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Postural Orthostatic Tachycardia Syndrome (POTS): A Primer for Nurse Practitioner Practice

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ABSTRACT

Postural Orthostatic Tachycardia Syndrome (POTS):
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Postural orthostatic tachycardia syndrome (POTS) is a form of orthostatic intolerance (OI) that affects 0.2% of the population and is over-represented in women of childbearing age. It is caused by autonomic dysfunction and hypovolemia that presents with marked tachycardia and with minimal change in blood pressure upon standing. Orthostatic symptoms must be present including: lightheadedness, nausea, chest pain, palpitations, shortness of breath, and nausea and must improve with recumbence. The three main subtypes of POTS are neuropathic POTS associated destruction of peripheral nerves and venous pooling, hypovolemic POTS associated with low blood volume, and hyperadrenergic POTS associated with inappropriate sympathetic activation. It is easily diagnosed by hemodynamic testing, but is difficult to treat. Treatment involves increased fluid and salt intake, exercise, and pharmacologic measures. POTS is a chronic illness that significantly affects quality of life. The purpose of this article is to describe the clinical presentation, the underlying physiological and pathological processes involved, the diagnostic criteria, and current management strategies for postural orthostatic tachycardia syndrome (POTS).

Keywords: Postural orthostatic tachycardia syndrome (POTS), autonomic dysautonomia, near syncope, non-neurogenic seizure

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TABLE OF CONTENTS

Abstract ii

Acknowledgments iii

Postural Orthostatic Tachycardia Syndrome (POTS): A Primer for NP Practice 1

Introduction 1

Clinical Presentation 2

Case Study 2

History of Present Illness 3

Pathophysiology 4

Normal Physiology 4

POTS Pathophysiology 4

Subtypes 5

Diagnosis 6

Prognosis 7

Management 8

Non-Pharmacological Management 8

Pharmacological Treatment 9

Discussion 10

Conclusion 12

References 13

Appendix A 16

Table 1 *Medications in Treatment of POTS. Used with Permission of the Authors* 16

Postural Orthostatic Tachycardia Syndrome (POTS): A Primer for NP Practice

Introduction

Postural Orthostatic Tachycardia Syndrome (POTS) affects an estimated 0.2% of the population, yet it is relatively unknown to healthcare providers.[1, 2] It predominantly affects females (5:1) during the reproductive years between ages 14 and 50.[1-5] While there have been no known mortalities from POTS, it is a chronic, often severely debilitating condition.[3]

The defining features of POTS are pronounced tachycardia while standing without hypotension causing significant symptoms which improve with recumbence. However, POTS is associated many non-orthostatic symptoms as well.[6, 7]

Similar constellations of symptoms were recognized by DaCosta as early as the U.S. Civil War; however, Schondorf and Low described the phenomenon and coined the term as postural orthostatic tachycardia syndrome.[7, 8] Little was understood about the cause of POTS in 1993, but it is now known to be a heterogenous syndrome with a common final pathway.[2-4] Many different pathophysiological processes occur independently or together leading to POTS. Its onset may be insidious and progressive, or it may occur suddenly after an illness or major stress to the body.[4, 9]

It is not uncommon for patients with POTS to be misunderstood and misdiagnosed initially, delaying appropriate treatment. The purpose of this article is to describe the clinical presentation, the underlying physiological and pathological processes involved, the diagnostic criteria, and current management strategies for postural orthostatic tachycardia syndrome (POTS).

Clinical Presentation

Case Study

S.P. is a 37-year-old female who collapsed while on vacation at an amusement park. Before that morning, she functioned as business owner, mother, and socially-engaged community member. At the moment of her collapse, she lost her ability to function. She was unresponsive for two hours. She heard the noises around her and was aware of her surroundings, but unable to lift her head or respond, she maintained some muscle control but was tremulous during the episode. Over the next several months, similar episodes happened repeatedly. She had severe orthostatic intolerance and standing for any length of time would elicit another episode of near-syncope and tremulousness.

She was seen at the ED multiple times for evaluation of her symptoms and was admitted for a video EEG to rule out a seizure disorder. The symptoms presented did not exactly match multiple emergency conditions, but symptoms such as altered mental status, weakness, tremulousness, chest pain and palpitations, shortness of breath, and abdominal pain mimicked emergency conditions. The severity of the symptoms was not well-explained by her history. At each ED visit medical staff were concerned that they were missing something and they questioned whether this might be a psychiatric illness. The neurologist opined that S.P. had psychogenic pseudoseizures, a manifestation of conversion disorder. This differential diagnosis was enticing as it explained the symptoms well and especially accounted for the “non-neurogenic” seizures. One provider felt that S.P. fit the quintessential profile of a person with conversion disorder: a woman in her reproductive years experiencing a trauma that was too great for her mind to handle causing her body to respond by losing physical function. However, S.P. did not have a history of significant trauma or sources of great unhappiness, shame, or guilt in

her life. The provider had an answer in psychology and stopped looking for a better explanation for her symptoms.

S.P. returned to her primary care provider who understood postural orthostatic tachycardia syndrome (POTS) and he diagnosed her using a relatively uncomplicated and low-tech test. She was lucky; her diagnosis took less than a month.

History of Present Illness

Up to fifty percent of patients diagnosed with POTS had an identifiable antecedent event, most often a viral illness; however, surgery, trauma, concussion, or pregnancy can also trigger POTS. While the individual symptom profile varies, all must have orthostatic symptoms that worsen with standing and improve with recumbence. The signs and symptoms of POTS reflect central nervous system (CNS) hypoperfusion, autonomic nervous system (ANS) activation, and underlying conditions.[2]

Orthostatic symptoms include lightheadness, near syncope, chest pain, palpitations, blurred or tunnel vision, tremulousness, shortness of breath, nausea, and paresthesia. CNS symptoms are often present, including impaired sleep, headache, mental clouding, depression, and anxiety.[2, 7] Cognitive symptoms often persist even when lying supine, which may be indicative of unknown pathophysiologic effects of POTS on the central nervous system.[10] Most patients report extreme fatigue and a significant majority develop chronic pain.[11]

Other manifestations of systemic autonomic involvement include: gastroparesis, abdominal pain, post-prandial bloating, constipation, poor thermoregulation, diaphoresis or anhidrosis, increased urinary output or urinary retention, and weakness.[4, 11] Symptoms are exacerbated by heat, illness, dehydration, exercise, alcohol use, and menstruation. Symptoms are worse in the morning.[4] Physical signs may include acrocyanosis, hypermobility, impaired

sweating, dermatologic changes, tremulousness, and altered attention, and cognitive processing.[1, 4]

Pathophysiology

Normal Physiology

Normally when a person stands, around 25% of the blood in the thoracic cavity is displaced downward by gravity causing a significant drop in stroke volume; the body's compensatory mechanisms are extensive including sympathetic activation increasing heart rate and vascular tone. When a person stands, the heart rate typically increases by 10 to 15 beats per minute (bpm) and the diastolic blood pressure increases by approximately 10 points while the systolic blood pressure is unchanged.[3, 7]

POTS Pathophysiology

With POTS an exaggerated fluid shift causes an exaggerated sympathetic response causing the heart rate to increase more than 30 bpm (40 bpm in children and adolescents) while maintaining a normal or elevated blood pressure. Defining POTS purely as a type of orthostatic intolerance (OI) is inaccurate; rather, it is a disorder of the autonomic nervous system with systemic effects. For this reason, many patients experience symptoms that are not directly related to orthostatic intolerance. For nurse practitioners (NPs) unaware of the autonomic basis of POTS, the constellation of symptoms creates an unclear diagnostic picture. The autonomic nervous system is involved in all automatic processes in the body; therefore, patients with POTS frequently have other symptoms of autonomic dysfunction including significant cognitive, gastrointestinal, thermoregulatory, and other symptoms.[4, 11]

Subtypes

The literature is unclear regarding the subtypes of POTS. There is a lack of consistency in the classification of POTS. The literature generally refers to three subtypes of POTS: neuropathic, hyperadrenergic, and hypovolemic. These subtypes address broader mechanisms leading to orthostatic tachycardia. Each subtype has multiple associated causes and could be classified with more specificity; however, there is no uniformity in the literature regarding further classification. POTS can be primary if idiopathic or secondary if there is a known underlying cause. Identification of underlying processes is essential in the effective treatment of POTS.[12] A patient with POTS may have multiple subtypes reflecting the causes of their symptoms. Additionally, there is no ICD-10 code specific for POTS. Some practitioners use a code related to autonomic dysfunction, others may classify it as orthostatic hypotension, or as other specified cardiac arrhythmia.[13]

Neuropathic POTS affects up to 50% of patients with POTS. It is caused by loss of nerve fibers usually of small and distal postganglionic fibers in the lower extremities, especially in the feet and toes. There is an inability of the distal vasculature to constrict leading to venous pooling evident by acrocyanosis. Those with neuropathic POTS frequently have abnormalities with the sudomotor fibers as well affecting thermoregulation and may have decreased sweat production.[2, 4, 5]

Hyperadrenergic POTS is caused by an overactive sympathetic nervous system (SNS). People with adrenergic POTS will have increased norepinephrine levels (>600 pg/ml) with orthostasis; they may have normal or increased levels of norepinephrine when supine. Autonomic storms cause hypertension, tachycardia, and diaphoresis independent of orthostatis. Patients with hyperadrenergic POTS are prone to greater symptom burden related to SNS

activation, such as increased tremulousness (sometimes referred to as pseudoseizures), anxiety/panic symptoms, and palpitations.

Approximately 70% of patients with POTS have hypovolemic POTS.[3] Research shows that patients with hypovolemic POTS have low blood plasma volume and decreased RBC count.[2, 4] Many have abnormalities in the renin angiotensin aldosterone system with decreased renin and aldosterone response to changes in blood and stroke volume and decreased metabolism of angiotensin II.[2, 4, 5]

Many other conditions and processes contribute to the presentation of POTS. Some processes that have been shown to be involved in subsets of patients with POTS include autoimmunity to α1, β1, or β2 adrenergic receptors, mast cell activation disorders, poor vascular tone caused by Ehlers Danlos Syndrome (hypermobility type), and NET transporter protein deficiency.[2-4, 14] Chronic fatigue syndrome (CFS), concussion, migraine, celiac disease, and IBS are frequently comorbid with POTS and may contribute to the presentation. POTS is often associated with autoimmune disorders—especially Sjőgren's disorder, systemic lupus erythematus (SLE), and Hashimoto thyroiditis. [3, 4, 14]. When there are known comorbidities, treatment of the comorbidities tends to improve POTS symptoms.[12]

Diagnosis

To be diagnosed with POTS, a patient must have an increase of heart rate on standing at least 30 bpm (40 bpm in adolescents) or have a standing heart rate of >120 bpm and have orthostatic symptoms that improve with recumbence. The patient should have had symptoms for at least six months; though in some cases, acute onset is adequately severe as to warrant diagnosis.[2, 3, 7]

The primary diagnostic test is orthostatic vital signs with a prolonged standing evaluation at two, five, and ten minutes; if the patient is unable to tolerate standing, the evaluation can include a head up tilt test (HUT) using a tilt table.[3, 7, 14] Cardiac causes should first be ruled out by ECG, and if needed: holter monitor, echocardiogram, and stress test. Tachycardia in POTS is sinus tachycardia. Laboratory testing should include a CBC, CMP, and TSH.[3, 4]

Other diagnostics identify underlying causes, comorbidities, and the subtypes of POTS and should guide treatment. Further laboratory testing may include supine and upright serum metanephrine levels, 24-hour urine, A1C, Vitamin B12 levels, ANA, viral and bacterial screenings, and enzyme and hormone levels. Symptoms may warrant further infectious, autoimmune, autonomic, gastrointestinal, genitourinary, cognitive/psychological, and sleep studies.[3, 4] Common differential diagnoses include: anemia, thyrotoxicosis, inappropriate sinus tachycardia and other cardiomyopathies, adrenal insufficiency, pheochromocytoma, panic disorder, paraneoplastic syndrome, and amyloidosis.[4, 5]

Prognosis

Much of the early literature indicates that full recovery is quite common and downplays the chronic nature of the disorder.[3, 5, 11] While some patients experience a complete resolution of symptoms, most will see significant improvement within the five years of diagnosis, but others may require at least non-pharmacologic treatment throughout their lives.[1, 2, 5, 15]

The level of impairment and the effect of POTS on quality of life can be quite significant. Results of a study by Pederson and Brook showed that patients with POTS have more days with poor health, more extreme fatigue and low energy, activity limitations, and poorer sleep than controls; they were also at much higher risk for suicide.[16] Approximately 25% of patients with POTS are unable to work.[1, 6]

Management

Non-pharmacological treatment creates a solid foundation for positive outcomes by expanding blood volume and venous return. This base is essential for effective treatment of POTS. The main components of non-pharmacological treatment include: 1) increased fluid and sodium intake, 2) a graded aerobic exercise program, 3) use of compression garments, 4) trigger avoidance, and 5) physical countermeasures. Fluid and electrolyte supplementation, exercise, and the use of compression garments are discussed below.

For some non-pharmacological treatment is enough; however, frequently pharmacological treatment is needed. Raj, Opie, and Arnold propose that cognitive behavioral therapy (CBT) can help patients adjust to life with a debilitating chronic illness.[10] If possible multidisciplinary treatment approach is best and may include both physical/occupational therapy and mental health services.[2, 10]

Non-Pharmacological Management

Increased fluid and sodium intake. Because patients with POTS tend to have a lower total blood volume, it is recommended that they consume at least 2to 3 liters of fluid per day. To keep fluid in the intravascular space, it is important to increase sodium intake to as much as 10 to 12 grams.[2] To achieve this, most require salt supplementation using salt tablets. Increasing salt in the diet also increases thirst and aids with fluid consumption.[12, 17]

Intravenous fluids can significantly improve symptoms; however, the Heart Rhythm Society' 2015 consensus statement recommends that intravenous fluids be used as a rescue effort in acute decompensation, and not as a chronic treatment.[12, 17 18]

Exercise. Exercise is the most important and challenging element of treatment. It requires frequent contact with a provider to work through the difficulties during the acute phase of illness.

Fu, et al. described a reconditioning exercise protocol in detail in their 2010 article on the cardiac origins of POTS.[19] A similar exercise regimen with more specifics was outlined the Children's Hospital of Philadelphia (CHOP). It can be accessed at: https://www.dysautonomiainternational.org/pdf/CHOP_Modified_Dallas_POTS_Exercise_Program.pdf

A person with acute exacerbation of POTS should start with fully recumbent exercises. Fu, et al. described the Patients should exercise at regular intervals, generally every other day.[17] Exercising too much can exacerbate symptoms. Patients can void symptom exacerbation by using a heart rate monitor to ensure their heart rate stays within the defined moderate intensity exercise levels (usually between 140-150 bpm), using solely recumbent exercise modalities at first to decrease orthostatic symptoms, increasing the minutes gradually, and having appropriate intervals for rest, both during exercise and between sessions.

Compression garments. Waist high, medium compression garments (at least 30 mmHg) are recommended to help prevent fluid pooling in the lower extremities. If needed, an abdominal binder can limit splanchnic pooling, manifest by a feeling of abdominal fullness.[7]

Pharmacological Treatment

Medications are used to treat the underlying pathophysiological dysfunction. Medications target low blood volume, tachycardia, peripheral vasoconstriction, and sympathetic activation. Providers can prescribe medications to treat the most problematic symptoms of POTS, such as mental clouding, insomnia, constipation, tremulousness, and fatigue. Treating comorbid autoimmune disorders, infections, and chronic pain disorders in addition to treating the vascular mechanisms and symptoms associated with POTS improves outcomes.

Due to lack of clinical trials and large randomized control studies, most evidence for pharmacological treatment comes from small studies. Because the physiologic mechanisms of POTS vary significantly among patients, the effect of medications on the treatment of POTS varies as well. Both fludrocortisone and midodrine can be effective in increasing blood volume. Midodrine is very short-acting and is given three times a day, but can cause supine hypertension, so it is only given during waking hours. Generally, propranolol in low doses (10-20 mg TID) improves tachycardia and symptomology of POTS but may increase fatigue.[12, 14]

For patients with hyperadrenergic POTS, clonidine and alpha-methyldopa can decrease central sympathetic activation, but the CNS effects of fatigue, drowsiness, and slowed cognition can be problematic. Pyridostigmine increases the acetylcholine available in autonomic ganglia and in the muscarinic synapses in the heart—improving tachycardia and symptoms of POTS—but the GI and urinary side effects are often not tolerated well.[2, 12] Ivabradine, a medication new to market in the United States, has shown promise in trials in Europe by decreasing tachycardia and improving symptoms of POTS by affecting the "funny" sodium channels of the sinus node.[2, 12, 20] Pharmacological treatment is a balancing act and patients with POTS tend to be more sensitive to the intended and unintended effects of medications.[18]

Appendix A lists important medications in the management of POTS and helpful prescribing guidelines presented previously in Practical Neurology and used with permission of the authors.

Discussion

It is not uncommon to find a provider who has never heard of POTS or one who questions its validity as a medical diagnosis. However, there is strong evidence and sufficient research legitimizing POTS as a physiologic syndrome with distinct pathophysiology affecting

both the autonomic nervous and cardiovascular system. It is neither a psychiatric diagnosis nor simply a functional diagnosis. Hypervigilance with physical sensations and anxiety frequently coexist with symptoms of POTS, but they do not cause POTS.[2] A delayed diagnosis of POTS often leads to an initial misdiagnosis of a psychiatric disorder. Patients with POTS frequently have mild to moderate depression and subclinical anxiety, but psychiatric disorders are found with similar prevalence in patients with POTS as in the general population.[1, 10]

Patients with POTS are high utilizers of healthcare due to the impact of their symptoms on quality of life and the similarity of their symptoms to emergency conditions. On average a patient with POTS sees an average of seven providers and takes four years to receive a correct diagnosis. Over 25% see more than ten providers before receiving a correct diagnosis.[1] As NPs become more aware of the clinical manifestations of POTS, the time to diagnosis would be expected to decrease significantly.

When NPs are aware of and understand POTS, it is relatively easy to diagnose, but it is difficult to treat. Significant provider time and support is required to develop an effective treatment plan. Additionally, it may take several medication trials to find a regimen that works. While some patients experience great progress quickly and are back to a functional level within months, for most, this is a chronic illness that impacts every aspect of their quality of life. Early diagnosis and treatment can halt the deconditioning that occurs over time with POTS and can make the path to recovery a little less steep.

It would make sense to refer this patient to a special given the complexities of the clinical course and the intricacies of treatment, but there are too few specialists in POTS.[1] And which specialist should the NP refer to? While this is primarily a neurological disorder, the key symptomology lies squarely in the territory of cardiology. There are interdisciplinary specialty

clinics for POTS and other autonomic disorders scattered throughout the country, but as of 2018, only approximately 40 physicians were board certified in Autonomic Disorders in the United States.[1] Patients frequently wait months for an appointment with a provider with experience in treating POTS; therefore, NPs must become well-versed in the diagnosis and treatment of POTS.

Conclusion

POTS is a highly relevant syndrome that significantly impacts patients' lives—much more prevalent than would be expected from a syndrome that no one has ever heard of before. Articles about POTS and autonomic disorders historically have been found in journals for cardiovascular and autonomic disorders. They are rarely found in the literature for nurse practitioners. As more articles about POTS appear in literature for NPs, awareness and understanding of POTS will improve. Continued research will yield greater understanding of the pathophysiology of POTS and will lead to better treatment outcomes. The body of knowledge is growing, and it will be essential to stay up to date to effectively treat individuals with POTS.

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Appendix A

Table 1
Medications in Treatment of POTS. Used with Permission of the Authors.

Medication	Dose	Mechanism of Action	Side Effects	Notes
Propranolol	10-20 mg orally four times a day	β-adrenergic receptor antagonist	Bradycardia, bronchospasm and hypotension	May help in lower doses and is not well tolerated in higher doses
Midodrine	2.5-10 mg orally every 4 hours of TID	α-1 adrenergic receptor agonist	Scalp paresthesia, piloerection, urinary retention and supine hypertension	Do not take 4 hours before bedtime to avoid supine hypotension
Fludrocortisone	0.05-0.2 mg/day orally or every other day	Expands blood volume through renal reabsorption of sodium	Hypertension, hypokalemia, and edema	Monitor for low serum potassium
Pyridostigmine	30-60 mg orally TID	Acetylcholinesterase inhibitor	Diarrhea and abdominal cramping	It helps but is not too potent by itself
Clonidine	0.05-0.2 mg BID	Central sympatholytic α-2 receptor agonist	May cause sedation and hypotension	Decreases plasma norepinephrine; can lead to rebound due to short half-life
Methyldopa	125-250 mg orally BID	Central sympatholytic (false neurotransmitter)	Sedation and hypotension	Longer half-life, so often better tolerated
Desmopressin (DDAVP)	0.2 mg orally as needed	Acute blood volume expansion	Water retention and hyponatremia	Carefully monitor for hyponatremia.
Ivabradine	5-7.5 mg qd or bid	Funny channel blocker	Bradycardia	No randomized trials for pots
Modafinil	100 mg orally twice daily	Stimulant	May exacerbate tachycardia in some patients	Approved for sleep disorders, but may help with concentration in POTS

Medications commonly used to treat the symptoms of postural tachycardia syndrome (POTS). These medications can be used alone or in combination.
Jones, PK, et al. Practical Neurology 2016: 16:431-438. Doi:10.1126/practneurol-2016-001405[14]