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Prolonged Ambulatory Oesophageal pH and Pressure Recording in Healthy Adults in Singapore

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ABSTRACT

Background/Aim of Study: Data on prolonged ambulatory oesophageal pH and pressure monitoring in normal subjects in the East are limited. This study aimed to define the normal characteristics of ambulatory oesophageal pH and motility among healthy adults in Singapore.

Method: Prolonged ambulatory oesophageal pH and pressure recording was performed on 10 healthy volunteers using a one-channel pH probe, a two channel pressure probe, a portable digital data recorder and a computerised data analysis system. The median (range) number of episodes with pH < 4 and the percentage of total time with pH < 4 were 24% (4% - 56%) and 3.0% (0.2% - 4.0%) respectively. They were greater in the upright than supine positions.

Results: The median percentages of peristaltic and simultaneous contractions were 65.8% - 80.5% and 10.6% - 12.7% respectively. The frequency, amplitude and duration of peristaltic contractions were greater during mealtimes than between meals in the upright position.

Conclusion: This study provides the first data on prolonged ambulatory oesophageal pH and manometry in healthy Singaporean adults.

Keywords: oesophageal pH monitoring, oesophageal manometry, gastro-oesophageal reflux, oesophageal motility disorder, non-cardiac chest pain

INTRODUCTION

Ambulatory oesophageal pH monitoring is currently considered the most accurate test to determine the presence of gastro-oesophageal reflux, with a reported sensitivity of 93% and specificity of 93%[1]. In the past few years, prolonged ambulatory oesophageal manometry has been introduced as a diagnostic tool in the work-up of patients with various oesophageal motility disturbances, particularly in the setting of non-cardiac chest pain. It has the advantage, over standard manometry, of allowing oesophageal motor activity to be monitored over an entire circadian cycle in a variety of physiologic conditions. This multiplies the amount of data on which a diagnosis can be based and increases the probability of documenting an intermittent abnormality. These two techniques, in particular the ambulatory pressure monitoring, are still relatively new in this part of the world. There are few published reports on the use of ambulatory pH monitoring in Asia[2], and literature on ambulatory oesophageal manometry amongst Asian populations are even more scarce. In the West, studies that aimed to define normal values for ambulatory oesophageal pH and pressure monitoring have yielded variable results[3]. The variation is due in part, to differences in the study populations and in part to variations in instruments used, techniques of data acquisition as well as methods of analysis. It might thus be expected that these data would not be entirely applicable to our local patient population.

The aim of the present study was to assess the normal patterns of ambulatory oesophageal pH and motility among Singaporean adults.

METHODS

Subjects

The study group comprised 10 ambulatory paid volunteers recruited from student residence halls at the National University of Singapore. There were seven males and three females. Their ages ranged from 20 to 32 years (median, 23 years). All except for one were Chinese. Only one of the volunteers was a cigarette smoker. These volunteers were without symptoms suggestive of gastro-oesophageal reflux disease (eg. chest pain, heartburn, acid regurgitation, and odynophagia), and had no symptoms suggestive of impaired oesophageal transit (eg. dysphagia). They did not have a previous history of oesophageal, gastroduodenal, or biliary surgery. Each volunteer was interviewed and when appropriate, underwent physical examination to ensure that they had no obvious medical illnesses. All volunteers gave written informed consent. The study was approved by the Ethics Committee of the National University Hospital, Singapore.

Standard oesophageal manometry

After an overnight fast, standard manometry was performed in all the subjects as described previously[4] before ambulatory monitoring. The position of the lower oesophageal sphincter was determined and its distance from the nose measured.

24-hour oesophageal pH and pressure recording

Subsequently, 24-hour recording using two

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connected catheters – one for measuring pH, and the other for measuring pressure was carried out. The pH catheter consisted of a monocrystalline antimony electrode (Synectics Medical, Stockholm, Sweden) which was placed 5 cm above the upper border of the manometrically determined lower oesophageal sphincter. A separate silver/silver chloride reference electrode (Synectics Medical, Stockholm, Sweden) was attached to the skin of the non-dominant shoulder. The manometry catheter contained three solid state pressure micro transducers positioned 5 cm apart and radially offset by 120° (Synectics Medical, Stockholm, Sweden). These transducers were placed in the body of the oesophagus, the lowest being 3 cm above the upper border of the lower oesophageal sphincter. Both the pH and pressure catheters were connected to a portable digital data recorder (Microdigitrapper 4MB, Synectics Medical, Stockholm, Sweden) which was able to continuously sample oesophageal motor and pH activity, at a rate of 4 Hz, for at least 24 hours. Before each recording, the machine was calibrated, by immersion of the pH catheter in standard buffers of pH 1.07 and 7.01 (Buffer No 5001 and 5002, Synectics Medical, Stockholm, Sweden) and by exposure of the pressure catheter to air (ie., at 0 mmHg) and immersion into a water column at 50 mmHg. The pH and pressure catheters were tied together and passed through the nose (anaesthetised with 1% lignocaine spray) into the oesophagus. The catheters were then taped to the nose so that the pH tip and lowest pressure transducer were 5 cm and 3 cm respectively above the upper border of the manometrically determined lower oesophageal sphincter. The subjects returned to their home or working place and assumed their normal activities. They were asked to eat their usual diet but to avoid drinks and foods with pH below 4. No restrictions were made regarding smoking and alcohol ingestion as well as the timing and duration of recumbence and meals. They were, however, requested to push the event button when they assumed the supine position, when they arose, and at the beginning and end of each eating episode, and in addition, note the times at which these happened. The subjects returned to the hospital the following day to remove the apparatus.

Data analysis

The data were transferred from the data recorder to a personal computer and analysed with the help of a computer programme (Multigram GI version 6.01, Gastrosoft Inc., Texas, USA). The analysis of both pressure and pH signals were done separately for the total, upright and supine portions of the recording and in the case of the pressure data, also for the perprandial portion. In the analysis of pH data, six reflux variables were calculated: (1) number of recorded reflux episodes; (2) number of reflux episodes lasting $>$ 5 min; (3) longest reflux episode in minutes, and percentage time the oesophageal pH was below 4 ie., oesophageal acid exposure during (4) the overall recording period; (5) the upright period, and (6) the recumbent period[5]. In the analysis of pressure data, the amplitude and duration of contractions, the percentage of multi-peaked contractions, the percentage of peristaltic, simultaneous and isolated contractions were calculated for the different oesophageal levels[6].

Definitions

The onset of reflux episode was defined as a drop in the oesophageal pH to less than 4 for at least 4 seconds and its end as the first rise above 4[1]. In case of a subsequent fall of pH below 4 within 5 seconds, both consecutive reflux episodes were interpreted as one single complex. A measurable contraction wave was defined as a rise in pressure above 15 mmHg for between 1.0 and 7.0 seconds. The pressure threshold was chosen since smaller contractions may be difficult to be distinguished from artefacts, and tiny contractions are not considered physiologically or clinically relevant[7]. The amplitude of contraction was defined as the difference between the baseline pressure and the maximum pressure during the pressure event. The duration of contractions was determined as the time elapsed between the onset and the end of the pressure event. Multi-peaked contractions were ones in which the amplitude rose and fell several times, all the while remaining above the contraction threshold of 15 mmHg. They must also fulfil all of the following criteria: the amplitude of the secondary peak was at least 10% of that of the main peak, the trough-to-peak duration was at least 0.5 seconds, the trough was a drop of at least 15% of the main peak amplitude. Contractions were considered peristaltic if their peaks occurred in successive channels, one after the other, at least 0.3 seconds apart. If the interval between the contraction peaks in two adjacent levels was shorter than 0.3 seconds, simultaneous contractions were said to have occurred. Isolated contractions represented those which occurred in one channel but not in the others, ie. contraction amplitude $>$ 15 mmHg in one channel and $<$ 15 mmHg in the other channels.

Statistical analysis

The number of reflux episodes and contractions occurring per day were normalised to numbers per 24 hours. Likewise, meal-related, upright and supine numbers were normalised to numbers per 16 hours and numbers per 8 hours respectively. Because the pH-metry and motility data were found to be skewed, these were expressed as medians and range, the upper reference limit was established as the 95th percentile of the variables, and the non-parametric tests of analysis of variance and Wilcoxon signed ranked were used as appropriate to detect any difference between groups. P values $<$ 0.05 were required for significance. All statistics were performed using the Statistical Package for Social Sciences for Window (SPSS, Chicago, IL, USA).

RESULTS

The mean recording time was 16.3 (95% confidence interval (CI), 12.5 – 20.1) hours and comprised 10.2 (95% CI, 7.9 – 12.5) hours in upright position and 6.2 (95% CI, 3.0 – 9.4) hours in supine position.

pH data

The pH data from the ten volunteers are shown in Table I. A total of 239 acid reflux episodes were observed in these subjects. Most of the episodes occurred in the upright (88%) rather than supine positions (12%), the difference being statistically significant ($p < 0.05$). Altogether nine (4%) episodes lasted more than 5 minutes with only one episode lasting more than 10 minutes. The duration of the longest reflux episode, and the percentage of time that the oesophageal pH remained below 4 were also greater in the upright period than during the supine period.

Motility data

Table II gives the median (range) values for various parameters of the ambulatory motility recording at the proximal, middle and distal oesophageal sites. The large ranges indicate considerable variability of the measured parameters between the subjects. As seen, the median (range) frequencies, amplitudes and durations of contractions were similar at the different oesophageal levels. More than half (median %, 65.8 – 80.5) of the contractions were of peristaltic nature, and a fair percentage (median %, 10.6 – 12.7) of simultaneous contractions was registered physiologically in all the subjects. There were more peristaltic and simultaneous contractions detected by the middle transducer than the proximal transducer and this is because the latter was associated with an increased number of isolated waves.

The contraction characteristics in the three predefined periods ie. meal, upright and supine periods are shown in Table III. It can be seen that there were more contractions per minute during meals than during the two non-meal periods, and this was significant in the middle and distal portions of the oesophagus. The amplitude and duration of mid-oesophageal contractions, and the frequency of distal peristaltic contractions were also significantly greater during mealtime than during the upright period. Compared with the upright and supine periods, the meal period showed a lower median frequency of simultaneous contractions; the differences however did not reach statistical significance. Upright and supine periods did not differ in any of the measured parameters.

Table I – pH data from 10 volunteers

	Total	Upright	Supine	Upright vs Supine
No of episodes/subject	24 (4-56)	24 (0-45)	1 (0-16)	< 0.02
No of episodes > 5 min	1.0 (0-2)	0 (0-2)	0 (0-2)	NS
Longest episodes (min)	6.0 (1.4-11.6)	4.5 (0.9-11.6)	0.1 (0-3.2)	< 0.02
% time pH < 4	3.0 (0.2-4.0)	2.9 (0.3-4.8)	0.1 (0-3.3)	< 0.02

Values are given in median (range)
Upper limits of normal (95th percentiles) are equal to maximum values in all variables

Table II – Motility data from 10 normal volunteers

	Proximal	Middle	Distal	P
Contractions/min	1.4 (0.8-2.4)	0.9 (0.5-1.8)	1.0 (0.7-1.9)	NS
Amplitude (mm Hg)	36.1 (30.2-52.9)	32.7 (22.9-64.0)	33.6 (27.8-85.8)	NS
Duration (sec)	1.8 (1.8-2.3)	1.8 (1.3-2.5)	1.8 (1.5-2.8)	NS
% multi-peaked	1.6 (0.1-15.8)	0.3 (0-2.6)	1.4 (0.2-4.7)	NS
% peristaltic waves	65.8 (31.3-85.4)	80.5 (53.9-90.2)*	78.6 (56.7-87.6)	< 0.05
% simultaneous waves	10.6 (2.5-18.9)	12.7 (7.3-27.6)*	11.6 (8.1-24.2)	< 0.05
% isolated waves	22.0 (3.5-66.3)	3.1 (1.3-36.8)*	7.9 (2.4-34.0)	< 0.05

* $p < 0.02$ versus proximal
Values are given in median (range)
Upper limits of normal (95th percentiles) are equal to maximum values in all variables

DISCUSSION

Prolonged oesophageal pH monitoring results can be affected by factors pertaining to study subjects such as ethnic origin and social habits (eg. alcohol, tobacco), physical activity such as exercise and posture, and variations in methodology such as probe characteristics, probe positioning, the make of the monitor, and the type of software used for analysis[8]. Thus even though 24-hour pH monitoring is the best available test to study gastro-oesophageal reflux; it is necessary for each laboratory to study their own normal populations to minimise these variables.

Prolonged ambulatory oesophageal manometry is a new research tool introduced primarily for the investigation of non-cardiac chest pain. Compared to the analysis of oesophageal pH data, the analysis of pressure recording is much more complex. Not only must contraction amplitude and duration be measured; contraction sequences such as peristaltic, simultaneous and non-transmitted contractions must also be differentiated. Furthermore, inter-individual variation in contraction amplitudes and duration is considerable, as shown in the present study, such that the use of 'normal values' to describe a patient's oesophageal motor profile as normal or as pathological was considered by one group of workers to be of limited value[3]. On the other hand, several studies have indicated that pathological ambulatory manometric profiles of certain oesophageal motility disorders such as achalasia[9] and scleroderma[10] could be accurately determined. The interpretation of these profiles would not have been possible without knowledge of the oesophageal motility patterns seen in healthy subjects under normal conditions. Furthermore, ambulatory recordings within an individual are highly reproducible[3]; thus any significant abnormality detected in a person at any time should never be dismissed as a transient non-event. For these reasons, normal ambulatory pressure values obtained on healthy subjects are useful, and should be derived by each motility laboratory from its own normal population, for reasons mentioned in our previous discussion on pH monitoring.

The pH results were in keeping with the many other studies of long-term pH monitoring showing that in control subjects, acid reflux episodes do occur, but are few in number and short-lived, with most occurring in the upright position[11]. Such reflux has been termed physiological reflux[12], implying it is not associated with symptoms or pathological changes. Oesophageal pH was often scored according to the scoring system devised by Johnson and DeMeester[5].

Table III – Motility data during meals, upright and supine time periods

	Meals	Upright	Supine	P
Contractions/min				
Proximal	2.1 (1.0-3.5)	1.2 (0-1.7)	0.9 (0.1-2.6)	NS
Middle	1.4 (0.5-3.1)[ab]	0.9 (0-2.0)	0.3 (0.2-1.5)	< 0.05
Distal	1.2 (0.8-3.5)[ab]	1.1 (0-2.2)	0.5 (0.1-3.0)	< 0.05
Amplitude (mm Hg)				
Proximal	38.7 (28.2-63.1)	36.2 (19.8-40.0)	34.7 (26.2-48.3)	NS
Middle	47.0 (22.9-81.3)[a]	31.2 (26.0-60.0)	32.2 (24.0-68.8)	< 0.05
Distal	36.3 (23.6-94.5)	34.4 (27.9-62.6)	38.5 (23.6-103.1)	NS
Duration (sec)				
Proximal	2.2 (1.5-2.8)	1.8 (0.8-2.0)	1.9 (1.8-2.5)	NS
Middle	2.3 (1.3-2.8)[a]	1.8 (1.0-2.5)	1.9 (1.3-3.0)	< 0.05
Distal	2.0 (0.8-2.0)	2.0 (1.8-2.8)	1.9 (0.8-3.0)	NS
% multi-peaked				
Proximal	1.0 (0-11.7)	0.2 (0-10.3)	1.6 (0-22.5)	NS
Middle	0.1 (0-3.5)	0.2 (0-1.4)	0 (0-8.1)	NS
Distal	0.8 (0-9)	0.6 (0-6.3)	0 (0-3.7)	NS
% peristaltic waves				
Proximal	73.6 (37.4-98.2)	84.6 (47.3-91.5)	64.0 (23.9-100)	NS
Middle	89.1 (45.1-98.2)	84.9 (65.7-91.0)	80.5 (49.5-89.3)	NS
Distal	88.2 (73.7-93.8)[a]	71.6 (57.1-85.7)	81.7 (51.1-90.0)	< 0.05
% simultaneous waves				
Proximal	6.8 (0.9-18.3)	10.4 (6.8-27.3)	7.8 (0-26.3)	NS
Middle	7.6 (1.8-37.0)	12.6 (8.2-25.9)	11.4 (7.1-32.7)	NS
Distal	10.4 (2.7-17.9)	13.5 (6.8-24.4)	11.5 (8.8-25.0)	NS
% isolated waves				
Proximal	14.9 (0.8-60.7)	3.5 (0-36.5)	27.4 (0-74.3)	NS
Middle	2.6 (0-49.8)	2.1 (0.5-15.9)	3.6 (0-42.8)	NS
Distal	5.0 (0-14.5)	8.5 (3.0-27.0)	7.1 (0-39.2)	NS

a < 0.05 versus upright values
b < 0.01 versus supine values
Values are given in median (range)

However, there is now a consensus that the percentage time with pH < 4 ie., oesophageal acid exposure time is the most useful discriminator between physiological and pathological reflux[8]. Our upper limit of normal for acid exposure time based on the upper 95th percentile was 4.0%. This value was similar to the normal values published in most Western research centres[8]. Previous studies have shown that acid reflux episodes in control subjects are principally caused by transient lower oesophageal sphincter relaxation[13]. Using the number of reflux episodes as a surrogate indicator of the frequency of transient lower oesophageal sphincter relaxation, we found no difference in the number of transient sphincteric relaxations occurring over 24 hours between our control subjects and those of the West[14].

The current study found equal contraction amplitudes and durations at the different recording channels, consistent with the findings described by other groups[15]. The constant proportions of peristaltic and simultaneous contractions at various oesophageal levels were also not different from those reported by others[15]. In the present study, isolated contractions were seen more frequently in the proximal than the distal part of the oesophagus. This finding is in variance with that of another group who found more isolated contractions distally than proximally, and suggested that these contractions represented spontaneous activity generated by the more irritable smooth muscle part of the oesophagus[16]. Further studies, including the use of a bigger sample size, are required to determine if the discrepancy between their and our findings were genuine. During meals, oesophageal contractions generally become more frequent, peristaltic, stronger and of longer duration. These changes, which have previously been noted[11,15-17], presumably are physiological and function to effectively propel swallowed food down the oesophagus. One unexpected finding from the present study was the absence of diurnal variations in oesophageal contraction patterns, otherwise previously shown by several workers[15-17]. They have uniformly demonstrated that peristaltic contractions, which are predominantly under voluntary control, become less frequent at night. It is not clear why our finding should be different from the rest. One possible explanation is a type II error because of the small sample size. However, the total absence of difference in any of the contraction parameters between the upright and supine periods makes this possibility less likely.

This study can be criticised because of the small number of subjects studied and the young age of the subjects. Thus, any potential contribution of age and gender on oesophageal pH and motor activity could not be adequately studied. Recently, Richter et al[18] compared the pH values for healthy subjects studied at three centres in the United States and found age to have no major effect on the pH parameters. Males however, were found to have significantly more acid exposure than females, and the discrepancy was attributed possibly to gender differences in parietal cell mass and gastric acid secretion. Another study[19] also found acid exposure to be similar in asymptomatic individuals who were < 65 years old and those who were ≥ 65 years old whilst it was greater in males than females. In contrast, when the composite score[5] was used to express oesophageal acid exposure, there was no difference between males and females in one recent study[14]. Thus, while gender may have some influence on pH parameters, the magnitude of the effect does not appear to be marked. In most studies, oesophageal motility data have been shown not to be influenced by either sex[16] or age[15]. On the basis of available data, we thus believe the normal values derived from our present study may be used for comparison with patients of all ages and both sexes in our population.

In conclusion, the present study provides the first data on prolonged ambulatory oesophageal pH and manometric recordings in healthy Singaporean individuals.

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CORRIGENDUM

As a matter of record, the Editor of the SMJ wishes to include the following 2 references to an earlier article, *Doctors' and Lawyers' Perspectives of Child Abuse and Neglect in Singapore* (Singapore Med J 1998; 39(4):160-165).

1. Elliott JM, Tong CK, Tan PEMH. Attitudes of the Singapore public to actions suggesting child abuse. Child Abuse and Neglect 1997; 21:445-464.

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