REFLEX CONTROL OF INTESTINAL GAS DYNAMICS AND TOLERANCE IN HUMANS

Running title: reflex control of intestinal gas dynamics

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Abbreviations used in this paper: SF\textsubscript{6}, sulfurhexafluoride

Key words: intestinal gas, gut reflexes, intestinal distension.

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Intestinal transit of gas is normally adapted to the luminal gas load, but in some patients impaired transit may lead to gas retention and symptoms. We hypothesized that intestinal gas transit is regulated by reflex mechanisms released by segmental distension at various gut levels. In 24 healthy subjects we measured gas evacuation and perception of jejunal gas infusion (12 ml/min) during simultaneous infusion of duodenal lipids mimicking the postprandial caloric load (Intralipid®, 1 Kcal/min). We evaluated the effects of proximal (duodenal) distension (n=8), distal (rectal) distension (n=8) and sham distension, as control (n=8). Duodenal lipid infusion produced gas retention (366±106 ml) with low abdominal perception (1.5±0.8 score). Distension of either the duodenum or rectum during lipid infusion expedited gas transit and prevented retention (-120±164 ml and -124±162 ml retention, respectively; p<0.05 vs control). However, the tolerance to the intestinal gas load differed markedly depending on the site of distension: perception remained low during rectal distension (2.6±0.7 score; N.S. vs control), but increased during duodenal distension (4.4±0.7 score; p<0.05 vs control). We conclude that focal gut distension, either at proximal or distal sites, accelerates gas transit, but the symptomatic response depends on the site of stimulation.

**Key words**: intestinal gas, intestinal transit, gut reflexes, gut sensitivity, abdominal distension, bloating, gut distension, gut tone, rectal distension, rectal tone.
INTRODUCTION

Intestinal gas handling in healthy subjects is a dynamic and efficient process, that allows the normal gut to accommodate, propulse and evacuate large gas loads without inducing symptoms (29;31). However, in some patients with functional abdominal symptoms these mechanisms apparently fail. We have recently evidenced that a large proportion of patients with the irritable bowel syndrome and functional bloating have impaired transit and tolerance of intestinal gas and develop gas retention, distension, and symptoms in response to gas loads that are well tolerated by healthy subjects (6;31). Hence, intestinal gas handling, i.e. accommodation, transit and evacuation, is a complex and important process in gut homeostasis, but the mechanisms that govern gas dynamics remain to be established.

Previous studies have shown that gut distension releases inhibitory reflexes (23;26) and exacerbates perception by spatial summation (28). Conceivably, these phenomena could be released by focal gas bubbles trapped within a gut loop. Hence, we hypothesized that gas transit and tolerance is regulated by reflex mechanisms released by focal gut distension. To clearly establish whether these regulatory mechanisms depend on the site of stimulation, we selected two test sites widely apart: duodenum and rectum. Our specific aim was to compare the effects of distension at either of these two sites on gas transit and tolerance in healthy subjects. Intestinal gas dynamics was assessed using a new technique developed in our laboratory, that measures gas evacuation and perception during continuous infusion of gas into the jejunum (29). The experiments were performed during duodenal infusion of nutrients at a rate that mimics the postprandial caloric load, and induces retention of intestinal gas loads (32;33).
MATERIAL AND METHODS

Participants

Twenty-four healthy individuals (10 women and 14 men; age range 19-31 years) participated in the study after giving written informed consent. Subjects completed a pre-entry questionnaire to determine the absence of gastrointestinal symptoms, including constipation (36), difficult gas evacuation, feeling of excessive abdominal gas or excessive gas evacuation. The studies were performed according to the Declaration of Helsinki, and the protocol for the study had been previously approved by the Institutional Review Board of the Hospital General Vall d’Hebron.

Intraluminal tubes

Jejunal tube assembly: We used a multilumen polyvinyl tube assembly (4.9 mm OD) that incorporated a gas infusion channel (1.2 mm ID) with multiple side holes at the tip of the tube, a lipid infusion channel (1.2 mm ID) opening 20 cm proximally, and a distending bag (6 cm long, 18 cm perimeter, 150 ml capacity) made of ultrathin polyethylene and mounted air tight over the tube assembly with the distal end 5 cm from the tip (Figure 1).

Rectal tube assembly: Another polyvinyl tube assembly (7 mm OD) incorporated a gas collection channel (3.5 mm ID) opening by multiple side holes over the 3 distal cm of the tube, and an oversized distending bag (25 cm perimeter, 400 ml capacity) air tight mounted over the tube at 5 cm distance from the tip (Figure 1). This tube arrangement allowed gas to be collected from the rectum also during rectal distension, because the surrounding bag never collapsed the gas collection channel.

Measurement of gas transit

Jejunal gas infusion: Gas was infused continuously into the proximal jejunum at 12 ml/min using a modified volumetric pump (Asid Bonz PP 50-300; Lubratronics, Unterschleissheim,
Germany). We infused a gas mixture containing 88% nitrogen, 6.5% carbon dioxide, and 5.5% oxygen, bubbled into water for saturation, mimicking the partial pressures of venous blood gases to minimize diffusion across the intestinal-blood barrier (13;24). A non-absorbable, stable gaseous marker, 5% sulfurhexafluoride (SF$_6$), was added to the gas mixture infused during the first 10 minutes of infusion (21).

**Measurement of anal gas evacuation:** Intestinal gas evacuation was collected via the rectal tube connected to a barostat (3;4) (Figure 1). The barostat provides a low-resistance collection line: a minimal pressure increment (0.25 mm Hg above atmospheric pressure) produced by gas evacuation immediately activates the pump (<5-millisecond lag) and displaces the volume along the line. Both pressure and volume were recorded on a paper polygraph (model 6006; Letica, Barcelona, Spain) so that gas evacuation was continuously monitored. A sample of gas evacuated (flatus) during each 30-min period was stored in metallized bags (Gas collection 750 ml, QuinTron, Milwaukee, WI) for later analysis of SF$_6$ concentration by infrared absorbance after determination of standard curves (16).

**Measurement of abdominal girth changes:** Subjects were placed in bed (see Procedure below), and then a non-stretch 48-mm wide belt with a metric tape measure was adjusted around the abdomen over the umbilicus by means of two elastic bands. Girth measurements were taken at 10-min intervals while the subjects were breathing relaxedly as the average of inspiratory and expiratory determinations over three consecutive respiratory excursions as described and validated before (29).

**Duodenal lipid infusion**

The experiments were performed during a continuous infusion of lipids (Intralipid® 20%; Pharmacia and Upjohn, San Cugat del Vallés, Spain) diluted in saline, at a rate of 0.5 ml/min
(1Kcal/min) using a volumetric pump (Asid Bonz PP 50-300; Lubratronics, Unterschleissheim, Germany).

**Gut distension**

Duodenal or rectal distension at fixed wall tension levels was performed by means of a computerized tensostat (10). The tensostat is a computerized air pump (Tensostat/Barostat, Sicie, Barcelona, Spain) connected via a double-lumen tube (2 mm ID for air transmission, i.e., inflation/deflation, and 0.8 mm ID for pressure transmission) to a high compliance intraluminal bag. Oversized bags were used, and we assumed that during the distension, air in the duodenum would conform to a cylindrical shape (6 cm long) and intrarectal air to a spherical shape. Based on transmural pressure and volume, the system calculates the tension on the gut wall by applying LaPlace’s law ($T = \frac{P}{R}$ for the cylinder, and $T = \frac{P}{2R}$ for the sphere), and drives the pump to maintain the desired tension level. Transmural pressure in the duodenum and the rectum was calculated by subtracting from the intraluminal pressure the intraabdominal pressure at each site. The latter was determined as the minimal distending pressure that detected respiratory variations (4;10). The distension level was individually adjusted by applying 4 g stepwise increments every minute up to a level of clear perception without discomfort. A detailed description of the tensostat and validation studies have been previously published (10).

**Perception measurement**

Subjective perception was measured at 10 min intervals during the studies, using a method that has been previously validated in detail, and extensively used in visceral sensitivity studies (1;2;14;29;37). Abdominal perception was measured by means of four graphic rating scales graded from 0 (no perception) to 6 (pain), specifically for scoring the following abdominal sensations: a) pressure/bloating, b) cramp/colicky sensation, c) stinging sensation, and d) other types of sensation (to be specified), respectively. Participants were asked to score any perceived sensation (one or more perceived simultaneously) on the scales. If two or more sensations were
simultaneously rated the highest score, instead of the mean or the cumulative score, was computed for comparisons. In previous studies we have observed that rectal distension in healthy subjects induces perception of sensations such as rectal filling, repletion, desire to evacuate and tenesmus, that are referred not to the abdomen, but deep into the pelvi-perineal region and invariably recognized by the subjects as originating from the rectum. In the present study, perception of rectal sensations (any kind of sensation without distinction, i.e., rectal filling, repletion, desire to evacuate, tenesmus) was measured by a separate rating scale also graded from 0 (no perception) to 6 (painful sensation). Additionally, a tick box (yes/no) was used to mark belching. The location and extension of the perceived sensations was measured by means of an anatomical questionnaire, that incorporated a diagram of the abdomen divided into nine regions (epigastrium, periumbilical area, hypogastrium, both hypochondria, flanks, and iliac fossae). Participants were instructed to mark the location, i.e. abdominal region(s) or extraabdominal, where the sensations were perceived.

Procedure

During the two days preceding the study participants were instructed to follow a diet excluding gas-producing foodstuffs. Participants were required to have one bowel movement within the 12 h prior to the study. Otherwise, the study was postponed. On the day of the study participants were intubated after an 8-h fast. With the bag finely folded, the intestinal tube assembly was orally introduced and was positioned under fluoroscopic control with the gas infusion port located 5 cm caudally to the angle of Treitz, the distending bag in the distal duodenum, and the lipid infusion port in the proximal duodenum. The rectal tube was then introduced. The studies were conducted in a quiet, isolated room with the subjects placed supine in bed at an angle of 30 degrees.

Before starting the study the distending bag was defolded by injecting air (50 ml in the duodenal bag and 100 ml in the rectal bag) under controlled pressure (< 20 mmHg). The bag was then completely deflated, connected to the system, and the distending tension level was
individually adjusted as previously described (see Gut distension above).

Fifteen minutes after starting the duodenal lipid infusion, gut distension either at the duodenum or the rectum (see Experimental design below), and jejunal gas infusion were both started and maintained for the subsequent 3 h study period. To prevent orad pooling of secretions, the duodenal distension was discontinued for 1 min at 15-min intervals.

Experimental design

Each subject participated only in one experiment. In three different groups of subjects (n=8 each) studies were randomly performed either with duodenal distension, with rectal distension or with sham distension, as control (Figure 1).

Data analysis

In each subject, the volume of gas retained within the gut at different time points was calculated as the difference between the volume of gas infused and the volume of gas recovered. The intensity of abdominal perception was measured by the score rated in the scales, as detailed before (see Perception measurement). In each subject we also counted the number of times each abdominal sensation was scored to calculate the frequency (as percent distribution) of each specific sensation. In the anatomical questionnaire the percentage of stimuli referred to over more than one abdominal region was calculated. Rectal perception was analysed separately. Changes in abdominal girth throughout the study were referred to measurements taken at the beginning of the study before gas infusion was started.

Statistical analysis

In each subject perception and girth change data were averaged over 30-min intervals. In each group of subjects mean values (±SE) of the parameters measured were calculated. Since some subjects did not complete the procedure, the effect of the various stimuli tested were compared using in each subject the values corresponding to the last 30 min of the study. The
Kolmogorov-Smirnov test was used to check the normality of data distribution. Comparisons of parametric data were performed by the Student’s $t$ test, paired for intragroup and unpaired for intergroup comparisons; comparisons of non-parametric data, including perception, were performed by the Wilcoxon signed rank test for paired data and the Mann-Whitney $U$ test for unpaired data. The frequency of symptoms was compared by the Chi-square test.
RESULTS

Effect of intestinal nutrients (control experiments)

During the first 60 min of duodenal lipid infusion, gas evacuation from the rectum was slow, which resulted in some degree of retention. Later on, gas evacuation increased until steady-state dynamics was achieved and gas outflow matched inflow which resulted in a fairly constant volume of gas being retained within the gut (375±12 ml mean retention between 60-180 min of the study) (Figure 2). In this period, the number of gas evacuations was 14 ±1/h with a mean volume of 50±2 ml per evacuation. Overall the subjects developed significant abdominal distension (7±2 mm girth increment; p<0.05). Recovery of SF₆ was 97±11% at 180 min.

All subjects, but one who developed frank gas retention, tolerated completion of the procedure with minimal symptoms (0.9±0.4 score by the end of the study; Figure 3), described as pressure/fullness (85±12%), colicky sensation (28±18%) and stinging sensation (32±18%). These sensations were predominantly referred to the abdominal midline (65±20% epigastrium, 71±16% periumbilical and 25±19% hypogastrium) and in 63±21% of the cases over more than one abdominal region.

Duodenal distension

Mild duodenal distension accelerated gas transit and evacuation, and modified the pattern of gas retention. Immediately after application, duodenal distension prompted gas evacuation (40±16 ml during the first 10 min versus 9±7 ml in control studies; p<0.01). During the first hour gas retention was only marginally smaller than in the control experiments (Figure 2), but later the effect of duodenal distension became more pronounced. At termination of the studies the balance of gas retention was negative, i.e. subjects evacuated 120±164 ml more gas than infused (p<0.05 vs control). During duodenal distension the subjects did not develop objective abdominal distension (2±1 mm mean girth increment; p<0.05 vs control). Recovery of SF₆ was 96±1% at 180 min.

Duodenal distension was individually adjusted at a level of mild abdominal perception.
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(2.3±0.2 score; 37±8 g). However, perception steadily increased during the study (Figure 3) up to a level of 4.4±0.7 score in the last 30 min (p<0.01 vs initial perception and vs control). Furthermore, half of the subjects did not tolerate completion of the procedure, and required termination of the study at 112±15 min. To note, the volume of gas retention at termination of the study was not significantly different in the subjects that tolerated the procedure and in those that did not (-70±164 ml and 102±170 ml, respectively). The main symptoms were pressure/fullness (65±15%), colicky sensation (63±14%), and stinging sensation (28±13%), and were referred to the epigastrium (45±14%), periumbilical region (71±11%) and hypogastrum (28±13%), predominantly (in 79±11% of the cases) over more than one area.

Rectal distension

Mild rectal distension markedly expedited gas transit and evacuation, an effect that was patent from the beginning of the study. During the first 10 min 54±15 ml were evacuated (p<0.05 vs control), and this expeditious evacuation was maintained throughout the study, which virtually prevented gas retention within the gut (Figure 2). In fact, from 120 min onwards the balance of retention became negative, indicating that even gas present in the gut before the initiation of the study was being expelled. The number of evacuations was 15±1/h with a mean volume of 55±5 ml, and the subjects did not develop abdominal distension (2±2 mm girth change; N.S.). Only one subject retained gas, exhibited substantial abdominal distension (13 mm girth increment), and required discontinuation of the study at 60 min. SF₆ recovery at 180 min was 96±3%.

Rectal distension was individually adjusted to induce mild rectal sensation (2.8±0.1 score; p<0.05 vs control and duodenal distension; 38±5g). During the first 60 min of the study, rectal perception decreased to a level that was then sustained throughout the study and was comparable to the rectal perception reported both by the duodenal distension and control groups (1.8±0.4 score, 1.5±0.6 score, 1.5±0.4 score during the last 30 min of the study, respectively; N.S.). Abdominal perception was not significantly different than in the control experiments: it
was initially very low, increased slightly during the first hour, and then remained stable until the end of the study (Figure 3). During the last 30 min of the study perception score was 2.6±0.7, significantly lower than in the duodenal distension experiments (p<0.05). The type of abdominal symptoms (63±21% pressure/fullness, 63±21% colicky sensation and 16±13% stinging sensation) and the referral pattern (55±19% epigastrium, 73±17% periumbilical region, 28±17% hypogastrium with 54±21% of the sensations perceived over more than one area) were not significantly different than in the control group.

**Local responses to distension**

Obviously, intraabdominal pressure at the duodenal and rectal sites was markedly different (10±1 mmHg and 20±1 mmHg, respectively). Duodenal and rectal distensions were individually adjusted to produce mild perception, and the resulting tension levels were remarkably similar at both sites (37±8 g and 38±5 g, respectively). However, at a fixed tension level, duodenal volume exhibited a progressive reduction along the study, reflecting a tonic contraction (from 55±6 ml at the beginning to 33±6 ml at the end of the study; p<0.05) (Figure 4). By contrast, rectal volume exhibited an initial expansion, which then remained steady until the end of the study, but these rectal changes were not statistically significant (Figure 4).
DISCUSSION

We have shown that intestinal gas dynamics is influenced by reflex mechanisms released by mechanical stimuli in the gut, and that the specific effects on gas transit and perception depend on the site of stimulation.

For this study we adapted a model of intestinal gas retention in healthy subjects (32;33) based on the infusion of a physiological dose of lipids directly into the duodenum, which mimics the postprandial state (22). During duodenal lipid infusion, about 400 ml of the gas infused was retained into the gut. Taking into account that the fasting gut normally contains about 200 ml of endogenous gas (29;31;35) the total volume of intraluminal gas (endogenous plus infused) actually tripled. Gas evacuation was collected via an intrarectal cannula, thus preventing potentially confounding effects of the anus on gas retention.

Using this model we have shown that either duodenal or rectal distension accelerated gas transit and eliminated the gas pooling by the end of the 180 min study period. However, the early effects of focal gut distension were remarkably different for each site. Thus, whereas duodenal distension had no significant effect on the initial gas retention, rectal distension accelerated gas evacuation and prevented retention from the very beginning of the experiment. By the end of the studies, however, both duodenal and rectal distension resulted in the evacuation of about 150 ml more gas than infused, a volume that probably represented most of the endogenous gas present in the gut at the beginning of the study (29;31;35). Hence, the distension stimuli induced complete clearance of intestinal gas and reduced the dead space in the gut conduit to a minimum. To note, the time-point for inflection in the gas retention curve towards negativization was similar in both duodenal and rectal distension groups, but during duodenal distension complete clearance took longer due to the initial retention. Hence, focal gut distension appears to trigger a gas propulsive activity that even overcomes the normal inhibitory effect of lipids.
Given the problems in standardizing gut distension in different individuals and at different regions of the gut, distensions were individually adjusted based on their intensity of conscious perception, at a level inducing mild sensation well below the discomfort threshold. Hence, the determinant of distension was the perceptual response. Once the distension level was established, the tension was kept constant over-time by means of a computerized tensostat. The tensostat has been previously validated in the stomach (10) and the rectum (9), showing that perception depends on wall tension rather than on intraluminal pressure or volume. However, we wish to acknowledge that this concept has not been validated in the small bowel. Since the level of distension was adjusted based on perception, plausibly the same purpose would have been achieved using either fixed volume or fixed pressure distensions by means of a barostat. Perception at the selected distension levels was similar in the duodenum and the rectum (2.3±0.2 score and 2.8±0.1 score, respectively; N.S.), and interestingly, the tension levels applied at the two sites were remarkably similar (37±8 g and 38±5 g, respectively; N.S.), whereas the intraluminal pressures (23±3 mmHg and 34±1 mmHg, respectively; p<0.05) and the volumes (55±6 ml and 168±13 ml, respectively; p<0.05) were different. During duodenal distension, abdominal perception progressively increased over time, even to uncomfortable levels in half of the subjects. We have previously shown that mild jejunal distension at fixed volume applied by means of a distending balloon and without concomitant gas infusion, induced steady perception over-time (28). In the present studies, during duodenal distension plus concomitant gas infusion abdominal perception increased, and although the methodology differed, i.e., the tensostat instead of the fixed volume distension was used, it could be speculated that duodenal distension sensitized the gut to the gas overload via spatial summation phenomena known to heighten perception (28;30). Rectal distension, in contrast, was not associated with significant abdominal perception. Hence, the effect of gut distension on perception of a gas load markedly depends on
the area of stimulation. The spatial summation phenomena observed with duodenal, but not rectal distension, suggest that the gas load distended the small bowel rather than the colon, but the organization of the afferent input from different gut regions, small bowel, colon and rectum, remains largely unknown (15;27). The type of abdominal symptoms and referral patterns were similar in the three study groups, duodenal, rectal and control, providing further evidence that gut distension simply increased perception of the gas loads.

The tensostat allowed also to study focal motor effects at the site of distension. The duodenum proximal to the gas infusion site exhibited a progressive reduction in volume, reflecting a contraction. In contrast, the rectum had a relaxatory response. Conceivably, these changes in muscular tone were related to the intestinal motor response to the gas loads, since we have previously shown that prolonged distension of the jejunum does not induce any change in local muscular activity (contraction or relaxation) (28). It is also unknown whether lipids act by relaxing the intestine and increasing capacitance or by increasing resistance due to segmental contractions (5;8;12;17;25). Bowel distensions have been shown to release inhibitory intestino-intestinal reflexes (23;26), but stimulatory responses can also be elicited under some circumstances (5;7;19;20). In this regard, the reduced dead space observed in our studies may be related to decreased capacitance secondary to tonic contraction of the intestine.

Evacuation of infused gas normally requires a lag-time of about one hour, during which the gas infused is retained in the gut (31;32). However, this initial retention was not observed in a previous set of studies using an unperceived balloon to prevent gaseous backflow (29). Comparison of these early data with the results of the present studies would suggest that gas propulsive reflexes may be also released by unperceived gut stimuli, and hence, that they may operate under physiological conditions. It is conceivable that these reflexes are part of the physiological peristaltic reflex in response to an intraluminal bolus (5;34). However, since in the
present study only gut distensions above the perception threshold were tested, it cannot be excluded that perception of the distending stimulus had an added effect on enhanced gas clearance.

We have recently shown that patients with the irritable bowel syndrome and functional bloating have impaired dynamics and tolerance of intestinal gas loads (6;31;33), and it is plausible to speculate that such impaired gas handling may result from failure of the physiological reflex mechanism that normally propulses and evacuates gas. This working hypothesis fits well within the framework of a sensory-reflex dysfunction in the pathophysiology of the irritable bowel syndrome and related functional disorders, as evidenced by other studies (11;18).
Reference List


28. Serra, J., F. Azpiroz, and J. R. Malagelada. Perception and reflex responses to intestinal distention in humans are modified by simultaneous or previous stimulation.


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Figure 1. Method. Gas was infused into the jejunum and collected via a rectal cannula passing through the rectal distending balloon. Abdominal distension was measured by a tape measure, and perception by a graphic rating scale. Lipids were infused into the duodenum mimicking the postprandial caloric load. The effects of duodenal distension (D), rectal distension (D), and sham distension, as control, were tested.
Figure 2. Effect of gut distension on intestinal gas retention. Both duodenal and rectal distension prevented gas retention ($p<0.05$ vs sham distension for both), but the later exhibited an earlier effect. Data are gas retention at 30-min intervals.
Figure 3. Effect of gut distension on intestinal gas tolerance. In contrast to sham and rectal distension, duodenal distension induced progressively worsening abdominal symptoms, and 4/8 subjects required discontinuation of the study at 112±15 min. (p<0.05 vs sham and rectal distension). Data are average values over 30-min intervals.
Duodenal and rectal tone response to intestinal gas loads. Using respective tensostats, intestinal gas infusion was shown to be associated to a significant duodenal contraction (volume decrease) ($p<0.05$ vs basal volume) but to a mild rectal relaxation (volume increment). Data are average values over 30-min intervals.