Impaired reflex control of intestinal gas transit in patients with abdominal bloating

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Background: Patients with abdominal bloating and distension exhibit impaired transit of intestinal gas which may lead to excessive gas retention and symptoms. Furthermore, we have previously shown that intestinal gas transit is normally accelerated by rectal distension. We hypothesise that in patients with functional bloating this modulatory mechanism fails and impairs gas transit.

Methods: In 12 healthy subjects and eight patients with abdominal bloating we compared, by paired studies, the effect of rectal versus sham distension on intestinal gas transit. Gas was infused into the jejunum (12 ml/min) for three hours with simultaneous perfusion of lipids into the duodenum (Intralipid 1 kcal/min) while measuring evacuation of gas per rectum.

Results: In healthy subjects, duodenal lipid infusion produced gas retention (409 (68) ml) which was prevented by rectal distension (90 (90) ml; p<0.05 v sham distension). In contrast, rectal distension in patients with abdominal bloating failed to reduce lipid induced gas retention (771 (217) ml retention during rectal distension v 730 (183) ml during sham distension; NS; p<0.05 v healthy controls for both).

Conclusion: Failure of distension related reflexes impairs intestinal gas propulsion and clearance in patients with abdominal bloating.

MATERIAL AND METHODS

Participants
Eight patients complaining of abdominal bloating (six women, two men; aged 23–56 years) and 12 healthy individuals (six women, six men; aged 19–40 years) participated in the study. The predominant symptom in patients was abdominal bloating, with no detectable abnormalities in routine testing and no concomitant diseases. Five patients fulfilled the Rome II IBS criteria (three were constipation predominant and two diarrhoea predominant) and the other three patients fulfilled Rome II functional bloating criteria and had a normal bowel habit. All patients were symptomatic at the time of the study. Healthy subjects completed a pre-entry questionnaire to determine the absence of gastrointestinal symptoms, including constipation, difficult gas evacuation, feeling of excessive abdominal gas, or excessive gas evacuation. The study protocol was approved by the Institutional Review Board of the University Hospital Vall d’Hebron, and all subjects gave written informed consent to participate in the study.

Intraluminal tubes

Orointestinal tube
A multilumen polyvinyl tube assembly incorporated a gas infusion channel (1.2 mm ID) opening at the tip of the tube and a lipid perfusion channel (1.2 mm ID) opening 20 cm proximally. The gas infusion port was fluoroscopically positioned 5 cm distal to the angle of Treitz and the lipid perfusion port in the proximal duodenum.

Rectal tube assembly
A high compliance oversized bag (25 cm perimeter, 400 ml capacity) made of ultrathin polyethylene was airtight mounted over a polyvinyl tube assembly (7 mm OD) 5 cm from the tip. The assembly incorporated a gas collection channel (3.5 mm ID) opening by multiple side holes over the distal 3 cm of the tube, as well as inflation (2 mm ID) and pressure recording channels (0.8 mm ID) opening within the bag. Distension of the rectal bag never collapsed the internal 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 5.3% oxygen, bubbled into water for saturation, mimicking the partial pressures of venous blood gases to minimise diffusion across the intestinal-blood barrier. To verify the completeness of recovery and absence of leaks, a non-absorbable stable gaseous marker, 5% sulphur hexafluoride; IBS, irritable bowel syndrome.
hexafluoride (SF₆), was added to the gas mixture during the first 10 minutes of the infusion.

Measurement of anal gas evacuation
Intestinal gas evacuation was collected via the rectal tube connected to a barostat, and the volume of gas evacuated was continuously recorded on a paper polygraph (model 6006; Letica, Barcelona, Spain), as previously described. A sample of gas evacuated (flatus) during each 30 minute period was stored in metal bags (gas collection 750 ml; Quin Tron, Milwaukee, Wisconsin, USA) for later analysis of SF₆ concentration by infrared absorbance after determination of standard curves.

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 while the subjects were breathing in a relaxed manner as the average of inspiratory and expiratory determinations over three consecutive respiratory excursions, as described and validated previously.

Duodenal lipid infusion
The experiments were performed during continuous duodenal perfusion of a lipid emulsion (Intralipid 20%; Pharmacia and Upjohn, San Cugat del Vallís, Spain) at a rate of 0.5 ml/min (1 kcal/min) using a volumetric pump (Asid Bonz PP 50–300; Lubratronics, Unterschleissheim, Germany).

Rectal distension
Distension at fixed wall tension levels was performed by means of a computerised air pump (Tensostat/Barostat, Sicie, Barcelona, Spain) connected to the rectal bag. Assuming that during the distension air within the oversized bag conforms to a spherical shape, the tensostat calculates the tension that during the distension air within the oversized bag was stored in metal bags (gas collection 750 ml; Quin Tron, Milwaukee, Wisconsin, USA) for later analysis of SF₆ concentration by infrared absorbance after determination of standard curves.

Perception measurement
Conscious perception was measured during the studies using a method that has been extensively used and previously validated in detail. Abdominal perception was recorded using a graded questionnaire to score the intensity and type of sensations perceived, and an anatomical questionnaire to measure the location and extension of the perceived sensations. The graded questionnaire included four graphic rating scales specifically for scoring four possible abdominal sensations: (a) pressure/bloating; (b) cramp/colicky sensation; (c) stinging sensation; and (d) other type of sensation (to be specified). Each sensation was independently scored on the respective rating scale from 0 (no perception) to 6 (painful sensation). Participants were asked to score any sensation on the respective rating scale from 0 (no perception) to 6 (painful sensation). The questionnaire included an additional scale to score rectal perception, and a tick box (yes/no) to signal belching. The questionnaire presented to patients had another tick box to signal the repetition of customary symptoms. The anatomical questionnaire incorporated a diagram of the abdomen divided into nine regions corresponding to the epigastrum, periumbilical area, hypogastrium, both hypochondria, flanks, and iliac fossae. Participants were instructed to mark the location (that is, abdominal region(s) or extra-abdominal) where the sensations were perceived.

Procedure
During the two days preceding the study, participants were instructed to follow a diet excluding legumes, vegetables, garlic, onion, nuts, cereals, wholemeal bread, and fizzy drinks. The night before the study they had a light dinner that could consist of meat, fish, eggs, rice, pasta, and/or white bread but were instructed to avoid dairy products, salad, fruit, and alcoholic beverages. Patients were administered a glycerine suppository the night before the study. All participants were required to have one bowel movement within the 12 hours prior to the study or otherwise the study was postponed. On the day of the study participants were intubated after an eight hour fast. The studies were conducted in a quiet isolated room with the subjects placed supine in bed at an angle of 30°.

Before starting the study the rectal bag was unfolded by injecting 100 ml of air under controlled pressure (<20 mm Hg). The bag was then completely deflated and connected to the tensostat. Fifteen minutes after starting the duodenal lipid infusion rectal distension was applied. During duodenal lipid infusion and rectal distension gas was continuously infused into the jejunum and rectal gas evacuation was recorded for the subsequent three hour study period. Conscious perception and girth changes were measured at 10 minute intervals.

Experimental design
Main studies
In patients (n = 8) and healthy controls (n = 8), the effects of rectal distension and sham distension (as control) were studied in random order on separate days with an interval of one week.

Ancillary study
The level of rectal distension tested in the main studies was individually adjusted, and was lower in patients than in controls (19 (3) g ν 34 (4) g, respectively; p<0.05) due to their increased rectal perception. Hence to validate that the different effects of rectal distension in patients and healthy subjects was not related to the level of distension, in an additional group of healthy subjects (n = 4) the effect of 19 g rectal distension (the mean tension level applied to patients) and sham distension, as control, were studied in random order on separate days with a one week interval, following the same procedure as in the main studies.

Data analysis
In each subject the volume of gas retained within the gut was calculated as the difference between the volume of gas infused and the volume of gas recovered. Perception was measured by the score rated in the scales. In each subject we counted the number of times each abdominal sensation was scored in the repeat measurements during the study to calculate the frequency (as per cent distribution) of each specific sensation. In the anatomical questionnaire we calculated the percentage of sensations referred over each abdominal region, as well as the percentage referred over more than one region. Rectal perception was analysed separately. Changes in abdominal girth during the study
were referenced to girth measurement at the start of the study (that is, before gas infusion was started).

**Statistical analysis**

In each group of subjects, mean values (SEM) of the parameters measured were calculated. The Komolgorov-Smirnov test was used to check the normality of data distribution. Comparisons of parametric normally distributed data were performed by the Student’s t test, paired tests for intragroup comparisons, and unpaired tests for intergroup comparisons; otherwise the Wilcoxon signed rank test was used for paired data and the Mann-Whitney U test for comparisons; otherwise the Wilcoxon signed rank test was used for paired data and the Mann-Whitney U test for unpaired data. Correlations between paired data were examined by linear regression analysis. The frequency of sensations was compared using the χ² test. In each group of subjects we calculated the mean values (SEM) for the frequency of each sensation using individual data of per cent distribution.

**RESULTS**

**Intestinal gas retention**

In healthy subjects, duodenal lipid perfusion induced retention of the gas infused but simultaneous rectal distension expedited gas transit and virtually abolished lipid induced gas retention (figs 1, 2). Patients with abdominal bloating exhibited significantly greater gas retention that was not modified by rectal distension (figs 1, 2). Rectal distension was individually adjusted at the beginning of the experiments to induce a mild rectal sensation but this perception level was achieved in patients at significantly lower rectal tensions than in healthy subjects (19 (3) v 34 (4) ml, respectively; p<0.05). However, in an additional group of healthy subjects, 19 g rectal wall tension, a level equivalent to that tested in patients, effectively expedited gas transit and reduced the volume of gas retained in the gut (198 (73) ml gas retention by the end to the experiments v 318 (74) ml during sham distension in the same subjects; p<0.05). By the end of the study, recovery of the SF₆ bolus administered at the beginning of the infusion was 97 (1)% in healthy subjects and 97 (2)% in patients, respectively (pooled data for experiments with and without rectal distension).

**Perception of rectal distension**

At the beginning of the studies, rectal distension induced a mild rectal sensation both in healthy subjects (score of 3.0 (0.1); p<0.05 v 0.4 (0.3) score during sham distension) and in patients (2.5 (0.2) score; p<0.05 v 0.8 (0.3) score during sham distension; NS v controls). Interestingly, 19 g rectal wall tension in healthy subjects induced significant effects on gas transit with insignificant rectal perception (score of 1.5 (0.6); NS v 0.3 (0.3) score during sham distension). In healthy subjects, rectal perception remained steady throughout the study period; by the end of the study the perception score was 2.7 (0.4) during rectal distension in the main studies, 1.0 (0.3) during sham distension, and 1.5 (0.6) during 19 g rectal distension in the ancillary studies (NS v beginning of the study for all). In contrast, rectal perception in patients progressively increased during the study up to a score of 4.1 (0.4) by the end of the experiments (p<0.05 v study start and v controls).

**Abdominal symptoms**

Intestinal gas retention was associated with abdominal distension (r = 0.62; p<0.0001). Hence in healthy subjects...
abdominal bloating have a gut motor dysfunction with impaired reflex control of gas propulsion.

Rectal distension was produced by means of a tensostat because it could "normalise" wall mechanoreceptor stimulation in subjects with different rectal compliance. Stimulus standardisation under these conditions could not have been achieved by applying either volume or pressure (barostat) driven distensions as perception seems to be related to wall tension rather than to intraluminal pressure or expansion.13 14 We adjusted wall tension individually at the level of mild perception, well below the discomfort threshold. It is important to note that rectal distension did not influence perception of abdominal sensations during gas infusion in healthy subjects or in patients with abdominal bloating. Rectal distension neither modified the type of abdominal symptoms nor the referral pattern during infusion of gas.

As previously described,23 patients exhibited rectal hyper-sensitivity, as evidenced by the significantly lower rectal wall tension required to induce perception. However, the lack of gas propulsion reflex seemed unrelated to the lower rectal tension tolerated by patients as in the ancillary study we showed that applying the same low tension level to healthy subjects as to patients effectively accelerated their gas transit. Nor could the presence of symptoms in patients explain their absent reflex on gas propulsion because we have previously shown that uncomfortable duodenal distension in healthy subjects stimulates gas propulsion.4

Evacuation of infused gas normally requires a lag time of approximately one hour, during which the gas infused is retained in the gut.24 25 However, this initial retention was not observed in a previous set of studies using an unperceived balloon to prevent gaseous backflow.1 These early data, together with the results of the present studies and particularly the ancillary experiment, would suggest that gas propulsive reflexes may also be released by unperceived gut stimuli and hence that they may operate under physiological conditions.

The tensostat also allowed study of the changes in tone at the site of distension. The rectum distal to the gas infusion site exhibited a progressive increment in intrabag volume, reflecting relaxation. Conflicting results have been reported with regard to the effect of rectal distension on phasic colonic motility,22 23 which may be explained by the different experimental conditions tested, particularly the level of rectal distension. Nevertheless, the effects of rectal distension on phasic and tonic gut motor activity may well be different. We have previously shown that both types of motor activity evolve independently,24 and gas movement might be determined by changes in capacitance produced by regional tonic contraction rather than by focal phasic contractions.

In conclusion, it is plausible to speculate that impaired gas handling in patients with bloating may result from failure of physiological reflexes that normally modulate gas accommodation, propulsion, and evacuation. The precise pathophysiological relevance of our data remains uncertain because in patients with either IBS or functional bloating, intestinal gas volume is similar to that in healthy subjects, at least under fasting basal condition.24 25 Nevertheless, the added value of our observations rests in the objective demonstration of altered reflex control of gut motility in patients with abdominal bloating. These data are particularly relevant within the framework of a sensory reflex dysfunction in the pathophysiology of IBS and related functional disorders.24 25

ACKNOWLEDGEMENTS
Supported in part by the Spanish Ministry of Education (Dirección General de Enseñanza Superior del Ministerio de Educación, Cultura, BFI 2002-03431), the Instituto de Salud Carlos III (grant C03/02 and 02/3036), and the National Institutes of Health, USA (grant DK57064). Dr Passos had a scholarship from the Brazilian Fundación Carolina de Inversiones y Desarrollo, Argentina.
Conflict of interest: None declared.

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Conflict of interest: None declared.

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