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

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INTESTINAL MOTILITY

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 vs 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 vs 730 ± 183 ml during sham distension; NS; p < 0.05 vs 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 (SF₆), was 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.

Abbreviations: SF₆, sulphur hexafluoride; IBS, irritable bowel syndrome
hexafluoride (SF₆), was added to the gas mixture during the first 10 minutes of the infusion. 1–3

Measurement of anal gas evacuation
Intestinal gas evacuation was collected via the rectal tube connected to a barostat, 10–11 and the volume of gas evacuated was continuously recorded on a paper polygraph (model 6006; Letica, Barcelona, Spain), as previously described. 1 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. 12

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. 1

Duodenal lipid infusion
The experiments were performed during continuous duodenal perfusion of a lipid emulsion (Intralipid 20%; Pharmacia and Upjohn, San Cugat del Vallés, 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. 13–14 Assuming that during the distension air within the oversized bag conforms to a spherical shape, the tensostat calculates the tension on the rectal wall based on transmural pressure and conforms to a spherical shape, the tensostat calculates the tension. Transmural pressure on the rectal wall is based on Laplace’s law (T = P × R/2), and drives the pump to maintain the desired tension level. Transmural pressure was calculated by subtracting from intraluminal pressure the intra-abdominal pressure determined at the beginning of the study as the minimal distending pressure that detected respiratory variations. 11–13 In each individual the distending tension level was then 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 published previously. 13

Perception measurement
Conscious perception was measured during the studies using a method that has been extensively used and previously validated in detail. 15–18 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 in the repeat measurements during the study to calculate the frequency (as per cent distribution) of each specific sensation. In the anatomical questionnaire we counted the number of times each abdominal sensation was scored in the repeat measurements during the study to calculate 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...
Figure 1  Effect of gut distension on gastrointestinal gas retention in healthy controls and patients with abdominal bloating. Rectal distension accelerated gas evacuation and prevented lipid induced retention in healthy subjects (p < 0.05 v sham distension) but had no effect in patients. #p < 0.05 versus sham; $p < 0.05$ versus healthy controls.

Figure 2  Individual data for gas retention by the end of the study.

Figure 3  Effect of gut distension on abdominal perception. In healthy subjects, abdominal perception remained low during both sham and rectal distension. In contrast, patients with abdominal bloating developed significantly greater perception than healthy subjects under both study conditions ($p < 0.05$ v controls for both).

**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 of 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 in both 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...
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... abdominal region; NS over their abdomen (in 78 (7)% of cases over more than the hypogastrium; pooled data for sham and rectal distension). These sensations were predominantly referred to the abdominal midline (35 (15)% epigastrum, 67 (14)% periumbilical, and 57 (15)% hypogastrum) and in 57 (17)% of cases over more than one abdominal region. Similar type of perception, although milder, was reported during rectal distension (data not shown). Patients also reported similar types of symptoms and referral patterns during both sham and rectal distension. Predominant symptoms in patients were pressure/bloating (53 (8)% of the time) and cramp/colicky sensations (27 (5)% of the time) which were referred to the abdominal midline (22 (7)% epigastrum, 58 (6)% periumbilical, and 65 (9)% hypogastrum; pooled data for sham and rectal distension). Patients tended to perceive these sensations more diffusely over their abdomen (in 78 (7)% of cases over more than the abdominal region; NS v controls). Interestingly, patients recognised the perceived sensations as their usual clinical symptoms on 95 (3)% of occasions.

Rectal responses to distension

Intra-abdominal pressure estimates were 20 (1) mm Hg in controls and 18 (1) mm Hg in patients (NS v controls). At a fixed tension level, rectal volume tended to increase but the increment was not statistically significant (volume increased from 141 (17) ml at the beginning of the study to 230 (22) ml at the end in healthy subjects, and from 129 (17) ml to 160 (20) ml in patients; NS v study start and v controls for both). Intrarectal volume was smaller in patients due to the lower tension levels tolerated but overall compliance was similar in both groups.

DISCUSSION

Our data indicate that patients with abdominal bloating have abnormal reflex control of intestinal gas transit which results in impaired tolerance of intestinal gas loads.

We have previously shown that in healthy subjects, intraluminal lipids dose dependently inhibit propulsion of intestinal gas loads, and that focal gut distension induces prokinetic activity that counterbalances the normal inhibitory effect of lipids. Hence intestinal gas transit appears to be normally regulated by a fine balance of stimulatory and inhibitory reflexes. However, in contrast with healthy subjects, patients with abdominal bloating, both IBS and functional bloating have impaired handling of intestinal gas loads, resulting in gas retention, abdominal distension, and symptoms. We have recently shown that these patients exhibit exaggerated responses to intestinal lipids: a low lipid dose, not producing detectable effects in healthy subjects, induced marked inhibition of gas transit in patients. The present studies showed that not only is the inhibitory response to lipids upregulated but the prokinetic effect of focal gut distension also seems to be impaired. Indeed, rectal distension failed to induce propulsive reflexes, and by the end of the experiments patients retained about 1 litre more gas in the gut than healthy subjects. Hence patients complaining of 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. 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, patients exhibited rectal hypersensitivity, 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.

Evacuation of infused gas normally requires a lag time of approximately one hour, during which the gas infused is retained in the gut. However, this initial retention was not observed in a previous set of studies using an unperceived balloon to prevent gaseous backflow. 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, 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, 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. 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.

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