Comorbid Conditions Do Not Differ in Children and Young Adults with Functional Disorders with or without Postural Tachycardia Syndrome

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Objective To determine if several multisystem comorbid conditions occur more frequently in subjects with tilt-table defined postural tachycardia syndrome (POTS) compared with those without.

Study design Retrospective chart review of 67 subjects aged 6-24 years, referred to a tertiary care neurogastroenterology and autonomic disorders clinic for a constellation of functional gastrointestinal, chronic pain, and autonomic complaints. All patients underwent formal autonomic testing, Beighton scores assessment for joint hypermobility (0-9), and fibromyalgia tender points (0-18) (43 subjects).

Results Twenty-five subjects (37%) met tilt table criteria for POTS. The median age of 16 years (range, 12-24 years) in the POTS group differed from 15 years (range, 6-21 years) in the no-POTS group ($P = .03$). Comorbidities including chronic fatigue, sleep disturbances, dizziness, syncope, migraines, functional gastrointestinal disorders, chronic nausea, fibromyalgia, and joint hypermobility did not differ between groups. All subjects with fibromyalgia by tender point-examination had a Beighton score ≥ 4 ($P = .002$).

Conclusions Comorbid conditions are equally prevalent in children and young adults with and without tilt-table defined POTS, suggesting that POTS itself is not a cause of the other comorbidities. Instead, POTS likely reflects another comorbid condition in children with functional disorders. Dizziness and syncope, classically associated with POTS, are not predictive of a diagnosis of POTS by tilt table, a test that is still required for formal diagnosis. These results suggest a paradigm shift in the concept of POTS as the physiological basis of many functional symptoms. *(J Pediatr 2015;167:120-4)*.

Postural tachycardia syndrome (POTS) is characterized by an increased heart rate (HR) while upright without a significant drop in blood pressure (BP), and associated orthostatic symptoms such as dizziness, palpitations, and lightheadedness. It affects females more than males.[1] Although the definition is based on increased HR with orthostatic symptoms while upright, patients with POTS frequently voice complaints beyond what one might attribute to the cardiovascular arena such as dizziness, lightheadedness, fatigue, etc, clearly reflecting other comorbidities.[2,3] We have previously reported that POTS is associated with sleep complaints in the majority of subjects, gastrointestinal symptoms in about 80%, severe fatigue (60%), and headaches with migraine features (about 45%).[3] Patients and physicians often focus on the presence of POTS as the etiology of the constellation of comorbid symptoms, and are discouraged when the tilt test fails to diagnose POTS, interpreting this finding as an absence of any etiology for their systemic symptoms. On this background, we set out to determine whether subjects referred to a tertiary neurogastroenterology and autonomic disorder clinic reported more comorbid symptoms in the presence compared with the absence of POTS. The aim of this study was to answer this question by determining if comorbidities such as functional gastrointestinal disorders (FGIDs), fibromyalgia, migraine, sleep problems, dizziness, nausea, and other complaints are more prevalent in adolescents and young adults with POTS than those without. We hypothesized that if these comorbidities relate to POTS per se, the number of comorbidities in the POTS group would exceed the number of comorbidities in the group without POTS. However, if POTS is just 1 of many co-equal comorbid disorders, its presence would not influence the remaining comorbid burden.

Methods

This was a cross-sectional, Institutional Review Board-approved review of retrospective data of 67 pediatric and young adult patients seen in the outpatient Pediatric Neurogastroenterology and Autonomic Disorders Clinic at Children's

BP	Blood pressure
FGID	Functional gastrointestinal disorder
HR	Heart rate
OI	Orthostatic intolerance
POTS	Postural tachycardia syndrome

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Hospital of Wisconsin. All subjects were new patients consecutively evaluated by a gastroenterology-neurology physician team between February 2012 and February 2013. In this interdisciplinary clinic, subjects undergo a detailed review of systems, general and neurologic examination, fibromyalgia tender point examination,[4] and hypermobility evaluation through a Beighton score.[5] Because this was a retrospective chart review, not every subject had all comorbidities recorded in the chart. Although the most likely possibility is that the absence of recorded symptoms is due to a negative review of systems, rather than assuming this fact, we performed the statistical analysis based on the total number of subjects in which the presence or absence of the specific symptom was documented. There was no significant difference between missing values in the 2 groups.

We collected data on the following information from systematic chart reviews as was previously described[6]: (1) demographics and medical history; and (2) comorbid symptoms including chronic fatigue, sleep disturbances, dizziness, syncope, chronic nausea, gastrointestinal symptoms with FGID diagnoses based on fulfillment of Rome III criteria, and migraine headaches as documented in medical records by the neurologist per the 1997 International Headache Society pediatric migraine criteria.[7] Of the 67 subjects included and classified according to the pediatric 2006 Rome III criteria for FGIDs,[8] 59 (88%) met at least 1 pediatric Rome criterion. We chose the requirement for subjects to meet at least 1 Rome criterion in order to meet the current definition of a FGID. We also evaluated if they met >1 Rome criteria (presumably worse disease), to determine if subjects with POTS may have more gastrointestinal symptoms than those with no-POTS. We defined sleep disturbance by 2 or more of the following 3 criteria: (1) time to fall asleep >30 minutes; (2) frequent night-time awakenings; and (3) feeling unrefreshed in the morning. A diagnosis of chronic fatigue required at least 6 months duration,[9] and chronic nausea was defined as bothersome nausea several times per week for a minimum of 2 months as is the duration used for all pediatric Rome criteria.[8] We defined dizziness as recurrent dizziness in upright sitting/standing position, and syncope as minimum 3 episodes of temporary loss of consciousness in a lifetime. We further reviewed physician-performed hypermobility scores based on the validated 1999 Beighton scale (0-9) (performed in 43 subjects)[5] and fibromyalgia tender point scores (0-18) (43 subjects) as defined by the 1990 American College of Rheumatology criteria.[4] Hypermobility was defined as having a Beighton score ≥4. Subjects were considered having fibromyalgia if they had 11 or more tender points rating of pain present on a numeric pain rating scale of ≥4/10.

Autonomic Function Tests

Autonomic testing is performed as a clinical tool in our practice.[10] Patients underwent a tilt table test with the patient supine for 10 minutes on a motorized tilt table before head-up tilt to 70° for 30 minutes (or 40 minutes if there is history of syncope). Continuous beat-to-beat BP and HR were monitored during the study. POTS was defined as an increase in HR >40 bpm during the first 10 minutes of the head-up tilt test, without a sustained decrease in BP (drop in diastolic BP >10 mm Hg or systolic BP >20 mm Hg) in the presence of symptoms of orthostatic intolerance (OI) while upright, such as dizziness, lightheadedness, tunnel vision, nausea, etc.[11,12]

Statistical Analyses

Fisher exact test was used to compare categorical variables. The Mann-Whitney test was used to compare continuous variables. Statistical analysis was performed with SPSS v 21 (SPSS Inc, Chicago, Illinois). A P value of <.05 was considered significant.

Results

In the entire cohort, 89% were Caucasians, 2% African American, 3% Hispanic, and 6% other, with 69% female. POTS criteria were met in 25 subjects (37%). There was no significant difference in sex or race distribution between groups. Although estimating the time of symptom onset was not very well defined as parents may have poor recall (some parents reported onset in infancy), the POTS group (N = 19) described a median time of 13 (range 4-16) years and the non-POTS (N = 31) of 11 (range 0-18) years for onset of symptoms (P = .059). The median age in the POTS group was 16 years (range 12-24 years of age) compared with 15 years (range 6-21 years of age) in the no-POTS group (P = .03). Five (7%) were adults (19-24 years). By definition, the peak HR while upright was significantly higher in the POTS group (median 120 [range 88-163] bpm) vs the no-POTS group (median 105 [range 61-147] bpm) ($P \leq .001$), and the baseline HR prior to tilt was not significantly different between the groups (POTS = median 78 bpm, range 40-106 bpm; no-POTS = median 78 bpm, range 40-129 bpm). One subject in the no-POTS group had a baseline HR >120 bpm, but the increase in HR while upright was <40 bpm.

The most common chief complaints included headaches/migraine (51%), dizziness (34%), abdominal pain (27%), nausea (22%), and fatigue (15%). Many subjects had more than 1 chief complaint.

Comorbidities in the POTS and no-POTS groups did not differ (**Figure 1**). **Figure 2** summarizes the number of comorbidities per subject per group. When we included the subject with baseline HR >120 bpm into the POTS group, the prevalence of comorbidities in the 2 groups was not significantly different. Of the subjects with POTS, 7 (33%) fainted later during the tilt. To understand if the presence of any orthostatic disorder might be associated with a higher burden of comorbidities, we grouped subjects with other orthostatic disorders such as orthostatic hypotension (n = 3), syncope without POTS (n = 6), or POTS (n = 25) and compared them with the subjects without an orthostatic disorder. These 2 groups (orthostatic vs nonorthostatic) still showed no significant difference in