients with endoscopically proven oesophagitis were excluded. Two groups of 10 consecutive patients were selected to serve the purpose of the present study. Group one consisted of 10 patients with pathological acid gastro-oesophageal reflux ($\text{pH} \leq 4$ during more than 2.4% of the recording period),³ and group two comprised 10 patients without pathological acid gastro-oesophageal reflux. The two groups consisted of nine men and one woman, median age 58 and 37 years (range, 20–67 and 21–58 years), respectively. For comparison, the results from 26 normal volunteers, 18 with acid reflux, described in an earlier investigation, were used.⁷

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APPARATUS

A combined pH- and pressure probe (Radiometer GK 282 C and two polyethylene catheters, Clay Adams PE 160) was introduced transnasally after local anaesthesia with Lidocain-spray[®]. By means of manometric criteria, the probe was positioned and fixed with the electrode 5 cm proximally to the gastro-oesophageal sphincter and the pressure catheters 8 and 23 cm proximally to the sphincter as described earlier.⁸ Conversion of the signals were achieved by a pH-meter (PHM 28 D) and microtip transducers (Millar PC-350) in connection with a continuous flush system (Intraflo R CFS 03) and transferred to an analogous tape recorder (Lyrec TR 47) as earlier described.⁸ During playback with a time compression of 64 fold, the signals were printed out on a mingograph (Siemens Elema 803) with a paper speed of 10 cm/sec.

EXPERIMENTAL CONDITIONS

The monitoring was initiated one hour after a light meal and was then carried out between 8 pm and 8 am. During this time the subjects were in the supine position and were not allowed to eat, drink, or smoke.

DATA ANALYSIS

A reflux episode was defined as a sudden fall >2 pH units to a $\text{pH} \leq 4$.³ Pressure amplitudes were classified into propagating, simultaneous, reverse and upper and lower segmentary contractions.^{7,8} When a distal pressure peak occurred after a proximal pressure peak within an interval of one to 5.8 sec a propagating peristaltic contraction was registered. A simultaneous contraction was defined as an interval between pressure peaks of one second or less. When a distal peak preceded a proximal peak within an interval of one to three seconds a reverse contraction was noted. Pressure peaks outside these limits were regarded as segmentary contractions. A relative pressure amplitude change of 8 mm Hg and a rise time of 1 mm Hg/sec were required for a pressure peak to be registered.⁸

The recorded pressure activity was divided into periods of contractile activity lasting ≤ 60 sec (short activity periods) and periods with pressure activity greater than 60 sec. Contractions occurring within 30 sec of the preceding contraction were included in the same period. The end of a period of pressure activity was defined as a period of more than 30 sec without any further pressure activity.⁷ Motor activity was defined as related to a reflux episode, if the time from the last contraction to the sudden fall in pH was less than 30 sec.^{7,9} An example of a short activity period related to an episode of reflux is shown in Figure 1. The number of the various types of peristaltic

Fig. 1 Episode of reflux preceded by a short activity period terminating in an upper segmentary contraction. (P) propagating pressure activity; (S) simultaneous contraction; (R) reverse pressure activity; (x) segmentary contractions. Time related amplitudes are indicated.

contractions were counted irrespective of the length of the activity period or its relation to reflux. The type and velocity of the last contraction in short activity periods and of the last contractions before reflux were registered. The interval between a reflux episode and the pressure amplitude of a preceding contraction (if <30 sec) was also measured.

STATISTICAL ANALYSIS

As a measure of quality the relative occurrence of the different types of contractile activity were used, assuming that this would at least fulfil the requirements for an ordinal scale. No tests requiring stronger assumptions were used and no assumptions were made regarding the distribution of the material. The Pratt's test was used in cases of two related samples. The Kruskal-Wallis and Friedmans non-parametric analysis of variances were used in cases of more than two independent or related samples, respectively. The Pratt's test and Friedmans test were used to test for interaction, which was considered present when the different groups made different contributions to the results when moving from one circumstance to another. For evaluation of correlation, the Spearman's rank correlation coefficient was calculated. In order to reduce the risk of committing errors of the first kind, a combination of values for the patient groups in cases of related samples and a combination of values for different circumstances in cases of independent samples were tested first, and exclusively in cases of significance, a multiple comparison procedure was carried out.^{10,11} p Values less than 0.05 were considered significant.

Table Total number of reflux episodes and number of reflux episodes related to pressure activity, as well as number of short activity periods and total contractile activity during 12 hours of simultaneous registration of pH and pressure activity in 20 duodenal ulcer patients and 18 asymptomatic subjects

	Reflux episodes (n)			Reflux episodes after pressure activity (n)			Short activity periods unrelated to reflux (n)			Contractions during normal pH (total n)		
	Total	Median	Range	Total	Median	Range	Total	Median	Range	Total	Median	Range
Asymptomatic subjects with acid reflux (n = 18)	81	3	1–15	67	3	0–15	1379	78	37–109	10664	617	220–984
Duodenal ulcer without pathological acid reflux (n = 10)	53	5	0–18	48	4	0–18	974	91	76–143	8463	757	459–1394
Duodenal ulcer with pathological acid reflux (n = 10)	205	19	11–38	184	16	8–33	652	62	27–103	5723	454	309–1186

Results

The number of reflux episodes and the pressure activity in the different subjects groups are shown in the Table. Two hundred and ninety nine episodes of acid reflux were preceded within 30 sec by pressure activity. Fifty nine per cent were preceded by short periods of pressure activity, 27% by long activity periods, and 15% by a single contraction.

The relative number of the different types of contractions in activity periods before reflux were not significantly different from the number in activity periods not followed by a fall in pH. The last contraction of pressure periods before reflux

episodes, however, consisted more frequently of a simultaneous, reverse or upper segmentary contraction than the last contraction of short activity periods not followed by reflux ($p<0.01$) (Fig. 2), and this was also true when only short activity periods prior to reflux were considered (Fig. 3). Patients with pathological reflux made a greater contribution to this difference than the other groups ($p<0.05$). The interval from the last contraction to a fall in pH was shorter, if the contraction was terminated in or confined to the upper part of the oesophagus (simultaneous, reverse or upper segmentary) compared with propagating or lower segmentary contractions ($p<0.001$) (Fig. 4). This difference was most marked in subjects without pathological reflux ($p<0.05$). In cases of propagating pressure activity before reflux no correlation could be shown between the peristaltic velocity and time to reflux.

Fig. 2 Relative frequency of simultaneous (S), reverse (R), and upper segmentary (US) pressure waves. (ur) last contraction of short activity periods unrelated to reflux; (pr) last contraction prior to all reflux episodes preceded by pressure activity; (UD-patR) duodenal ulcer patients with pathological acid reflux; (UD-R) duodenal ulcer patients presenting with reflux within the normal range; (N-R) asymptomatic subjects with at least one episode of reflux preceded by pressure activity.

Fig. 3 Relative frequency of simultaneous (S), reverse (R), and upper segmentary (US) pressure waves. (ur) last contraction of short activity periods unrelated to reflux; (pr) last contraction of short activity periods prior to reflux. Remaining abbreviations as in Fig. 2.

The contraction frequency was greater during short activity periods preceding reflux than during long activity periods before reflux or any type of period unrelated to reflux ($p<0.001$) irrespective of subject group. The last contraction of a short activity period without reflux was more likely to be progressive than the pressure activity within the rest of the period ($p<0.001$), regardless of subject group (Fig. 5).

Relatively more reflux episodes followed pressure periods terminated by an upper segmentary contraction in patients with pathological reflux as compared with the two groups without pathological reflux ($p<0.05$). In addition, a relatively higher number of reflux episodes were preceded by a short activity period in patients with pathological reflux as compared with non-pathological refluxers ($p<0.02$) (Fig. 6).

Discussion

In normal subjects a decreased resting pressure in the gastro-oesophageal sphincter has been shown to play a minimal role in the production of gastro-oesophageal reflux episodes. Dent *et al*¹ found this factor responsible in less than 2% of reflux episodes in healthy subjects. In patients with reflux induced oesophagitis Dodds *et al*⁸ found that only one third of the recorded reflux episodes could be attributed to a low resting sphincter pressure or a low sphincter pressure in combination with increased intragastric

pressure. Most of the spontaneously occurring reflux episodes recorded in normal subjects and patients with gastro-oesophageal reflux disease occurred during inappropriate relaxation of the gastro-oesophageal sphincter – that is, sphincter relaxation not triggered by the passage of a bolus.^{1,5,12} Sphincter relaxation and reflux are frequently preceded by peristaltic activity,^{1,5,6} but a proportion of the contractions preceding reflux are not propagating peristalsis elicited by swallowing.^{1,6,12} These observations suggest that reflux may result from a sphincter relaxation triggered by a non-propagating peristaltic contraction or insufficiently bolus transporting propagating peristalsis. Acid reflux during the night is probably the most important factor in the development of reflux changes in the oesophagus.^{13,14} Acid clearance both in normal subjects and in patients with reflux disease is prolonged during the night.¹⁵ Reflux episodes and oesophageal contractile activity during the night have been shown to occur during transient arousal from sleep,¹ contractions during the night occurring predominantly in brief bursts.^{1,7} An increased occurrence of non-propagating contractions in these clusters of activity has been observed.¹ In dog experiments triggering of lower oesophageal sphincter relaxations have been achieved by stimulation of the striated upper portion of the oesophagus.¹⁵ We therefore evaluated the relationship between reflux episodes and the activity pattern in

Fig. 4 Intervals from pressure activity to reflux. (P) propagating pressure waves; (S) simultaneous contractions; (R) reverse pressure waves; (US) upper segmentary contractions; (LS) lower segmentary contractions. Unbroken lines are related median values for the three subject groups. Remaining abbreviations as in Fig. 2.

Fig. 5 Pattern of pressure activity unrelated to reflux episodes. Relative frequency of propagating (P) and non-propagating (S+R+US) pressure activity, when considering the initial part (a) and the last contraction (b) in short activity periods as well as the remaining pressure activity (c). Unbroken lines are related median values for the four subject groups. (N) asymptomatic subjects without reflux during the monitoring period. Remaining abbreviations as in Fig. 2.

- oesophageal reflux episodes. A study in normal subjects. *Scand J Gastroenterol* 1986; **21**: 711–7.
- 8 Wallin L, Madsen T, Boesby S, Sørensen O. Gastro-oesophageal acid reflux and oesophageal peristalsis. Method for 12-hour simultaneous recording of pH and peristaltic activity in the oesophagus. *Scand J Gastroenterol* 1979; **14**: 481–7.
 - 9 Madsen T, Wallin L, Boesby S, Larsen VH. Oesophageal peristalsis in normal subjects. Influence of pH and volume during imitated gastro-oesophageal reflux. *Scand J Gastroenterol* 1983; **18**: 513–8.
 - 10 Bradley JV. *Distribution-free statistical tests*. Englewood Cliffs: Prentice-Hall, 1968.
 - 11 Conover WJ. *Practical non parametric statistics*. Wiley: New York, 1971.
 - 12 Baldi F, Ferrarini F, Balestra R, *et al*. Oesophageal motor events at the occurrence of acid reflux and during endogenous acid exposure in healthy subjects and in patients with oesophagitis. *Gut* 1985; **26**: 336–41.
 - 13 Orr WC, Robinson MG, Johnson LF. Acid clearance during sleep in the pathogenesis of reflux esophagitis. *Dig Dis Sci* 1981; **26**: 423–7.
 - 14 Orr WC, Johnson LF, Robinson MG. Effect of sleep on swallowing, esophageal peristalsis, and acid clearance. *Gastroenterology* 1984; **86**: 814–9.
 - 15 Price LM, El-Sharkawy TY, Mui HY, Diamant NE. Effect of bilateral cervical vagotomy on balloon-induced lower esophageal sphincter relaxation in the dog. *Gastroenterology* 1979; **77**: 324–9.