ORIGINAL ARTICLE

Electric Activity of the Colon in Subjects With Constipation Due to Total Colonic Inertia

An Electrophysiologic Study

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Background: Idiopathic constipation may result from colonic inertia, which affects the whole colon or is localized to an area of the colon. The colon exhibits electric activity in the form of slow waves or pacesetter potentials (PPs) and action potentials (APs), which are coupled with elevated colonic pressure. The APs are claimed to be responsible for colonic motor activity.

Hypothesis: Colonic electric activity is disordered in patients with constipation due to colonic inertia.

Methods: Electric activity was studied in 11 patients with colonic inertia and constipation (mean±SD age, 42.8±6.6 years; 7 women) who underwent total colectomy. Eight volunteers who had no gastrointestinal complaints (mean±SD age, 40.6±5.8 years; 5 women) acted as controls. Control subjects underwent laparotomy for hernia repair (n=7 patients) and for removal of a mesenteric cyst (n=1 patient). During the operation, 2 monopolar silver–silver chloride electrodes were applied to the cecum and the ascending, transverse, descending, and sigmoid colon.

Results: Electric waves (PPs and APs) were recorded from all parts of the colon in control subjects. The waves were monophasic, negatively deflected, and had regular rhythm. The wave variables from the 2 electrodes of each segment of the colon were identical and reproducible. They progressively increased aborally. In the colonic inertia group, 5 patients had recorded waves from the cecum and ascending colon but no waves from the rest of the colon. The wave variables were significantly lower than those of the controls ($P=.02$). In the remaining 6 patients, no waves were registered from the whole colon.

Conclusions: Regular electric waves were recorded from the colons of control subjects. The aboral increase of their frequency, amplitude, and conduction velocity suggests that colonic motile activity increases analward, reaching its maximum in the sigmoid colon to expel its solid contents. We postulate that constipation in patients with colonic inertia is attributable to weak or absent electric activity, the cause of which is unknown. A disorder of the interstitial cells of Cajal, which generate electric activity, is suggested to have a role in inducing diminished or absent colonic motor activity, a point that should be investigated.

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CONSTIPATION IS a common coloproctologic problem that may be attributed to recognizable causes.[1-10] In many cases, however, the cause is unknown, and the condition is considered idiopathic.[11-22] In most of these cases, findings from barium enema examination prove the colon to be of normal length and diameter, and colonoscopy confirms its normal appearance.[23] The rectoanal inhibitory reflex is preserved.[11,24] Three groups of patients with idiopathic constipation can be identified: patients with colonic inertia who have delayed transit throughout the colon,[11] patients with a localized area of delayed transit (ie, the right, left, or sigmoid colon),[12] and patients with outlet obstruction.[1-10] Evaluation of anorectal dysfunction must be performed in such cases.

Colectomy specimens from patients with colonic inertia commonly show a degenerated enteric nerve plexus[25,26]; whether this plexus degeneration is congenital or acquired is not known. Gut regulatory peptides, which influence colonic motility, may be involved in the pathogenesis of colonic inertia.[27] Reduced levels of vasoactive intestinal polypeptide, calcitonin-related peptide, and motilin were found in the colonic wall.[28,29]

See Invited Critique at end of article

The colon exhibits electric activity in the form of slow waves, or pacesetter po-

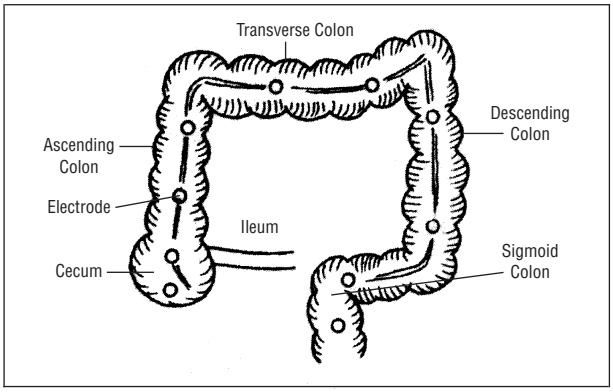

Figure 1. Sites of electrodes applied to the colon.

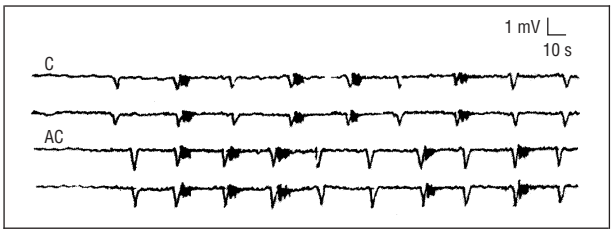

Figure 2. Electric waves recorded from the electrodes applied to the cecum (C) and ascending colon (AC) of a subject with no gastrointestinal complaints.

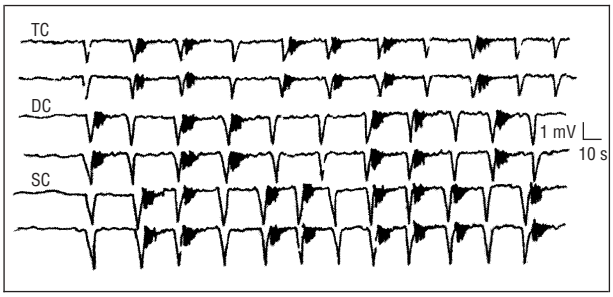

Figure 3. Electric waves recorded from the electrodes applied to the transverse (TC), descending (DC), and sigmoid (SC) colon of a subject with no gastrointestinal complaints.

tentials (PPs), and fast activity spikes, or action potentials (APs).[30-33] The PPs have a constant frequency, amplitude, and conduction velocity, whereas the APs occur randomly, are inconsistent, and follow or are superimposed over the PPs. The APs are coupled with increased intracolonic pressure and are suggested to be responsible for colonic motility.[30-33]

Because electric activity is thought to be accountable for colonic motor activity, we hypothesize that colonic electric activity is disordered in patients with constipation due to colonic inertia. The current study investigated this hypothesis.

METHODS

SUBJECTS

The study sample comprised 11 patients with chronic constipation due to total colonic inertia. Mean±SD age was 42.8±6.6 years (age range, 36-54 years); 7 were women, and 4 were men. The duration of constipation varied from 12 to 26 years (mean±SD, 16.8±7.2 years). Stool frequency was less than once per week. All patients used enemas, laxatives, and digitation to induce defecation. Results of laboratory workups were unremarkable. Findings from proctoscopy, colonoscopy, and barium enema studies were normal. Colonic transit studies were performed using 20 radiopaque markers administered to the patients with a normal diet and no laxatives.[12] Daily abdominal radiographs were performed for 1 week, and the number of markers in the right colon, the left colon, and the rectosigmoid area was assessed. Study subjects were selected from a population that was scheduled for total colectomy because of colonic inertia that had failed to respond to medical measures.

Eight subjects acted as controls (5 women and 3 men; mean±SD age, 40.6±5.8 years; age range, 34-52 years). They had no gastrointestinal complaints in the past or at the time of presentation, and they had normal stool frequency. The colon was exposed during operative repair of huge abdominal incisional hernia in 7 patients and during laparotomy for removal of a mesenteric cyst in 1 patient.

All subjects gave their informed consent before being enrolled in the study. Our Faculty Review Board and Ethics Committee approved the study.

METHODS

Mechanical bowel preparation was performed using isotonic sodium chloride solution enemas for 1 day preoperatively and on the day of the operation. Electric activity was recorded when the abdomen was opened under general anesthesia and the colon was being exposed. The same anesthesia was used for all patients. We used monopolar silver–silver chloride electrodes (SmithKline Beckman, Los Angeles, Calif) that were 2 mm in diameter and covered by an insulating vinyl sheath, except for the tips. Two electrodes were fixed by electrode gel to the cecum and the ascending, transverse, descending, and sigmoid colon (**Figure 1**). Signals from the electrodes were fed into an alternating current amplifier with a frequency response within ± 3 dB from 0.016 Hz to 1.0 kHz and were displayed on a UV recorder at a sensitivity of 1 mV/cm. The indifferent electrode was a metal disk applied to the abdominal skin.

A 10-minute time lapse was given for the gut to adapt to the electrodes. For each subject, a 20-minute recording was performed before any manipulations were done for the scheduled operation. Narcotics were not given to patients prior to or during the 20-minute recording period.

The results were analyzed statistically using *t* tests. $P<.05$ was considered to be statistically significant. Values are given as the mean±SD.

RESULTS

No adverse effects related to the test were encountered, and all subjects were evaluated.

ELECTRIC COLONIC ACTIVITY OF CONTROLS

Electric waves were recorded from all electrodes applied to the colon. The PPs were registered as monophasic waves with a large negative deflection and had a regular rhythm (**Figure 2** and **Figure 3**). The frequency, amplitude, and conduction velocity of the PPs recorded from the cecum and the ascending, transverse, descending, and sigmoid colon are exhibited in the **Table**. Action potentials were superimposed on, or followed ran-

Frequency, Amplitude, and Conduction Velocity of the Pacesetter Potentials Recorded From the Cecum and the Ascending, Transverse, Descending, and Sigmoid Colon of Control Subjects

	Mean ± SD (Range)		
	Frequency, Cycles/min	Amplitude, mV	Conduction Velocity, cm/s
Cecum	4.6 ± 0.9 (3-5)	0.8 ± 0.3 (0.6-1.0)	3.9 ± 1.1 (3.3-4.8)
Ascending colon	4.8 ± 1.1 (4-6)	1.1 ± 0.2 (0.9-1.2)	4.3 ± 1.1 (3.6-5.2)
Transverse colon	5.1 ± 1.1 (4-6)	1.4 ± 0.3 (1.2-1.6)	4.8 ± 0.8* (3.9-5.5)
Descending colon	5.8 ± 0.8* (5-7)	1.8 ± 0.5* (1.4-2.1)	4.9 ± 0.7* (4.3-5.6)
Sigmoid colon	6.1 ± 0.8* (5-7)	2.1 ± 0.4* (1.8-2.4)	5.3 ± 0.9* (4.6-5.9)

*$P<.05$ vs the cecum.

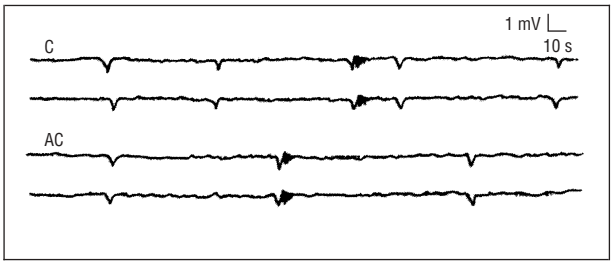

Figure 4. Diminished electric activity recorded from the electrodes applied to the cecum (C) and the ascending colon (AC) of a patient with colonic inertia.

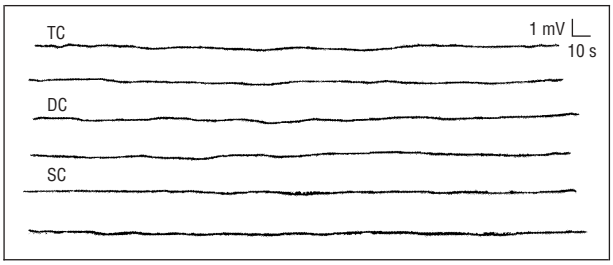

Figure 5. No electric activity recorded from the electrodes applied to the transverse (TC), descending (DC), and sigmoid (SC) colon of a patient with colonic inertia.

domly, the PPs. They occurred as negative deflections and did not accompany each PP (Figure 2 and Figure 3). The frequency, amplitude, and conduction velocity of the electric waves had identical readings from the 2 electrodes of each segment of the colon and were reproducible in the same subject. However, these variables differed from one colonic segment to the other. They progressively increased aborally so that the highest values were recorded from the sigmoid colon (Table). Electric activity was present throughout all the recording sessions.

ELECTRIC ACTIVITY OF PATIENTS WITH COLONIC INERTIA

Electric activity varied in the different segments of the colon and from patient to patient. In 5 of 11 patients, PPs were recorded from the cecum and the ascending colon but were absent in the transverse, descending, and sigmoid colon (**Figure 4** and **Figure 5**). The recorded waves from the cecum and the ascending colon exhibited significantly diminished frequency and amplitude compared with the values of controls ($P=.02$ and $P=.04$);

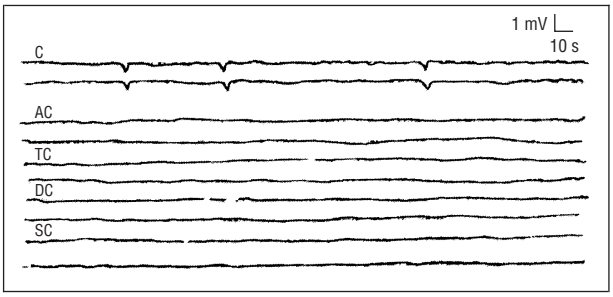

Figure 6. Occasional pacesetter potentials recorded from the cecum (C) of a patient with colonic inertia; no waves recorded from the ascending (AC), transverse (TC), descending (DC), and sigmoid (SC) colon.

the mean ± SD frequency was 2.2 ± 0.9 cycles/min (range, 1-3 cycles/min), the amplitude was 0.3 ± 0.06 mV (range, 0.1-0.4 mV), and the conduction velocity was 2.6 ± 1.1 cm/s (range, 1.3-3.4 cm/s). Action potentials were infrequently recorded compared with those of controls (Figure 4). The above-mentioned electric pattern was registered during the whole 20-minute recording period. These patients had a higher stool frequency than the remaining 6 patients, although the stool frequency was less than once per week.

In the remaining 6 patients, no waves were recorded from the colon during the 20-minute session. In 1 patient, occasional PPs were registered from the cecum (**Figure 6**) but not from the rest of the colon; no APs were recorded.

COMMENT

Electric waves are thought to be responsible for conducting colonic motility.[30-33] This motor activity is suggested to be induced by APs,[34,35] and it has been demonstrated that APs are coupled with elevated colonic pressure.[34,35] However, PPs were not associated with colonic pressure changes, and their exact function is not known. It has been suggested that they pace the APs in terms of direction and frequency.[34]

The current study shows that the colons of control subjects without gastrointestinal tract complaints exhibited electric activity from all segments. The waves showed regular rhythm and were reproducible when recorded from the same electrodes of each colonic segment. We observed that the frequency and amplitude of the electric waves increased gradually as we proceeded aborally

from the cecum. Thus, the frequency and amplitude were greater in the ascending colon than in the cecum and were greatest in the sigmoid colon. This supposedly denotes that the motile activity of the colon increases gradually analward, reaching its maximum in the sigmoid colon. The incremental aboral increase in colonic motor activity seems to be related to the functional activity of the different segments of the colon. Thus, the left colon presumably needs to exert greater motile activity to propel its semisolid contents than does the right colon, the contents of which are fluid. The highest wave frequency and amplitude are assumed to provide the strong motor activity needed to expel the solid stools that accumulate in the sigmoid colon.

In patients with colonic inertia, most or all segments of the colon recorded no electric waves, which presumably resulted in an absence of motile activity and would explain the colonic inertia and consequent constipation in these patients. In fewer than half the patients with colonic inertia, the right colon recorded occasional PPs, pointing to weak motor activity. The stool frequency of these patients was higher than that of the other patients, who exhibited no waves. It is apparent from this study that stool frequency is closely related to the electric activity of the colon. Inertia constipation was associated with diminished or absent colonic electric activity.

We do not know the cause of the absent electric waves in the colon. Studies have claimed that electric waves are generated from pacemakers, which are suggested to consist of interstitial cells of Cajal (ICC).[36-39] These cells appear to be the pacemaker cells in the smooth muscle layers of the gut. They may also be involved in neurotransmission.[40] Accordingly, it seems that the ICC are responsible for generating the motile activity of the gut, including the colon, and that colonic inertia results from a pathologic process involving these cells. This is evidenced by the fact that the investigations in the current work and other studies,[23] including colonoscopy and barium enema studies, had normal findings; no apparent abnormalities were recorded. The only common abnormal finding was delayed colonic transit. Therefore, we propose that the cause of colonic inertia may be a derangement of the pacemakers resulting from disordered ICC.

Previous studies have shown that blocking the ICC networks in animals using neutralizing antibodies disrupted the electrical rhythmicity and neural response of the gut.[40] Other studies have shown that regular motor activity was not obtained after removal of the colonic plexus of ICC.[41]

In conclusion, regular electric waves were recorded from the colons of control subjects. The waves' frequency, amplitude, and conduction velocity increased aborally, suggesting that colonic motile activity increased analward and reached its maximum in the sigmoid colon in order to expel the solid contents. In colonic inertia, no electric waves were recorded from the whole colon in more than 50% of patients; weak electric activity from the right colon was recorded in 5 of 11 patients with colonic inertia. We postulate that constipation in such patients is attributable to weak or absent electric activity, the cause of which is not known. Interstitial cells of Cajal are suggested to have a role in inducing diminished or absent colonic motor activity, a point that needs to be investigated.

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Invited Critique

Colonic inertia is a poorly understood disease process. Few studies have investigated the molecular, humoral, and physiological mechanisms that govern motility in the large intestine. Recent data have pointed toward abnormalities in the specialized cells within the muscle layers of the bowel wall, known as ICC. These cells are thought to be involved with the myoelectrical activity of the colon. The role of ICC in colonic dysmotility and in disorders such as colonic inertia remains unknown.

The article by Shafik et al compares colonic electrical activity in normal patients with that of patients with colonic inertia. This is accomplished by performing electrophysiologic studies intraoperatively. Shafik et al found significant differences in colonic electrical activity between the 2 groups. Although the data are compelling, the interpretation of the results is difficult for various reasons. A number of stimuli, including neurotransmitters, gut hormones, and intestinal peptides, can affect colonic electrical activity, and the impact of anesthesia, narcotics, and operative manipulation on these factors should not be overlooked. Although both groups were subject to similar external stimuli, their responses may have differed. The reduced or absent electrical stimuli seen in the inertia group may represent an exaggerated response to the operative environment as a result of an already diseased gut. In addition, it is not clear whether the electrical abnormalities that are detected in this and other studies are acquired as a result of years of chronic constipation or whether they are part of the disease process itself. To date, there is little evidence to correlate the symptoms of colonic inertia with the degree of electrophysiologic derangement. Future studies with larger groups of patients and controls for comorbid conditions, external stimuli, physiological testing, and bowel habits would resolve many of these issues. Shafik et al, however, are to be congratulated for providing the much-needed starting point from which these future studies will be based.

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