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Prevalence of Colonic Motor or Evacuation Disorders in Patients Presenting with Chronic Nausea and Vomiting Evaluated by a Single Gastroenterologist in a Tertiary Referral Practice

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Abstract

Background—Nausea and vomiting are thought to result from upper gastrointestinal dysfunctions. Our clinical observations led to the hypothesis that colonic motor dysfunction is associated with nausea and vomiting.

Methods—We reviewed electronic medical records (EMR) of 149 patients presenting with complaints of nausea and/or vomiting in a tertiary gastroenterology practice to investigate the association with disorders of colonic motor or evacuation disorders. We extracted demographics, gastric emptying (GE in 149) and colonic transit (CT in 138) of solids, ascending colon emptying half time (AC $t_{1/2}$), rectal evacuation by anorectal manometry (ARM) in 91 and balloon expulsion test (BE) in 55 patients. We estimated the proportions with delayed GE or CT, based on the 5th percentile of GE (in 319) and CT in 220 healthy volunteers using same method.

Key Results—Among 11 patients with nausea and/or vomiting with only GE measured, 5 had delayed and 6 normal GE. Among the 149 patients, 77 (52%) patients had evacuation disorders, confirmed by objective tests in 68 patients, and clinical examination in 9 patients. In the 138 patients with both GE and CT measured, 106 (76%) had both normal GE and CT, 11 (8%) only delayed GE, 16 (11%) normal GE with delayed CT, and 5 (3%) delayed GE and CT. Among 21 patients (15%) with delayed CT, 9 had slow AC $t_{1/2}$ and 12 evacuation disorder.

Conclusions & Inferences—In patients with chronic nausea and/or vomiting in gastroenterology practice, evaluation of colonic motility and rectal evacuation should be considered, since about half the patients have abnormal functions that conceivably contribute to the presenting nausea and/or vomiting.

Keywords

nausea; vomiting; colonic motility; rectal evacuation

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INTRODUCTION

Nausea is an unpleasant subjective sensation of the imminent need to vomit; it is typically experienced in the epigastrium or throat (1) and is described as feeling queasy or sick to the stomach and may be associated with retching or vomiting. Vomiting is the forceful expulsion of the gastric contents that may be preceded by nausea. These and other upper gastrointestinal symptoms in the dyspepsia complex are commonly experienced by people in the community (2) and are thought to arise in the gastroduodenal region (1). Among patients evaluated at referral centers with such upper gastrointestinal symptoms, about 60% have either delayed or accelerated gastric emptying (GE) or reduced gastric accommodation (3, 4). The symptoms of nausea and vomiting are predominant symptoms in patients attending emergency departments because of gastrointestinal illnesses (5).

Epidemiological studies show that there is overlap between several functional gastrointestinal disorders, including symptoms that form part of the dyspepsia complex (such as nausea or vomiting) and irritable bowel syndrome and constipation (6). Sarosiek et al. recently demonstrated that, among patients with known gastroparesis evaluated in a multicenter study, less than 50% had delayed GE of a wireless motility capsule (WMC); however, there was prolongation of colonic transit (CT) time in the patients with “gastroparesis symptoms”, suggesting that dysmotility beyond the stomach is present and could be contributing to symptom presentation in such patients (7). Given the multicenter nature of that study and the potential for reduced sensitivity for the WMC to identify delayed GE of digestible food, we tested the hypothesis that a subset of patients with chronic or recurrent nausea and/or vomiting has colonic motor or evacuation disorders with or without delayed GE. The rationale for this hypothesis was also supported by evidence that voluntary suppression of defecation delays GE (8) and by a report of dyspeptic symptoms in children with constipation that have been attributed to activation of a cologastric brake (9).

Thus, our aim was to determine the prevalence of colonic motor or evacuation disorders in patients presenting with chronic and/or recurrent nausea and/or vomiting evaluated by a single gastroenterologist in a tertiary referral practice.

METHODS

This medical records review study was approved by the Mayo Clinic Institutional Review Board for patients who had given prior unrestricted consent to use their medical records for such research.

Study Population and Medical Records Review

We reviewed electronic medical records of a consecutive series of all the patients with presenting complaints of nausea and/or vomiting evaluated between January 1, 1994 and June 30, 2012 by a single physician (MC) in a tertiary clinical center in the Midwest USA. Patients were all examined by the same gastroenterologist, and clinical features suggestive of rectal evacuation disorder (dyssynergic defecation or descending perineum syndrome) were routinely sought as previously recommended (10) and noted in the electronic medical record. Patients presented with the primary complaints of nausea and/or vomiting, and the presence of constipation or features of abnormal defecation were identified by evaluation during the presentation to this gastroenterologist. None were being treated for constipation at the time of presentation to Mayo Clinic with nausea or vomiting.

Patients had undergone exclusion (including upper gastrointestinal endoscopy), either by the referring physician or at Mayo Clinic, of alternative diagnoses such as peptic ulceration, NSAID-induced ulcers, and *H. pylori* infection as clinically indicated. Eating disorders were

excluded by clinical evaluation. None of the patients were taking medications that could be the cause of nausea or vomiting, such as opiates or antidepressants.

The patients consisted mainly of non-Hispanic, non-Latino, Caucasian white population. The presenting complaint of these patients was chronic and/or recurrent nausea and/or vomiting. In addition to measurement of GE of digestible solids, most of these patients also underwent measurement of CT of solid particles by validated scintigraphy (as described below) and, when clinically indicated, anorectal manometry and balloon expulsion tests to assess rectal evacuation function.

Patients were excluded if they did not undergo tests of anorectal function or CT, or if the isotope had not reached the colon by 24 hours in order to eliminate confounding the evaluation of CT by slow gastric or small bowel transit. Patients with diagnosis of rumination syndrome and post-fundoplication syndrome were excluded.

Details on the data abstracted from the Mayo Clinic electronic medical records are summarized in Appendix Table 1, including age, gender, BMI, presence of nausea and/or vomiting separately; GE at 1, 2 and 4 hours (h), and CT [measured by geometric center (GC) at 24 and 48h]. Ascending colon emptying $T_{1/2}$ (AC $t_{1/2}$ h) was calculated from the nuclear medicine studies. Anorectal manometry (ARM) tests, balloon expulsion studies, and anorectal angle change tests are described elsewhere (11) and, when available, were also recorded.

Physiological Measurements

Gastric emptying studies—To evaluate GE, an established scintigraphic method was used (12). Overnight fast was followed by subjects ingesting a ^{99m}Tc -labeled meal consisting of two scrambled eggs, one slice of whole wheat bread, and one glass of skim milk (296 kcal, 32% fat). Abdominal images of 2 minutes duration were obtained with anterior and posterior gamma cameras following ingestion of the radiolabeled meal and at 1, 2 and 4 hours in clinical studies. No participants were taking any prescription or over-the-counter medications for the 48 hours prior to and during the testing of GE. The performance characteristics of this scintigraphic GE have been recently reported (13).

Gastrointestinal and colonic transit studies—In addition to the measurement of GE described above, we used a validated scintigraphic method (14,15) to evaluate CT. The relationships with bowel function, performance characteristics and responsiveness to treatment using this method are described in detail in the previous work (15,16). The testing was done on patients after stopping medications that could interfere with the study.

After an overnight fast, patients ingested a delayed-release methacrylate-coated gelatin capsule packed with 0.1 mCi ^{111}In adsorbed on activated charcoal with the aid of a glass of water (250ml). Subjects were instructed to standardize the caloric intake and general content of lunch 4 hours and dinner 8 hours after swallowing the capsule. There was no bowel preparation prior to scintigraphy. Anterior and posterior images of 2 minutes duration were acquired at 4, 6, 24 and 48 hours, and ^{111}In counts were quantified within a 247 keV (610%) window and corrected for decay of the isotope and tissue attenuation (geometric mean of anterior and posterior counts). Images were obtained at 4, 6 and 24 hours in 138 participants; 48-hour images were available in 16 patients.

Anorectal manometry and balloon expulsion studies—Anorectal manometry was performed after a sodium phosphate enema (Fleet®, Lynchburg, Virginia, USA) approximately 1 hour before testing. Patients were positioned in the left lateral position. Between 1994 and 2007, anal sphincter pressures were measured by a low compliance

pneumohydraulic manometric perfusion system (0.5ml/min perfusion rate) and a polyvinyl catheter (4.8mm outer diameter; Arndorfer Medical Specialties, Greendale, WI, USA) connected to a computerized software program (Medtronic, Minneapolis, MN, USA). The method has been described elsewhere (17). Resting and squeeze anal sphincter pressures were recorded three times at 1cm levels in the anal canal and referenced to intra-rectal pressure. A rest period of 45 seconds separated sequential squeeze measurements.

From 2008 onwards, a trans-anal, solid-state, high-resolution probe with closely spaced solid-state sensors (16 channels at each level) was used. This allowed simultaneous high-resolution measurements of circumferential pressures in the rectum and throughout the anal canal. The results of this technique are significantly correlated with traditional manometry (18). The high-resolution probe also measures the rectoanal pressure difference. After the anal manometry study, a latex balloon was inserted into the rectum and filled with 50ml water. Additional traction weights were subsequently added if the patient was unable spontaneously to expel the balloon from the rectum, and the weight required to assist balloon expulsion was recorded (19,20). The maximum weight tested was 576 grams.

Data Analysis

Transit endpoints—The geometric mean of counts obtained on anterior and posterior images of the stomach were estimated at 1, 2 and 4 hours after correction for isotope decay. Colonic transit was assessed by calculating the geometric center (GC), which is the weighted average of radioactivity in the different segments of the colon [ascending colon=AC, transverse colon=TC, descending colon=DC, rectosigmoid=RS, stool (21)]:

$$(\%AC \times 1 + \%TC \times 2 + \%DC \times 3 + \%RS \times 4 + \% \text{ stool} \times 5) / 100 = GC$$

Ascending colon half-emptying time (AC t_{1/2}) was calculated by linear interpolation of AC content at all times when imaging demonstrated isotope in the AC, which is from 4 to 48 hours.

Normal values—Normal values were estimated in studies conducted using the same methods in our laboratory. For the definition of normal values, images had been obtained every 15 minutes during the first 2 hours and every 30 minutes during the subsequent 2 hours. The definition of delayed GE was based on the 5th percentile of pooled data using the same method (300kcal ^{99m}Tc-labeled egg meal) in 319 healthy volunteers: GE at 2h <25.0% and GE at 4h <76%. The definition of delayed CT for males (M) and females (F) was based on the 5th percentile of 220 healthy volunteers using the same method (¹¹¹In-charcoal-delayed release capsule): GC24h <1.3(F), 1.5 (M); GC48h <1.9 (F), 2.1 (M). The definition of slow AC t_{1/2} was >28.5 hours based on the 95% percentile from 36 healthy volunteers. The data and distribution for these healthy volunteers are included in Appendix Table 2.

Anorectal manometry and balloon expulsion—Maximum resting and squeeze anal pressures were the highest pressures recorded in the anal canal during resting or squeezing (17) and were expressed in mmHg. The amount of weight in grams required to facilitate expulsion of the rectal balloon was recorded and censored above 576 grams.

Diagnosis of rectal evacuation disorder was based on clinical examination findings by a single experienced gastroenterologist if confirmed by at least 1 of 2 criteria:

1. Abnormal balloon expulsion test (inability to expel the balloon from the rectum with <200g added) (22,23);
2. High resting anal sphincter pressure (maximum pressure >90 mmHg) (22,24,25).

The criteria were developed from a review of the published data for adults studied in Minnesota (25) and Iowa (24).

Statistical analysis—Data are summarized as mean $\pm$ SD overall and by GE and CT subgroups. Data from previous studies in healthy volunteers were used to specify normal limits (5th percentiles) in order to characterize delayed GE or CT in the patient cohort. The proportions (%) of patients outside these limits in each subgroup were calculated. The association of subgroup with demographic characteristics was assessed using the Kruskal-Wallis test (age and BMI), and Fisher's exact test (gender).

RESULTS

Participant Characteristics

The demographic characteristics of overall patients and the comparison for groups based on gastric and colonic transit studies are represented in Table 1. There were no significant differences in age or BMI in the different groups. Females outnumbered males in all subgroups with 82% of the overall cohort being women. No association of gender with subgroup based on gastric and colonic transit studies was observed. Among the 138 patients who had colonic transit measured (that is excluding the 11 with only GE measured), 3 had diabetes mellitus and none had thyroid disease or class II or III obesity (that is BMI>35kg/m²).

Evaluation of Gastric Emptying

Eleven patients underwent only GE test: 5 of these were delayed, 2 of which had the diagnosis of diabetic gastroparesis, and 6 were normal.

Evaluation of both Gastric and Colonic Transit

Among the 149 patients with nausea and/or vomiting: all had a GE test; 138 (93%) had CT measured at 24h (GC24hr); and 91 (61%) had the AC $t_{1/2}$ calculated. The summary data are provided in Table 2.

A comparison of groups based on gastric and colonic transit studies (n=138) is presented in Table 3: 11 (8%) had delayed GE with normal CT, 16 (11%) had normal GE with delayed CT, and 5 (3%) had delayed GE and CT. AC $t_{1/2}$ was slow in 9 patients, and 12 patients had clinical diagnosis of evacuation disorder among the group of patients with delayed CT.

Evaluation of Rectal Evacuation

Among 149 patients with nausea and/or vomiting, 77 (52%) were diagnosed with rectal evacuation disorder, including 68 patients with objective findings consistent with dyssynergic defecation (DD); in 9 patients, the diagnosis was based on digital examination including 7 with descending perineum syndrome (manifested as with excessive perineal descent of >3.5cm on perineal inspection and digital rectal examination while the patient was instructed to strain as though she/he was trying to defecate) and 2 with DD in whom ARM and BE results are not available. The criterion for excessive perineal descent of >3.5cm on all examinations conducted by a single gastroenterologist was based on the 10th to 90th percentile range of 0.3 to 3.5cm in 94 patients with "spastic" evacuation disorders due to puborectalis spasm or anismus (11). The majority (70 of 77) of these patients with evacuation disorders were therefore consistent with dyssynergic defecation. The vast majority of these patients with evacuation disorders had normal CT (58 of 70) and normal GE (71 of 77).

Combination of Delayed Colonic Transit and Disordered Evacuation

Among 21 patients with delayed colonic transit, there were 12 (52%) patients with diagnosis of evacuation disorder: DD in 11 patients, and descending perineum syndrome in 1 patient.

Impact on Patient Management

Among the 77 patients who had evacuation disorders, pelvic floor retraining program was recommended in 72 patients; 4 patients eventually underwent colectomy after the pelvic floor had been retrained with the aid of biofeedback. Fiber supplementation (n=18), prokinetics (n=23), laxatives (n=69), antiemetics (n=12) and other medications (n=17) were also prescribed to these patients according to their clinical characteristics. It is important to note that a single patient could receive multiple therapies.

Among the 21 patients with delayed CT, pelvic floor retraining therapy was prescribed in 11 with evacuation disorder. Fiber supplementation (n=4), prokinetics (n=4), laxatives (n=9), surgery (n=2), antiemetics (n=2) and other medications (n=2) were also prescribed to these patients in accordance with their clinical characteristics. In this analysis, a single patient may have received multiple therapies.

DISCUSSION

We report that patients presenting with chronic and/or recurrent nausea and/or vomiting have delayed CT and evacuation disorder. These disorders occur independently of generalized motility disorders which would be manifested with delayed GE in addition to the delayed CT. These observations from a single gastroenterologist's tertiary referral practice suggest that, when clinically indicated by careful history and examination findings, the diagnostic strategy in patients with chronic and/or recurrent nausea and/or vomiting should incorporate tests of colonic motility and rectal evacuation.

In the present cohort of 138 patients presenting with chronic and/or recurrent nausea and/or vomiting who underwent measurements of both GE and CT, more patients had delayed CT (n=21) compared to isolated delay in the GE of solids (n=16). This phenomenon was also observed in a previous multicenter study that evaluated transit with a wireless motility capsule (7). In addition, Bonapace et al. (26) used scintigraphic transit measurements in a single center cohort of patients with upper GI symptoms: they observed 31% had delayed CT, whereas 17% had both GE and CT delayed. However, that study did not appraise the cause for the delayed CT and, specifically, the potential role of the rectal evacuation dynamics as a cause of the delays in GE and CT (26). Our study shows that, in patients presenting with chronic nausea and/or vomiting at a tertiary care center, about 50% of the overall cohort and 50% of those with delayed CT have rectal evacuation disorder.

It may appear surprising that, in this tertiary referral practice involving 149 patients with recurrent and/or long-term nausea and/or vomiting, only 21 had delayed gastric emptying. However, this proportion is consistent with a previously reported cohort of 214 patients with upper gastrointestinal symptoms evaluated at Mayo Clinic over a three-year period (3). Thus, among the 214 patients, 14.4% of patients had delayed GE, and 13.3% of the patients with functional dyspepsia had delayed GE. The prevalence of delayed GE among community (rather than tertiary) patients from Olmsted County, Minnesota with upper gastrointestinal symptoms consistent with functional dyspepsia was not different from that of community controls (27). Thus, the proportion of participants with abnormal GE of solids (<70min [accelerated] or >150min [delayed] GE half-time) was 3 of 17 in the control group, 4 of 21 in the meal-unrelated dyspepsia group, and 2 of 14 in the meal-related dyspepsia group (27).

The mechanisms that are involved in nausea and vomiting in these patients require further consideration. Nausea and vomiting arise from stimulation of the chemoreceptor trigger zone or the vomiting center on the floor of the 4th ventricle (28). Vagal and spinal afferents convey sensations to induce nausea or vomiting symptoms from a variety of gastrointestinal as well as non-gastrointestinal organs, including the gall bladder, small and large bowel, and ureter in common conditions such as biliary, intestinal and renal colic. The observation that lower GI disorders are associated with nausea and vomiting can be explained by the induction of viscerovisceral reflexes that alter gastric functions. Indeed, these symptoms may be initiated by painless rectal distention in healthy volunteers (29), and upper GI symptoms are observed in patients with colonic disorders (30).

We believe it is significant that in 77 (52%) of our overall cohort of 149 patients with nausea and/or vomiting, in whom clinical evaluation identified clues suggestive of colonic dysfunction, there was evidence of rectal evacuation disorders, with the majority (70 of 77) having dyssynergic defecation. In this group with evacuation disorders, 12 were found to have delayed colonic transit, which was presumed to be secondary to the rectal evacuation disorder. These observations are consistent with a study by Shahid et al. (31) who reported the association of upper GI transit disorders with different types of constipation: delayed GE in 32% of patients with dyssynergic defecation and in 21% of patients with combined slow transit constipation and dyssynergic defecation. However, that study focused on overall upper GI symptoms, unlike our study appraised patients with presenting complaints of chronic and/or recurrent nausea and/or vomiting.

Our patients were managed mainly by pelvic floor retraining (n=72) and laxatives (n=69), reflecting their clinical and diagnostic characteristics. Similarly, in the 21 patients with delayed CT, pelvic floor retraining therapy (n=11) and laxatives (n=9) were the main recommendations.

The advantages of this study are the relatively large number of patients presenting with chronic or recurrent nausea and/or vomiting and the single-physician appraisal in a tertiary clinical practice with the use of standardized, validated tests for gastrointestinal and colonic transit and anorectal function tests.

The limitations of this study are its retrospective nature (which limits our ability to establish causality), incomplete data gathering (such as the lack of colonic transit measurement in 11 of the 147 patients), and the tertiary referral population which limits generalizability. Another limitation is the lack of anorectal tests in a cohort of patients with nausea and/or vomiting without suggestion of colonic motor disorder in order to appraise the frequency of defecation disorder in an unselected cohort (which would contrast with the highly selected patients in our study, of whom 55% had evidence of evacuation disorder). Another limitation is that the current analysis does not assess whether the identification and treatment of the colonic transit delay or evacuation disorder actually improved patients' nausea or vomiting. However, our study identifies a subset of patients presenting to a gastroenterologist with chronic and/or recurrent nausea and/or vomiting who have delayed colonic motility and evacuation disorders. .

In conclusion, in patients with chronic or recurrent nausea and/or vomiting, the history should screen for constipation, the clinical examination should seek evidence of colonic dysfunction or features to suggest an evacuation disorder (10), and diagnostic tests should include gastrointestinal and colonic transit measurements and anorectal function tests. These approaches may provide further information about the pathophysiology of the underlying problem and enhance the management of these patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

GE	gastric emptying
CT	Colonic transit
GC	geometric center
AC	ascending colon
TC	transverse Colon
DC	descending colon
RS	rectosigmoid colon
AC t1/2	ascending colon emptying half-time
BMI	body mass index

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Demographic characteristics of overall patients, patients with normal gastric emptying and colonic transit, patients with delayed gastric emptying and normal colonic transit, patients with normal gastric emptying and delayed colonic transit, and patients with delayed gastric emptying and colonic transit.

Table 1

Data Mean $\pm$ SD	N	Overall patients	N	Normal GE and CT	N	Delayed GE, normal CT	N	Normal GE, delayed CT	N	Delayed GE and CT
Age (years)	138	41.5 $\pm$ 15.5	106	41.5 $\pm$ 15.3	11	44.5 $\pm$ 19.1	16	38.2 $\pm$ 14.8	5	46.4 $\pm$ 14.2
BMI (kg/m ²)	130 [#]	23.2 $\pm$ 5.6	101	23.2 $\pm$ 5.1	10	26.6 $\pm$ 11.0	14	20.7 $\pm$ 2.9	5	22.6 $\pm$ 3.8
Female N (%)	138	113 (82%)	106	86 (81%)	11	9 (82%)	16	14 (88%)	5	4 (80%)

GE=gastric emptying, CT=colonic transit

[#] In 8 patients, BMI was not recorded in the episode of care when the tests were performed.

Table 2

Summary data on 149 patients (entire cohort) presenting with chronic or recurrent nausea and/or vomiting to a single physician in a tertiary care center, 1994-2012, and comparison of values with data of healthy volunteers (319 for gastric emptying, 220 for colonic transit, and 36 for ascending colon half emptying time).

	N (%)	Mean $\pm$ SD	5% cutoff for transit studies for healthy volunteers
GE at 2h (%)	149 (100%)	53.9 $\pm$ 21.3	<25%
GE at 4h (%)	149 (100%)	86.9 $\pm$ 15.2	<76%
GC at 24h	139 (93%)	2.3 $\pm$ 1.2	<1.3 (F), <1.5 (M)
GC at 48 h	16 (10%)	2.8 $\pm$ 1.1	<1.9 (F), <2.1 (M)
AC t _{1/2} (h)	91 (61%)	17.8 $\pm$ 11.2	>28.5

GE=gastric emptying, GC=geometric center, ascending colon half emptying time (AC t_{1/2}), F=females, M=males

Table 3

Comparison of groups based on gastric and colonic transit studies

Data Mean $\pm$ SD	N	Overall patients	N	Normal GE and CT	N	Delayed GE, normal CT	N	Normal GE, delayed CT	N	Delayed GE and CT
GE 2h (%)	149	53.9 $\pm$ 21.2	106	60.1 $\pm$ 18.0	11	20.6 $\pm$ 6.9	16	53.3 $\pm$ 14.4	5	26.2 $\pm$ 8.3
GE 4h (%)	149	86.9 $\pm$ 15.2	106	91.9 $\pm$ 8.1	11	60.0 $\pm$ 17.3	16	90.1 $\pm$ 7.2	5	61.4 $\pm$ 26.4
GC 24h	138	2.3 $\pm$ 1.1	106	2.5 $\pm$ 1.1	11	2.6 $\pm$ 1.1	16	1.0 $\pm$ 0.3	5	1.1 $\pm$ 0.1
GC 48h	16	2.8 $\pm$ 1.1	12	2.9 $\pm$ 0.9	0	-	3	2.7 $\pm$ 1.9	1	1.4
AC t _{1/2} (h)	91	17.8 $\pm$ 11.2	75	15.4 $\pm$ 9.3	5	17.3 $\pm$ 12.4	8	33.1 $\pm$ 10.2	3	37.6 $\pm$ 5.6

GE=gastric emptying, GC=geometric center, ascending colon half emptying time (AC t_{1/2}), CT=colonic transit