Colonic manometry in children with chronic intestinal pseudo-obstruction

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Abstract
Pressure changes were evaluated in the transverse, descending, and rectosigmoid colon of 30 children with chronic intestinal pseudo-obstruction. Twenty-two had severe lifelong constipation and eight had symptoms suggesting a motility disorder exclusively of the upper gastrointestinal tract. Based on prior antroduodenal manometry, 24 children were diagnosed as having a neuropathic and six a myopathic form of intestinal pseudo-obstruction. On the day of study, endoscopy was used to place a manometry catheter into the transverse colon and intraluminal pressure was recorded for more than four hours. After a baseline recording, we gave a meal to assess the gastrointestinal response. Colonic contractions were noted in 24 children. The six children with no colonic contractions had a hollow visceral myopathy and constipation. In the children with colonic contractions, fasting motility did not differentiate children with and without constipation. After the meal, in all eight children without constipation there was (1) an increase in motility index (2-3 SEM 0-3) mm Hg/min basal + 8-4 (SEM 1-1) mm Hg/min postprandial; p<0.001, and (2) at least one high amplitude propagated contraction (HAPC). In the 16 constipated children with colonic contractions the motility index did not significantly increase after the meal (2-1 SEM 0-3) mm Hg/min basal + 3-1 (SEM 0-4) mm Hg/min postprandial and 12 of them had no HAPCs (p<0.01 v group without constipation). In summary, children with a clinical diagnosis of chronic intestinal pseudo-obstruction, constipation is associated with absence of HAPCs, and the gastrocolonic response or with total absence of colonic contractions. It is concluded that studies of colonic manometry are feasible in children and may document discrete abnormalities in those with intestinal pseudo-obstruction with colonic involvement.

Chronic intestinal pseudo-obstruction (CIP) is a heterogeneous group of disorders that vary in cause, severity, course, and response to treatment. Pathophysiology of the various subtypes of CIP is only now being elucidated. There is a wide range of abnormalities of gastric, small intestinal, and colonic myoelectric activity and contractions, and in nerve and muscle histopathology. To diagnose and intervene appropriately it is often necessary to be able to evaluate the complete gastrointestinal tract. Oesophageal, anorectal, and antroduodenal manometry are diagnostic tools in many paediatric centres, but little is known about colonic manometry. Previous study of colonic pressures in paediatric patients has been limited mainly to the rectosigmoid area, because of relative inaccessibility of the proximal colon. Information concerning motility of the entire colon has been obtained by indirect measures such as the movement of radioopaque markers or barium to assess colonic transit time. Newer techniques provide more specific and often complementary information about colon transit and motor activity. Manometry, electromyography, and scintiscanning have been used in adults in the investigation of colon motility but only recently have these been extended to the study of paediatric patients.

The aim of our study was to clarify the pathophysiology of constipation in children with CIP and to correlate abnormal motility patterns with distinctive clinical presentations or pathology.

Methods
Before each study informed consent was obtained from a parent, and assent was obtained from any subject seven years of age or older.

SUBJECTS
Thirty children, 1-1 to 11-6 years of age (mean age 4-1 years, 18 female), were referred by paediatric gastroenterologists for evaluation of severe symptoms unresponsive to conventional management (Table I). Duration of symptoms was at least one year in every patient (mean 3-7 years). All the patients carried a diagnosis of chronic intestinal pseudo-obstruction based on recurrent symptoms of bowel obstruction without physical lesion. Before colon manometry, all underwent antroduodenal manometry to discriminate between disorders of myopathic or neuropathic origin. Nine patients had a diagnosis based on a small bowel full thickness biopsy (Table II). From these studies, it was established that 24 children had a neuropathy (mean age 4-4 years) and six a myopathy (mean age 3-2 years). Eight of the children with neuropathy did not have constipation, diarrhoea, or any other symptoms of colonic disease (mean age 4-5 years).

STUDY DESIGN AND INSTRUMENTATION
We prescribed a clear liquid diet for all children during the 48 hours before study. On the day before study, the patients underwent a preparation for colonoscopy, designed for each patient on the basis of the patient's age, symptoms, and ability to tolerate lavage solutions. We infused a
TABLE I Symptoms and the means of alimentation in patients with and without constipation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Constipation (n=22)</th>
<th>Non-constipation (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than one bowel movement a week</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Chronic abdominal distension</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Recurrent urinary tract infections</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Tube feeding</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

balanced electrolyte solution (Colyte, Reed, and Carnick, Piscataway, NJ) through a pre-existing gastrostomy or through a nasogastric tube in those able to tolerate enteral feedings. We used enemas when it was not possible to utilise the enteral lavage. No additional colonic preparation was used on the morning of the study, and the patients fasted for at least five hours before colonoscopy.

On the day of the study a colonoscopy was performed with minimal air insufflation and minimal sedation (midazolam 0.05 mg/kg intravenously). After reaching the mid-transverse colon, a soft tipped teflon biliary guidewire (length 480 cm, diameter 0.052 cm; Wilson-Cook, Wilson-Salem, NC) was inserted through the colonoscope. The guidewire was positioned in the transverse or ascending colon and the colonoscope was withdrawn, leaving the guidewire in position. A seven lumen manometric catheter, with recording orifices radially oriented and spaced 15 cm apart (Arndorfer Medical Specialities, Greendale, Wis), was then advanced over the guidewire. The guidewire was removed and the catheter taped to the patient’s thigh.

The subjects were placed supine under a gamma camera and we waited at least one hour to allow the patients to recover from the procedure. The position of the manometric catheter was confirmed on the persistence oscilloscope of the gamma camera by introducing into the catheter, via the proximal recording orifice, 2 ml of 0.9% NaCl solution containing 4 MBq (0.1 mCi) of 99mTc DTPA. This marker remained in the catheter until it was removed by aspiration after confirmation that the recording sites were in the distal half of the transverse colon, the splenic flexure, the descending colon, the sigmoid colon, and the rectum. The catheters were continuously perfused at 0.1 ml/min with distilled water by a low compliance capillary system (Arndorfer Medical Specialities). Pressure was transmitted to transducers (Statham P231A, Statham Instruments, Oxnard, CA) and recorded on a rectilinear recorder (Beckman R611, Beckman Instruments Inc, Fullerton, CA) and on a personal computer system.

After at least 120 minutes of fasting recording, the patients were fed. The complex liquid meal was designed for each patient on the basis of age and current mode of nutritional support. In those enterally fed (n=18) we gave 240 ml of whole milk or infant formula. In those on parenteral nutrition (n=12) we gave the maximum amount of milk the patients were able to ingest without symptoms, and at the end of the test we emptied the gastric content via their gastrostomies. The minimum volume given to each patient was 90 ml. The two groups of constipated and non-constipated children received a similar amount of milk (190 (10) ml v 210 (13) ml respectively). Each subject’s upper body was tilted slightly to provide comfortable drinking. Each subject was asked to consume the meal in less than 10 minutes. We recorded motility for at least 90 minutes after the meal.

STUDY EVALUATION

Motor activity

A colonic motility index was calculated with a computerised program, by measuring the area under the pressure records for the 60 minute period immediately preceding and the 60 minute period immediately after completion of the meal. The motility index was expressed as mm Hg/min. The motility indices obtained from the different recording sites were averaged to obtain only one basal and one postprandial motility index for each patient. Only contractions greater than 5 mm Hg were included in the analysis.

Patterns of colonic motor contractions were identified visually. Movement artefacts gave rapid fluctuations that occurred simultaneously at all recording sites and were easily differentiated from colonic contractions and discarded from analysis. Non-propagating contractions were defined as contractions that did not propagate at least 15 cm between the recording ports. Propagating contractions were those that appeared at adjacent recording sites within 30 seconds of each other. These were defined as antegrade or retrograde based on their aboral or oral propagation respectively. High amplitude propagated contractions (HAPCs) were defined as contractions with amplitude of at least 100 mm Hg in at least two recording sites, propagating for at least 30 cm (over three or more recording sites).

<table>
<thead>
<tr>
<th>Pathology</th>
<th>No of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopathy (hollow visceral myopathy)</td>
<td>4</td>
</tr>
<tr>
<td>Neuropathy (absence or immaturity of myenteric plexus)</td>
<td>5</td>
</tr>
<tr>
<td>Antroduodenal motility (n=30):</td>
<td></td>
</tr>
<tr>
<td>Myopathy (coordinated contractions of low amplitude)</td>
<td>6</td>
</tr>
<tr>
<td>Neuropathy (absence of migrating motor complex, uncoordinated contractions of normal amplitude)</td>
<td>24</td>
</tr>
</tbody>
</table>

Statistical analysis

The Wilcoxon signed rank test was used to compare the differences between motility index during the baseline period and postprandial period. A χ² test was used to compare percentage of children with and without HAPCs in the different groups of patients. Results are expressed as mean (SEM).
TABLE III  Summary of quantitative results

<table>
<thead>
<tr>
<th></th>
<th>Non-constipation</th>
<th>Neuropathy</th>
<th>Myopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients:</td>
<td>8</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>With fasting HAPCs</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>With postprandial HAPCs</td>
<td>8*</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>With retrograde contractions</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Fasting motility index (MI)</td>
<td>3-2 (0-3)</td>
<td>2-1 (0-3)</td>
<td>0</td>
</tr>
<tr>
<td>Postprandial MI</td>
<td>8-4 (1-1)**</td>
<td>3-1 (0-4)</td>
<td>0</td>
</tr>
<tr>
<td>Patients with 2 fold increase in MI</td>
<td>8**</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*p<0.01 non-constipation v neuropathy and myopathy; **p<0.001 fasting MI. Motility index expressed as mean (SEM) mm Hg/min.

Results
Table III summarises the results. Twenty-two patients had colonic contractions during fasting and after the meal. Two children had contractions only after feeding. In six subjects there were no contractions during the entire study. Sixteen children had both propagated and non-propagated contractions, one had only propagated contractions and the other seven only non-propagated contractions. Retropulsive contractions were recorded in four constipated and in one non-constipated patient. HAPCs (Fig. 1) constituted 57% of the propagated contractions. When HAPCs were excluded from the propagated contractions, there was no difference in the percentage of propagated and non-propagated contractions in the group of patients with and without constipation. In 65% of episodes, HAPCs were associated with the passage of flatus, or stool, or both. In most cases, HAPCs began from the most proximal recording site and migrated to the sigmoid region. Only 21% of HAPCs were associated with the passage of flatus, or stool, or both. In most cases, HAPCs began from the most proximal recording site and migrated to the sigmoid region. Only 21% of HAPCs were propagated to the rectum. Mean speed of propagation of the HAPCs was 0.9 (0-3) cm/s (range 0.5-2.2 cm/s).

All eight children in the non-constipated group had contractions in both fasting and fed states. The postprandial colonic motility index increased significantly, when compared with basal values, in this group of children (3.2 (0-3) mm Hg/min basal v 8.4 (1-1) mm Hg/min postprandial, p<0.001). There was no correlation between volume or caloric content of the meal (analysed as ml/kg and Kcal/kg) given to the patient and the increase of his postprandial motility index. All non-constipated subjects had HAPCs within 30 minutes after beginning the meal. They averaged 3-6 HAPCs during the first 60 minutes after the meal (range 1-12). Three of eight subjects also had HAPCs during fasting.

Postprandial HAPCs were found only in four of 16 subjects with neuropathic disorders, a significant decrease compared with the non-constipated group (p<0.01) (Fig. 2). No patient with neuropathy had HAPCs during fasting. There was no difference in the speed of HAPCs between patients with neuropathy and non-constipated patients. The presence of HAPCs had a 67% predictive value for not having constipation, and the absence of HAPCs had a 100% predictive value for having constipation. There were no manometric features in the fasting motility that differentiated the patients without constipation from those with neuropathy and constipation. By contrast with the non-constipated subjects, the patients with neuropathic constipation had no significant increase in their postprandial motility index (2.1 (0-3) mm Hg/min basal v 3.1 (0-4) mm Hg/min postprandial, NS). A twofold increase in motility index after the meal was present in two patients with neuropathy and in all non-constipated patients (2/16 v 8/8, p<0.001). Although four patients with neuropathy and constipation had HAPCs and two had a twofold increase in motility index after the meal, no patient with neuropathy had both these features.

The six children with myopathy had no contractions at any time. Therefore their motility index was zero before and after the meal. The absence of contractions throughout the entire study distinguished subjects with myopathy from the non-constipated group and from the patients with neuropathy.

Two patients in the non-constipated group had, during fasting, a rectal motor complex (RMC), a cluster of contractions at a rate of 7-9/min found only in the rectum (Fig. 3).

There were no adverse events during the studies.

Discussion
In this study we investigated colonic motility in children with chronic intestinal pseudo-obstruction. We divided the study population into two groups: subjects with symptoms sug-
Figure 3: Colon manometry from a child without constipation. There are non-propagating contractions in the transverse colon and a rectal motor complex in the rectum that lasts six minutes and has a frequency of contractions of 7–2/min.

Figure 3 shows examples of colon manometry from a child without constipation. The transverse colon, descending colon, sigmoid colon, and rectum are depicted. The manometry tracing in the rectum shows a rectal motor complex that lasts for six minutes with a frequency of contractions ranging from 7 to 2 contractions per minute.

The text discusses the role of rectal motor activity, or migrating motor complex, in the healthy colon during sleep. It is noted that non-constipated patients have these motor patterns, whereas constipated patients may have altered patterns.

In the transverse colon, there are non-propagating contractions that are characteristic of the interdigestive cycle of the gastrointestinal tract. These patterns are not seen in constipated patients.

The descending colon and sigmoid colon show a similar pattern of contractions, indicating the presence of a migrating motor complex. The rectum, however, shows a distinct motor pattern with a rectal motor complex that lasts for six minutes.

The study elucidates the importance of these motor patterns in the healthy colon and the potential implications for patients with constipation. It highlights the need for further research to understand the pathophysiology of constipation and its associated motor abnormalities.
Colonic manometry in children with chronic intestinal pseudo-obstruction

Evidence that HAPCs can be induced by distention of the lumen or by luminal irritants such as olive oil and bisacodyl. In the evaluation of CIP in childhood, colon manometry complements the radio-opaque marker test. The last often reveals the site of functional obstruction and can differentiate among colonic inertia, hindgut dysfunction, and outlet obstruction. Manometry distinguishes between myopathy, neuropathy, and normal colonic function. There were no contractions recorded from children with myopathy. We assume that contractions were totally absent or failed to occlude the intestinal lumen. It is possible that a dilated colon would generate only very low amplitude contractions that are not distinguished during manometric studies. In colonic neuropathies contractions were present, but the gastrocolonic response was absent and there were fewer HAPCs.

Scintigraphy is a less invasive approach to the study of bowel motility than manometry. It allows the study of regional transit of solids in the unprepared human colon without the need for colon intubation. There are limitations to the use of scintigraphy in children with pseudo-obstruction, such as the very long transit time for orally ingested capsules to reach the colon, the impossibility of peroral cannulation of the right colon, and the poor patient cooperation with lying quietly under a gamma camera. Also, scintigraphy may not differentiate clearly between neuropathy and myopathy.

In conclusion, colonic manometry is a safe and effective means to evaluate colonic motility in children with CIP. Colon manometry could be used as a diagnostic tool in selected patients to clarify the pathophysiology of severe colonic disorders.

The results of this study were presented in part at the Digestive Disease Week held in San Antonio, Texas, USA, May 1990.