Gastric Electrical Activity Becomes Abnormal in the Upright Position in Patients With Postural Tachycardia Syndrome

*Shaista Safder, †Thomas C. Chelimsky, *Mary Ann O'Riordan, and *Gisela Chelimsky

ABSTRACT

Objectives: Some patients with functional abdominal pain report worsening of symptoms in the upright position. Many of these have a postural tachycardia syndrome (POTS). We investigated whether the electrical activity of the stomach changes during the upright portion of a tilt table test in patients with and without POTS.

Patients and Methods: All of the children undergoing autonomic testing were offered enrollment in this institutional review board–approved prospective study between October 2007 and January 2009. Electrogastrography was recorded 10 minutes in the supine position and during the entire upright portion of tilt. Children were divided into 2 groups: POTS and No-POTS. Findings were correlated with this grouping using Fisher exact test and either Student *t* test or Wilcoxon rank sum test as appropriate.

Results: Forty-nine patients participated (35 girls), with a mean age of 14.7 + 3.5 years, 25 with POTS and 24 without. The POTS and No-POTS groups did not differ in baseline normal gastric activity. The change from supine to standing showed a significant difference in the electrogastrographic tracing between the POTS and No-POTS groups ($P < 0.04$–0.09), best seen in channels 1 and 4. In particular, gastric activity became more abnormal in the upright position in the POTS group, whereas the opposite occurred in the No-POTS group.

Conclusions: The electrical activity of the stomach changes during the upright position in children with POTS, but not in children without this diagnosis. These changes could relate to their report of worsening pain in the upright position.

Key Words: electrogastrography, functional gastrointestinal disorders, motility, orthostatic intolerance, postural tachycardia syndrome, tilt table testing

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From the *Department of Pediatrics, and the †Department of Neurology, Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital and Case Medical Center, Cleveland, Ohio.

Address correspondence and reprint requests to Gisela Chelimsky, MD, 11100 Euclid Ave, Department of Pediatrics, University Hospitals of Cleveland, Cleveland, OH 44106 (e-mail: Gisela.chelimsky@UHhospitals.org).

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Functional gastrointestinal disorders (FGIDs) are defined as a variable combination of chronic or recurrent gastrointestinal symptoms, in the absence of structural or biochemical abnormalities (1). Although more than 90% of children with chronic abdominal pain are diagnosed as having an FGID (2,3), the pathophysiology of FGIDs remains elusive. Interestingly, FGIDs share many symptoms with a seemingly distant disorder of cardiovascular autonomic regulation, postural tachycardia syndrome (POTS). POTS is characterized by an orthostatic rise in heart rate accompanied by symptoms of orthostatic intolerance, such as dizziness, fatigue, nausea, and light-headedness. When carefully evaluated, these subjects also report frequent gastrointestinal symptoms such as nausea, vomiting, and bloating (4,5). In parallel, recent reports have described non-gastrointestinal symptoms such as dizziness, headaches, and light-headedness in patients with FGID (6,7). Not only is the overlap of symptoms between the 2 groups intriguing but also the 2 diagnoses (POTS and FGID) often overlap in the same subject. Finally, improvement of the gastrointestinal symptoms often occurs with treatment that targets orthostatic intolerance (8).

Diverse pathophysiological mechanisms appear to contribute to FGIDs, including altered motility, visceral hyperalgesia, brain–gut disturbances, genetic and environmental factors, and psychosocial factors, among many. In support of a role for motility, patients with functional dyspepsia demonstrate abnormalities in electrogastrography (EGG) and antroduodenal motility studies (9). Similar findings are found in children, who have either slow gastric emptying or abnormal EGG tracing (10,11). However, no physiological or motility study to date has attempted to elucidate the preponderance of symptoms in the upright position and the responsiveness of these symptoms to improved orthostatic tolerance, or attempted to link autonomic control of the splanchnic circulation with the symptom mechanism. The purpose of the present study was to begin an investigation of the differences in the physiological state of the gastrointestinal tract in the supine and upright positions. We chose EGG because it is a noninvasive measure of gastric electrical activity that can easily be performed during a tilt table study. We studied children with FGID in the supine and upright positions and compared children with POTS to those without.

The main question that we tried to answer in the present study was whether there were changes in electrical activity of the stomach in subjects with orthostatic intolerance more than in subjects without it as determined by tilt table testing, and whether tilt-EGG has potential as a diagnostic tool for patients with FGIDs in the setting of orthostatic intolerance.

PATIENTS AND METHODS

Study Design

A prospective University Hospitals Case Medical Center institutional review board–approved study was conducted from

October 2007 to January 2009 at the autonomic laboratory. All of the children undergoing autonomic testing were offered enrollment in the study. We excluded children with a known organic gastrointestinal disease or genetic/metabolic abnormality, although 2 patients who were enrolled were later found to have an organic disorder (the first eventually had small bowel Crohn disease—but had no gastrointestinal symptoms at the time of testing—and the second had Behcet disease, having the only autonomic test in our cohort to be read as an "unusual study" because of supine hypotension posttilt without POTS). The referring services for the autonomic testing included gastroenterology (20.5%), neurology/neurosurgery (20.5%), cardiology (20.5%), primary care providers (36%), and genetic/metabolic service (1.5%). Many of the patients were referred by the department of pediatric gastroenterology to evaluate dysautonomia as a possible cause for their gastrointestinal complaints after organic disorders had been excluded. The remainder was referred for evaluation of dysautonomia for presenting symptoms such as dizziness, syncope, migraines, and hyperhidrosis. Patients underwent autonomic testing in conjunction with EGG supine and upright during the tilt test. All of the subjects that had any abdominal pain as part of their symptoms were evaluated by pediatric gastroenterology as part of the multidisciplinary autonomic clinic where most of the patients were seen after the testing.

The tilt table test is performed by having the subject supine for 20 minutes on a motorized tilt table before an upright tilt to 70°. Continuous blood pressure (BP) and heart rate (HR) are monitored noninvasively in the supine position for the last 3 minutes supine, and then upright for 30 minutes, or up to 40 minutes when the subject had a history of syncope. Patients were reclined if they developed presyncope. Four leads were placed on the skin. The normal vasomotor response to the tilt test is a decrease in diastolic BP of <10 mmHg (diastolic usually increases by approximately 5 mmHg), in systolic BP of <20 mmHg, and an HR increase of <30 bpm (12). EGG was recorded using a Digitraper-EGG (Alpine, Stockholm, Sweden) for 10 minutes in the supine position and during the entire upright portion of tilt.

The data obtained from the EGG recording were derived from the 4 standard recording channels in the recumbent and upright positions for each patient. The leads were placed as shown in Figure 1. Data were analyzed for the percent of time of recording

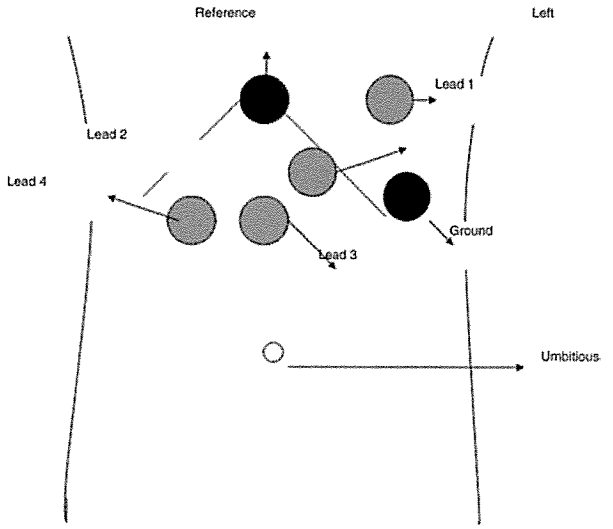

FIGURE 1. Location of the EGG leads in the subjects. EGG = electrogastrography.

that the subject demonstrated normal gastric electrical activity, bradygastria, tachygastria, and arrhythmia for all of the recording channels. The Alpine Digitraper-EGG device produces a computer reading that calculates the percent of each type of electrical activity. The definition of tachygastria is a frequency of 3.5 to 7.0 cpm, bradygastria of 1.0 to 2.5 cpm, and normal gastric activity of 2.5 to 3.5 cpm (13).

To answer our question regarding changes in electrical activity based on orthostatic intolerance during the tilt test, the subjects were divided into 2 groups: POTS and No-POTS. The No-POTS group could include children with syncope (n = 7). The designation of POTS was made based on an HR rise >30 bpm during the first 10 minutes of the tilt up position associated with symptoms of orthostasis. The objective was to determine whether patients with POTS demonstrate altered EGG measurements when going from supine to upright compared with patients without POTS. This was done in 2 stages. The first stage used a priori, non–data-driven definitions of change for all of the EGG channels for all measures as a screen for potentially fruitful measures. The second used data-driven cutpoints in the distribution of change measures to maximize the difference between POTS and No-POTS for those measures identified in the first stage. For the first stage, the change from lying to standing was categorized in the following manner; no change was designated as 0 ± the standard error (SE) of the respective supine measurement, a negative change was defined as <0−SE, and a positive change was defined as >0 + SE.

Analyses were done for all 4 of the channels for the percentage of normal gastric activity, percent bradygastria, percent tachygastria, and percent of gastric arrhythmia from the total recording time. In the first stage, Fisher exact test was used to determine the association of change in electrical activity of the stomach between the supine and upright position in the POTS group versus the No-POTS group. A Cochran-Armitage trend test was used to look for directional significance. This is more informative with 3 ordinal categories: negative, none, and positive.

The second part of the data analysis was a sensitivity analysis. Distributions of the differences were examined visually for evidence of bimodality, and to identify potential cutpoints. The Fisher exact test was used to determine the association of change in electrical activity of the stomach based on all of the potential cut points in the POTS group versus the No-POTS group, and the results for the most significant associations were reported. Fisher exact test and either Student *t* test or Wilcoxon rank sum test were used for other 2-group comparisons.

RESULTS

Of the 57 enrolled subjects, 8 were excluded because of a technically inadequate recording in the upright position. Thus, 49 subjects completed the study. Twenty-five subjects fulfilled the criteria for POTS and 24 did not. The mean age was 14.7 ± 3.5 years (POTS group: 14.3 ± 2.4; No-POTS group: 15 ± 4.1). Thirty-five (71%) were girls (49% girls in POTS group and 51% girls in No-POTS group) and 14 (29%) were boys. The gastrointestinal symptom complexes are summarized in Table 1. There was no statistical difference between the prevalence of dyspepsia symptoms in the POTS versus the No-POTS group ($P = 0.28$). There was no difference between the POTS and No-POTS groups in relation to baseline percent of normal gastric activity. In the POTS group, 18 subjects had <70% of normal gastric activity on baseline supine electroencephalography versus 14 subjects in the No-POTS group ($P = 0.38$).

The most promising measurements in the electrogastrographic tracing between the POTS and No-POTS groups with regard to change from supine to standing were in channel 1

TABLE 1. Summary of gastrointestinal symptom complex in each group

	POTS	No-POTS
Dyspepsia	11	7
Constipation	2	2
Gastroesophageal disease	2	1
Irritable bowel syndrome	4	5
Functional abdominal pain	2	1
No gastrointestinal complaints	10	11

A few subjects had 2 groups of symptoms. POTS = postural tachycardia syndrome.

($P = 0.04$), and channel 4 ($P = 0.08$) for normal electrical gastric activity, in channel 4 for bradygastria ($P = 0.07$), in channel 1 for tachygastria ($P = 0.04$), and in channel 1 for gastric arrhythmia ($P = 0.09$) based on the Cochran-Armitage test for trend. In the POTS group, gastric activity becomes more abnormal in the upright position, whereas the opposite is true in the No-POTS group (Table 2). The raw data are described in Figure 2 for POTS and No-POTS groups.

When the results were analyzed using data-derived cut-points that best separated the POTS and No-POTS groups with regard to electrogastrographic changes, more significant changes were observed with several at $P < 0.05$ (Table 3).

DISCUSSION

This is the first study of posturally mediated changes in gastric electrical activity. We and others have previously reported the presence of POTS in patients with FGIDs (7). Equally well recognized is the presence of abdominal symptoms compatible with a diagnosis of FGID in patients with POTS (4). To our knowledge however, the concept that FGID symptoms could themselves represent an orthostatic process has not been entertained, and the gastric electrical changes observed in the present study could be the first measurement of a physiological abnormality potentially leading to upper gastrointestinal tract symptoms in some patients.

Our results do not directly explain the pathogenesis of the gastrointestinal symptoms. However, one could easily envision that an increase in gastric arrhythmia or bradygastria associated with decreased normal electrical activity would lead to delayed gastric emptying or inadequate gastric accommodation (10) accounting for nausea, abdominal discomfort, or vomiting. The EGGs of patients with gastric accommodation or emptying problems typically demonstrate the abnormalities we demonstrate here (14). This could explain why the abdominal complaints of some of our patients are maximized in the upright position or with exercise, and respond to treatment aimed at their orthostatic symptoms (15). The findings of increased bradygastria and tachygastria in children with POTS in channels 1 (fundus) and 4 (antrum) further support the possibility of either decreased fundic accommodation and/or delayed gastric emptying.

A recent study demonstrated that patients with FGID experiencing abdominal pain and nausea often demonstrate abnormal gastric emptying. These investigators found no correlation between gastric emptying time and rate of increase in heart rate in their tilt table test. However, the present study did not address the issue of whether orthostatic intolerance could contribute to symptom pathogenesis (16). The emphasis was on correlation rather than on physiology, because the gastric emptying study and tilt study were done on different days, and there was no attempt to investigate any link between orthostatic stress and gastric function. Finally, the test of gastric emptying does not evaluate gastric accommodation, which may be playing a much more important role in symptom pathogenesis.

Several mechanisms could explain how a change in position could induce EGG abnormalities. We have previously described 3 groups of children with FGID based on response to autonomic testing and replication of symptoms during tilt. We had found a group who had mainly POTS and replicated the gastrointestinal symptoms during the upright portion of the tilt test that we labeled "gastrointestinal vasomotor dysautonomia," a second group with more generalized autonomic dysfunction that did not replicate the symptoms (we called them "gastrointestinal neuropathic dysautonomia"), and a third group of children who have FGID and a normal response to autonomic testing. Along these lines, one may consider a direct vascular explanation, with abnormal splanchnic blood flow perhaps explaining the change in gastric function, a

TABLE 2. Trend of changes in electrogastrographic activity in POTS and No-POTS subjects in supine and upright positions

	Negative change (%)	No change (%)	Positive change (%)
Normal, channel 1			
No-POTS	8/24 (33.3)	4/24 (16.7)	12/24 (50.0)
POTS	15/25 (60.0)	4/25 (16.0)	6/25 (24.0)
Normal, channel 4			
No-POTS	11/24 (45.8)	4/24 (16.7)	9/24 (37.5)
POTS	18/25 (72.0)	2/25 (8.0)	5/25 (20.0)
Bradygastria, channel 4			
No-POTS	10/24 (41.7)	5/24 (20.8)	9/24 (37.5)
POTS	4/25 (16.0)	7/25 (28.0)	14/25 (56.0)
Tachygastria, channel 1			
No-POTS	5/24 (20.8)	6/24 (25.0)	13/24 (54.2)
POTS	2/25 (8.0)	2/25 (8.0)	21/25 (84.0)
Arrhythmia, channel 1			
No-POTS	13/24 (54.2)	3/24 (12.5)	8/24 (33.3)
POTS	8/25 (32.0)	3/25 (12.0)	14/25 (56.0)

POTS = postural tachycardia syndrome.

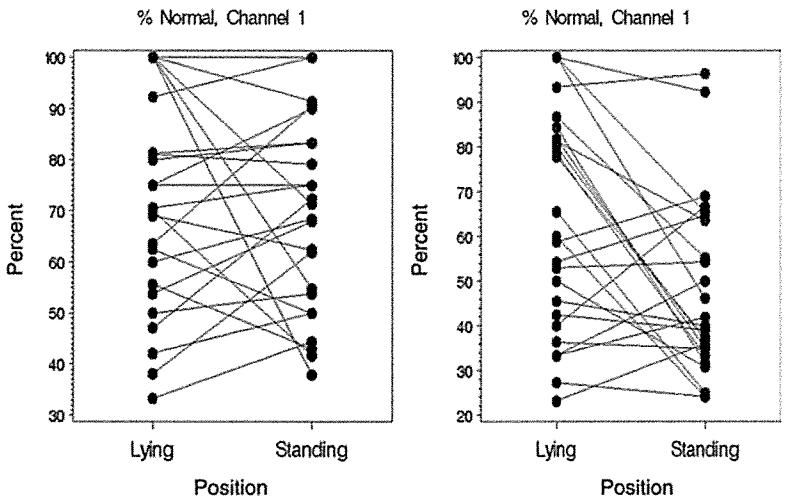

FIGURE 2. Changes in percent of normal gastric activity in subjects with No-POTS (left) and POTS (right) when they are tilted. POTS = postural tachycardia syndrome.

neuropathic explanation mediated through some type of neural reflex, or a pharmacological mechanism involving nitric oxide or other vasoactive molecules. These mechanisms are not mutually exclusive (8).

In addition, a vascular mechanism may occur directly, through some type of local vasodilator resulting in excessive pooling and distention of the mesenteric vasculature, with EGG findings being secondary to the vascular abnormalities, or through some type of sympathetically mediated reflex affecting gastric electrical activity first and vessels second.

Studies by Stewart et al (17) may shed some light on these possibilities. They have described 3 types of subjects with POTS based on blood perfusion to the lower extremities and splanchnic beds. "Low-flow POTS" includes patients with absolute hypovolemia and abnormal local vascular regulatory mechanisms. "High-flow POTS" with either normal or increased blood volume have inadequate vasoconstriction in the lower extremities in all of the positions. "Normal-flow POTS" is the only group with position-dependent abnormalities, being normovolemic and healthy appearing at rest, but demonstrating thoracic hypovolemia with splanchnic hypervolemia in the upright position in the face of decreased lower-body blood flow (17). One could speculate that this last group could correspond to our patients with position-dependent symptoms of FGID, which we have labeled "gastrointestinal vasomotor dysautonomia." The splanchnic hyperemia is not well understood, but Stewart hypothesizes that peripheral vasoconstriction compensates for blood pooling in the abdomen because of either selective splanchnic denervation or overexpression of locally mediated vasoactive substances like nitric oxide, substance P, or vasoactive intestinal polypeptide antagonizing the sympathetic vasoconstriction during the orthostatic stress (17). In this light, it is of interest that children with posturally dependent gastrointestinal symptoms seem to respond better to fluid expansion treatment and low-dose fludrocortisone (8).

A primary neuropathic mechanism could also account for our findings. Both the gastric pacemaker and the splanchnic vascular

TABLE 3. Summary of change in gastric electrical activity with position in subjects with POTS and No-POTS

	Cutoff points		*P*
% Normal gastric activity in channel 1	≤−2.0	>2.0	
No-POTS	8/24 (33.3)	16/24 (66.7)	0.03
POTS	16/25 (64.0)	9/25 (36.0)	
% Tachygastria in channel 1	≤0.3	>0.3	
No-POTS	11/24 (45.8)	13/24 (54.2)	0.02
POTS	4/25 (16.0)	21/25 (84.0)	
% Arrhythmia in channel 1	≤0.3	>0.3	
No-POTS	15/24 (62.5)	9/24 (37.5)	0.06
POTS	9/25 (36.0)	16/25 (64.0)	
% Normal gastric activity in channel 4	≤0	>0	
No-POTS	11/24 (45.8)	13/24 (54.2)	0.01
POTS	20/25 (80.0)	5/25 (20.0)	
% Bradygastria in channel 4	≤−1	>−1	
No-POTS	9/24 (37.5)	15/24 (62.5)	0.09
POTS	4/25 (16.0)	21/25 (84.0)	

POTS = postural tachycardia syndrome.

beds are under neural control. A peripheral process such as a focal autonomic neuropathy or a central nervous system process such as dysregulation of the controlling central autonomic network could produce these abnormalities. In this regard, it is of interest that patients with POTS (6) and at least a subset of subjects with FGID (18) frequently harbor an autonomic neuropathy. Finally, a vasoactive agent such as nitric oxide is likely to be playing a role somewhere in the chain of events leading to abdominal pain and nausea, but it appears less likely to constitute the primary abnormality.

The present exploratory study demonstrates that with upright position on a tilt table study, abnormal gastric electrical activity increases in patients with POTS, whereas it decreases in patients without POTS. These changes could reflect vasomotor, neuropathic, or pharmacological abnormalities that affect gastric function in the upright position. In addition, these abnormalities could contribute to some of the gastrointestinal symptoms in the upright position in patients with POTS. Because POTS and FGID are closely associated, these findings may well apply in some patients with FGID as well. Additional studies will establish whether these electrical changes bear any relation to measures of splanchnic perfusion. It will also be important to know whether EGG normalizes when symptoms resolve after treatment aimed at orthostatic intolerance. If so, tilt-EGG could become an important diagnostic tool.

REFERENCES

1. Drossman DA. Introduction. The Rome Foundation and Rome III. *Neurogastroenterol Motil* 2007;19:783–6.
2. Stickler GB, Murphy DB. Recurrent abdominal pain. *Am J Dis Child* 1979;133:486–9.
3. Stanghellini V, Ghidini C, Maccarini MR, Paparo GF, Corinaldesi R, Barbara L. Fasting and postprandial gastrointestinal motility in ulcer and non-ulcer dyspepsia. *Gut* 1992;33:184–90.
4. Sandroni P, Opfer-Gehrking TL, McPhee BR, Low PA. Postural tachycardia syndrome: clinical features and follow-up study. *Mayo Clin Proc* 1999;74:1106–10.
5. Kanjwal Y, Kosinski D, Grubb BP. The postural orthostatic tachycardia syndrome: definitions, diagnosis, and management. *Pacing Clin Electrophysiol* 2003;26:1747–57.
6. Al-Shekhlee A, Lindenberg JR, Hachwi RN, Chelimsky TC. The value of autonomic testing in postural tachycardia syndrome. *Clin Auton Res* 2005;15:219–22.
7. Sullivan SD, Hanauer J, Rowe PC, Barron DF, Darbari A, Oliva-Hemker M. Gastrointestinal symptoms associated with orthostatic intolerance. *J Pediatr Gastroenterol Nutr* 2005;40:425–8.
8. Safder S, Chelimsky TC, O'Riordan MA, Chelimsky G. Autonomic testing in functional gastrointestinal disorders: implications of reproducible gastrointestinal complaints during tilt table testing. *Gastroenterol Res Pract* 2009;2009:868496.
9. Jacob G, Costa F, Shannon JR, et al. The neuropathic postural tachycardia syndrome. *N Engl J Med* 2000;343:1008–14.
10. Friesen CA, Lin Z, Hyman PE, et al. Electrogastrography in pediatric functional dyspepsia: relationship to gastric emptying and symptom severity. *J Pediatr Gastroenterol Nutr* 2006;42:265–9.
11. Leung MW, Wong BP, Chao NS, Chung KW, Kwok WK, Liu KK. Electrogastrography in the management of pediatric functional dyspepsia and motility disorder. *J Pediatr Surg* 2006;41:2069–72.
12. Schondorf R, Low P. Idiopathic postural orthostatic tachycardia syndrome: an attenuated form of acute pandysautonomia? *Neurology* 1993;43:132–6.
13. Pfister CJ, Hamilton JW, Nagel N, Bass P, Webster JG, Tompkins WJ. Use of spectral analysis in the detection of frequency differences in the electrogastrograms of normal and diabetic subjects. *IEEE Trans Biomed Eng* 1988;35:935–41.
14. Koch K. Electrogastrography: physiological basis and clinical application in diabetic gastropathy. *Diabetes Technol Ther* 2001;3:51–62.
15. Chelimsky G, Chelimsky T. Familial association of autonomic and gastrointestinal symptoms. *Clin Auton Res* 2001;11:383–6.
16. Chitkara DK, Camilleri M, Zinsmeister AR, et al. Gastric sensory and motor dysfunction in adolescents with functional dyspepsia. *J Pediatr* 2005;146:500–5.
17. Stewart JM, Medow MS, Glover JL, Montgomery LD. Persistent splanchnic hyperemia during upright tilt in postural tachycardia syndrome. *Am J Physiol Heart Circ Physiol* 2006;290:H665–73.
18. Chelimsky G, Boyle JT, Tusing L, Chelimsky TC. Autonomic abnormalities in children with functional abdominal pain: coincidence or etiology? *J Pediatr Gastroenterol Nutr* 2001;33:47–53.