Published in final edited form as:

Clin Auton Res. 2013 August ; 23(4): 163–167. doi:10.1007/s10286-013-0193-y.

Gastric Emptying in Postural Tachycardia Syndrome: A Preliminary Report

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Abstract

Purpose—Autonomic neuropathy is widely recognized to be associated with upper gastrointestinal symptoms and abnormal (i.e., rapid or slow) gastric emptying. While patients with postural orthostatic tachycardia syndrome (POTS) may also have gastrointestinal symptoms, our understanding of gastric emptying disturbances in POTS is very limited. The objectives of this study were to evaluate the relationship between gastric emptying disturbances and gastrointestinal symptoms in patients with POTS.

Methods—We retrospectively reviewed the medical records of 22 well-characterized patients with POTS and upper gastrointestinal symptoms in whom autonomic (i.e., postganglionic sudomotor, cardiovagal, and adrenergic) functions and gastric emptying were evaluated using standardized techniques and scintigraphy respectively. Medical records were reviewed retrospectively to assess clinical features, gastric emptying, and autonomic functions.

Results—Over 70% of patients had nausea and/or vomiting, which was the most common GI symptom; other common symptoms were abdominal pain (59%), bloating (55%), and postprandial fullness/early satiety (46%). Over one-third of patients had abnormal (i.e., rapid [27%] or delayed [9%]) gastric emptying. Gastric emptying disturbances were not significantly associated with GI symptoms, autonomic symptoms or autonomic dysfunction.

Conclusions—Over one third of patients with POTS and gastrointestinal symptoms have abnormal, more frequently rapid than delayed gastric emptying. These findings need to be confirmed in a larger cohort of patients.

Keywords

dumping; dysautonomia; orthostatic intolerance; CASS; COMPASS

INTRODUCTION

In the gastrointestinal (GI) tract, autonomic dysfunction is primarily associated with abnormalities in motor and sensory function, which can manifest as a variety of symptoms

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On behalf of all authors, the corresponding author states that there is no conflict of interest.

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or syndromes (e.g., dysphagia, gastroparesis, chronic intestinal pseudo-obstruction, constipation, diarrhea, and fecal incontinence) [7, 9, 15, 22]. While vagal neuropathy can cause antral hypomotility and delay gastric emptying (GE) [5, 28], dysautonomia is also associated with rapid gastric emptying (GE) [15, 24], presumably due to sympathetic dysfunction.

Postural orthostatic tachycardia syndrome (POTS) is characterized by symptoms of orthostatic intolerance and an excessive orthostatic increase in the heart rate without concomitant orthostatic hypotension [31]. Some common symptoms (e.g., lightheadedness, presyncope and weakness) are attributed to cerebral hypoperfusion while others (e.g., palpitations, tremulousness, shortness of breath and chest pain) to autonomic overactivity [23, 31]. Gastrointestinal (GI) symptoms are also common; indeed, nearly 40% and 25% of adults with POTS have bloating and nausea respectively and a smaller proportion have other symptoms (i.e., vomiting, abdominal pain, constipation or diarrhea) [21, 31]. Abdominal pain, nausea, and vomiting are also common in children with POTS [3]. In addition, GI symptoms are more common in POTS patients with than without an autonomic neuropathy [2].

However, our understanding of GE disturbances in POTS is very limited. Three patients in the original report of POTS had abnormal gastrointestinal motility [24]. Both accelerated and delayed gastric emptying have been reported in adolescent POTS patients [3]. Prompted by clinical observations, this study reviewed the records of patients with POTS who were enrolled in autonomic research studies and also underwent assessment of GE at our institution. A better understanding of the relationship between gastrointestinal motility disorders and POTS is particularly important because GI symptoms may not only impair quality of life, but also limit oral fluid and salt intake, which is necessary to manage the disorder.

METHODS

We retrospectively reviewed the medical records, results of autonomic function and gastric emptying tests, and standardized questionnaires of patients with POTS who participated in autonomic research studies and who also underwent GE assessment by scintigraphy for GI symptoms between January 1998 and June 2011. There was no overlap between these patients and a previous study from our institution assessing gastric emptying in adolescents [3]. POTS was defined by an excessive orthostatic heart rate increment of at least 30bpm during head-up tilt associated with symptoms of orthostatic intolerance such as lightheadedness and faintness [20]. Stricter HR criteria (heart rate increment $\geq$ 40bpm) were used for adolescents [26]. A single physician reviewed and abstracted information from medical records. The study was approved by the Institutional Review Board at Mayo Clinic.

Autonomic function tests

Postganglionic sudomotor, cardiovagal, and adrenergic functions were assessed in all patients [18]. Postganglionic sudomotor function was tested in four areas (forearm, proximal lateral aspect of the leg, medial distal aspect of the leg, and proximal foot) with the quantitative sudomotor axon reflex test (QSART). Cardiovagal functions were assessed by evaluating heart rate responses to deep breathing and the Valsalva ratio. Adrenergic function was assessed using blood pressure and heart rate response to Valsalva maneuver and head-up tilt using beat-to-beat blood pressure recordings (FinometerTM) with sphygmomanometric validation.

Composite autonomic severity score (CASS)

CASS is a validated semiquantitative composite score of autonomic dysfunction graded from 0 to 10, composed of sudomotor (0–3), cardiovagal (0–3), and adrenergic subscores (0–4). The degree and distribution of autonomic dysfunction are evaluated by the total CASS score and subset scores [19].

Composite autonomic symptom score (COMPASS)

COMPASS is a validated instrument to quantitate autonomic symptoms across eleven domains of autonomic function; it is based on the Autonomic Symptom Profile, a questionnaire composed of 169 questions pertaining to autonomic nervous system function [29]. For this study, analysis of COMPASS was limited to the total score and GI subscores.

Gastrointestinal Symptoms

In addition to COMPASS, upper GI symptoms (i.e., nausea, vomiting, heart burn, regurgitation, postprandial fullness or early satiety, bloating, and abdominal pain) were recorded by reviewing medical records. A minimum duration of 6 months was required for symptoms to be considered present.

Gastric-Emptying Scintigraphy

GE was assessed by scintigraphy using a 300-kcal mixed meal containing ^{99m}Tc -sulfur colloid labeled eggs in all patients [6]. For our laboratory, normal values for GE are 11–39% at 1 hr, 40–76% at 2 hr, and 84–98% at 4 hr. Delayed emptying was defined as values below the lower limit of normal range at 2 or 4 hr, and rapid emptying was defined by values above the upper limit of normal range at 1 or 2 hr [30].

Statistical Analysis

Based on GE, patients were categorized into 3 groups: normal, delayed, and rapid. Univariate associations between various categorical variables and GE characterized as normal or rapid was assessed using Chi-square or Fisher's exact test as appropriate. Nonparametric (Spearman's rho) correlation analysis was used to assess correlations between GE and CASS score and subscores, COMPASS (total and GI subscores), and the heart rate increase during head-up tilt. Continuous data were expressed as mean $\pm$ SD, while discrete variables were shown as counts and percentages. For all tests, p values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS statistical software and version 11 for Windows (SPSS Inc. Chicago, Ill).

RESULTS

Twenty two patients with POTS in whom GE was evaluated were included in this study. The age of subjects ranged from 13 to 46 years (mean $\pm$ SD, 28.5 $\pm$ 10.9 years) and 19 (86%) were females. None of the patients had an underlying organic disorder that explained gastrointestinal or neurological symptoms and none were taking medications that could potentially affect GE during the GE study. Autonomic function and gastric emptying tests were performed within a timespan of 2 weeks in 15 and 3 months in 18 of 22 patients. The 4 patients with a longer time-interval between autonomic function and gastric emptying tests were documented to have orthostatic and gastrointestinal symptoms prior to both tests. The most frequent upper GI symptoms were nausea and/or vomiting (82%), abdominal pain (59%), bloating (55%), and postprandial fullness/early satiety (46%) (Tables 1 and 2). Patients reported nausea under varying circumstances, e.g., intermittent or continuous, associated with food intake or heat exposure or orthostasis or migraines and with or without vomiting. Three patients with nausea also reported that the head-up tilt study induced or

aggravated nausea. None of these patients had cyclic vomiting syndrome. Twenty one patients had an upper gastrointestinal endoscopy performed either at our institution or elsewhere after onset of symptoms. The endoscopy was normal in 17 patients and revealed minor abnormalities (i.e., esophagitis, gastritis, or diaphragmatic hernia alone) in the remaining patients. Five patients had an upper gastrointestinal series, which was normal in 4 patients and revealed a diaphragmatic hernia with gastroesophageal reflux in 1 patient.

Fourteen (64%) patients had normal, 2 (9%) had delayed, and 6 (27%) had rapid GE (Table 1, 2). The frequencies of various GI symptoms were not associated with rapid (versus normal) GE (Table 1). None of these patients had cyclic vomiting syndrome. Because only 2 patients had delayed GE, associations with GI symptoms were not evaluated.

CASS revealed autonomic impairment in 14 patients (61%), which was invariably mild, as indicated by a maximum total CASS score of 3 (Table 2). Nine patients had POTS alone (i.e., without adrenergic, sudomotor or vagal dysfunction). Ten patients (43%) had mild adrenergic dysfunction, 7 patients (32%) had sudomotor dysfunction and 4 (18%) had both. However, none had cardiovagal dysfunction.

There was no significant correlation between GE at 1 or 2hr and autonomic symptoms or autonomic dysfunction (i.e., heart rate increase on head-up tilt, CASS score and subscores, COMPASS, and GI subscores of COMPASS). Correlations between GE and COMPASS scores were based on data in 12 of 22 subjects who completed this instrument.

DISCUSSION

The main finding of this preliminary study is that approximately one in four patients with POTS had rapid GE. These observations extend a previous study which showed that adolescents with POTS with GE disturbances [3]. However, associations between gastric emptying with GI symptoms and separately with autonomic symptoms and autonomic function tests were not significant in this study.

Rapid GE was more common than delayed GE in this cohort. While the link between autonomic neuropathy and delayed GE is well recognized [5, 28], autonomic neuropathy is also associated with rapid GE [15]. Indeed, in one study of patients with autonomic neuropathy, rapid was more prevalent than delayed GE [15]. Since the sympathetic nervous system normally inhibits GI motility; excessive sympathetic activation, as occurs in some patients with POTS, would be anticipated to delay, not accelerate gastric emptying [17]. However, it is conceivable that rapid GE is the result of sympathetic denervation of the upper gastrointestinal tract. Indeed, the concept that POTS may represent a limited autonomic neuropathy was suggested in the first systematic description of this syndrome [24]. Features of sympathetic autonomic denervation in POTS include reduced norepinephrine spillover in the lower extremity, denervation supersensitivity in the lower extremity veins, and distal sudomotor denervation [13, 14, 24, 27]. Moreover, 20% of patients with POTS had cardiac sympathetic denervation, as evaluated by ¹²³I-Meta-iodobenzylguanidine (MIBG)-single photon emission computed tomography [12]. Also of interest, patients with neuropathic POTS had more GI symptoms than non-neuropathic POTS [2]. However, further studies to ascertain the prevalence of GE disturbances and GI autonomic dysfunctions, for example with the pancreatic polypeptide response to sham feeding as an index of vagal function and superior mesenteric arterial flow to evaluate sympathetic function, in larger cohorts of patients with POTS are necessary [8, 11].

Confirming previous studies, GI symptoms were common in patients with POTS [23]. However, symptoms were not useful for distinguishing between rapid and normal gastric emptying [4]. Hence it is necessary to assess GE to ascertain whether GE is normal, delayed

or rapid in patients with upper GI symptoms [1]. By delivering an excessive amount of nutrients and distending the small intestine, rapid GE can cause symptoms of functional dyspepsia (e.g., postprandial satiety, nausea, bloating, and fullness) and vasomotor symptoms [10, 15, 16, 25]. Moreover, rapid gastric emptying with dumping of nutrients into the small intestine may also exaggerate orthostatism in the postprandial state. In turn, rapid GE can be explained by one or more of the following mechanisms: impaired fundic relaxation and accommodation, greater antral contraction, or lower pyloric resistance [1].

This study was limited by its retrospective nature and the small number of patients. Moreover, although GE data and autonomic function tests were available for all patients, only 12 of 22 patients completed a COMPASS questionnaire.

In conclusion, 36% of patients with POTS in this cohort had delayed (9%) or rapid (27%) gastric emptying. However, associations between gastric emptying disturbances and symptoms and separately with autonomic dysfunction were not significant. These findings need to be confirmed and further evaluated in a larger cohort of patients with POTS.

Acknowledgments

This study was supported by USPHS NIH Grant P01 DK068055 and UL1 RR024150-01* from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and the NIH Roadmap for Medical Research. PL's contribution was supported in part by the NIH (NS 44233). WS is supported by K23NS075141.

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Table 1

Gastric emptying and reported frequency of gastrointestinal symptoms in patients with Postural orthostatic tachycardia syndrome.

Symptoms	Normal gastric emptying (N = 14)	Delayed gastric emptying (N = 2)	Rapid gastric emptying (N = 6)	Overall Totals (N = 22)
Nausea/Vomiting	12	1	5	18 (82%)
Bloating	8	2	2	12 (55%)
Post-prandial fullness/Early satiety	7	1	2	10 (46%)
Upper abdominal pain	5	1	2	8 (36%)
Lower abdominal pain	2	1	1	4 (18%)
Abdominal pain – unspecified	3	0	2	5 (23%)
Heart burn/Regurgitation	3	1	2	6 (27%)

The symptom totals in each column exceed the total number of subjects because some patients had more than one symptom.

Table 2

Gastric emptying (%), CASS scores, NE, and DHPG.

No.	Sex	Age	Type	GE1	GE2	GE4	CASS_Sudo	CASS_Vagal	CASS_Adren	CASS_Total	HR increase
1	F	39	Normal	32	58	94	0	0	0	0	34
2	F	34	Normal	10	41	85	0	0	0	0	45
3	F	18	Normal	19	55	86	0	0	0	0	34
4	F	34	Normal	36	74	99	0	0	0	0	67
5	M	30	Normal	26	52	98	1	0	0	1	40
6	F	44	Normal	32	67	91	0	0	0	0	44
7	F	37	Normal	35	58	99	1	0	1	2	70
8	F	33	Normal	23	62	92	0	0	0	0	48
9	F	46	Normal	10	55	94	0	0	1	1	55
10	F	28	Normal	34	55	95	0	0	0	0	78
11	F	16	Normal	19	58	89	0	0	1	1	54
12	F	21	Normal	31	65	93	0	0	1	1	60
13	F	18	Normal	21	52	91	0	0	1	1	47
14	F	19	Normal	24	57	94	0	0	0	0	38
15	F	43	Delayed	10	29	65	3	0	0	3	31
16	F	23	Delayed		32	64	1	0	2	3	44
17	F	43	Rapid	50	85	100	2	0	1	3	36
18	F	37	Rapid	32	86	100	1	0	1	2	82
19	M	16	Rapid	58	75	95	0	0	1	1	45
20	M	13	Rapid	60	84	100	0	0	1	1	51
21	F	18	Rapid	60	76	94	0	0	0	0	53
22	F	18	Rapid	46	72	88	1	0	0	1	30

GE1, gastric emptying (%) 1hr; GE2, gastric emptying (%) 2hr; GE4, gastric emptying (%) 4hr; CASS_Sudo, sudomotor CASS SCORE; CASS_Adren, adrenergic CASS SCORE; CASS_Vagal, vagal CASS SCORE; CASS_Total, total CASS SCORE; HR-I, heart rate increase during head-up tilt;