Unraveling childhood constipation: Pathophysiology, diagnostics and treatment

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CHAPTER 3

Colonic manometry and colonic scintigraphy as a diagnostic tool for children with severe constipation

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ABSTRACT

Background and Objective: In adults, colonic manometry and colonic scintigraphy are both valuable studies in discriminating normal and abnormal colonic motility. The objective of this study was to compare the diagnostic yield and tolerability of colonic manometry and colonic scintigraphy in children with severe constipation.

Methods: Twenty-six children (mean age 11.4 years, 77% boys) who had received colonic manometry and colonic scintigraphy as part of colonic motility evaluation were included. Manometry was performed as per department protocol. After swallowing a methacrylate-coated capsule containing Indium-111, images were taken at 4, 24, and 48 hours, and geometric centers were calculated. Results of both tests were categorized in 3 groups: normal, abnormal function in the distal part of the colon and colonic inertia. Cohen's Kappa was used for the level of agreement. Patients and parents completed a questionnaire regarding their experience.

Results: Colonic scintigraphy showed normal transit time in 20%, delay in the distal colon in 48%, and colonic inertia in 32% of patients. Colonic manometry was normal in 40%, abnormal in the distal colon in 40%, and colonic inertia was diagnosed in 20%. The Kappa score was 0.34. All 5 patients with colonic inertia during manometry had a similar result by scintigraphy. Eighty-eight percent of patients preferred scintigraphy over manometry and 28% of parents preferring colonic manometry over scintigraphy.

Conclusions: Colonic manometry and colonic scintigraphy have a fair agreement regarding the categorization of constipation. Scintigraphy is well tolerated in pediatric patients and may be a useful tool in the evaluation of children with severe constipation.
INTRODUCTION

Childhood constipation is a common problem with a worldwide prevalence of 0.7% to 29.6%. It has a significant effect on quality of life and contributes significantly to health care financial burden. Children with severe constipation not responsive to dietary, behavioral and medical treatment require further investigation. Accurate assessment of colonic motility and transit can be essential in the investigation, because patients with abnormal colonic function may require different treatment strategies. The most frequently used method to measure colonic transit time in children with defecation disorders is with ingestion of radio-opaque markers. This non-invasive and simple method is widely accessible and monitors the progress of ingested plastic markers through the colon; however, this test can be used only as a gross indicator of transit. Another test to assess colonic transit is scintigraphy, which involves the measurement of the location of an ingested radioisotope as it transits through the gastrointestinal tract. The colon can be divided into more segments than is feasible with the use of radio-opaque markers. Furthermore, multiple images can be obtained without increasing radiation dosage. The use of scintigraphy was first demonstrated by Krevsky et al. in 1986 and since that time several methods have been used; however, normative scintigraphy data for children are lacking. Colonic manometry is another valuable diagnostic test in differentiating normal colonic motor function from colonic neuromuscular disorders on a segmental level. It allows for provocative maneuvers, and it has been found to be well tolerated in children; however, manometry requires hospital admission to place a catheter in the colon under endoscopic or fluoroscopic guidance. Successful catheter placement and maintenance in the cecum for the duration of the study is not always possible, limiting the information obtained about the proximal colon. Manometry is also not widely available, with only a few pediatric centers worldwide performing the test routinely in children. The primary aim of this study was to compare the diagnostic yield and tolerability of colonic manometry and colonic scintigraphy in children with severe constipation.

METHODS

Patients
The charts of all of the patients with longstanding intractable constipation referred for testing to the Motility Center at Nationwide Children’s Hospital and who had received both colonic manometry and colonic scintigraphy as part of their colonic motility evaluation were reviewed. Symptoms at the time of evaluation, results of colonic manometry and colonic scintigraphy, and interpretation of the findings of both tests were collected. Patients and their parents were asked to complete a brief questionnaire asking them about their experience with each study as well as their overall preference. The study protocol was approved by the Nationwide Children’s Hospital Institutional Review Board.
Manometry protocol
A clear liquid diet was recommended to all patients for at least 24 hours before the study. On the day before the study, patients underwent preparation for colonoscopy by drinking or receiving through a nasogastric catheter a balanced electrolyte solution containing polyethylene glycol. On the morning of the study the manometry catheter was placed using endoscopy with fluoroscopic control to place the tip of the catheter into the proximal colon. A water-perfused manometry catheter, with eight recording sites spaced 10-15 cm apart was used. Manometric recording was started after complete recovery from sedation. During the study, patients were awake and required to remain in bed, and a trained observer was present at the bedside throughout the entire study. All of the motility studies included at least 1 hour of fasting and 1 hour postprandial after finishing a high calorie meal. The position of the catheter was confirmed with an abdominal X-ray after the meal. If no high-amplitude propagated contractions (HAPCs) were observed during fasting or in the postprandial period, bisacodyl (0.2 mg/kg, max of 10mg) was administrated through the central lumen of the catheter.

Manometry data analysis
Patterns of colonic motor contractions were identified visually. Contractions with an amplitude of at least 80 mm Hg, lasting more than 10 seconds and propagating for at least 30 cm, were considered HAPCs. The gastrocolonic response was defined by an increase in colonic motility that occurred within 30 minutes after beginning a meal. The studies were categorized into 3 different groups: 1) Normal: presence of HAPCs and a gastrocolonic response; 2) Distal colon dysfunction: absence of HAPCs in the descending and/or sigmoid colon after administration of bisacodyl; and 3) Colonic inertia: no gastrocolonic response and no HAPCs through the entire colon after administration of bisacodyl.

Scintigraphy protocol
The patient fasted the night prior to the test. A 2-cm pH sensitive capsule, containing the radioisotope Indium-111, was administrated by mouth. The methacrylate-coated capsule dissolves in the cecum. The patient received a meal in the Nuclear Medicine Department and the first images were obtained 4 hours after ingestion of the capsule. The patient then ate and drank normally, with the exception of the avoidance of caffeinated beverages during the study. Images were acquired at 24 and 48 hours from the time of ingestion.

Scintigraphy data analysis
For each subject, the colon was divided anatomically into the following 4 regions of interest (ROI): 1) ascending colon; 2) transverse colon; 3) descending colon; 4) rectosigmoid colon. The stools were considered a fifth ROI. Overall colonic transit was quantified by the geometric center (GC) or center of radioactivity. The GC was calculated by multiplying the fraction (%/100) of counts in each ROI by the ROI number (1-5) and sum the products. The sum represents the GC at the time of image collection at 4, 24, and
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48 hours. A low GC value indicates that a higher amount of tracer in the proximal colon, while a high GC value is consistent with an increased amount of tracer in the distal colon or with elimination in the stool. In patients with distal abnormality or functional outlet obstruction, progression of the tracer may be normal at the 24 hour mark, but there is little evacuation at the 48 hour mark. In patients with slow colonic transit, the majority of the tracer remains in the proximal colon throughout the entire study. Normal values are based on adult data from Camilleri and Zinsmeister and were considered the following: mean GC at 4 h = 1.2 (range 0.7 - 1.7); mean GC at 24 h = 2.7 (range 1.6 - 3.8); mean GC at 48 h = 3.9 (range 3 - 4.8).³

Statistical analysis
The level of agreement between colonic manometry and colonic scintigraphy was assessed using Cohen’s κ statistic. The opinion and preferences of the patient and the parents were collected from the questionnaire, and summarized using descriptive statistic. A P value ≤ 0.05 was considered significant.

RESULTS
Patients
Between August 2008 and January 2011, 26 children (77% boys) with severe constipation unresponsive to standard medical treatment underwent both colonic manometry and colonic scintigraphy. The mean age of the patients was 11.4 years (6-19 years). The mean age of onset of defecation problems was 3 years and 9 months. Besides stooling difficulties, 69% of the patients reported at least one episode of fecal incontinence per week and 73% experienced abdominal pain regularly. At the time of referral, 50% of the patients used a combination of oral laxatives and retrograde enemas, 46% used only oral laxatives and 4% only daily enemas.

Scintigraphy
Scintigraphy data were obtained in 25 patients. In one patient the capsule did not release the radioactive tracer properly and the child was therefore excluded from further analysis. All patients, except for one, swallowed the capsule. In the latter patient the capsule was placed during an upper endoscopy. In 50% of the patients colonic scintigraphy and manometry study were performed in the same week, whereas in the other 50% there was at least one week between the two studies (mean 4.5 weeks, range 1-16 weeks). The median GC at the 24 hour scan was 1.61 (range 0.52-4.12). The median GC at the 48 hour scan was 2.73 (range 0.61-4.95). Colonic scintigraphy showed normal transit time in 20%, delay in the distal colon in 48%, and colonic inertia in 32% of the patients (Figures 1 and 2).
**Figure 1:** An example of a normal scintigraphy study at 24h (1a) and 48h (1b), study of a patient with dysfunction of distal part of the colon at 24h (2a) and 48h (2b), and study of a patient with colonic inertia at 24h (3a) and 48h (3b).

**Manometry**
Placement and maintenance of the catheter in the right side of the colon during the entire colonic manometry was achieved in 52% of the patients. Colonic manometry showed normal motility in 40%, abnormal motility pattern in the distal colon in 40%, and colonic inertia was diagnosed in 20% of the patients (Figure 2).

**Comparison**
In 14 patients (56%) both colonic scintigraphy and colonic manometry showed similar results. In 8 patients with a normal manometry, scintigraphy showed a delayed transit time, whereas in 3 patients the manometry revealed abnormal motility in the distal colon, while scintigraphy showed normal transit. All 5 patients diagnosed as having colonic inertia by manometry had similar results with scintigraphy. The calculated sensitivity for scintigraphy was 0.8. The $\kappa$ score was 0.34, indicating a fair agreement between the two studies.

**Questionnaire**
The questionnaire was completed by 25 patients. Data about overall patient and parental preferences demonstrated that 88% of the patients preferred scintigraphy over manometry. Mentioned reasons for this preference included increased comfort, less preparation time, lack of anesthesia and lack of catheter placement. Scintigraphy was preferred by 60% of parents; manometry by 28% of the parents, and 12% reported no difference between the two tests. Parents with a preference for manometry believed that it offered more detailed information and were pleased that it could be accomplished in 1
day versus 3 days. The variance in opinions between patients and parents for scintigraphy and manometry was significantly different ($P = 0.02$). Asked about the experience with both studies, 12% of patients described manometry as significantly unpleasant and 52% of parents expressed concerns about manometry for their child. Reasons for the reported difficulties and concerns with manometry included catheter placement, anesthesia risks, length of study, and discomfort for the child. None of the patients or parents described scintigraphy as unpleasant.

Figure 2: Categorization of constipation by colonic scintigraphy and colonic manometry ($k = 0.34$)

DISCUSSION

This is the first study comparing the diagnostic yield and tolerability of colonic manometry versus colonic scintigraphy in children with severe constipation. Colonic manometry and colonic scintigraphy had a fair agreement regarding the categorization of constipation. Scintigraphy was well tolerated in pediatric patients and in the majority it was preferred over manometry.

Patients with constipation who do not respond to standard dietary, behavioral, and medical treatments warrant further evaluation to identify the behavioral and physiologic components of their defecatory disorder. Patients with constipation have been traditionally categorized as having normal colonic function, functional outlet obstruction/fecal retention, or colonic inertia/slow transit. Knowledge of the subgroup of constipation may help direct therapy. A patient with functional constipation and stool withholding may respond best to laxatives combined with dietary changes and behavioral modifications, whereas a patient with slow transit constipation may benefit from enemas, colonic lavage or a surgical intervention. The use of antegrade enemas may be indicated when there is an abnormality limited to distal colon or when the rectosigmoid is dilated. Segmental colectomies can be used when there is a motility disorder involving only a segment of the colon.
Part III

While the use of radio-opaque markers has been the most common method used to assess colonic transit, it has been suggested that this method may assign markers to incorrect bowel segments and does not provide accurate data on transit through each colonic region.\(^1\)\(^,\)\(^2\) Also, there is a concern that indigestible solid particles do not move with a meal and may not be handled by the colon in the same manner as stool.\(^2\)\(^2\) The disadvantages of scintigraphy are the higher costs compared to radio-opaque markers\(^8\) and the inconvenience of having to visit the department three days in a row for the acquisition of the images. Comparison of scintigraphy and transit marker studies is difficult because of the different dynamics of the two methods.\(^1\) Nevertheless, there are a number of studies that have performed simultaneous comparison of radioisotope and plastic markers in healthy adult subjects. These studies show a significant difference in the descending colon, where more patients were diagnosed as having prolonged transit by scintigraphy than by plastic marker study.\(^8\)\(^,\)\(^1\)\(^1\) Comparison of scintigraphy and transit marker studies for the evaluation of constipation in children has not been performed.\(^2\)\(^3\) Some authors argue that scintigraphy is a more reliable technique and should now become the criterion standard in transit studies.\(^1\)\(^1\)\(^,\)\(^2\)\(^1\)

Our results show that colonic scintigraphy is well tolerated in the pediatric population. None of the patients or parents described scintigraphy as unpleasant. Almost 90% of the patients and 60% of the parents preferred scintigraphy over manometry. Scintigraphy has been criticized for excessive radiation dose.\(^4\) The radiation dose given to a patient during a scintigraphy study, however, is equivalent to that of two plain abdominal x-rays – the same number of films often used in standard radio-opaque marker studies.\(^4\)\(^,\)\(^9\) There has also been some concern about the short duration of imaging. While there has been some disagreement about the time period required to assess colonic transit\(^4\)\(^,\)\(^6\), functional outlet obstruction has been found to be apparent by 24 to 48 hours, with most of the tracer held up in the rectosigmoid. Determining the total time to excretion would not add any extra useful information, so there is no need to pursue further imaging and unnecessary additional radiation exposure.\(^4\)

Colonic manometry is a valuable diagnostic test in providing information about colonic function on a segmental level;\(^7\)\(^,\)\(^1\)\(^2\) however, the availability of colonic manometry studies is limited to a few pediatric referral centers. Additionally, colonic manometry studies are described as lengthy and somewhat uncomfortable, requiring the use of general anesthesia for introduction of catheters.\(^2\)\(^3\) Therefore, the identification of children who would likely benefit from manometry would be helpful.\(^2\)\(^3\) On the other hand, during the manometry parents get to directly observe the motility tracing and any provocative manoeuvres done during the testing. After administration of bisacodyl for example many patients experience an urge to defecate and the observation of the child’s response to the urge can be enlightening for the parents who may now recognize stool withholding behavior that previously they had interpreted as attempts to defecate. These factors make manometry seem more tangible and concrete. Furthermore, during manometry testing there is continuous presence of nursing staff or the physician. This may be reassuring to
the parents as well.\textsuperscript{24,25} This is in line with the results of our study, which indicated that despite the expressed concerns, almost 30\% of the parents preferred manometry over scintigraphy. All parents were indeed present during the manometry studies in our series.

We found a fair agreement between scintigraphy and manometry and a sensitivity of 80\% for scintigraphy compared to colonic manometry. This is comparable with previous studies in healthy adult subjects showing a high sensitivity in the detection of motility disorders of the colon.\textsuperscript{9,22,26} In this study colonic scintigraphy identified more patients with abnormal colonic transit, while manometry categorized more patients as having normal colonic function. All 5 patients with manometry indicative of slow colonic transit, however, also had scintigraphy studies consistent with slow colonic transit. This suggests that scintigraphy can be used as a screening tool for patients with constipation to determine which patients require additional manometry testing.

Three patients with colonic inertia on scintigraphy had normal manometry studies. Having a diagnosis of colonic inertia has important clinical consequences; therefore, we suggest that an abnormal scintigraphy study suggesting colonic inertia should be confirmed before any medical or surgical treatment choices will be made. In addition, an abnormal colonic scintigraphy even in the presence of normal colonic manometry may have important clinical implications that are presently unclear. Scintigraphy can also provide useful information regarding the proximal colon when the manometry catheter does not reach the proximal colon. Differences between both study results can be related to the fact that patients underwent preparation before colonic manometry. Second, stimulants are used during the study, whereas scintigraphy is done without clean-out and the use of stimulations. The amount of time between the two studies had no significant influence on disagreement between both tests. Tipnis et al. studied the colonic transit time measured by radio-opaque markers and colonic manometry in children with chronic constipation. They found a good correlation between the two study results and concluded that, although sensitive, oro-anal transit time was not specific for predicting whether the whole colon or a segment of the colon was affected by either a neuropathic or myopathic disease process. They concluded that transit studies may be helpful to predict which children should be referred for colonic manometry, and that manometric testing remains an important step in the evaluation of children with slow transit constipation.\textsuperscript{23}

Scintigraphy does have some limitations that warrant further discussion. There is the possibility of capsule malfunction, as occurred in one of our patients. A second limitation is that to date, normative scintigraphy data for children are lacking. There are also age limitations, because younger children may not be able to swallow the capsule. Variations in the protocol used for scintigraphy with regard to the number of ROIs as well as the normal values used have been described.\textsuperscript{27} Although it may not be available at all institutions, scintigraphy could certainly be more available than colonic manometry.

Larger scale future studies are needed to explore the use of scintigraphy in children, including normal pediatric GC values, possible sex and age differences such as those
suggested in previous studies\textsuperscript{28}, the reproducibility and intra-subject variability,\textsuperscript{11} the influence of the use of previous medications such as stimulants and stool softeners, and the cost effectiveness of scintigraphy compared to radio-opaque marker studies and manometry.

CONCLUSIONS

Colonic manometry and colonic scintigraphy have a fair agreement regarding the categorization of constipation. Scintigraphy is well tolerated in pediatric patients and may be a useful tool in the evaluation of pediatric patients with severe constipation.

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REFERENCES


