

Colonic Propulsive Impairment in Intractable Slow-Transit Constipation

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Hypothesis: Intractable constipation, especially of the slow-transit subtype, may represent several pathophysiologic entities with a common final symptomatic appearance. An overall impairment of colonic propulsive activity may represent a major disease mechanism.

Design: Case series.

Setting: Tertiary university hospital.

Subjects: Twenty-nine severely constipated patients with clinical and homogeneous features of slow-transit constipation that were unresponsive to conventional medical measures and 16 age-matched healthy volunteers.

Interventions: Twenty-four-hour manometric recordings obtained in patients and controls to assess high- and low-amplitude colonic propulsive activity.

Results: Compared with controls, patients showed heavily reduced high-amplitude propagated activity (average, <1 event per subject per day). No differences were found in low-amplitude propagated activity.

Conclusions: Patients with severe constipation that is refractory to medical treatment may display an important reduction of colonic forceful propulsive activity. This may justify a surgical approach, which may offer the best results in such patients. It is, however, important to obtain thorough physiologic documentation before such a drastic approach is considered. The residual low-amplitude propulsive activity might represent a partially compensatory mechanism in these patients. Studies in more homogeneous groups of such patients are needed.

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FUNCTIONAL constipation encompasses a group of functional disorders that exhibit persistent difficult, infrequent, or seemingly incomplete defecation and infrequent, lumpy, or hard stools.¹ This symptom is very common and may occur in up to 20% of populations, depending on demographic factors, sampling, and the definitions employed.² The term *constipation* is probably better viewed as a sort of semantic umbrella, covering pathophysiologic subtypes, among which 2 major groups may now be identified: slow-transit constipation (STC) and pelvic floor dysfunction. A third group includes patients with both STC and pelvic floor dysfunction.³

Slow-transit constipation is thought to have, as a primary defect, slower than normal movement of contents from the cecum to the rectum.^{4,5} However, it is likely that the term *STC* encompasses a range of disorders with a definite common abnormality—prolonged colonic transit time⁶—as shown by the heterogeneity of

the clinical signs and symptoms.⁷⁻⁹ Although a few studies have shown that severely constipated patients may have altered anorectal¹⁰⁻¹² and colonic¹³⁻¹⁵ motor function, no data exist on colonic propulsive function in homogeneous and consistent groups of such patients.

The purpose of our study was to assess colonic propulsive activity in a relatively large group of STC patients with homogeneous characteristics and a particularly severe clinical picture. Our working hypothesis was that such activity was particularly impaired in these patients.

METHODS

PATIENTS

Twenty-nine severely constipated women (age range, 37-52 years) entered the study. The patients' characteristics not only fulfilled the Rome II criteria for functional constipation¹⁶ but they exceeded the criteria in symptom duration and severity. The study inclusion criteria were (1) long-standing (>3 years) history of constipa-

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tion; (2) fewer than 1 evacuation per week; (3) absence of frequent (>2 episodes per month) or chronic abdominal pain; (4) sensation of incomplete evacuation in more than one quarter of defecations; (5) negative history for (sub)occlusive episodes; (6) no history of major abdominal or pelvic surgery; and (7) unresponsiveness to appropriate medical treatment. All patients retained more than 20% of 40 ingested radiopaque markers within the colon after 96 hours, which is the mean + 2 SDs for healthy controls studied in our laboratory.¹⁷ Causes of secondary constipation were excluded by drug history (special care was taken in excluding the use of antidepressants^{18,19}), physical examination, and laboratory screening (blood chemical analysis, thyroid hormones, and, where appropriate, oral glucose tolerance test, sex hormone profiles, and antinuclear antibodies). To exclude organic diseases or mechanical causes of constipation and megacolon or megarectum, each patient underwent double-contrast barium enema, colonoscopy, and abdominal ultrasound scans. The absence of Hirschsprung disease was demonstrated by normal relaxation of the internal anal sphincter on anorectal manometry.²⁰ No patient had evidence of pelvic floor dyssynergia, as documented by anorectal manometry and defecography.

CONTROLS

Sixteen healthy volunteers (8 men, 8 women; age range, 35-48 years) were recruited as a control group, matched for age but not for sex. However, there is evidence that gender does not influence colonic propulsive activity.^{21,22} No volunteer complained of abdominal pain, abdominal distention, or disturbances in bowel habits. The average defecation frequency was 1 per day. A careful drug history was obtained for each subject to ascertain that none had taken drugs known to influence gastrointestinal motility during the 2 weeks before the study. No volunteer had previously undergone abdominal or pelvic surgery.

PROCEDURE

Twenty-four-hour colonic motor activity in patients and controls was studied by a previously described manometric technique.²³⁻²⁵ After an overnight fast, an 8-lumen manometric probe with side holes spaced 12 cm apart (outer diameter, 4.5 mm; inner diameter for each lumen, 0.8 mm) was introduced into the colon by a colonoscope. Bowel cleansing was achieved with a semi-liquid diet for 2 days and magnesium sulfate (30 g by mouth 36 hours before colonoscopy) and tap water enemas (12 and 6 hours before the procedure). The probe was positioned by advancing it together with the endoscope, with the tip of the probe fixed to the tip of the colonoscope by a silk thread held by biopsy forceps inside the operative channel of the endoscope. Intravenous diazepam (5 mg) was used for sedation. Once the desired portion of the viscus was reached (at least the proximal part of the transverse colon), the forceps were opened and the colonoscope gently withdrawn, aspirating air as completely as possible. The probe was then connected to external physiologic pressure transducers and to a low-compliance pneumohydraulic system, perfusing bubble-free distilled water at a constant rate of 0.2 mL/min. At this perfusion rate, distal occlusion of individual recording ports yields a rise rate of more than 100 mm Hg/s. Intraluminal pressures were recorded by a multichannel paper recorder coupled to the transducers (paper speed, 0.5 mm/s).

After the probe was positioned, a radiologic control was made to assess catheter placement. Then the patients were moved to the motility laboratory, where they rested for 2 to 4 hours to allow elimination of the air from the colon and recovery from the endoscopy procedure. Thereafter, a 24-hour recording was obtained. During the recording, 2 1000-kcal mixed meals and a 450-kcal breakfast were served, as previously described.²⁶ At the end of the recording session, a fluoroscopic check was ob-

tained to ascertain that no major (>10 cm) displacement of the probe had occurred.

After careful explanations about the aims of the study, both patients and controls gave informed consent. The studies were carried out in accordance with local ethical guidelines, following the recommendations of the Declaration of Helsinki.

DATA ANALYSIS

All data were calculated manually by one of us (G.B.). High-amplitude propagated contractions (HAPCs) were defined as pressure waves that (1) were observed at 3 ports sequentially with a delay of 1 to 10 seconds between peaks seen at adjacent sites and (2) had amplitudes of at least 75 mm Hg of absolute pressure or a 50-mm Hg increase from the baseline at all 3 sites.²⁷ Low-amplitude propagated contractions (LAPCs) were defined as for HAPCs but with amplitudes of less than 50 mm Hg of absolute pressure at all 3 sites.²⁸ The following HAPC and LAPC variables were taken into consideration for both groups: (1) the total number per 24 hours; (2) their mean amplitude (in millimeters of mercury), by subtracting mean resting colon pressure from the peak of pressure waves; and (3) their correlation with abdominal sensations, pain, or flatus. To be correlated, a propulsive event of either amplitude would have to occur within 10 minutes from the event, signaled on the tracing by an event marker operated by the patient, who could not view the tracing itself.

STATISTICAL ANALYSIS

The *t* test was used for unpaired data. Data are expressed as mean ± SEM. *P* < .05 indicates rejection of the null hypothesis.

RESULTS

The probe was positioned near the hepatic flexure in 25 patients and 12 controls; in the remaining subjects, it was positioned between the mid and the distal transverse colon. The fluoroscopic check at the end of each recording showed that no major displacement of the catheter had occurred. Each subject was able to complete the study without discomfort.

In STC patients, the average number per subject per day of HAPCs was decreased to a significant and important extent with respect to controls (0.62 ± 0.2 vs 5.5 ± 0.78 ; *P* < .001), whereas no differences were found in HAPC amplitude (106.3 ± 8 vs 109.5 ± 7 mm Hg; *P* = .98) and LAPC variables (average number per subject per day, 50.9 ± 10 vs 46.3 ± 8 ; *P* = .96; average amplitude, 19.4 ± 1.8 vs 22.5 ± 2.4 mm Hg; *P* = .87) (**Table**).

Concerning relationships with abdominal sensations, HAPCs were associated with a defecatory stimulus in 4 controls (25%); no patients reported such sensation. Low-amplitude propagated contractions were associated with the passage of flatus on at least 1 occasion in 4 controls (25%) and in 2 patients (7%), and with mild defecatory stimulus in 9 patients (31%) on at least 1 occasion, especially following meals.

COMMENT

The pathophysiologic mechanisms of STC are still widely debated.²⁹ This study demonstrates that in severe constipation that is refractory to conventional medical treatment, the forceful colonic propulsive activity equivalent to

HAPC and LAPC Variable in Patients With Slow-Transit Constipation and Controls*

Variable	Patients (n = 29)	Controls (n = 16)	P Values
HAPC			
No. per 24 h	0.62 ± 0.2	5.5 ± 0.78	<.001
Amplitude, mm Hg	106.6 ± 8	109.5 ± 7	.98
LAPC			
No. per 24 h	50.9 ± 10	46.3 ± 8	.96
Amplitude, mm Hg	19.4 ± 1.8	22.5 ± 2.4	.87

Abbreviations: HAPC, high-amplitude propagated contraction; LAPC, low-amplitude propagated contraction.

*Data are given as mean ± SD unless otherwise indicated.

mass movements, ie, the HAPC, is so impaired that it is detectable, on average, on less than 1 occasion per day. This is a notable finding, especially because it was consistently present in a relatively large group of patients with homogeneous characteristics. Although there was minimal propagated activity, as evidenced by the preservation of LAPCs (which may exert some propulsive activity in humans³⁰), this activity was not entirely able to compensate for the lack of HAPCs (as happens in less severe forms of STC through an increase of such an activity [G.B., unpublished data, 2003]), since their number showed no increment with respect to controls. It is conceivable that in a more advanced stage, the loss of LAPCs might lead to a true colonic inertia, in which no propulsive activity is recorded.

In constipated patients who are unresponsive to medical measures, a history of surgery is often indicated.³¹ When a thorough physiologic assessment reveals convincing evidence of STC and no evidence of outlet obstruction, total colectomy with ileorectal anastomosis may offer sustained relief of constipation.^{32,33} It remains to be established whether an adjunct assessment by means of colonic manometry may offer further evidence to support a surgical approach, for instance, through a demonstration of ineffective propulsive colonic capability. Our institution now uses such an approach for selected cases.³⁴ However, this technique is not yet readily available, is somewhat invasive, and is not easy to apply in the routine practice of surgery. This technique, therefore, might be best used in cases where STC is suspected but cannot be proven by the conventional methods. Careful physiologic evaluation is strongly advisable for patients with STC that has been unresponsive to conventional therapy. We recommend this to obtain the best results and, possibly, suggest a more targeted therapeutic approach.

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