Relationships Between Gastric Accommodation and Gastrointestinal Sensations in Healthy Volunteers. A Study Using the Barostat Technique and Two- and Three-Dimensional Ultrasonography

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The origin of postprandial gastrointestinal sensations and their relation to gastric accommodation remain unclear. Our aim was to investigate the relation between antral and fundal accommodation and sensations. (A) In eight healthy volunteers fundus accommodation was measured using a barostat after a 200-ml (300-kcal) liquid nutrient. Antral area (AA) was measured using ultrasound. Data on bag volumes, AA, and sensations were assessed. (B) In another eight healthy volunteers gastric volume was measured after a 500-ml (300-kcal) liquid nutrient using 2-D/3-D ultrasound. Sensations were scored using VAS. Distal and proximal volumes were calculated from 3-D datasets. (A) Fullness was correlated with AA (r = 0.48, P = 0.002). Fullness and bag volume were not correlated. (B) Fullness was correlated with AA (r = 0.77, P < 0.001) and distal volume (r = 0.75, P < 0.001). Proximal volume was not correlated with fullness (r = 0.10, P = NS). We conclude that fullness is related to antral volume and area rather than proximal volume. The gastric antrum may play a key role in normal appetite regulation.

KEY WORDS: three-dimensional ultrasonography; gastric volume; barostat; gastric accommodation.

Regulation of satiety and induction of upper gastrointestinal sensations are still poorly understood. Several studies have demonstrated the involvement of chemo- and mechanoreceptors at the level of the duodenum and stomach in producing upper gastrointestinal sensations (1–4). The site at which this gastric distension occurs may also play an important role (5, 6). In the physiological state the proximal stomach accommodates after meal ingestion. Gastric accommodation can be described as a reduction in gastric tone and increase in compliance. This physiological response makes it possible for solids or liquids to be ingested without a significant rise in gastric pressure. Abnormal postprandial proximal gastric accommodation has been reported in several studies. Most studies that have investigated gastric accommodation have made use of the barostat technique to quantify the increase in volume of the proximal stomach after meal ingestion in conditions (7–10) such as functional dyspepsia (11) and diabetes mellitus (8, 12). Reduced proximal gastric accommodation has been reported to be related to symptoms such as early satiety and weight loss (11), although other studies have not confirmed this relation (13). However,

Digestive Diseases and Sciences, Vol. 50, No. 9 (September 2005) 0163-2116/05/0900-1654/0 © 2005 Springer Science+Business Media, Inc.

Manuscript received December 15, 2003; accepted May 3, 2004.

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other relevant postprandial upper gastrointestinal sensations such as nausea, fullness, and pain were found not to be related to proximal gastric dysaccommodation, underlining that the pathogenesis of these symptoms is not yet established.

Recently we reported that the presence of a barostatic bag induces an increase in antral area (AA) and proximal gastric volume, demonstrating that the intragastric bag influences the magnitude of the accommodation response after meal ingestion (14). These observations and the fact that the barostat technique does not allow quantification of the distal gastric accommodation and is unpleasant for the patient led to the development of less invasive techniques to asses change in gastric volume as a reflection of gastric accommodation. These techniques include magnetic resonance imaging (MRI) (15, 16), single-photonemission computed tomography (SPECT) (17, 18), and two- and three-dimensional ultrasonography (2-D and 3-D US) (19). Several studies showed that 3-D US can be used to accurately estimate volumes of hollow organs including the stomach (20-25). Using 2-D US, impaired proximal gastric accommodation was observed in a large proportion of patients with diabetes mellitus and functional dyspepsia, confirming findings of barostatic studies (12, 26, 27). Recently, several studies demonstrated that both fasting and postprandial antral size are larger in patients with functional dyspepsia than healthy controls (28, 29). Using 3-D US we tested the hypothesis that the gastric antrum plays an important role in generating postprandial sensations. The aim of this study was therefore to investigate gastric accommodation using the barostat, 2-D US, and 3-D US and to assess the relationships between accommodation of the proximal and distal stomach and upper gastrointestinal sensations in healthy volunteers.

MATERIALS AND METHODS

The study consisted of two parts. In total 16 healthy volunteers without gastrointestinal symptoms or previous gastrointestinal surgery or diseases were asked to participate in the study after giving written informed consent. Eight healthy volunteers (five male and three female; mean age, 23; age range, 18–26; mean weight, 69 kg) participated in study A, in which proximal gastric volume changes were measured using the barostat technique and distal gastric volume was studied using 2-D US. Eight other healthy volunteers (three male and five female; mean age, 23; age range, 20–37; mean weight, 63 kg) participated in study B, in which gastric volume changes were studied using 2-D and 3-D US. The protocol was approved by the ethics committee of the University Medical Center Utrecht.

Study A

Experimental Design and Barostat Measurements. In this study proximal gastric volume changes were measured using the

barostat technique, and AA changes by 2-D ultrasonography. The studies commenced at 9.00 AM, after an overnight fast. The subjects were placed in bed in a sitting position, leaning slightly backward (at a 110° angle). A polyethylene bag with a maximum capacity of 1000 ml attached to a double-lumen tube (Ventrol; outer diameter, 6 mm; length, 120 cm) was introduced into the proximal stomach transorally and then slowly unfolded by manual inflation of 200 ml of air. Thereafter the bag was completely deflated and connected to the barostat device. After a 15-min rest period minimal distension pressure (MDP) was determined by increasing the pressure in the bag in 1-mm Hg increments. MDP was defined as the lowest pressure level that provided a mean intrabag pressure of 30 ml (8, 12). Thereafter intrabag pressure was set at 1 mm Hg above MDP (MDP + 1) for the remainder of the study. A 15-min equilibration period was followed by a baseline recording of 15 min. After this baseline period subjects were asked to drink 200 ml Nutridrink (1.5 kcal/ml; Nutricia; Zoetermeer, the Netherlands; 12 g protein, 11.6 g fat, and 36.8 g carbohydrates) within 3 min using a straw. Barostatic bag volumes were monitored at MDP + 1 for 60 min after liquid nutrient ingestion. Volume and pressure recordings were stored in a personal computer (sample frequency, 1 Hz). A positive accommodation response was defined as mean postprandial volume minus mean baseline volume >64 ml (11).

Measurement of Antral Area. In study A, AA was measured before bag placement, before liquid nutrient, and at 5, 15, 30, 45, and 60 min after liquid nutrient. Measurement of AA was performed with a standard duplex US scanner (Esaote AUS; Pie Medical; Maastricht, the Netherlands) with a 3.5-MHz curved probe. The AA was measured in a standardized sagittal section in which the antrum, the superior mesenteric vein, and the aorta were visualized simultaneously (30). The AA was outlined between antral contractions and with subjects suspending their breathing in expiration and calculated automatically using the built-in caliper and calculation program of the ultrasound scanner (26, 31, 32) (Figure 1). Data are expressed as square centimeters. All US measurements at each time point were performed twice. The mean of the two measurements was used for further analysis.

Sensations. Directly before each AA measurement the upper gastrointestinal sensations hunger, nausea, fullness, and pain were scored using a 100-mm-long visual analog scale (VAS).

Study B

Experimental Design. Subjects were placed in a comfortable chair leaning slightly backward. First, AA was measured using the same method as in study A. Next, a 3-D US measurement of the total stomach was performed as described below. After this fasting ultrasound scan a 500-ml, 300-kcal liquid nutrient (200 ml Nutridrink [1.5 kcal/ml; 12 g protein, 11.6 g fat, 36.8 g carbohydrate; Nutricia] mixed with 300 ml of water) was ingested within 3 min. At 5, 15, 30, 45, and 60 min after the liquid nutrient, AA and 3-D US measurements were repeated.

Sensations. Sensations were scored as in study A.

Measurements of Gastric Volumes Using 3-D US. A standard ultrasound scanner (Esaote-Pie Medical; Maastricht, the Netherlands) with a 3.5-MHz curved probe with an attached position sensor was used to perform this study. The probe was placed on the abdominal wall and the stomach was localized. With a fluent left-to-right lateral sweeping movement (20, 21, 24, 25), the total stomach was visualized from fundus to pylorus. During



Fig 1. Example of an ultrasonographic measurement of the antral area (1) with the typical landmarks, liver, (2), superior mesenteric vein (3), and aorta (4), visualized in one sagittal plane.

this sweep approximately 400 sagittal images were digitized and stored into the PC using InVivo ScanNT software (MedCom GmbH, Darmstadt, Germany). During all sweeps the position and the orientation of the US probe were recorded continuously by a magnetic tracker system. This system consists of a transmitter generating a pulse magnetic field and a receiver (sensor) attached to the US probe, defining position and orientation in relation to the transmitter. The tracker transmitter was positioned at a maximum distance of 60 cm from the patient.

Using specialized software (InVivo; Medcom GmbH) the computer calculated images of transverse and longitudinal planes on the basis of the information in the sagittal images and the measured position and orientation of the US probe. Regions of interest (ROIs) were then drawn using the original sagittal US images. The ROIs were constructed using the outer profile of the muscularis propria of the gastric wall. After delineation of the gastric wall in the sagittal plane, the computer calculated ROIs



Fig 2. Example of performance of 3-D analysis software with ROIs drawn in the three planes. The lower-left panel shows the original 2-D sagittal sections, whereas the upper-left image demonstrates the transverse plane and the lower-right the longitudinal plane. The upper-right panel shows the constructed 3-D image of the stomach.

in the other two planes and created a 3-D image of the stomach (Figure 2). Using this 3-D reconstruction the total gastric volume was calculated. In addition, partial gastric volumes were calculated. The proximal gastric volume was calculated using a dividing plane 10 cm from the diaphragm downward perpendicular to the longitudinal axis of the stomach. The gastric volume within this 10-cm region represented the proximal part. The distal volume was calculated by constructing a plane perpendicular to the antral axis at the point where the antrum, liver, superior mesenteric vein, and aorta could be seen simultaneously. The gastric volume from this plane to the pylorus represented the distal part. The volumes of the proximal and distal parts were calculated and used for further analysis.

Statistical Analysis

Data are presented as mean values \pm SE. Barostat and AA variables were compared using a two-sided Student's *t*-test. Relationships between gastrointestinal sensations and volume or area variables were assessed using partial correlation, controlling for subjects. The partial correlations procedure computes partial correlation coefficients that describe the linear relationship between two variables while controlling for the effects of one or more additional variables. This statistical method corrects for intrinsic correlation. Significance was accepted at the 5% level. All statistical analysis was performed with SPSS 10.0 for MS Windows (SPSS Inc.).

RESULTS

All procedures were tolerated well and all volunteers completed the study.

Antral Area and Volume Changes

Study A. MDP in the fasting state was $6.3 \pm 0.3 \text{ mm}$ Hg. The fasting volume of the barostat bag at MDP + 1 was 99.6 ± 3.9 ml. After the liquid nutrient an increase in intrabag volume of at least 64 ml was observed in all subjects. The mean maximum volume of the intragastric barostat bag was 347 ± 30.7 ml. The maximum volume was reached 30 min after ingestion of the nutrient (Figure 3A). In the fasting state, the AA was not affected by the presence of the intragastric bag, $2.8 \pm 0.28 \text{ cm}^2$; with intragastric bag, $3.3 \pm 0.39 \text{ cm}^2$; P = NS.). Five minutes after nutrient ingestion the AA had increased significantly ($3.3 \pm 0.39 \text{ vs.}$ 9.94 ± 1.53 cm²; P = 0.002). Maximum AA was reached 15 min postprandially ($11.09 \pm 1.43 \text{ cm}^2$) (Figure 3B).

Study B. Using the 3-D US technique the fasting gastric volume was 35.9 ± 4.1 ml. At 5 min after the liquid nutrient a significant increase in gastric volume was observed (488 ± 6.4 ; P < 0.001). During the postprandial hour a 37% linear decrease in gastric volume (Figure 4) to 336.7 ± 4.1 ml occurred. The mean fasting AA was 3.26 ± 0.41 cm², which was comparable to that in study A (P = NS). AA also increased significantly after liquid



Fig 3. Mean intragastric bag volume as measured by gastric barostat (A) and mean antral area (B) before (time 0) and after administration of a mixed liquid meal. Ingestion of the meal induces a rapid and sustained increase in intragastric bag volume as well as antral area.

nutrient ingestion $(3.26 \pm 0.47 \text{ vs. } 13.9 \pm 1.37 \text{ cm}^2; P < 0.001)$. Maximum AA occurred 5 min after the liquid nutrient. Calculated distal volumes changed significantly after the liquid nutrient $(2.85 \pm 0.42 \text{ vs. } 24.1 \pm 2.0 \text{ ml}; P < 0.001)$. Proximal gastric volumes could not be measured in the fasted condition.

Gastrointestinal Sensations

Study A. Five minutes after the liquid nutrient a significant increase in sensation fullness $(15.4 \pm 5.2 \text{ vs.} 41.3 \pm 5.7; P < 0.001)$ was observed as well as a sig-



Fig 4. Mean measured gastric volume using the 3-D US technique. A linear decrease can be observed during the first postprandial hour.

Digestive Diseases and Sciences, Vol. 50, No. 9 (September 2005)



Fig 5. Mean hunger (A) and fullness (B) sensation scores in studies A (squares) and B (diamonds) measured using the VAS. In both studies a significant decrease in hunger and increase in fullness are seen directly after liquid nutrient ingestion.

nificant decrease in sensation hunger $(63.5 \pm 6.8 \text{ vs.} 37.3 \pm 8.0; P = 0.02)$ (Figure 5). There were no significant changes in scores for the sensations pain $(11.1 \pm 7.1 \text{ vs.} 13.8 \pm 7.7; P = \text{NS})$ and nausea $(14.1 \pm 8.3 \text{ vs.} 12.0 \pm 6.2; P = \text{NS})$.

Study B. Immediately after the liquid nutrient a significant increase in sensation fullness was observed (7.2 \pm 3.5 vs. 53 \pm 5.1; *P* < 0.001) as well as a decrease in sensation hunger (43.4 \pm 8.3 vs. 20 \pm 7.2; *P* = 0.03) (Figure 5). No changes were found in the sensations pain (10.2 \pm 7.2 vs. 8.8 \pm 4.8; *P* = *NS*) and nausea (0.8 \pm 0.49 vs. 1.0 \pm 0.42; *P* = NS).

Relation Among Antral Area, Gastric Volume Data, and Gastrointestinal Sensations

Study A. The increase in AA showed a moderate but significant relation with the increase in sensation fullness after the liquid nutrient (r = 0.48, P = 0.002). In contrast, a negative, nonsignificant relation was observed between change in barostat bag volumes and change in sensation fullness (r = -0.21, P = NS). Other sensations were not related to gastric volume data.



Fig 6. Scatter plots demonstrating the relation between increase in fullness and increase in antral area (A), increase in distal volume (B), and proximal volume (C).

Study B. In this part a relation between increase in AA and distal gastric volume and increase in fullness was observed (0.77, P < 0.001, and r = 0.75, P < 0.001, respectively) (Figure 6A and B). In contrast, increase in fullness was not related to proximal gastric volume (r = 0.10, P = NS) (Figure 6C). Pain, hunger, and nausea were not related to AA or gastric volume data.

DISCUSSION

Many studies have focused on the relation between upper gastrointestinal sensations and different aspects of gastric function. Most recent studies investigated this relationship using the barostat technique. In the present study we used three different techniques to measure accommodation responses of the stomach. In study A the barostat technique was used to measure proximal gastric accommodation and 2-D US was used to measure AA, which reflects the volume of the distal stomach. No relation could be demonstrated between changes in barostatic bag volume and the upper gastrointestinal sensations fullness, pain, hunger, and nausea, which is in concordance with findings of others in healthy volunteers and patients with functional dyspepsia (11, 13). On the other hand, AA did show a moderate, but statistically significant correlation with sensation fullness. In study B we solely applied noninvasive 2-D and 3-D US techniques to measure accommodation. Three-dimensional ultrasound has been developed to enhance accuracy in volume estimation (19, 24, 25, 33). With this method not only the total stomach volume can be calculated, but also partial gastric volumes and intragastric distribution of the meal (21). Intragastric air can potentially limit visualization of the gastric outline by ultrasound. However, in our studies, which were carried out with subjects in seated position, air-fluid interfaces were not encountered. This observation is in concordance with the results presented by Gilja et al. (27, 34, 35) and encourages the use of 3-D US in studies of the stomach. Future studies should investigate if 3-D US can be used in studies using solid meals. In this study a total gastric volume decrease of 37% within the first postprandial hour was observed. If we equate this volume decrease to gastric emptying, 37% of the liquid nutrient was emptied within this hour. Within the first 5 min after the nutrient mean of 536 (mean fasting volume + meal volume) -488 (mean volume at 5 min) = 48 ml had emptied from the stomach. This represents an emptying rate of about 6 ml/min. Since the energy density of our liquid nutrient was 0.6 kcal/ml (300 kcal/500 ml), this means an emptying rate of 3.6 kcal/min, which is comparable with findings of Hunt et al. (36) during the early gastric emptying phase. The results of our study demonstrate a clear relation between increase in AA and increase in fullness, as was previously demonstrated by Jones et al. (37). This relation was stronger in the absence of a barostat bag in the proximal stomach. The most likely explanation for this phenomenon is that the intragastric bag influences the gastric physiology and therefore interferes with sensation rating. Recently we demonstrated that presence of an intragastric bag in the proximal stomach has an effect on both proximal and distal gastric accommodation after a liquid nutrient (14). These observations make clear that the barostat technique is not ideal to measure gastric accommodation.

Digestive Diseases and Sciences, Vol. 50, No. 9 (September 2005)

Since 2-D US only reflects the gastric volumes, we developed a method to measure partial volumes. Proximally we drew a 10-cm downward line to calculate proximal volume. The proximal volume thus obtained did not correlate with any of the scored gastrointestinal sensations. However, the calculated distal volume did show a clear relation with fullness. Although gastric borders were drawn somewhat arbitrarily, the method provides more insight in the functional behavior of different parts of the stomach.

Our findings suggest that the gastric antrum plays an important role in symptom generation and might be involved in physiological appetite regulation. It has already been suggested that antral distention might play a major role in triggering the sensation fullness (37) as our study results confirm. Up to now it is not clear how this mechanism is mediated. It is, however, conceivable that this regulation is modified by multiple factors such as sympatic nerve activity and humoral activity (38–40). Antral distention will stimulate visceral mechanoreceptors. Mechanoreceptors in different regions of the stomach show different patterns of phasic contractile activity. It has been suggested that increased antral activity during antral distention gives rise to gastric discomfort (41, 42).

Future studies using the 3D ultrasound technique are likely to increase an understanding of the pathophysiology of functional gastric disorders, especially functional dyspepsia. Several studies reported a larger AA in a subgroup of patients with functional dyspepsia (28, 43, 43). Those findings taken together with our observations suggest that the gastric antrum plays an important role in symptom generation and might be involved in the impaired relaxation response of the proximal stomach in patients with functional dyspepsia.

In conclusion, this study, using three techniques to measure accommodation, has shown that postprandial fullness is related to antral volume and AA rather than to proximal gastric volume. This suggests that the gastric antrum is more important in functional gastric disorders than hitherto assumed. Our findings imply that the total stomach should be included in studies investigating accommodation and sensations in patients.

ACKNOWLEDGMENT

Dr. M. Samsom is a fellow of the Royal Netherlands Academy of Arts and Sciences.

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Digestive Diseases and Sciences, Vol. 50, No. 9 (September 2005)

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