Effect of distension and feeding on phasic changes in human proximal gastric tone

N K Ahluwalia, D G Thompson, J Barlow

Abstract

Background—Proximal stomach by virtue of its property of accommodation acts as a reservoir for the ingested food, but its role in emptying and the factors modulating it remain unexplored.

Aim—To assess the effects of distension and of feeding on proximal gastric tone.

Subjects—14 healthy volunteers with no current or past history of any gastrointestinal symptoms.

Methods—Isobaric changes in volume of the proximal stomach were recorded both during fasting and for the first 30 minutes after a meal.

Results—For a given degree of distension, the mean (SEM) intragastric pressure was consistently lower, immediately after meal ingestion (9.8 (1.1) mm Hg) than during fasting (12.9 (0.6) mm Hg; p<0.01). Proximal gastric tone was continuously variable with a frequency of fluctuation of 0.9–1.3/minute and an amplitude of 16.8 (2.2) mm Hg. Superimposed upon slower higher amplitude fluctuations in baseline tone. These variations in tone were unaffected by the degree of gastric distension or by food.

Conclusions—While proximal gastric tone decreases after meal ingestion consistent with accommodation, the fluctuations in tone are not an important factor in the modulation of nutrient emptying from the proximal stomach in the immediate postprandial period.

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Gastric emptying of food is determined by the coordinated motor activity of both the proximal and the distal stomach.1–3 The distal stomach is concerned with trituration of food particles to a small size before their delivery into the duodenum.4,5 The proximal stomach, in contrast, acts as a food reservoir, its tone being reduced after food ingestion.4,6 The modulation of the tone of the proximal stomach is suspected to be an important factor controlling gastric emptying, of liquids,2 however the exact mechanism by which the proximal stomach modulates gastric emptying remains unknown. It is probable that a major force for gastric emptying is the presence of a tonic pressure gradient between the stomach and the duodenum, with an additional mechanism being modulation of phasic contractions of the proximal stomach, which have been shown to occur in animals during the fasting state.7 In humans, the occurrence of ‘volume waves’ suggestive of changes in baseline tone have been described during the interdigestive state8,9 but the existence of phasic contractions and their role in modulating gastric emptying remains to be explored.

In recent years electronic barostat devices have been developed to study the contractions and relaxations of the proximal stomach.8,9 These devices are commonly used at an operating pressure, arbitrarily chosen to be the pressure that exists when the intragastric bag has a volume of 30 ml. We have recently characterised the pressure:volume relations of the human proximal stomach and found that the tone of the proximal stomach is directly related to the degree of distension.6 We also found that the relation between pressure and volume varies widely between subjects, so that for a given volume of distension intragastric pressure will be different.6 This led us to question whether, to maintain consistency between subjects while performing isobaric studies, it would be better to first characterise the pressure:volume plot and then select, using pre-defined criteria, the degree of distension required for each person.

As the effect of varying the degree of gastric distension on the frequency of the phasic variations in proximal gastric tone has not been studied, we performed the following study to assess the effect of distension on the variations in tone of the proximal stomach and, to find out if meal ingestion modified these variations.

Methods

SUBJECTS

Fourteen healthy volunteers (six males, eight females, mean age 29, range 23–42) without a current or past history of gastrointestinal disease, participated in the study after providing written informed consent.

CATHETER BAG ASSEMBLY

To induce selective distension of the proximal stomach, a bag, with a maximum diameter of 17 cm and capacity of 1200 ml was constructed from a 0.02 mm thick polyethylene sheet using a heat sealing device. The bag was sealed over the distal 10 cm of a 100 cm long 16 French gauge polyvinyl catheter, the proximal end of which was connected to the pressure-measurement device. Before, and after, each study the catheter bag assembly was tested for leakage, by inflating it underwater.
When inflated on the laboratory bench the intrabag pressure did not differ from atmospheric pressure until 1050 ml inflation was reached, after which a steep rise in pressure occurred for any additional increase in volume.

**BAROSTAT SYSTEM**

For all studies we used a computer driven pump system constructed in our laboratory, developed from the original Mayo Clinic design. Full details of the apparatus have been previously published, but are summarised below.

The pressure inside the intragastric bag was maintained using a transducer (Sensym, Farnell, Leeds, W Yorks, UK) attached to the proximal end of the catheter. Before its use, the transducer was calibrated from 0–64 mm Hg against an electronic digital manometer (DPI 700, Druck, Groby, Leicestershire, UK) in 256 steps, the accuracy of the pressure measurement being ±0.25 mm Hg. The voltage output from the transducer was fed into a desktop computer (Apple II, Europlus) after digital conversion of the signal by an analogue to digital card (DCP Interpack, DCP microdevelopments Limited, Lingwood, Norwich, UK), comprising an 8-bit converter with 8-bit digital input and output.

**The aspiration/injection pump**

The pump was constructed from a computer controlled motor connected to three 160 ml syringes, connected in parallel, giving a total capacity of 480 ml. The system and its connections were sufficiently rigid to ensure that any air injected into or aspirated from the bag equalled the corresponding change in the volume of the intragastric bag over the operating pressure used. The system was capable of transferring up to 15 ml air per second. However, for the purpose of our studies it was set to inject/ aspirate 1 ml air per second, to avoid any overshoot of volume exchange when monitoring small changes in tone.

**Pressure:volume recordings** – For studying the pressure:volume relations, the system was programmed to provide readings of pressure at five second intervals for 60 seconds at each inflation volume.

**Isobaric recordings** – When set to provide isobaric recordings, the intragastric bag pressure was sampled at one second intervals and relayed to the aspiration/injection pump via the computer interface. The software of the system then calculated from the intrabag pressure the change in volume required to maintain an isobaric state in the intragastric bag.

**TEST MEAL**

A commercially available iso-osmolar liquid meal (250 ml Fortison, Cow and Gate Limited, Clinical Products Division, Trowbridge, England) was used. The composition of the meal per 100 ml was, 100 kcal; 12·0 g carbohydrate; 4·0 g protein, and 4·0 g fat.

Before ingestion it was warmed to a temperature of 37°C.

In the control studies, 250 ml of iso-osmolar saline was used.

**STUDY PROTOCOLS**

All protocols were presented to, and approved by, the Salford District Ethics Committee.

Studies were carried out in the morning, after an overnight fast of at least 11 hours. Firstly, the bag, folded upon the catheter, was inserted through the mouth into the body of the stomach. The bag was next unfolded by inflating it to 400 ml and then withdrawn gently until slight resistance was encountered, indicating that the proximal end of the bag was at the gastro-oesophageal junction. The catheter was then advanced 2 cm, to ensure that the proximal end of the bag was clear of the lower oesophageal sphincter, the bag fully deflated, and the catheter attached to the cheek with adhesive tape. The subject was then positioned supine at an angle of 30° to the horizontal on a hospital bed.

**Determination of the study conditions for each subject**

To ensure consistency between subjects, a number of specific points on the gastric fundal pressure:volume curve, were first identified during a 30 ml stepwise inflation of the bag with air. At each inflation step, pressure readings were taken at five second intervals for one minute and the mean pressure calculated. The inflation procedure was continued until the maximum volume tolerated by the person was reached, after which the air was completely aspirated. From the pressure:volume plot obtained by this inflation, four study conditions were identified for each person (Fig 1). The ‘basal’ condition was identified as that volume beyond which further inflation resulted in greater than 1 mm Hg rise in pressure. The ‘plateau’ condition was identified as the volume, beyond which no further rise in pressure was seen despite continued inflation of the bag. The ‘prebasal’ condition was defined as the ‘basal’ volume minus 50 ml. The ‘mid-distension’ condition was defined as the volume that was half way between the ‘basal’ and ‘plateau’ volumes.

**Fasting variations in tone**

After determining the four study volumes for each person, isobaric variations in volume were recorded for 30 minutes, at each condition, the order of study being in ascending volume order. Between each recording condition, the bag was completely deflated for five minutes.

To perform each study, the intragastric bag was first inflated to the required volume for three minutes and the mean value for the 36 readings of intragastric pressure was calculated. The barostat system was then set to maintain this pressure for the next 30 minutes, while changes in intragastric volume were recorded.
Postprandial variations in tone

After the fasting study, each subject ingested the test meal over two to three minutes. Five minutes after the completion of meal ingestion a further 30 minute barostat study was performed at the ‘basal’ condition volume in the same manner as that described in the fasting state.

Repeat studies

In seven subjects, the protocol was repeated on a different day using 230 ml iso-osmolar saline instead of the test meal to allow the effect of the nutrient content of the meal to be distinguished from the effect of the meal volume.

DATA ANALYSIS

Initial inspection of the intragastric volumes showed continuous phasic variations for all study conditions except those at pre-basal volumes (Figs 2 and 3). These variations seemed to vary in cycle length from a few seconds to over a minute.

For each 30 minute study condition the mean amplitude and frequency of these variations was calculated after variations in volume of less than 10 ml (regarded as respiratory artefact) had been excluded.

STATISTICAL TESTS

The distribution of the data was tested by applying the Shapiro-Wilk test, and where the data were found to be normally distributed, the results are expressed in the text as mean (SEM).

Student’s paired t test was used to test the probability that differences between different study conditions were chance related, a p value of <0.05 being taken to show a biologically relevant difference. Where multiple comparisons were made, a p value of less than 0.01 was taken to represent a biologically relevant difference.

Results

Pressure:volume characteristics

During stepwise inflation, intragastric pressure increased progressively until a plateau phase was reached (Fig 1).

For the group, the basal volume was 176±8 (13-2) ml with a corresponding pressure of 14-5 (0-8) mm Hg, and the plateau volume was 438±9 (22-1) ml with a corresponding pressure of 26-4 (1-3) mm Hg.

Fasting variations in tone

During the pre-basal condition no variations were seen in any of the studies (Fig 2)

During the basal condition a continuous rhythmic pattern of phasic variations in volume was seen, superimposed on fluctuation (Fig 3) in baseline tone. This pattern was also seen during the mid-distension and plateau conditions.

At the plateau condition, the maximum variation in volume at the beginning of the study period was similar to that at the end (12-3 (10-6) ml v 22-1 (13-4) ml respectively, p=0.51, Fig 4), indicating that tone had not changed.

Postprandial variations in tone

The intragastric pressure recorded during the basal condition was consistently lower (p<0.01, Fig 5) after the meal than either
during fasting or after saline. In contrast, neither the amplitude nor the frequency of the phasic variations was changed after meal ingestion (Fig 6).

**Variations in tone after saline**

Neither the intragastric pressure nor the phasic variations in tone differed from fasting values in any subject (p>0.05 for all comparisons, Fig 6).

**Discussion**

Our study has shown that the proximal stomach, both during fasting and after meal ingestion, exhibits continuous phasic variations in tone that were independent of either the degree of distension or the nutrient content of the meal. Although phasic variations of the fundus have not been described before in humans, a similar pattern has been shown in canine fundal pouches. The failure to report similar variations in tone in earlier human studies may be due to differences in barostat design. We used a rigid syringe system, with a lower compliance than models used in earlier experiments and which may therefore not have detected the changes that were found.

The mechanism responsible for the generation of the phasic variations in tone is uncertain. The pacesetter potentials generated along the greater curvature of the corpus, which are responsible for antral contractions, do not seem to be responsible as they do not seem to propagate proximally to the fundus and also show a regular frequency of three per minute, which is more rapid than the variations noted in our study. However, bursts of spike activity occurring more rapidly than the pacesetter potentials have been demonstrated in the guinea pig fundus, just before and during phasic changes in muscle tone, and it is possible to speculate that the phasic variations in tone we have seen might have a similar electrophysiological basis.

The explanation for the fluctuation in baseline tone is similarly elusive and no gastric myoelectric correlate has yet been identified in animals or humans. It is possible to speculate that they are extragastrically controlled, an interpretation proposed by Azpiroz and Malagelada, the most plausible explanation being the result of spontaneously variable vagal efferent discharge. It remains to be discovered if human vagal efferent activity exhibits a similar rhythmic fluctuation, however, support for the conjecture comes from recent electrogastrographic studies in humans that indicate that the normal spontaneous variability of the electrical rhythmicity of the stomach is reduced in diabetics with vagal damage and autonomic neuropathy.

Our failure to show phasic variations at the lowest distension volume (prebasal condition) requires further comment. The most probable explanation is that at such small volumes of inflation no effective gastric distension is occurring and that mechano-receptors in the fundal wall are not being stimulated.
Phasic variations in proximal gastric tone

It is important to recognise that the findings reported in our study refer only to the first 30 minutes of the postprandial period and as we did not simultaneously measure gastric emptying, it is not possible to know either what was happening to gastric emptying when our study was conducted, or how much meal remained in the stomach at the end of the study period. It is known however, that the initial relaxation response to meal ingestion is followed by a later rise in baseline tone as gastric emptying proceeds so it is possible that the pattern of variations in tone could differ between the early and late postprandial phases. Additional more pronged studies are now indicated to consider this question.

In the fasting stomach, a triphasic cyclical contraction pattern, known as the migrating motor complex, is found. However, in our studies, no similar pattern was seen in proximal stomach tone. This contrasts with an earlier report that cyclical variations in tone of the fasting proximal stomach occur synchronised with the duodenal migrating motor complex. This discrepancy between the two studies is possibly related to the fact that in our study the stomach was initially distended to pressure:volume plot, before recording the variations in tone, because gastric distension has been noted to abolish the gastric migrating motor complex pattern.

Under continued isometric stretch in vitro, smooth muscle shows a decrease in tone with time, a phenomenon known as stress relaxation. In our study however, the gastric tone at the beginning of each study was similar to that at the end, suggesting that stress relaxation did not occur to any major degree. This is probably because the maximum distension achieved in our study (which was limited by subject discomfort) was insufficient to induce the stress-relaxation demonstrable in vitro.

In conclusion, our studies show that the distended proximal stomach undergoes continuous phasic variations in tone irrespective of either the degree of distension or the presence of nutrients. The mechanisms responsible for these variations now require further exploration.

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