Relations between upper abdominal symptoms and gastric distension abnormalities in dysmotility like functional dyspepsia and after vagotomy

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Abstract

Postprandial bloating and fullness are commonly found both in dysmotility like functional dyspepsia, and after vagotomy but the relation between gastric accommodation and symptom production has not been investigated. Intragastric pressure levels and symptoms developed during controlled distension of the gastric fundus were recorded in nine patients with functional dyspepsia, in seven patients after truncal vagotomy, and in 11 healthy volunteers. The procedure was repeated after ingestion of a liquid nutrient meal (250 ml; 250 kcal). Gastric tone, expressed as the average value of pressure over the distension period was lower in controls (median: 11.3 mm Hg) than in either the dyspeptic patients (median: 16.48 mm Hg) or postvagotomy patients (median: 19.12 mm Hg) ($p < 0.05$). Meal ingestion reduced gastric tone in controls, but no significant change occurred in either the dyspepsia or the postvagotomy patients. Volumes at which discomfort was elicited by distension during fasting were lower both in dyspeptic patients (median: 210 ml) and in postvagotomy patients (median: 180 ml) than in healthy volunteers (median: 660 ml) ($p < 0.05$). Discomfort thresholds were unaffected by meal ingestion. These results suggest that a disturbance of gastric relaxation may be related to symptom development in dysmotility like functional dyspepsia, while similarities between dyspeptic patients and postvagotomy patients suggest that the impaired gastric accommodation in functional dyspepsia may be due to an underlying vagal defect.

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early satiety, belching, nausea, and vomiting.² These symptoms often occur in clusters and are characteristically associated with food ingestion.

Several studies have suggested an association between the symptoms of dysmotility like dyspepsia and abnormalities of upper gastrointestinal motility, including abnormal gastric myoelectric activity,³ antral dysmotility,⁴ delayed gastric emptying,^{4,5} and disturbances of duodenal and jejunal motor activity.^{6,7} Nevertheless, these dysfunctions cannot fully explain the symptoms, because almost half the patients show no detectable abnormality of gastric manometric activity or gastric emptying⁸ and no correlation exists between symptom severity and those functional abnormalities that are found.^{5,9}

A similar symptom pattern to that characterising dysmotility like dyspepsia (particularly postprandial bloating), is commonly found in patients after bilateral truncal vagotomy¹⁰ in whom defective relaxation of the gastric fundus occurs in response to distension.¹¹ This similarity of symptom character, raises the possibility that a disturbance of the gastric accommodation process in response to food, might be common to the two conditions.

In a previous study¹² we assessed gastric accommodation mechanisms in normal subjects by determining intragastric pressure-volume relations during controlled gastric distension, both under fasting conditions and after meal ingestion, and showed that food increased gastric accommodation.

In this paper, we report a study designed to compare the relations between symptoms and gastric responses to distension, in patients with dysmotility like functional dyspepsia and in patients with similar upper abdominal symptoms after bilateral truncal vagotomy.

Methods

SUBJECTS

Nine patients with dysmotility like functional dyspepsia (five male and four female; median age: 40 years; range: 22-54), seven postvagotomy patients (six male and one female; median age: 45 years; range: 31-74), and 11 healthy asymptomatic volunteers (six male and five female; median age: 25 years; range: 22-44) participated in the study after giving informed consent. The protocol for the study had been previously approved by the Salford Health Authority ethics committee.

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Functional dyspepsia, also known as chronic idiopathic dyspepsia, is a common condition defined by upper abdominal symptoms that are not explained by any structural abnormality on conventional investigation.¹ Functional dyspepsia is now conventionally subdivided into ulcer like, reflux like, and dysmotility like groups² according to symptoms experienced. Symptoms in patients with dysmotility like dyspepsia include epigastric discomfort or pain, upper abdominal bloating,

Functional dyspepsia patients

All the patients with functional dyspepsia had been referred to our centre because of chronic, severe, upper abdominal symptoms, particularly bloating, related to meals. All had suffered from their symptoms for at least one year and regarded themselves as being seriously disabled. None had evidence of a peptic ulcer, previous gastric surgery or any systemic disease known to affect gastrointestinal motility. Common laboratory tests, upper digestive tract endoscopy, barium meal examination, and abdominal ultrasonography were normal in all.

Postvagotomy patients

All postvagotomy patients had been referred for assessment of postprandial symptoms. All had been submitted to bilateral truncal vagotomy and pyloroplasty for peptic ulcer three to 18 years (median: 10 years) before the study. All suffered from severe postprandial bloating, which had started soon after the surgery and which had caused them to reduce the size of their meals. In addition, three had dumping syndrome and three others had postprandial diarrhoea.

All drugs were stopped for at least 72 hours before the study in all patients.

Healthy volunteers

Volunteers were recruited from the medical personnel and student population of the University of Manchester. All were symptom free at the time of study and none gave a history of either digestive tract or systemic disease, or previous abdominal surgery.

STUDY DESIGN

Gastric accommodation was assessed both during fasting and after the ingestion of a standard meal, by serial measurement of intragastric pressure during stepwise fundal distension using an ultrathin polyethylene bag (capacity 1200 ml), mounted on a 14 French gauge polyvinyl catheter (RT 20 N, Pennine Health Care Products, Derby, UK). Details of the methodology have been previously published.¹² The catheter bag assembly was introduced through the mouth into the gastric fundus and the proximal end of the catheter was connected to a strain gauge transducer calibrated against a commercial electronic digital manometer (DPI 700, Druck, Grosby, Leicestershire, UK), capable of measuring intrabag pressure in the range 0 to 64 mm Hg with a maximum inherent error of 0.25 mm Hg. At each distension volume, a series of 12 consecutive readings of intrabag pressure were taken at five second intervals and averaged to give a mean value for intragastric pressure. Inflation of the bag in the air showed no increase in intrabag pressure until at least 1200 ml was introduced.

PROTOCOL

Bag insertion

All subjects were studied in the morning after

an overnight fast while reclining comfortably in a semirecumbent position in a quiet room. Firstly, the bag was folded upon the gastric tube, swallowed, and advanced until sited in the body of the stomach. The bag was then unfolded by inflation with 400 ml of air and the tube was gently withdrawn until resistance of the bag against the lower oesophageal sphincter was felt. The catheter was then reinserted 2 cm to ensure that the proximal end of the bag was clear of the gastro-oesophageal junction, the bag fully deflated, and the catheter fixed to the cheek with adhesive tape.

Fasting inflations

After a 10 minute rest period, the bag was progressively inflated in 30 ml increments at one minute intervals until the maximal tolerated volume was reached.

In previous studies with this technique it was found that the first distension of the stomach induced a variable degree of gastric relaxation, after which the pressure-volume relations remained constant during all subsequent fast-ing distensions.¹² In this study, therefore, a second inflation was performed immediately after the first, and the data from this second inflation were used to construct the fasting gastric pressure-volume curve.

Post-meal inflation

At the end of the fasting study, the bag was deflated and the subject was allowed to rest for 10 minutes before drinking 250 ml of a liquid mixed nutrient meal (Fortison, Cow and Gate, Trowbridge, composition: 1.0 kcal/ml; carbohydrate: 12.0%; protein: 4.0%; lipid: 4.0%). Five minutes after the end of meal ingestion, another graded gastric distension was performed to the maximal tolerated volume.

ASSESSMENT OF SENSATIONS ELICITED BY GASTRIC DISTENSION

At every 150 ml of gastric distension, subjects were asked to report their sensations. Subjects were specifically instructed to report the first time they felt uncomfortable. Gastric distension was stopped at the maximally tolerated volume, which corresponded either to the sensation of painful discomfort or to the development of nausea. Throughout the study, the subjects were kept unaware of the volume in the bag.

DATA ANALYSIS

Pressures recorded during each distension were plotted against the corresponding bag volumes for each subject studied. From these intragastric pressure-volume curves the following parameters were derived.

Gastric tone = an index of tone was obtained by adding all the values of intragastric pressure obtained from the inflations between 30 ml to the maximally tolerated volume and dividing this value by the number of inflation steps.

Figure 1: Pressure-volume relations (median values) for three series of controlled gastric distension ($\circ$ =first, fasting, $\triangle$ =second, fasting, and $\bullet$ =third, after a meal) in 11 control subjects, nine dysmotility like functional dyspeptic patients, and seven postvagotomy patients.

Figure 2: Individual values of intragastric pressure during gastric distension in fasting conditions and after meal ingestion in 11 control subjects, nine dysmotility like functional dyspeptic patients, and seven postvagotomy patients.

Volume at the onset of discomfort – the volume of inflation at which the sensation of discomfort was first reported.

Pressure at the onset of discomfort – the intra-gastric pressure recorded at the onset of discomfort.

Maximal tolerated volume – the volume of inflation at which distension was stopped.

Pressure at the limit of tolerance – the intra-gastric pressure recorded at the maximal tolerated volume.

STATISTICAL ANALYSIS

To avoid the assumption of a normal distribution of the data, the results are expressed as median and range of distribution. Non-parametric tests were used for the statistical analysis¹³; for comparisons between the three groups we used the Mann-Whitney U test. Paired data regarding fasting versus fed results were analysed by the Wilcoxon's signed rank matched paired test. Differences were taken to be biologically relevant for values of p of less than 0.05.

Results

PRESSURE:VOLUME CHARACTERISTICS

Figure 1 shows the intragastric pressure volume relations during the three gastric distensions in the three groups of subjects.

Fasting studies

Gastric tone – Fig 2 presents the data for the three subject groups. Values for controls ranged from 8.0 to 20.6 mm Hg (median: 11.3 mm Hg) and were significantly lower than those for either the functional dyspepsia patients or the postvagotomy patients. Values obtained in dyspeptic patients and postvagotomy patients were similar, however ($p < 0.20$).

Gastric stiffness – data for the slopes of the intragastric pressure-volume curves ranged from 43–115 mm Hg/30 ml in controls (median: 78 mm Hg/30 ml). Values obtained in functional dyspepsia patients (median: 75 mm Hg/30 ml; range: 41–192 mm Hg/30 ml) were similar ($p > 0.10$). In the postvagotomy group, values ranged 46–113 mm Hg/30 ml (median: 60.5 mm Hg/30 ml) and were again similar to both the control and dyspeptic groups ($p > 0.05$).

After meal

Gastric tone – data are again shown in Fig 2. In the control group, postprandial gastric tone was lower than during fasting. In contrast, no consistent reduction in tone occurred in either the functional dyspepsia, or the postvagotomy, patients ($p > 0.10$).

Gastric stiffness – was reduced by food in control subjects. Slope values ranged from 28.0 to 92.2 mm Hg/30 ml (median: 60.2 mm Hg/30 ml) and were consistently lower than in those found during fasting ($p < 0.05$). In functional dyspepsia patients, slope values

Figure 3: Volume (median and interquartile interval) within the intragastric bag at the onset of, and at the maximal tolerated, discomfort in fasting conditions and after meal ingestion in 11 control subjects (C), nine dysmotility like functional dyspeptic patients (FD), and seven postvagotomy patients (PV).

were also reduced by meal ingestion, with postprandial values (median: 43.5 mm Hg/30 ml; range: 21.0–114.0 mm Hg/30 ml), which were lower than fasting values ($p < 0.05$). In contrast, postvagotomy patients showed no change in stiffness after meal ingestion, slope values (median: 64.0 mm Hg/30 ml; range: 30.0–16.0 mm Hg/30 ml) remaining similar to those recorded during fasting ($p > 0.05$).

SENSORY RESPONSES TO DISTENSION

Fasting

Volume at onset of discomfort – in the control group, the inflation volume at the onset of discomfort was 660 ml (median) (range 510–990). Discomfort was elicited at lower volumes both in the dyspeptic patients (median: 210 ml) and in the postvagotomy group (median: 180 ml) ($p < 0.05$) (Fig 3).

Pressure at onset of discomfort – the pressure within the bag at the onset of discomfort was similar in all three subject groups (Fig 4).

Maximum tolerated volume – was similar in controls (660 ml (range: 540–900)), and in dyspeptic patients (median: 525 ml; range: 390–750), but both were higher ($p < 0.02$) than in postvagotomy patients (median: 440 ml; range: 210–660) (Fig 3).

Pressure at the limit of tolerance – was similar in all groups (Fig 4).

After meal

Volume at onset of discomfort – the volume at which discomfort was first reported in the normal subjects (median: 615 ml; range 330–850) was similar to fasting values (Fig 3). In the functional dyspepsia group, volumes (median: 240 ml; range: 120–660) were also similar to fasting and were again consistently lower ($p < 0.05$) than those recorded in the normal subjects. Values in the postvagotomy patients were also similar to fasting and lower ($p < 0.05$) than those seen in the normal subjects.

Pressure at the onset of discomfort – was reduced by meal ingestion (Fig 4) in the control subjects and the functional dyspepsia group. In contrast, values were not different from fasting (median: 17.9 mm Hg; range: 10.6–21.7) in the postvagotomy group.

Maximum tolerated volume and pressure – neither the maximum tolerated distension volumes nor the pressures were changed by food in any of the groups studied.

Discussion

The results of this study show that patients with dysmotility like functional dyspepsia show abnormally raised proximal gastric tone after meal ingestion, and an increased sensitivity to distension, suggesting that a disturbance in gastric relaxation may be related to the symptoms.

Gastric relaxation is a property of the proximal stomach in response both to distension and to nutrient ingestion,¹⁴ mediated at least in part by an inhibitory non-adrenergic, non-cholinergic vagal pathway.^{14 15}

While an impairment in gastric relaxation after food has previously been suspected to be associated with postprandial symptoms in patients with functional dyspepsia,¹ three recent studies aiming at assessing intragastric pressure-volume relations in dyspeptic patients have failed to show any abnormality.^{16–18} It does not seem that methodological differences could account for the discrepancy between these previously reported results and our own data because the techniques used for assessing pressure-volume relations seem to be similar in all studies. The most probable explanation therefore seems to lie in patient selection, we studied a more homogeneous subgroup of dyspeptic patients, including only those with dysmotility like symptoms and excluding those with other dyspeptic symptom patterns, which were included by others and which might have reduced the possibility of showing an abnormality.

After bilateral truncal vagotomy in dogs, an impaired gastric relaxatory response to intra-intestinal nutrient¹⁵ and to feeding¹⁹ has been seen, showing that the relaxation is vagally mediated. Our study seems now to confirm this abnormality in humans. It is of further interest to note that the abnormalities in the dyspeptic patients resemble closely those found in postvagotomy patients suggesting perhaps a common aetiology for the development of symptoms in the two conditions. Our

Figure 4: Pressure (median and interquartile interval) within intragastric bag at the onset of, and at the maximal tolerated, discomfort during fasting and after meal ingestion in 11 control subjects, nine dysmotility like functional dyspeptic patients, and seven postvagotomy patients. Abbreviations as in Fig 3.

work thus not only supports the concept that, in humans, intact vagal pathways are of major importance in the mediation of gastric relaxatory response to distension and to food, but also suggests that a neural defect may participate in the production of gastric tone abnormalities in functional dyspepsia although it remains uncertain where precisely in the pathway such a defect might occur.

Our method of estimating gastric tone by averaging intragastric pressures measured during distension probably includes components of both basal tone and the relaxatory response to distension. In the fasted state, gastric tone seems to be the consequence of a balance between excitatory cholinergic¹⁴ and non-adrenergic, non-cholinergic inhibitory vagal efferents, the second entailing nitric oxide release.²⁰

It seems unlikely that the increased fasting gastric tone in dyspeptic patients is caused by cholinergic hyperactivity because measurements of vagally mediated gastric acid secretion²¹ and pancreatic polypeptide release²² in functional dyspepsia are normal. It seems more probable therefore that the increased fasting tone is the result of defective neural inhibitory pathways. These defects do not necessarily imply damage to the vagus nerve trunks,

however, as the destruction of intramural ganglia and intrinsic nerve fibres of the stomach also impairs gastric accommodation to a similar degree to vagotomy.²³

The postvagotomy patients, showed normal gastric wall stiffness in the fasted state, but, unlike controls and dyspeptic patients, failed to show a reduction in stiffness after meal ingestion. This is unlikely to be explained simply by an abnormality of the passive viscoelastic properties of the stomach, which it has been suggested, exists after vagotomy,²⁴ as gastric stiffness reflects more than the passive elastic characteristics of the stomach, being changed by meal ingestion¹² as well as by intragastric lipids and osmolytes.²⁵

Both the dyspepsia and postvagotomy patients reported the onset of discomfort at an abnormally low volume both under fasting conditions and after meal ingestion although it is important to note that the intragastric pressure at which discomfort was triggered was similar to that in the normal subjects. Previous experimental work in humans²⁶ has suggested that epigastric fullness and abdominal discomfort may be elicited either by excessive distension of a relaxed stomach or by the development of increased gastric muscle tone. As intramural tension can be expressed as a function of both gastric wall stretch (which is related to intragastric volume) and gastric tone (which is related to intragastric pressure),¹² it follows that if intragastric pressure is similar, and the volume is less, then the discomfort must be the result of either changed mechanoreceptor sensitivity or increased tone in the gastric wall. As our data show that in the fasted stomach tone is increased in both patient groups studied, this seems to be the most plausible explanation for the increased discomfort and is thus consistent with the view that a failure of the stomach to relax in response to meal ingestion is the cause of postprandial bloating, not only in postvagotomy patients but also in dysmotility like dyspepsia.

After vagotomy, defective postprandial gastric relaxatory responses and increased intragastric pressure probably contribute to the accelerated initial phase of gastric emptying known to occur in the condition.²⁷ This contrasts, however, with the reports of either normal⁹ or delayed^{4,5} gastric emptying in functional dyspepsia. We have, however, recently described abnormal intragastric distribution of ingested food in dysmotility like dyspeptic patients and found an increased transfer of intraluminal contents from the fundus to the antrum even when overall gastric emptying was normal.²⁸ The results of this study now suggest that the cause of such intragastric food maldistribution may be impaired fundal relaxation.

In conclusion, our results show that dysmotility like functional dyspepsia patients with postprandial bloating symptoms show, defective gastric accommodation both to distension and to food, and a lower threshold for the onset of abdominal discomfort. These results, which parallel those found in a group of postvagotomy patients with similar symptoms

suggest a common underlying neural defect of vagally mediated pathways. The precise nature of this defect in the dyspeptic patients remains to be determined, however.

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