Mechanisms of intestinal gas retention in humans: impaired propulsion versus obstructed evacuation

JORDI SERRA, FERNANDO AZPIROZ, AND JUAN-R. MALAGELADA
Digestive System Research Unit, Hospital General Vall d’Hebron, Autonomous University of Barcelona, 08035 Barcelona, Spain

Received 29 November 2000; accepted in final form 28 February 2001

Serra, Jordi, Fernando Azpiroz, and Juan-R. Malagelada. Mechanisms of intestinal gas retention in humans: impaired propulsion versus obstructed evacuation. Am J Physiol Gastrointest Liver Physiol 281: G138–G143, 2001.—To explore the clinical role of intestinal gas dynamics, we investigated two potential mechanisms of gas retention, defective propulsion and obstructed evacuation. In healthy subjects, a gas mixture was continuously infused into the jejunum (4 ml/min) during a 2-h control period of spontaneous gas evacuation and 2) during a 2-h test period either with impaired gut propulsion caused by intravenous glucagon (n = 6) or with obstructed (self-restrained) anal evacuation (n = 10) while anal gas evacuation, symptom perception (0–6 scale), and abdominal girth were measured. Impaired gut propulsion and obstructed evacuation produced similar gas retention (558 ± 58 ml and 407 ± 85 ml, respectively, vs. 96 ± 58 ml control; P < 0.05 for both) and abdominal distension (8 ± 3 mm and 6 ± 3 mm, respectively, vs. 1 ± 1 mm control; P < 0.05 for both). However, obstructed evacuation increased symptom perception (2.3 ± 0.6 score change; P < 0.05), whereas gas retention in the glucagon-induced hypotonic gut was virtually unperceived (−0.4 ± 0.7 score change; not significant). In conclusion, the perception of intestinal gas accumulation depends on the mechanism of retention.

intestinal transit; visceral sensitivity; bloating; intestinal tone; anal function

IN CONTRAST to the better-studied transit patterns of solid and liquid gut content, the physiology and pathophysiology of intestinal gas remain poorly understood. We recently developed a new methodology to evaluate intestinal gas dynamics. Our method consists of infusion of gas into the jejunum and collection of the anal gas effluent for correlation of intestinal gas retention, objective abdominal distension, and subjective symptom perception (20). In a large dose-response study (20), we previously demonstrated that, by and large, healthy subjects tolerate a wide range of intestinal gas loads because normal individuals propel and evacuate gas expeditiously, thus preventing intra-abdominal pooling. In contrast, in a further study (21) we demonstrated that a large group of patients with unexplained abdominal symptoms, specifically those with irritable bowel syndrome (IBS) (24) have impaired handling of intestinal gas; a large proportion manifested gas pooling and symptoms that mimicked their customary complaints. On the basis of these studies we concluded that functional (unexplained) abdominal symptoms may be related to impaired handling of intestinal gas. However, the mechanisms responsible for poor gas tolerance remain unknown.

The goal of the present study was to compare the effects of two key mechanisms of intestinal gas retention, specifically, defective propulsion and obstructed flow. To address this goal, we correlated intestinal gas transit, abdominal distension, and symptom perception in response to standardized gas loads (20). Defective intestinal gas propulsion was modeled by pharmacological inhibition of gut motor activity with glucagon (6–8, 16, 19), and obstructed gas flow was modeled by voluntary restraint of anal gas evacuation.

MATERIALS AND METHODS

Participants

Thirty healthy individuals (13 women, 17 men; age range 19–26 yr) participated in the study after giving their written informed consent. Subjects completed a preentry questionnaire to rule out the presence of gastrointestinal symptoms, particularly those of constipation (24), difficult gas evacuation, feeling of excessive abdominal gas, or excessive gas evacuation. The protocol for the study had previously been approved by the Institutional Review Board of the University Hospital Vall d’Hebron, and the studies were performed according to the Declaration of Helsinki.

Jejunal Gas Infusion

We used an intestinal polyvinyl tube assembly (3.2-mm OD) that incorporated a gas infusion channel (1.6-mm ID) with multiple side holes over the 2-cm distal segment. A separate gastric polyvinyl tube (3.2-mm OD) was used to measure possible gaseous reflux and/or swallowing into the stomach.

A gas mixture containing 88% nitrogen, 6.5% carbon dioxide, and 5.5% oxygen bubbled in water for saturation was infused. These proportions were chosen to mimic the partial pressures of gases in venous blood and hence minimize diffusion across the intestinal-blood barrier (9, 15). In some

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
experiments a nonabsorbable, stable gaseous marker, 0.5% sulfur hexafluoride (SF₆), was added to the final mixture (13). Gas was infused continuously into the proximal jejunum at 4 ml/min with a modified volumetric pump (Asid Bonz PP 50–300; Lubratronics, Unterschleissheim, Germany).

Measurement of Gas Evacuation

Intestinal gas evacuation was measured via an anal cannula that fit hermetically between the buttocks (20). Anal gas was collected via a leak-proof, low-resistance collection line using a barostat (3, 4), and the volume was automatically recorded on a paper polygraph (model 6006, Letica, Barcelona, Spain) as previously described (20). The subjects were provided with an event marker to signal every gas expulsion for later correlation with the volume recording.

Measurements of Abdominal Girth Changes

Once the subjects were in bed (see Procedures), 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 in a relaxed manner as the average of inspiratory and expiratory girth determinations over three consecutive respiratory excursions.

Perception Questionnaire

A graded questionnaire was used to measure the intensity and type of sensations perceived, and an anatomic questionnaire was used to measure the location and extension of the perceived sensations (2, 10, 18, 20). The graded questionnaire, which included four graphic rating scales graded from 0 (no perception) to 6 (pain), was used to specifically score sensation. The questionnaire included two additional scales for scoring the feeling of rectal gas retention and belching, which were analyzed separately. Every 10 min participants were asked to score any perceived sensation (1 or more perceived simultaneously) on the scales. The anatomic questionnaire incorporated a diagram of the abdomen divided into nine regions corresponding to epigastrium, periumbilical area, hypogastrum, and both hypochondria, flanks, and iliac fossae. Participants were instructed to mark the location, i.e., abdominal region(s) or extra-abdominal regions, where the sensations were perceived.

Procedures

General procedure. During the 2 days preceding the study, all participants were placed on a diet excluding gas-producing foodstuffs. On the day of the study, participants were orally intubated after an 8-h fast. The intestinal tube assembly was positioned 5 cm caudal to the angle of Treitz under fluoroscopic control. The studies were conducted in a quiet, isolated room with the subjects lying supine in bed at an angle of 30°. A 30-min equilibration period was permitted before intestinal gas infusion and collection began. During the 4-h study period, intestinal gas was continuously infused (4 ml/min) and gas evacuation was recorded. In the studies with SF₆ infusion (see Obstructed gas evacuation), a sample of gas evacuated (flatus) in each 30-min period was stored in metallized bags (gas collection 750 ml; QuinTron, Milwaukee, WI) for later analysis. Perception and abdominal girth were regularly measured from the beginning to the end of the study at 10-min intervals.

Obstructed gas evacuation. Before starting the study, participants were instructed that the study consisted of a 2-h control period, during which they could evacuate rectal gas ad libitum, and a 2-h test period, during which they had to inhibit anal evacuation and retain gas. They were further reminded that they were to signal every gas evacuation for correlation with the automated evacuation recording and that perceived sensations, including feeling of rectal gas retention, would be scored every 10 min. The instructions were repeated in the eventuality of anal gas evacuation during the retention period. To verify that the gas collected during the test period corresponded to intestinal gas involuntarily released, SF₆ was added to the gas mixture infused during the first 30 min of the study.

Impaired gas propulsion. At the beginning of the study, an intravenous line was established and saline was continuously perfused at 25 ml/h using an infusion pump (Perfusor model; Braun, Melsungen, Germany). During the control period saline was perfused alone, and during the test period glucagon (Glucagon Novo, Novo Laboratories, Madrid, Spain) was administered as a 4.8 μg/kg bolus followed by a 9.6 μg·kg⁻¹·h⁻¹ continuous infusion. This dose produces a profound inhibition of gut motor activity (7, 8, 19).

Experimental Design

Each of the 30 individuals participated in one experiment only. Each experiment consisted of a 2-h control period and a 2-h test period. Four groups of subjects were studied as follows.

Obstructed gas evacuation. The effect of restrained anal gas evacuation was studied in 10 subjects. In four subjects the test period preceded the control period, and in the other six the test period followed the control period.

Impaired gas propulsion. The effect of inhibition of gut motor activity was studied in six subjects, with the control period preceding the test period.

Sham test. Putative time effects of gas infusion were studied in six subjects, in whom two consecutive control periods were tested, i.e., gas was continuously infused for 4 h during basal conditions (without test intervention).

Validation study. The effect of restrained gas evacuation per se on abdominal perception was evaluated in eight subjects; the subjects were studied without jejunal intubation and gas infusion but otherwise followed the same procedure as described above (see Obstructed gas evacuation); the order of the control and test periods were randomized.

Data Analysis

In each subject, the volume of gas retained within the gut at different time periods was calculated as the difference between the volume of gas infused and the volume of gas recovered. At the same time periods, SF₆ concentration in the evacuated gas was measured by infrared absorbance after determination of standard curves (11).

Obstructed gas evacuation. Before starting the study, participants were instructed that the study consisted of a 2-h control period, during which they could evacuate rectal gas ad libitum, and a 2-h test period, during which they had to inhibit anal evacuation and retain gas. They were further reminded that they were to signal every gas evacuation for correlation with the automated evacuation recording and that perceived sensations, including feeling of rectal gas retention, would be scored every 10 min. The instructions were repeated in the eventuality of anal gas evacuation during the retention period. To verify that the gas collected during the test period corresponded to intestinal gas involuntarily released, SF₆ was added to the gas mixture infused during the first 30 min of the study.

Experimen...
the test period (480 ml infused over 2 h, 333 ml of gas infused in 2 h) in whom the control period preceded the obstructed evacuation group and 6 to the impaired propulsion group in the 12 subjects (6 allocated to the obstructed evacuation group and the other to the impaired propulsion group) in whom the control period preceded the test period (480 ml gas infused over 2 h, 333 ± 60 ml evacuated, 147 ± 60 ml retained, 1.5 ± 0.3 perception score, 1 ± 1 mm girth change) were similar to those in the 4 subjects (allocated to the obstructed evacuation group) in whom the control period followed the test period (960 ml gas infused over 4 h, 843 ± 170 ml evacuated, 118 ± 170 ml retained, 1.5 ± 0.7 perception score, -1 ± 3 mm girth change). Furthermore, in the sham test group the results were similar in the first (480 ml gas infused over 2 h, 341 ± 93 ml evacuated, 139 ± 93 ml retained, 1.7 ± 0.7 perception score, -1 ± 2 mm girth changes) and second (960 ml gas infused over 4 h, 813 ± 134 ml evacuated, 147 ± 134 ml retained, 1.3 ± 1.0 perception score, 1 ± 2 mm girth change) control periods.

Statistical Analysis

In each subject we averaged the three values of perception and girth changes measured during the last 30 min of the control and test periods; gas data are values measured at the end of each period (at 120 and 240 min). Mean or grand mean values (±SE) of the parameters measured were calculated in each group. Parameters were compared between groups by the Mann-Whitney U-test. Within each group, parameters during control and test periods (final gas retention and last 30 min average of perception and girth change) were compared using the Wilcoxon signed-rank test. Correlations of paired data were examined by linear regression analysis.

RESULTS

Basal Conditions (Control Period)

Overall, during the control period healthy subjects (n = 16) appropriately handled the 4 ml/min gas load (i.e., 480 ml infused in 2 h) and evacuated gas volumes matching those infused with minimal gas retention (Fig. 1); the number of gas evacuations during the 2-h control period was 10 ± 2, and the gas volume per evacuation was 45 ± 7 ml. Only two subjects (one allocated to the obstructed evacuation group and the other to the impaired propulsion group) retained >400 ml of gas (470 and 425 ml, respectively). Overall, gas infusion did not produce abdominal symptoms or abdominal distension. The correlation between reported and recorded gas evacuation was excellent (r = 0.96; P < 0.0005). No subject reported belching, and no gas was collected through the gastric venting tube.

The order of the control and test periods did not influence the end results. In fact, the results at the end of the control period in the 12 subjects (6 allocated to the obstructed evacuation group and 6 to the impaired propulsion group) in whom the control period preceded the test period (480 ml infused over 2 h, 333 ± 60 ml evacuated, 147 ± 60 ml retained, 1.5 ± 0.3 perception score, 1 ± 1 mm girth change) were similar to those in the 4 subjects (allocated to the obstructed evacuation group) in whom the control period followed the test period (960 ml gas infused over 4 h, 843 ± 170 ml evacuated, 118 ± 170 ml retained, 1.5 ± 0.7 perception score, -1 ± 3 mm girth change). Furthermore, in the sham test group the results were similar in the first (480 ml gas infused over 2 h, 341 ± 93 ml evacuated, 139 ± 93 ml retained, 1.7 ± 0.7 perception score, -1 ± 2 mm girth changes) and second (960 ml gas infused over 4 h, 813 ± 134 ml evacuated, 147 ± 134 ml retained, 1.3 ± 1.0 perception score, 1 ± 2 mm girth change) control periods.

Obstructed Gas Evacuation

Self-restrained anal gas evacuation significantly reduced the volume of gas evacuated, resulting in a final gas retention at the end of the test period of 407 ± 85 ml of the gas infused (P < 0.05 vs. control). Voluntary inhibition of anal gas evacuation reduced both the number of gas evacuations (5 ± 3 evacuations in 2 h; P < 0.05 vs. control period) and the gas volume per evacuation (22 ± 8 ml; P < 0.05 vs. control period). Gas retention during restrained evacuation was associated with abdominal distension (Fig. 2) and perception of abdominal symptoms (Fig. 3); during the last 30 min of the test period mean girth increment was 6 ± 3 mm and mean perception score was 3.3 ± 0.6 (P < 0.05 vs. control period for both). Self-restrained anal gas evacuation was less effective toward the end of the test period, when gas retention and symptoms were greater (the number of evacuations from the first to the last 30-min intervals of the 2-h test period was 0.8 ± 0.7, 0.9 ± 0.5, 1.0 ± 0.7, and 1.8 ± 0.6, respectively). Both abdominal distension and perception of symptoms correlated with the volume of gas retained inside the gut (both R = 0.78; P < 0.05). No significant differences were observed in gas retention, perception of symptoms, or abdominal distension between the subjects.
who inhibited gas evacuation during the first and second parts of the experiment (data not shown). In the subjects who restrained anal evacuation during the first part of the experiment (test preceding control period), clearance of retained gas occurred within the first 30 min of the subsequent control period during free gas evacuation (315 ± 129 ml/30 min anal gas collection) with concomitant symptom relief (perception score decreased by 29 ± 20% in 30 min).

The most frequent abdominal symptoms reported during restrained anal evacuation were pressure and/or bloating (51 ± 9%) and cramp and/or colicky sensation (40 ± 7%). These symptoms were largely (84 ± 7%) referred to the lower abdominal midline (periumbilical area and hypogastrium), and 63 ± 10% of the sensations were located in a single abdominal area. Eight of the ten subjects also reported sensation of rectal gas retention (3.1 ± 0.5 score), but no subject reported belching and no gas was collected through the gastric venting tube.

Impaired Intestinal Propulsion

Infusion of glucagon markedly reduced intestinal gas evacuation and produced significant gas retention, similar to that produced by obstructed evacuation (Fig. 1). Glucagon infusion significantly reduced the number of evacuations (1 ± 0 evacuations in 2 h; P < 0.05 vs control) but not the volume of gas per evacuation [44 ± 12 ml; not significant (NS) vs. control]. Gas retention was associated with abdominal distension (8 ± 3 mm increment in abdominal girth; P < 0.05 vs. control period; Fig. 2). In contrast to the situation observed during obstructed gas evacuation, gas retention during glucagon administration did not increase perception; during the last 30 min of the test period, perception was virtually identical (-0.4 ± 0.7 score change; NS) to that in the control period (Fig. 3). The main symptoms reported were cramp and/or colicky sensation (50 ± 17%) and pressure and/or bloating (34 ± 15%), which were largely (77 ± 16%) referred to the lower abdominal midline (periumbilical area and epigastrium) and predominantly (76 ± 12%) located in a single abdominal area. During the study, only two subjects reported mild rectal sensation (perception score 2). Belching was never reported during the studies, and only in one subject was a small amount of gas (45 ml) collected through the gastric venting tube. However, 80–115 min after the start of glucagon infusion, five subjects suddenly developed severe nausea in addition to their other symptoms, which led to discontinuation of the study. Hence, the total duration of the study (control plus test periods) was 224 ± 6 min; 900 ± 27 ml of gas were infused, 343 ± 78 ml of gas were evacuated, and at the end of the study 558 ± 68 ml of gas were retained (586 ± 78 ml in the subjects with nausea and 445 ml in the subject without).

Validation Study

During the 2-h control period without intestinal gas infusion, subjects evacuated 107 ± 33 ml of gas (4 ± 1 evacuations in 2 h) and, as expected, did not develop abdominal distension (−2 ± 1 mm girth change) or abdominal symptoms (0.4 ± 0.3 perception score). Voluntary inhibition of anal gas evacuation reduced the total volume of gas evacuated to 23 ± 17 ml (1 ± 1 evacuations; P < 0.05 vs. control period). However, in these experiments without exogenous intestinal gas infusion and pooling, the subjects did not develop abdominal symptoms (1.4 ± 0.6 perception score; NS) or abdominal distension (1 ± 3 mm girth increment; NS).

DISCUSSION

We have shown that disturbed intestinal gas dynamics may produce different manifestations depending on the cause of the dysfunction. Whereas objective abdominal distension depends on the volume of the gas pooled inside the gut, subjective perception of abdominal symptoms depends on the intestinal motor response.

We previously showed (20) that in healthy subjects the gut adapts to a wide range of gas loads andpropels and evacuates as much gas as is infused. These data suggest that gas loads induce metered responses to prevent gas pooling, distension, and secondary symptoms (20). In the present studies we experimentally disturbed the normal dynamics of intestinal gas by modeling the two basic mechanisms that may interfere with intraluminal gas transit, impaired propulsion and obstructed flow. Obstructed gas flow was produced by voluntary anal gas retention. Most healthy subjects were able to effectively control gas outflow and consciously retained significant amounts of gas within the gut. Impaired gas propulsion was produced by administration of glucagon, which has been shown to inhibit motor activity throughout the gut (6–8, 16, 17, 19). Gas pooling due to obstructed evacuation produced symptoms that correlated with the volume of retention. In contrast, similar volumes of gas retention due to impaired propulsion by glucagon did not induce symptoms, thereby altering the normal positive correlation between retention and perception. Global analysis of
both sets of data indicate that perception of symptoms depends on the motor response of the gut to a given gas load rather than on the volume of retention. However, at this stage we are unable to ascertain the detailed mechanisms of symptom production.

Although we know that the gut responds appropriately to gas loads, the type of motor activity directly involved in gas handling remains unknown. Conceivably, intestinal capacitance, which is regulated by the tonic motor activity of the gut (16, 17), determines both gas accommodation and displacement. Hence, tonic contraction of the gut wall, by reducing capacitance, may displace large masses of gas through the gut. When the gut lumen is permeable to gas displacement, this propulsive activity evolves completely unperceived. However, in the event of a gut segment generating resistance to gas flow, gas would be trapped, and the contraction of the gut wall against the blocked gas volume would increase wall tension and thereby induce perception (8). Furthermore, focal gas pooling and distension may also trigger reflex phasic contractile activity responsible for the production of symptoms (5, 12, 22, 23). Indeed, the distribution of gas pooled in the gut during obstructed evacuation was conceivably more localized than during impaired propulsion by glucagon administration.

In the present studies we used a well-established methodology to measure transit and tolerance to standardized gas loads, which has been previously validated in detail (20, 21). This technique does not attempt to reproduce physiological conditions but has proven effective in demonstrating otherwise undetectable abnormalities in patients with IBS (21). Putative time effects of anal retention were firmly ruled out, because the effects recorded in the subjects inhibiting gas evacuation in the first versus the second part of the experiment were similar. Furthermore, the validation studies without intestinal gas infusion showed that restrained anal evacuation per se, that is, without effective gas pooling, did not induce abdominal symptoms, thus ruling out psychological influences, which should always be considered in the type of experimental setting used in these studies.

Glucagon administration induced severe nausea in most subjects before the end of the 2-h gas infusion period, an effect not directly attributable to glucagon at this dose but rather to gas retention in the immobilized gut. This dose of glucagon does not induce nausea when administered under basal conditions (7, 8, 19) but does so after ingestion of a meal. Using scintigraphic imaging, we observed that intravenous glucagon arrested gastric emptying without inducing symptoms for a relatively prolonged period of time, until sudden nausea developed (Moragas G, Azpiroz F, Malagelada J-R, unpublished observations).

The pathophysiological and therapeutic implications of our study may be highly significant because the experimental results help to explain the mechanism of abdominal symptoms in some clinical conditions. A large proportion of patients in a gastroenterological clinic complain of symptoms such as abdominal bloat-

ING, borborygmi, cramps, and visible distension for which no underlying cause can be detected after a thorough diagnostic investigation (24). These patients frequently attribute their symptoms to excessive intestinal gas. We previously showed (21) that this type of patient has impaired handling and tolerance of a gas load, sometimes with frank intestinal gas retention that becomes symptomatic (21). It is our contention that specific segments of the gut may generate a high-resistance barrier to gas flow and induce symptomatic retention. Moreover, focal intestinal distension may induce retrograde relaxatory reflexes (16, 17), spreading back the oral pooling of gas over a large gut segment. Owing to spatial summation phenomena, relatively mild distension at multiple levels of the gut could amount to symptomatic perception (18, 19), an effect presumably accentuated by the visceral hypersensitivity observed in patients with IBS (1, 14, 25). In the present study we induced retention at the most caudal level of the gut, taking advantage of its voluntary control, but admittedly this may not be the most prevalent mechanism of gas retention in IBS patients (21). However, it is a good model for the symptomatic consequences of impaired gut flow. Inhibiting motor activity, as we did experimentally with glucagon, increases tolerance but does not resolve gas pooling and hence would only delay the inevitable symptomatic crises. However, our studies do point a way forward. Pharmacological action directed toward focal resistance barriers, but without impairing gut capacitance and propulsion, theoretically would resolve the cause of both retention and symptoms.

The authors thank Nuria Ferrer and Isidre Casals, Serveis Científico-Tècnics of the Central University of Barcelona, for help in gas infrared absorbance analysis, Maite Casaus and Anna Aparici for technical support, Gloria Santalíestra for secretarial assistance, and Christine O’Hara for English language editing of the manuscript. This work was supported in part by the Spanish Ministry of Education (Dirección General de Enseñanza Superior del Ministerio de Educación y Cultura, PM97–0096), Generalitat de Catalunya (Direcció General de Recerca 1998GR-00113), and the U.S. National Institute of Diabetes and Digestive and Kidney Diseases (Grant DK-57064). J. Serra was supported by a scholarship from the Spanish Ministry of Education (CICYT).

REFERENCES


