Published in final edited form as:

Neurogastroenterol Motil. 2017 July ; 29(7): . doi:10.1111/nmo.13050.

Prospective Evaluation of Same Day versus Next Day Colon Manometry Results in Children with Medical Refractory Constipation

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Abstract

Background—We evaluated the change on colon manometry (CM) parameters and interpretation comparing results when the study is performed the same day after the motility catheter is placed under anesthesia or the following day.

Methods—CM catheter was placed with colonoscopy under anesthesia and recorded on day 1 and repeated on day 2. Study parameters including motility index (MI) during fasting, post-prandial and post-Bisacodyl challenge phase; gastrocolonic response; number, presence and propagation of high amplitude propagating contractions (HAPCs); and, study interpretation were compared between both days.

Key Results—MI (fasting, post-Bisacodyl phase, $p < 0.05$), HAPC number (10.1 vs. 6.6, $p = 0.01$) and proportion of patients having HAPCs (92% vs. 70%, $p = 0.002$) was significantly higher on day 2 vs. day 1. HAPC propagation improved on day 2 vs. day 1 (fully propagated, 49% vs. 37%; partially propagated, 43% vs. 33%; absent 8% vs. 30%). Study interpretation changed from day 1 to day 2. On day 1, 37% had a normal study and 63% had an abnormal study. On day 2, all patients with a normal study on day 1 remained normal, and patients with an abnormal study on day 1, 53% remained abnormal and 47% had a normal study.

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Industry sponsorship: None.

Professional medical writer assistance: None.

Specific author contributions: RAA: data collection; CM study interpretation; data analysis and interpretation; manuscript draft. SN: study concept and design; performance of colonic manometry; data analysis and interpretation; manuscript final draft approval. NH: data entry, analysis and interpretation. MA: data entry, analysis and interpretation. LR: study concept and design; performance of colonic manometry; data analysis and interpretation; manuscript final draft approval. All authors approved the final version of the manuscript.

Competing interest: the authors have no competing interests.

This work has not been previously published in abstract form in a meeting sponsored by the American Motility Society, European Neurogastroenterology and Motility Society, or Functional Brain Group.

Conclusions & Inferences—CM parameters are affected the day catheter is placed with colonoscopy under anesthesia. The number, presence and propagation of HAPCs was significantly higher/improved on day 2 compared to day 1. Overall, CM interpretation changed from abnormal to normal from day 1 to day 2 in 47% of the patients.

Graphical Abstract

This study highlights the changes in colon manometry parameters and study interpretation from the day the motility catheter is placed with colonoscopy under anesthesia to the following day.

Keywords

anesthesia; colon motility; colonic manometry; constipation; pediatrics

INTRODUCTION

Colonic manometry (CM) has been proven to be a useful tool in the evaluation and treatment of children with defecation disorders.^{1–4} CM has been instrumental in the identification of previously unrecognized normal physiologic patterns, including the association between the internal anal sphincter relaxation and the onset of proximal to distal colon contraction migration.⁵ In post-surgical patients CM has not only helped clarify the pathophysiology of recurrent symptoms⁶, but has also been proven to predict therapeutic outcomes in patients treated with antegrade colonic enemas via cecostomy.^{7, 8}

In children, colonic motility catheters are usually placed during colonoscopy with fluoroscopy guidance under general anesthesia. However, the timing on when to start the recording of the study varies. Some centers perform the study the same day right after catheter placement under anesthesia and others perform it the following day. A previous study showed that there is no difference.⁹ Another study suggested that there may be more colonic motor events recorded the day after anesthesia.¹⁰ There is also experimental evidence that anesthesia can affect gastrointestinal motility.^{11–13} Given the contradictory information and the fact that there has been an increase routine use of CM as part of the evaluation of children with chronic medical refractory constipation, it is important to know whether the test can be performed the same day the catheter is placed under anesthesia. Therefore, the primary aim of this study was to determine if there are differences in CM parameters when the study is performed the day of catheter placement with colonoscopy

under anesthesia compared to the following day. Secondary aims were to determine if there is difference in CM interpretation and, establish the presence of predictive factors that could explain differences in interpretation.

METHODS

Study design and patients

This was a single center prospective study that included patients with a history of chronic constipation refractory to medical therapy undergoing CM evaluation. Subjects with medical refractory constipation were defined as patients that have previously failed conventional medical therapy. All patients were admitted to the hospital and received a standardized bowel clean out with polyethylene glycol. The following day a colonic motility catheter (solid state or water perfused) was placed with colonoscopy under general anesthesia. The proximal end of the catheter was left in the cecum and the distal end in the rectum. The catheter was taped secured to each patients' thigh to avoid displacement. Medications that could affect colonic motility were discontinued 48 hours prior to catheter placement.

Colon manometry

The CM was performed as per previously described protocol.^{2, 5, 14} Either a solid-state (36 radially oriented pressure sensor, 3 cm spacing) or a water perfused (8 port longitudinal staggered sensor, 10–15 cm spacing) catheter was used as indicated according to patients' age, size and availability. CM recording was performed by a stationary motility unit (Medical Measurement Systems, New Hampshire USA). Briefly, the study consisted in recording of a fasting phase, post-prandial phase after a meal and post-Bisacodyl challenge phase (0.25 mg/kg divided in 2 doses given via the catheter lumen spaced by 20 minutes, maximum of 10 mg). The fasting phase was recorded for 60 minutes; the post-prandial phase was recorded for 60 minutes after a meal was given over 30 minutes; and, the post-Bisacodyl challenge phase was recorded for 90 minutes. To assess the colonic motility on each subject we evaluated the following CM parameters. The motility index (MI), a measurement of contractility for a selected segment and period of time (mmHg*cm*sec) was calculated on all of the above phases for a time frame of 60 minutes on the right colon (cecum-mid transverse colon), left colon (mid transverse-rectum) and whole colon. A normal gastrocolonic response to a meal was evaluated both visually (visual increase on the colon motor activity after meal ingestion) and by an increase in post-prandial motility index of at least 15%. High amplitude propagating contractions (HAPCs) were defined by an increase in intraluminal pressure of more than 60 mmHg that did not overlap with other contractions, lasting more than 10 seconds and less than 30 seconds propagating over a distance of 30 cm or more.¹⁴ HAPCs were considered to have full propagation if they reached the rectosigmoid and partial propagation if they did not reach the rectosigmoid. The presence, number and propagation of HAPCs was recorded on the 3 phases of the study. The study was considered normal if there was presence of the gastrocolonic response to a meal (except on those being evaluated for chronic intestinal pseudo-obstruction that did not receive a meal and only HAPCs were included in analysis) and presence of fully propagated HAPCs to the rectosigmoid (Figure 1). The study was performed on two separate days. On day 1, CM recording began once the patient was completely recovered and awake from

anesthesia. On day 2, all patients had an abdominal x-ray early in the morning to confirm catheter position and CM recording was repeated after an overnight 12-hour fast following the same protocol as on day 1. Only subjects that had the proximal end of the catheter reach the cecum during placement on day 1 and no displacement on day 2 determined by abdominal x-ray were included in the study. If there was significant catheter displacement, the subject was not included in the study. The MI, gastrocolonic response, presence, number and propagation of HAPCs, and overall CM interpretation results between day 1 and day 2 were compared. The same observer analyzed all traces blindly. Medications used during anesthesia, total anesthesia time, lapsed time between end of anesthesia and CM initiation, and combined antroduodenal manometry (ADM) catheter placement were documented.

Statistical analysis

Statistical analysis was carried out using IBM SPSS Statistics Software, version 21. Conventional descriptive statistics and non-parametric tests were performed for continuous variables. Results are expressed as mean values $\pm$ standard error of the mean (SEM) as indicated. Proportions were compared using Chi-squared and Fisher's exact test. Logistic regression analysis was used to establish the joint effect of different factors on CM interpretation. To ascertain if there was an independent effect of difficulty during colonoscopy or longer anesthesia time, patients that underwent a combined ADM and CM catheter placement were excluded from the predictive analysis. A p value of <0.05 was considered statistically significant.

Ethical approval

This study was approved by the Institutional Review Board of Boston Children's Hospital. Written informed consent was obtained from each of the patient's parent or guardian before any study-specific procedure was performed. Patient assent was obtained when age appropriate.

RESULTS

Patient population

A total of 60 patients undergoing CM at Boston Children's Hospital were included in the study. Mean age was 9.5 years (1.5–18.8), 53% were male and 83% had a diagnosis of functional constipation. The mean total anesthesia time at the time of colonoscopy and catheter placement was 99.6 ± 4.19 minutes. A total of 31 patients (52%) received Sevoflurane as a general anesthetic and 29 (48%) received Propofol. Other demographic and procedure related characteristics are shown in table 1.

Motility index

The mean MI was significantly higher on the right, left and whole colon during the fasting and post-Bisacodyl phase on day 2 when compared to day 1. However, no difference was observed on the calculated MI during the post-prandial phase (Table 2).

Gastrocolonic response

A total of 50 subjects (83%) received a meal on both days. The gastrocolonic response was visualized in 44/50 subjects on day 1 and 49/50 on day 2 (88% vs. 98%, $p=0.12$). The presence of the gastrocolonic response to a meal when there was a post-prandial increase in the motility index of at least 15% was assessed and we found no difference between both days ($p=0.20$).

High amplitude propagating contractions

The mean number of HAPCs was significantly higher on day 2 when compared to day 1 (10.1 ± 1.03 vs. 6.6 ± 0.97 ; $p=0.01$). In a similar manner, the percentage of subjects who had HAPCs was also significantly higher on day 2 when compared to day 1 (92% vs. 70%, $p=0.002$). On both days, HAPCs were visualized only during the post-Bisacodyl challenge phase except for 1 patient that had HAPCs during the post-prandial phase. There was also a significant improvement in HAPC propagation when comparing day 1 to day 2. We found that on day 1, 22/60 (37%) of the patients had fully propagated HAPCs, 20/60 (33%) had partially propagated HAPCs and 18/60 (30%) had absent HAPCs. On day 2 there was a change in HAPC propagation as 40/60 (67%) of the patients had fully propagated HAPCs, 15/60 (25%) had partially propagated HAPCs and 5/60 (8%) had absent HAPCs. Overall, there was a significant improvement in HAPC propagation when comparing both days, changing from partially to fully propagated, and from absent to partially propagated (figure 2).

Study interpretation

We also found that there was a significant change in the overall interpretation of the study. On day 1, 22/60 (37%) of the patients had a normal study and, 38/60 (63%) had an abnormal study. On day 2, all subjects that had a normal study on day 1 (22/22 or 100%) remained normal; 18 of those with an abnormal study on day 1 the study interpretation changed to normal (18/38 or 47%); and, the remainder subjects (20/38 or 53%) continued to demonstrate an abnormal CM. In other words, the change on interpretation from day 1 to day 2 was 18/60 (30%). Overall, in our patient population we found a normal CM in 40/60 (67%) on day 2.

A separate analysis was performed according to the patients' diagnosis. Amongst patients with functional and non-functional constipation we found no difference in the rate of studies changing from abnormal to normal on day 2 (16/50 or 32% vs. 2/10 or 20%, $p=0.45$). There was no difference as well in the presence of HAPCs between patients with functional and non-functional constipation (37/50 or 74% vs. 8/10 or 80%, $p=0.689$). We also evaluated the 18 patients with absent HAPCs on day 1. Of these, 15 had functional constipation and in 4 the study remained abnormal on day 2; and, 3 had non-functional constipation and only in 1 they study remained abnormal on day 2 (27% of functional constipation vs 33% of non-functional constipation patients, $p=0.817$). Exclusion of all non-functional constipation patients did not change the results of the study analysis.

Predictive factors

When analyzing predictive factors that could affect interpretation, patients with an abnormal study on day 1 had a significant longer anesthesia time compared to those who had a normal study (106.5 ± 5.5 vs. 87.7 ± 5.6 min; $p=0.03$). On univariate analysis, it was also found that there was a tendency for the study to remain abnormal on day 2 on patients who also had a longer total anesthesia time (115.5 ± 9.3 vs. 96.8 ± 4.6 min; $p=0.08$). The same results were seen even after excluding patients that had a study combined with an ADM (97.2 ± 5.1 vs. 83.5 ± 3.9 min; $p=0.053$). However, multivariate analysis demonstrated that there was no significant predictive factor associated with a change in study interpretation when controlled for other factors (Table 3).

DISCUSSION

We show for the first time that there is a significant change in CM parameters including the MI and HAPC number, presence and propagation when the study is performed the day following catheter placement with colonoscopy under anesthesia. This resulted in a significant change in CM interpretation. This study demonstrates that CM parameters are affected when the study is performed the day of colonoscopy under anesthesia and highlights that CM interpretation changed in a considerable proportion of patients the following day. These findings have major clinical implications as the diagnosis can vary significantly if the CM is performed the same day the motility catheter is placed with colonoscopy under anesthesia.

In the present study, we found that colonic motility changed from day 1 to day 2 as evidenced by a significant increase in the MI and improved propagation of the HAPCs. The presence of HAPCs is considered as a marker of colonic neuromuscular integrity and their absence, along with other criteria, defines colonic inertia.¹⁵ Therefore, the fact that there was a significant increase in the number, presence and propagation during day 2 suggests that anesthesia may have a significant effect that needs to be taken into account. Procedure performance (i.e. difficulty reaching cecum and manipulation during colonoscopy) could be an additional factor that might affect colon motility and study interpretation. In the present study, however, it is not possible to discern the separate effects of the anesthesia from colon manipulation during colonoscopy and catheter placement, and future studies that address these two variables separately will be needed.

We also observed a change in study interpretation based on HAPC propagation improvement: from partially to fully propagating contractions and more importantly from absent to partially and fully propagating contractions. These findings suggest that anesthesia may affect the MI and HAPCs. Our results are in accordance with a recent study by Liem *et al*¹⁰ that concluded that prolonged measurement provides more information and allows detection of motor events missed by the standard short duration manometry performed that same day after catheter placement, also suggesting a potential anesthesia effect on colonic motility that could lead to an erroneous interpretation. On the other hand, Ammoury *et al* found no difference on the MI or study interpretation when comparing results after catheter placement or the next day.⁹ However, their study population does not seem to represent patients with significant defecation disorders as the majority of the subjects (17/20) had a

normal CM already on day 1 that remained normal on day 2. They had 1 of the remainder 3 patients with an abnormal CM on day 1 change to normal interpretation on day 2, also demonstrating, like us, that approximately 30% changed from abnormal to normal. Therefore, the main discrepancy with their findings is that their baseline number of patients with a normal study was much higher (90%). We also found that all of the patients that had a normal study on day 1 remained normal on day 2, suggesting that if the colon motility is normal on the first day, it is unlikely to change on the second. However, those findings do not apply for those with an abnormal study on day 1, as 30% became normal on the second day. It is not possible for us to ascertain exactly the factors that will predict which patients will have better results on the second day. Nevertheless, we showed that the longer the anesthesia time the more likely the patient is to have an abnormal CM the first day. The exact mechanism on how anesthesia affect gastrointestinal motility is unknown. Experimental data suggest an inhibitory effect over smooth muscle cells via acetylcholine¹⁶ and calcium channel pathways^{17, 18} while under anesthesia but the mechanisms of potential effects hours later (hence affecting the performance of the colon motility study) are unknown. Still, multiple factors including mechanical, hormonal and neural mechanisms, are most likely affected by anesthesia as well.

One could argue that the changes observed from day 1 to day 2 over the HAPCs and overall interpretation could be due to day to day study variability. Nonetheless, in 2010 Rao *et al* investigated the day to day reproducibility of prolonged 24-hour CM performed 2 weeks apart in healthy adults and demonstrated that the study findings were reproducible, particularly for the assessment of key physiologic changes, including HAPCs.¹⁹ In their study, the colonic motility catheters were placed under minimal sedation unlike our own in which general anesthesia was used for catheter placement.

There are important limitations to the present study. Firstly, patients that had an ADM and CM simultaneously were included in this cohort and the effect of medications administered during ADM on colon motility is not known. We tried to correct this by performing a subgroup analysis excluding those subjects and the results did not change, so it is likely that those factors did not affect our results. Secondly, the gastrocolonic response -an indicator of normal colonic response to a meal- was not evaluated on all patients in this study due to the reasons explained above. In addition, the meal type and volume was not standardized and varied amongst patients and from day 1 to day 2 which could potentially affect the presence of gastrocolonic response. Finally, the manometry findings of the patients of this study were not compared to healthy controls and adult data cannot be extrapolated for comparison.

In conclusion, CM study parameters are affected the day the motility catheter is placed with colonoscopy under anesthesia and this may result in an important change in the CM study interpretation between day 1 and day 2. Although the effect of the CM results on therapeutic outcomes has not been evaluated, the possible effect of anesthesia on CM interpretation can carry important implications on patient care. We propose that patients with an abnormal study on day 1 be studied again on day 2 and those with a normal study on day 1 do not need to undergo a repeat study the next day. Future studies are needed to identify patients at risk of having a significant effect of anesthesia on colon motility and the potential impact on their outcome.

Acknowledgments

Guarantor of the article: Leonel Rodriguez MD, MS.

Financial support: This work was supported by National Institutes of Health, USA (K24DK082792A to SN).

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Abbreviations

ADM	antroduodenal manometry
CM	colonic manometry
HAPCs	high amplitude propagating contractions
MI	motility index
SEM	standard error of the mean

KEY POINTS

- This study suggests that colon manometry (CM) parameters and study interpretation change from when the study is performed the same day the motility catheter is placed under anesthesia compared to the following day.
- The motility index, characteristics of the high amplitude propagating contractions and CM study interpretation improved the day after anesthesia.
- Based on our findings we suggest that patients with an abnormal study the day the catheter is placed under anesthesia should have the study repeated the following day.

Figure 1.

High resolution CM trace depicting HAPCs with full propagation from cecum to rectum. Y-axis represents pressure (mmHg) and x-axis represents time (seconds).

Figure 2.

CM tracings of a patient with absent HAPCs on day 1 and fully propagated HAPCs on day 2. A) Study on day 1. Note the absence of HAPCs. B) Study on day 2. Note presence of HAPCs during post-prandial and post-Bisacodyl phase. C. Day 2 post-Bisacodyl phase segment (enhanced) where the HAPCs fully propagated to the rectosigmoid.

Table 1

Demographic and anesthesia data.

Demographics	
Subjects	N=60
Age – years (range)	9.5 (1.5–18.8)
Gender	
Male - no. (%)	32 (53)
Female - no. (%)	28 (47)
Weight - kg±SEM	36.1±2.64
Diagnosis	
Functional - no. (%)	50 (83)
Non-functional - no. (%)	10 (17)
Cecostomy follow-up- no. (%)	3 (30)
*History of congenital malformation- no. (%)	3 (30)
Hirschsprung's disease- no. (%)	2 (20)
Microcolon-hypoperistalsis syndrome- no. (%)	2 (20)
**Combined study - no. (%)	9 (15)
Anesthesia time	
Mean total anesthesia time - min±SEM	99.6±4.19
Mean end of anesthesia to study start time - min±SEM	96.2±4.91
Anesthesia type	
Sevoflurane - no. (%)	31(52)
Propofol - no. (%)	29 (48)

SEM, standard error of mean

* Gastrochisis, malrotation.

** Combined ADM and CM study: evaluation for chronic intestinal pseudo-obstruction.

Table 2

Motility index comparison between day 1 and day 2.

Phase	Day 1	Day 2	<i>p</i> value
Fasting			
Right colon	8.0±0.35	9.44±0.26	0.002
Left colon	8.12±0.33	9.65±0.23	0.0003
Whole colon	8.13±0.32	9.66±0.21	0.0001
Post-prandial			
Right colon	8.77±0.32	9.54±0.28	0.09
Left colon	9.39±0.28	9.90±0.27	0.23
Whole colon	9.26±0.26	9.89±0.25	0.10
Post-Bisacodyl			
Right colon	9.96±0.19	10.6±0.22	0.04
Left colon	9.66±0.29	10.58±0.20	0.01
Whole colon	9.66±0.27	10.66±0.18	0.003

* Mean motility index (mmHg*cm*sec)±SEM

Table 3

Predictive factors: multivariate analysis.

Variable	<i>p</i> value
Age	0.86
Gender	0.63
Weight	0.66
CM alone vs. combined with ADM	0.42
Anesthesia type	0.87
Total anesthesia time	0.99
Time end of anesthesia study start day 1	0.87
Time end of anesthesia study start day 2	0.72
Time end of anesthesia first Bisacodyl dose	0.39
Individual performing colonoscopy	0.53