Carol Rees Parrish, MS, RDN, Series Editor

The POTS (Postural Tachycardia Syndrome) Epidemic: Hydration and Nutrition Issues

John K. DiBaise

Tisha N. Lunsford

Lucinda A. Harris

Postural tachycardia syndrome (POTS) is one of the most common causes of orthostatic intolerance and is being increasingly recognized in clinical practice. A variety of non-orthostatic symptoms including gastrointestinal (GI) symptoms are also reported commonly in patients with POTS and pose a considerable management challenge, occasionally resulting in problems maintaining hydration and nutrition. The available evidence suggests that GI dysmotility occurs in POTS and may represent an important pathogenic mechanism. At present, the evaluation and treatment of POTS remains largely empirical. General lifestyle modifications to treat POTS may lead to improvement in both GI and non-GI symptoms, at least in the milder form of POTS. Symptoms refractory to these measures should prompt further diagnostic evaluation and appropriate dietary, pharmacologic and nutrition support management options. This review includes a brief background on POTS, conditions associated with POTS, and an overview of management including nutrition and hydration support.

CASE STUDY 1

A 20-year-old woman presented to clinic for further evaluation of a several year history of fullness and epigastric discomfort associated with eating and irregular bowel habits. Her weight was stable. She also described frequent migraine headaches, episodic palpitations and lightheadedness with progressively increasing episodes of syncope. A systems review was notable for profound fatigue, dry eyes and mouth and intermittent flushing and pruritus. These symptoms had impacted her ability to attend college. A previous GI evaluation demonstrated negative Helicobacter pylori urea breath test, routine labs including thyroid studies, pancreatic enzymes and celiac antibodies, and hepatobiliary ultrasound. Previous treatment with a proton pump inhibitor was without benefit. Additional testing included upper endoscopy and gastric emptying scintigraphy which were normal and autonomic testing including head-up-tilt testing which showed changes consistent with POTS, but without evidence of autonomic neuropathy. Further testing for mast cell activation was normal. Lifestyle modifications

John K. DiBaise, MD Professor of Medicine Tisha N. Lunsford, MD Assistant Professor of Medicine Lucinda A. Harris, MD Associate Professor of Medicine Mayo Clinic Scottsdale, AZ

including increased oral fluid (2-2.5 L/day) and salt intake (10 g/day), exercise training, and use of support garments provided some benefit, but the syncope and the GI symptoms persisted. A trial of an H2-receptor antagonist, cromolyn sodium and midodrine along with intravenous fluids (1 L normal saline) every week or two resulted in substantial benefit and allowed her to resume her schooling.

Orthostatic intolerance describes symptoms that classically develop in response to upright posture and resolve upon recumbency. Patients with orthostatic intolerance may present with both orthostatic hypotension and tachycardia or with orthostatic tachycardia alone. It is estimated that over 500,000 persons in the United States have some form of orthostatic intolerance.[1] Common symptoms of orthostatic intolerance include lightheadedness, blurred vision, altered cognition/brain fog, generalized weakness, syncope, palpitations, chest pain, dyspnea, tremors and paresthesias. Table 1 lists some causes of orthostatic intolerance.

Postural tachycardia syndrome (POTS) is one of the most common causes of chronic orthostatic intolerance[2] and is characterized by an excessive heart rate increase without a corresponding decrease in blood pressure.[3] Recent consensus criteria define POTS as an increase in heart rate of 30 beats per min or more (> 40 bpm in children aged 12-19 years) within 10 minutes of standing or head-up tilt in association with symptoms of orthostatic intolerance and in the absence of orthostatic hypotension and any precipitating factors.[4,5] (Table 2). The purpose of this review is to increase the awareness of this condition to clinical nutrition specialists who are increasingly being referred these complex patients. In this review, we will focus on a discussion of symptoms and conditions associated with POTS and provide an overview of its management including the potential need for nutrition and hydration support.

Table 1. Selected Causes of Orthostatic Intolerance.

- Volume depletion
  - Dehydration, blood loss, anemia
- Medications
  - Tricyclic antidepressants, phenothiazines, monoamine oxidase inhibitors, antihistamines
- Cardiac and neurologic disease
- Primary autonomic failure
- Secondary dysautonomia
  - Diabetes, adrenal insufficiency, thyroid disease, liver/kidney failure, alcohol abuse
- Postural tachycardia syndrome

Table 2. POTS Diagnostic Criteria

- Heart rate increase ≥ 30 bpm within 10 min of upright posture in adults (≥ 40 bpm in adolescents 12-19 years)
- Absence of orthostatic hypotension (sustained drop in blood pressure ≥ 20/10 mmHg within min of upright posture)
- Orthostatic intolerance symptoms for ≥ 6 months
- Absence of other causes such as dehydration, other medical conditions, medications and dietary influences

Background

Epidemiology

The prevalence of POTS has been estimated at about 170 cases per 100,000 individuals.[6] POTS occurs most commonly among adolescent girls and young women and is characterized by typical orthostatic symptoms and is often accompanied by a variety of nonorthostatic symptoms including dry eyes or mouth, headaches, myalgias and a variety of urinary and gastrointestinal (GI) complaints.[7] Both orthostatic and nonorthostatic symptoms can be debilitating and contribute substantially to diminished quality of life and overall sense of well being.[8,9]

The natural history of POTS does not seem to incur an increased mortality risk.[10] Overall, existing

data suggest that, while cure is uncommon, many POTS patients improve over time.[8,11] Patients who have an antecedent event (e.g., viral illness) and a more acute onset seem to do better, while those without an antecedent event are more likely to have a family history of similar symptoms and a less favorable outcome.[8]

Pathophysiology

Multiple pathophysiologic mechanisms are thought to participate in the clinical syndrome known as POTS.[10] POTS has been classified into neuropathic and hyperadrenergic subtypes based primarily on autonomic testing and plasma norepinephrine levels. Neuropathic POTS may involve partial autonomic denervation characterized by reduced total peripheral resistance with exaggerated orthostatic venous pooling in the lower limbs and resultant blood pressure instability.[12,13] In contrast, hyperadrenergic POTS is considered a centrally driven sympathetic activation characterized by supine vasoconstriction and tachycardia, pale and cold skin, and increased supine muscle sympathetic nerve activity.[13] These patients often present with episodes of tachycardia, hypotension, tachypnea and hyperhidrosis, which may be triggered by orthostatic stress, emotional stimuli and physical activity. In actuality, there is often overlap between these subtypes, and so it may be preferred clinically to not focus on labels for POTS subtypes, but rather to address the individual findings as appropriate.The presence of multiple symptoms that are severe and result in significant disability without demonstrable cause often raises the suspicion of a psychogenic origin. POTS shares a number of symptoms with panic disorder and anxiety including palpitations, lightheadedness, dyspnea, and tremulousness. Somatization, depression, anxiety and attention deficit have all been observed in POTS.[14] While psychological distress is often present in POTS patients, it is similar to others with chronic medical conditions.

Finally, many GI and non-GI symptoms seen in POTS patients are similar to those seen in patients with functional disorders.[15] The underlying pathophysiology of these disorders includes visceral hypersensitivity, central sensitization, somatic hypervigilance and behavioral amplification – processes that may also explain the heterogeneity of multiple etiologies of POTS, the poor correlation between symptom severity and extent of hemodynamic changes and other objective testing, and the persistence of orthostatic symptoms despite control of heart rate.[16] Because many of these conditions are not attributable to orthostatic intolerance and occur commonly in patients with functional disorders, this raises the question of whether any association between these conditions and POTS reflects an epiphenomenon rather than a causal relationship.[17]

Comorbidities in POTS

A number of chronic conditions are frequently seen in patients with POTS and contribute to symptom burden and reduced quality of life. Common comorbidities include chronic fatigue syndrome, fibromyalgia, interstitial cystitis, and migraine headaches. Other unique conditions that seem to occur with increased frequency in POTS are autoimmunity, the hypermobile form of Ehlers-Danlos syndrome (HM-EDS), and mast cell activation disorder (MCAD).

HM-EDS is a non-inflammatory heritable disorder of connective tissue characterized by hyperflexible joints, hyperelastic skin and musculoskeletal symptoms. GI symptoms occur commonly among HM-EDS patients and there is a well-recognized association between HM-EDS and functional GI disorders.[18] HM-EDS appears to be common in patients with POTS;[19] however, many POTS patients have similar GI symptoms and disorders without having HM-EDS. Furthermore, it is important to recognize that generalized joint hypermobility without actual EDS is probably more common in POTS.

Based on the description of flushing episodes associated with orthostatic intolerance in some POTS patients, it has been suggested that mast cell mediators might play a role in the pathogenesis of POTS. Unlike mastocytosis, idiopathic mast cell activation occurs in the absence of mast cell

proliferation and with episodic accumulation of mast cell mediators in the plasma or urine, usually present when symptomatic. Patients with MCAD typically present with episodic "attacks" of flushing, urticaria and pruritus accompanied by lightheadedness, dizziness, dyspnea, nausea, headache, diarrhea, and/or syncope; symptoms representative of the hyperadrenergic type of POTS with biochemical evidence of MCAD (20). Triggering events include prolonged standing, exercise, menses, meals, sexual intercourse and certain medications (e.g., aspirin, β-blockers). Diagnosis of MCAD requires biochemical documentation because other causes of flushing may occur in patients with POTS.

CASE STUDY 2

A 21-year-old woman presented with a 5-year history of intermittent nausea, vomiting and abdominal pain that began suddenly after a viral illness. Evaluation at the time of her initial symptoms revealed a moderate delay in gastric emptying and a mildly increased tissue transglutaminase antibody with increased intraepithelial lymphocytes but no villous blunting on duodenal biopsies. A gluten free diet was not instituted at that time. Five years later, she now complains of persistent GI symptoms, orthostatic symptoms (confirmed on exam) and a greater than 10% weight loss in the last 6 months. She also endorsed joint hypermobility by history. Autonomic testing confirmed the presence of POTS. Repeat serological testing for celiac disease was, once again, equivocal. A celiac disease permissive gene (HLA DQ2) was present, so a gluten challenge with duodenal biopsy was performed confirming the diagnosis of celiac disease. Deficiencies were also noted in iron, zinc and vitamin B12; iron and B12 were corrected with parenteral supplementation while zinc was corrected with an oral supplement. Musculoskeletal examination revealed a Beighton score of 7 (out of 10; greater than 5 is abnormal) and a clinical diagnosis of Ehlers-Danlos syndrome – hypermobility type was made. Despite institution of a gluten free diet, correction of micronutrients and implementation of routine lifestyle changes for POTS, the GI symptoms persisted limiting her oral intake and resulting in continued weight loss. Because of the gastroparesis, a trial of a nasojejunal tube feeding was initiated and was well tolerated leading to placement of a percutaneous gastrojejunal tube for long-term enteral nutrition support. Although her weight and overall sense of well-being improved, because of intermittent intolerance to the tube feedings due to unexplained episodes of worsening abdominal pain and nausea, she requires intermittent infusions of intravenous fluids several times monthly.

Gastrointestinal Concerns

Symptoms

GI symptoms occur commonly in POTS patients and contribute substantially to the frustration and disability experienced by these patients with respect to both the reduced quality of life and impaired intake of nutrition and hydration.[17] While the most commonly reported GI symptoms are nausea (86%), irregular bowel movements (71%), abdominal pain (70%), constipation (70%), heartburn (64%), and bloating (59%) (15), most patients report multiple symptoms that occur more than once weekly and do not improve with supine positioning.

Dysmotility

Abnormalities in GI motility have been suggested to contribute to the GI symptoms occurring in POTS. Loavenbruck and colleagues retrospectively reviewed the records of 163 adult patients (140 female; mean age 30 years) with POTS who also had undergone testing of gastrointestinal transit and autonomic function.[21] Gastric emptying was normal in 55 (34%), delayed in 30 (18%), and rapid in 78 (48%). Symptoms were not associated with alterations in gastric emptying; however, vomiting was more common in those with delayed emptying. In a small case series, Huang et al. reported on 12 POTS patients (11 female; mean age 32 years) who presented to a tertiary care GI motility clinic for evaluation of GI symptoms and underwent a variety of motility tests.[22] Disturbances in GI motility were found to involve not only the stomach, but also multiple segments of the gut spanning the esophagus to the anus.

Since POTS may result from dysautonomia, this same impairment in autonomic nerves may influence gut sensorimotor function and contribute to the symptoms that result.[15,23] Moreover, GI

symptoms may lead to a reduction in nutrient and fluid intake resulting in volume shifts and dehydration, further aggravating the autonomic symptoms. It is also important to recognize that because GI disorders associated with POTS may result in insufficient fluid intake or excess fluid loss leading to hypovolemia with subsequent orthostatic symptoms and tachycardia, orthostatic intolerance might be better considered a consequence of the GI disorder. It has also been suggested that a shared trigger, such as a prior infectious episode, may be responsible for both POTS and GI dysfunction. Finally, median arcuate ligament syndrome, also known as celiac artery compression syndrome, has been suggested to occur commonly in POTS patients (> 50%) and has been implicated in the development of GI symptoms in some.[24,25] Median arcuate ligament syndrome is characterized by a variety of dyspeptic symptoms often accompanied by weight loss attributed to impingement and compression of the celiac artery and/or celiac plexus by the median arcuate ligament. Although improvement has been suggested to occur in GI symptoms, orthostatic symptoms and quality of life following surgical division of the median arcuate ligament, caution is recommended in pursuing surgery as this radiographic finding may occur as a consequence of weight loss and not be the cause of the symptoms.

Nutritional Implications of POTS

The adverse nutritional consequences that may be seen in POTS are similar to those that may occur in any disorder that limits oral intake. These consequences can lead to weight loss and altered micronutrient levels.[26] Although its prevalence is uncertain in POTS, because of the GI dysmotility that occurs in many POTS patients, small intestinal bacterial overgrowth (SIBO) may develop. Although uncommon except in severe (usually postsurgical) stasis syndromes, steatorrhea secondary to fat maldigestion and malabsorption may occur in SIBO as a result of deconjugation of bile acids by intraluminal bacteria and a subsequent deficiency of intraluminal bile acids necessary for adequate micelle formation. The malabsorption of fat may also cause foul-smelling flatus and oxalate nephrolithiasis. These bacteria-derived deconjugated bile acids, such as lithocholic acid, may also exert a toxic injury on enterocytes that affects not only the absorption of fat, but also carbohydrate and protein. Deconjugated bile acids have secretomotor effects on the colon that may lead to diarrhea. Carbohydrate malabsorption may also result from intraluminal degradation of sugars by the bacteria and by impaired activity of disaccharidase and other brush-border hydrolase activity responsible for absorption of sugars. Carbohydrate malabsorption may cause diarrhea and a number of 'gas' symptoms including abdominal discomfort and bloating.

Altered Micronutrients

When fat malabsorption from SIBO or, more commonly, limitations in dietary fat intake are present in POTS patients, deficiencies in the fat-soluble vitamins A, D, E and K may occur. Iron, folate and vitamin B12 deficiency may also result from the restricted diet often seen in POTS patients. In addition, B12 deficiency may occur in the setting of SIBO as a result of inhibition of absorption by anaerobic organisms and by its consumption within the intestinal lumen by enteric microbes. Folate and vitamin B12 deficiency may result in a megaloblastic anemia and, in severe cases, B12 deficiency may result in a rare neurological syndrome. Because these deficiencies are often clinically silent, a high index of clinical suspicion and monitoring of micronutrient levels is suggested, particularly in those POTS patients with more severe clinical manifestations.

Case Study 3

A 37 year-old woman with Ehlers-Danlos syndrome described a 6-month history of debilitating nausea, vomiting and postprandial abdominal pain resulting in an inability to maintain her weight and hydration. Prior gastric emptying scintigraphy demonstrated a severe delay in emptying but treatment with a gastroparesis diet and prokinetic, antiemetic and antisecretory medications did not provide effective symptom relief. An attempt at enteral nutrition support via a nasojejunal tube was poorly tolerated despite trials of multiple enteral formulae. She was then referred to our clinic for ongoing weight loss and continued debilitating nausea, vomiting, weakness and recurrent syncope. Further diagnostic

(continued on page 21)

(continued from page 18)

evaluation including computed tomography of the abdomen and pelvis, upper endoscopy with duodenal biopsies and aspirate, and endoscopic functional lumen imaging probe of the pylorus was unremarkable. Because of her recurrent syncope, autonomic testing was conducted and revealed evidence of marked tachycardia and tachypnea with tilt-table testing consistent with a hyperadrenergic state and POTS. Due to the presence of severe protein-energy malnutrition, in addition to starting pharmacological therapies to promote vascular tone, control heart rate and promote GI motility, a decision was made to initiate parenteral nutrition in order to maintain her caloric needs and intravascular volume status. Over the next few months, her weight and energy level improved, the episodes of syncope diminished, and adjustments in her medications allowed for the slow reintroduction of a modest degree of oral food intake.

General Management

Evaluation

When POTS is suspected, referral for appropriate testing and/or to a specialist in POTS (e.g., neurologist, cardiologist) is encouraged. An awareness of the unique associations with POTS, particularly MCAD, EDS and autoimmunity, should prompt an assessment of these conditions when the appropriate history, signs and/or symptoms are present (Table 3). Testing is generally guided by the most prominent symptoms present. Given the number of conditions associated with POTS, there is the danger of unnecessary testing including, from a GI perspective, multiple endoscopic, radiographic and motility assessments. Importantly, nutritional assessment and counseling for all POTS patients is recommended, particularly those with moderate to severe symptoms. A suggested approach to the basic evaluation of POTS is shown in Table 4.[6]

Treatment

Given its complexity, a multidisciplinary approach to treatment is important. Setting realistic goals and treatment expectations is critical, particularly in the management of those patients with severe symptoms. As with any complex chronic medical condition, establishing an effective provider-patient relationship along with reassurance and education are essential steps in management. Patient education should include information about symptoms due to orthostatic intolerance and those that are not, as well as factors that may exacerbate their symptoms. Finally, a focus on the simultaneous treatment of the orthostatic and non-orthostatic symptoms and associated conditions is essential.

Because of the heterogeneity of POTS, there is not a single treatment algorithm that suits all patients. As such, it is important to recognize that, with respect to the management of the classical orthostatic symptoms affecting POTS patients, most treatment recommendations are derived from consensus opinions, and not high quality randomized controlled trials. This is underscored by the findings of a recent systematic review and meta-analysis on the treatment of POTS which identified only 25 case series and 3 small randomized controlled trials.[27] The investigators

Table 3. Tests When POTS Comorbidities Suspected

Condition	Testing
Autoimmunity	Paraneoplastic autoantibody profile, collagen vascular disease screening, celiac disease, thyroglobulin antibody
Dysautonomia	Autonomic testing of cardiovagal, sudomotor and adrenergic functions
Hypermobile Type – Ehlers-Danlos Syndrome	Screen by calculating Beighton score for generalized joint hypermobility; if vascular EDS suspected, an echocardiogram
Mast Cell Activation Disorder	Tryptase; 24-hour urine collection for n-methylhistamine, leukotriene E4 and 11-beta prostaglandin F2 alpha preferably during a flare
Median Arcuate Ligament Syndrome	Radiographic (duplex ultrasound, CT/MR angiography) imaging of the celiac artery using respiratory maneuvers

found that interventions increasing intravascular volume and peripheral or splanchnic vascular tone, reducing heart rate, and increasing exercise tolerance demonstrated moderate efficacy. However, significant heterogeneity among the studies was present in multiple factors including patient age, symptom severity, and the outcome measures used. While acknowledging this limited evidence-base, the general approach to managing orthostatic symptoms in POTS involves a variety of lifestyle modifications including volume restitution, physical conditioning, exercise training, support garments and pharmacotherapies. Increasing oral fluid (2-2.5 L/day [67-84 ounces]) and salt intake (10 g/day [See http://www.jdabrams.com/documents/wellness/USDA-Sodium-Content.pdf]) is an important first step in management of all POTS patients. Mild to moderate symptoms may respond to simple measures including avoidance of circumstances that precipitate symptoms such as orthostatic stress, emotional stimuli and physical activity, and use of pressure garments. More severely affected individuals will require medications such as fludrocortisone, midodrine, beta-blockers, pyridostigmine, and/or selective serotonin reuptake inhibitors. For suppression of symptoms of mast cell activation, H1 and H2 receptor antagonists, and cromolyn sodium are commonly used. Occasionally, periodic parenteral fluid administration either at home or at an infusion center is needed in those with severe orthostatic symptoms.

Given the varied GI symptoms in POTS, initial treatment focuses on the most prominent symptoms (Table 5).[28] In patients who do not respond to standard medical therapies, similar to the approach to orthostatic symptoms, treatment is empirical and not evidence-based. Antiemetics are commonly employed in POTS patients given the prevalence of nausea; combinations of antiemetics are sometimes needed. The utility of prokinetic and anti-dumping treatments in POTS patients with delayed or rapid gastric emptying, respectively, requires further study. For patients with immune-mediated GI dysmotility, corticosteroids and intravenous immunoglobulin are sometimes used.[29] When chronic pain is present, avoidance of opioids is encouraged due to the risk of opioid-induced bowel dysfunction and narcotic bowel syndrome. The use of neuromodulating agents

Table 4. Approach to the Evaluation of POTS

	Comment
Basic	Medical history – medications, comorbidities, diet, exercise, family history, details on nature of tachycardia.
	Physical exam – cardiovascular, neurologic, autonomic, musculoskeletal, others based on symptoms.
	Orthostatic vitals – blood pressure and heart rate while supine (> 5 min) and again after 1, 3, 5, and 10 min of standing.
Cardiac	Electrocardiogram to exclude prior cardiac condition or existing conduction defects.
	Holter monitor, echocardiogram, and/or exercise stress test when suspected structural or conduction defects.
Blood	Check for dehydration, anemia, hyperthyroidism, carcinoid and nutritional deficiencies.
	Supine and standing norepinephrine levels when hyperadrenergic POTS suspected.
	Autoimmune testing when concomitant autonomic neuropathy or GI dysmotility present.
Autonomic	When symptoms of autonomic neuropathy present, or in those whose symptoms do not markedly improve with treatment.
	Head-up tilt table testing when normal orthostatic vitals but high clinical suspicion, or in those with known/suspected seizure disorder.

(e.g., tricyclic antidepressants) as an alternative should be considered. For more refractory cases, the use of a combination of gut-directed and neuromodulating agents is often used and the combination of medications with psychological treatment should also be considered.[30]

Nutritional Management

Nutritional management of the POTS patient involves identification and correction of nutritional deficiencies. Given the prevalence of POTS in young women who may be underweight, POTS must be differentiated from eating disorders, which

Table 5. Approach to Treating Common GI Symptoms Seen in POTS

Symptom	Therapy or Treatment
Chronic Abdominal Pain	• Acid suppression – proton pump inhibitor, H_2 receptor antagonist • Antispasmodics – dicyclomine, hyoscyamine, peppermint oil • Neuromodulators – tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, anti-epileptic agents • Psychological therapy – cognitive behavioral therapy, hypnotherapy
Constipation	• Osmotic laxative – PEG3350, lactulose, milk of magnesia • Stimulant laxative – bisacodyl, senna • Chloride channel activator – lubiprostone • Guanylate cyclase-C agonist – linaclotide, plecanatide • 5-HT4 agonist[+] – prucalopride, tegaserod (females only)
Dehydration	• If oral intake possible – salt tablets and oral rehydration solutions • If limited/no oral intake – intermittent intravenous or enteral tube fluid boluses
Diarrhea	• Diet modification – soluble fiber, low FODMAP, gluten-free • Microbiome modification – rifaximin, Bifidobacterium infantis 35624 • Antidiarrheals – loperamide, diphenoxylate with atropine • Bile acid sequestrants – cholestyramine, colestipol, colesevelam • μ- and κ-opioid receptor agonist and δ-opioid receptor antagonist – eluxadoline** • 5-HT3 receptor antagonist – alosetron (females only)
Motility Disturbance	• 5-HT4 agonist[+] – prucalopride, tegaserod (off-label use if used for gastroparesis) • Dopamine D2 receptor antagonist – metoclopramide,[++] domperidone (requires IND application in U.S.) • Acetylcholinesterase inhibitor – pyridostigmine
Nausea/Vomiting	• Antiemetics* – ondansetron, promethazine, prochlorperazine, aprepitant, off-label use of carbidopa • Prokinetic agents –metoclopramide,[++] domperidone, pyridostigmine • Complementary medicine treatments – ginger tea, aromatherapy, STW5
Weight loss	• Oral nutrition supplements • Micronutrient supplementation (when deficiencies detected) • Enteral or parenteral nutrition support

*Patients may require multiple agents and care should be taken to monitor the electrocardiographic QT interval.

**Contraindicated in patients post cholecystectomy, patients having ≥3 alcoholic beverages/day, and moderate to severe hepatic insufficiency.

[+]Both agents recently gained FDA approval (availability anticipated in 2019).

[++]To minimize risk of tardive dyskinesia, recommended dose ≤20mg/day for up to 12 weeks.

can produce orthostatic intolerance in early stages. Importantly, a pattern of restricted eating distinct from actual eating disorders appears to be common among POTS patients and should be discerned and addressed when present. In those with identified micronutrient deficiencies, periodic monitoring is recommended. Because the often-accompanying GI symptoms and gut dysmotility may result in considerable weight loss and recurrent dehydration, POTS patients require special attention to their nutrition and hydration needs. In the individual with weight loss and malnutrition, oral nutritional supplements should initially be provided. Although a gastroparesis diet is often employed, the optimal diet in POTS requires further study, as does the role of dietary modification in POTS management. As weight loss and dehydration are common in those with severe symptoms, parenteral fluid and/or enteral or parenteral nutrition support is occasionally required; however, the prevalence of need of non-oral nutrition or hydration support in this population is unknown. We recently conducted a retrospective, exploratory cohort study of patients diagnosed with POTS over a 7-year period with a minimum of 6 months of follow-up.[31] Three hundred thirty-two patients with POTS over a 7-year period were included; 32 received non-oral nutrition or hydration support either at home or at an infusion center. Of these patients, 21 (66%) required parenteral fluids, 19 (59%) enteral nutrition and 9 (28%) parenteral nutrition. Those receiving enteral or parenteral nutrition or hydration support had more severe orthostatic and non-orthostatic symptoms, abnormal GI motility and autonomic testing, and exhibited greater healthcare utilization.

CONCLUSION

Because of its pathophysiologic heterogeneity, diversity of clinical presentation seemingly unrelated to orthostatic stress, and unpredictability of clinical response, patients with POTS pose a considerable management challenge and benefit from a multidisciplinary management approach. The variety of symptoms and comorbidities seen in POTS patients should be evaluated expeditiously and managed accordingly as they often exacerbate symptoms of orthostatic intolerance and may result in weight loss and other adverse nutritional outcomes. At present, the treatment of symptoms in patients with POTS remains largely empirical. While general lifestyle measures to treat POTS may lead to improvement in both orthostatic and non-orthostatic symptoms, refractory symptoms should prompt further diagnostic evaluation and appropriate dietary and pharmacologic management. Nutritional deficiencies should be monitored and corrected when present. ■

References

1. Robertson D. The epidemic of orthostatic tachycardia and orthostatic hypotension. Am J Med Sci 1999;317:75-77.
2. Schondorf R, Low PA. Idiopathic postural tachycardia syndrome: an attenuated form of acute pandysautonomia? Neurology 1993;43:132-137.
3. Low PA, Opfer-Gehrking TL, Textor SC, et al. Postural tachycardia syndrome (POTS). Neurology 1995;45(Suppl 5):S19-S25.
4. Singer W, Sletten DM, Opfer-Gehrking TL, et al. Postural tachycardia in children and adolescents: what is abnormal? J Pediatr 2012;160:222-226.
5. Sheldon RS, Grubb II BP, Olshansky B, et al. 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. Heart Rhythm 2015;12:e41-63.
6. Raj SR. Postural tachycardia syndrome (POTS). Circulation 2013;127:2336-2342.
7. Benarroch EE. Postural tachycardia syndrome: a heterogeneous and multifactorial disorder. Mayo Clinic Proc 2012;87:1214-1225.
8. Sandroni P, Opfer-Gehrking TL, McPhee BR, et al. Postural tachycardia syndrome: clinical features and follow-up study. Mayo Clin Proc 1999;74:1106-1110.
9. Benrud-Larson LM, Dewar MS, Sandroni P, et al. Quality of life in patients with postural tachycardia syndrome. Mayo Clin Proc 2002;77:531-537.
10. Arnold AC, Ng J, Raj SR. Postural tachycardia syndrome - Diagnosis, physiology, and prognosis. Auton Neurosci 2018 Feb 28. pii: S1566-0702(17)30354-5. [Epub ahead of print]).
11. Kimpinski K, Figueroa JJ, Singer W, et al. A prospective, 1-year follow-up study of postural tachycardia syndrome. Mayo Clin Proc 2012;87:746-752.
12. Jacob G, Costa F, Shannon JR, et al. The neuropathic postural tachycardia syndrome. N Engl J Med 2000;343:1008-1014.
13. Stewart JM, Montgomery LD. Regional blood volume and peripheral blood flow in postural tachycardia syndrome. Am J Physiol Circ Physiol 2004;28:H1319-H1327.
14. Raj V, Haman KL, Raj SR, et al. Psychiatric profile and attention deficits in postural tachycardia syndrome. J Neurol Neurosur Psychiatry 2009;80:339-344.
15. Wang LB, Culbertson CJ, Deb A, et al. Gastrointestinal dysfunction in postural tachycardia syndrome. J Neurol Sci 2015;359:193-196.
16. Khurana RK. Visceral sensitization in postural tachycardia syndrome. Clin Auton Res 2014;24:71-76.

(continued on page 26)

(continued from page 24)

17. DiBaise JK, Harris LA, Goodman B. Postural Tachycardia Syndrome (POTS) and the GI Tract: A Primer for the Gastroenterologist. Am J Gastroenterol. 2018;113:1458-1467.
18. Fikree A, Aktar R, Grahame R, et al. Functional gastrointestinal disorders are associated with the joint hypermobility syndrome in secondary care: a case-control study. Neurogastroenterol Motil 2015;27:569-579.
19. Wallman D, Weinberg J, Hohler AD. Ehlers-Danlos syndrome and postural tachycardia syndrome: a relationship study. J Neurol Sci 2014;340:99-102.
20. Shibao C, Arzubiaga C, Jackson Roberts II L, et al. Hyperadrenergic postural tachycardia syndrome in mast cell activation disorders. Hypertension 2005;45:385-390.
21. Loavenbruck A, Iturrino J, Singer W, et al. Disturbances of gastrointestinal transit and autonomic functions in postural tachycardia syndrome. Neurogastroenterol Motil 2015;27:92-98.
22. Huang RJ, Chun CL, Friday K, et al. Manometric abnormalities in the postural orthostatic tachycardia syndrome: a case series. Dig Dis Sci 2013;58:3207-3211.
23. Al-Shekhlee A, Linderberg JR, Hachwi RN, et al. The value of autonomic testing in postural tachycardia syndrome. Clin Auton Res 2005;15:219-222.
24. Ashangari C, Suleman A, Le TH. Median arcuate ligament syndrome in postural tachycardia syndrome (POTS. Autonom Neurosci 2015;192:124(abstract P17.16).
25. Abdallah H, Thammineni K, Hartas G, et al. Median arcuate ligament syndrome presenting as POTS. Autonom Neurosci 2015;192:123(abstract P17.111).
26. Adike A, DiBaise JK. Small intestinal bacterial overgrowth: nutritional implications, diagnosis and management. Gastroenterol Clin N Am 2018;47(1):193-208.
27. Wells R, Elliott AD, Mahajan R, et al. Efficacy of therapies for postural tachycardia syndrome: a systematic review and meta-analysis. Mayo Clin Proc 2018;93:1043-1053.
28. Camilleri M, Bueno L, Andresen V, et al. Pharmacologic, pharmacokinetic, and pharmacogenomic aspects of functional gastrointestinal disorders. Gastroenterology 2016;150:1318-1331.
29. Ashat M, Lewis A, Liaquat H, et al. Intravenous immunoglobulin in drug and device refractory patients with the symptoms of gastroparesis – an open label study. Neurogastroenterol Motil 2018 Mar;30(3).
30. Kizilbash SJ, Ahrens SP, Bruce BK, et al. Adolescent fatigue, POTS, and recovery: a guide for clinicians. Curr Probl Pediatr Adol Health Care 2014;44:108-33.
31. Tseng AS, Traub NA, Harris LA, et al. Factors Associated with Use of Non-Oral Nutrition and Hydration Support in Adult Patients with Postural Tachycardia Syndrome. JPEN J Parenter Enter Nutr 2018 Dec 18. [Epub ahead of print].