JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME: A SYSTEMATIC REVIEW

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Abstract : The hallmark of Postural Orthostatic Tachycardia Syndrome (POTS), a chronic illness, is orthostatic intolerance accompanied by an abnormal rise in heart rate when standing upright. Numerous symptoms, such as weariness, exercise intolerance, and gastrointestinal distress, are commonly experienced by patients. It generally affects primarily women between the ages of 20 and 50. POTS frequently starts with a viral infection, significant surgery, trauma, or pregnancy. Nonetheless, our understanding of the syndrome's pathophysiology is incomplete or lacking. There are no FDA-approved drugs for treating POTSonce it has been diagnosed. On the other hand, non-chemical therapeutic alternatives like exercise, increased fluid intake, tensing of the muscles, diet, and routine adjustments are usually used in conjunction with patient education to control it.

IndexTerms **- Postural Orthostatic Tachycardia Syndrome (POTS), weariness, exercise intolerance, orthostatic intolerance.**

I. INTRODUCTION

Postural Orthostatic Tachycardia Syndrome is characterized as a clinical syndrome that lasts for at least half a year. The primary diagnostic criterion is the absence of overt orthostatic hypotension during a head-up tilt test and an increase in heart rate equal to or greater than 30 min−1 or above 120 min−1.[1] One of the most prevalent types of chronic orthostatic intolerance in pediatric patients is POTS.[1]

Since tilt table testing and beat-to-beat hemodynamic monitoring are crucial components of the diagnostic workup, POTS can be challenging to identify.[2] Furthermore, One should rule out POTS in favour of other illnesses that might cause tachycardia, such as tachyarrhythmias, anaemia, severe deconditioning, dehydration, thyroid disease, usage of adrenergic medications, and emotional disorders.[2]

Because of the factors above, it is challenging to assess the overall prevalence; nonetheless, it is believed that approximately 500.000 persons in the USA alone suffer from POTS. Rather than an increase in the disease's overall prevalence, Robertson (1999) defined "the epidemic of orthostatic tachycardia and orthostatic intolerance" as an epidemic of disease recognition. Because of this, it is uncertain if POTS has been an underdiagnosed illness or if its occurrence is rising and signalling the start of an epidemic.[2]

II.CLASSIFICATION

POTS has been categorized in several ways by researchers. According to Dr. Blair Grubb, POTS can be classified as "primary" or "secondary." "Primary" (also called "idiopathic") POTS is defined as having no other discernible medical condition. When there is another medical condition that is known to cause or exacerbate POTS symptoms, it is referred to as "secondary" POTS.[3] Dr. Julian Stewart classified POTS into "high flow" and "low flow" categories based on the patient's lower limb blood flow.[4] Other researchers have used some notable features of the post-stroke syndrome to characterize the condition: hypovolemic POTS, linked to low blood volume; partial dysautonomic or neuropathic POTS, linked to a partial autonomic neuropathy; and hyperadrenergic POTS, linked to elevated norepinephrine levels.[3][5][6] Several POTS patients exhibit two or three of the various characteristics, indicating that these are not separate medical conditions. One patient may, for instance, have low blood volume, increased norepinephrine, and neuropathy.

III.EPIDEMIOLOGY

There is no data on how common POTS are.[7] A study calculated a minimum rate of 170 cases of POTS per 100,000 people; however, because of underdiagnosis, the true prevalence is probably higher.[7]According to a different study, there are at least 500,000 cases in the US.POTS affects women more frequently than men, with a 4:1 female-to-male ratio.[8][9]The majority of POTS patients are between the ages of 20 and 40, with an average age of 21.[10][8] POTS diagnoses are uncommon after the age of 40, possibly because symptoms get better with age.[7]

IV. ETIOLOGY

Specific postural orthostatic tachycardia syndrome subgroups have been identified based on a range of putative aetiologies outlined below. The ultimate common pathway is generally considered excessive tachycardia in the context of cardiovascular deconditioning.[11]

NEUROPATHIC

A length-dependent autonomic neuropathy known as neuropathic postural orthostatic tachycardia syndrome is primarily characterized by sympathetic denervation in the lower limbs, which results in decreased vasoconstriction and venous pooling.[12][13] A study found that a distal pattern of anhidrosis revealed by thermoregulatory sweat testing was associated with peripheral sudomotor denervation in 50% of POTS patients.[14] Despite normal systemic norepinephrine spillover, POTS patients have been found to have reduced norepinephrine spillover in their lower extremities, which suggests dysfunctional norepinephrine reuptake because of damaged terminal nerves.[15]It has also been noted that dependent acrocyanosis is a sign of peripheral venous pooling.[16]Therefore, an excessive cardiovascular response is required to maintain appropriate mean arterial pressures.

HYPERADRENERGIC

The hyperadrenergic subtype, which accounts for 30 to 60% of patients with POTS is characterized by elevated standing plasma norepinephrine levels of 600 pg/mL or higher. The primary symptoms of this subtype are palpitations, tremors, hypertension, anxiety, and tachycardia.[17][18] One case had a norepinephrine transporter (NET) loss of function gene mutation (SLC6A2), which led to inadequate norepinephrine transport and an elevated mean supine heart rate.[19] NET block is more commonly observed when drugs such as tricyclic antidepressants, sympathomimetics (methylphenidate), and norepinephrine reuptake inhibitors (bupropion) are causing pharmacologic inhibition.[17][18]When treating the cognitive side effects of post-oxygenase syndrome (POTS), such as depression, anxiety, and difficulty concentrating, these drugs are frequently helpful. As a result, it is wise.

HYPOVOLEMIC

Although the degree of hypovolemia varies between studies, reduced plasma, red blood cell, and total blood volumes are seen in up to 70% of patients with postural orthostatic tachycardia syndrome.[20][18][21] This physiologic low-volume state is persistent in POTS patients. It is correlated with a paradoxically low level of aldosterone and renin, indicating a potential disruption of the renin-angiotensin-aldosterone axis, essential for maintaining a sufficient plasma volume.[22] Patients with co-occurring gastrointestinal disorders may experience secondary hypovolemic states, which result in excessive fluid loss and inadequate volume intake (nausea, vomiting, diarrhoea).[17]

AUTOIMMUNE

Given the significant overlapping commonalities (female predominance, post-viral onset, elevated autoimmune markers) seen in other systemic autoimmune disorders like rheumatoid arthritis, lupus, and Sjogren's syndrome, one theory for postural orthostatic tachycardia syndrome is an autoimmunity hypothesis.[17][23] Increased autoantibodies have been shown in POTS in earlier research. Up to 25% of patients had positive antinuclear antibodies; the most common cause was Hashimoto thyroiditis.[24][25]According to one study, POTS patients had higher proinflammatory IL-6 levels that were linked to higher sympathetic drive—possibly as a result of long-term systemic immune activation.[26]In the POTS population, additional autoimmune markers, such as ganglionic AChR, G-protein coupled receptor, and different nonspecific autoantibodies, have also been observed.[27][28][29]

DECONDITIONING

Although its existence as a cause or effect is unclear, patients with postural orthostatic tachycardia syndrome frequently exhibit physical and cardiovascular deconditioning.[16][20]Furthermore, objective laboratory or autonomic findings do not always correlate with the degree of deconditioning.[30] Other healthy people placed in microgravity environments, like space flight, have also shown similar symptoms to POTS, indicating the physical and gravity-dependent roles underlying POTS.[11] Compared to healthy controls, POTS patients have been shown to have smaller hearts, with an average reduction in left ventricular mass of 16% and a reduction in plasma volume of 20%. Chronic fatigue, autonomic instability, and general functional impairment are well-documented conditions that lead to decreased physical activity and extended periods of bed rest.[31][32]

V.PATHOPHYSIOLOGY

Although the exact cause of POTS is unknown, episodes frequently follow surgery, viral illnesses, or trauma. In addition, women may develop symptoms right before their periods. Furthermore, in certain patients, genetic abnormalities might be involved.[33] A triggering event, like COVID-19, typically occurs weeks or months before the onset of POTS symptoms in patients.[34]

When a patient moves from a supine to a standing position, their regular physiological response is interrupted, which is the hallmark of post-stroke syndrome (POTS). An immediate reduction in blood volume to a volume of 500 mL to 800 mL upon standing is a normal physiological response.[35]Thirteen Blood pools in the legs and abdomen as a result, lowering blood pressure (BP) as a result of less blood returning to the heart. Sensing this drop in blood pressure, specialized cells called baroreceptors send signals to the brain, triggering autonomous nervous system in a compensatory manner.[35][36] Increased sympathetic activity during this reaction causes vasoconstriction, increased heart rate (HR), and increased stroke volume. Furthermore, there is a decrease in parasympathetic outflow, which raises HR even more. These combined responses maintain the cardiac output (CO) required for the brain and other organs to be perfused.[35]Thirteen Standing up from a supine position,

POTS results from an exaggerated compensatory response to the initial decline in BP and CO, which causes the patient to experience pronounced tachycardia.[37][36][38]

Though several mechanisms, including hypovolemia and deconditioning, have been proposed, the precise mechanism causing the autonomic dysregulation observed in POTS remains unknown. Reduction in blood volume and blood pooling in the legs after normal conditions are restored are two signs of deconditioning, a decrease in heart-muscle responsiveness that can occur occasionally following extended weightlessness.[39]sixteen Because a higher HR will be required to sustain CO, this may further exacerbate hypovolemic symptoms.[35]

A fresh explanation suggested is neuroendocrine dysfunction, in which cases may parade hyperadrenergic countries due to elevated cardiovascular adrenergic exertion distinct from tachycardia. Compared to cases without POTS, these cases generally have advanced catecholamine situations, which may be caused by a functional or acquired insufficiency in the norepinephrine transporter(NET). (38) Some POTS cases with a single point mutation have also been set up to have inheritable variations that affect reduced norepinephrine concurrence, sympathetic whim-whams activation, and loss of NET function. (40) Also, women are more likely to be diagnosed with POTS, and the inflexibility of their symptoms can change throughout the menstrual cycle, leading to changes in BP and vasoconstriction. (41) Nevertheless, experimenters suspect that POTS may have colourful causes, some of which may be abnormal regulation of BP; disabled function of jitters, especially in the lower extremities; and functional changes in heart and blood vessel.

VI. TREATMENT :

A.PHARMACOLOGICAL TREATMENT:

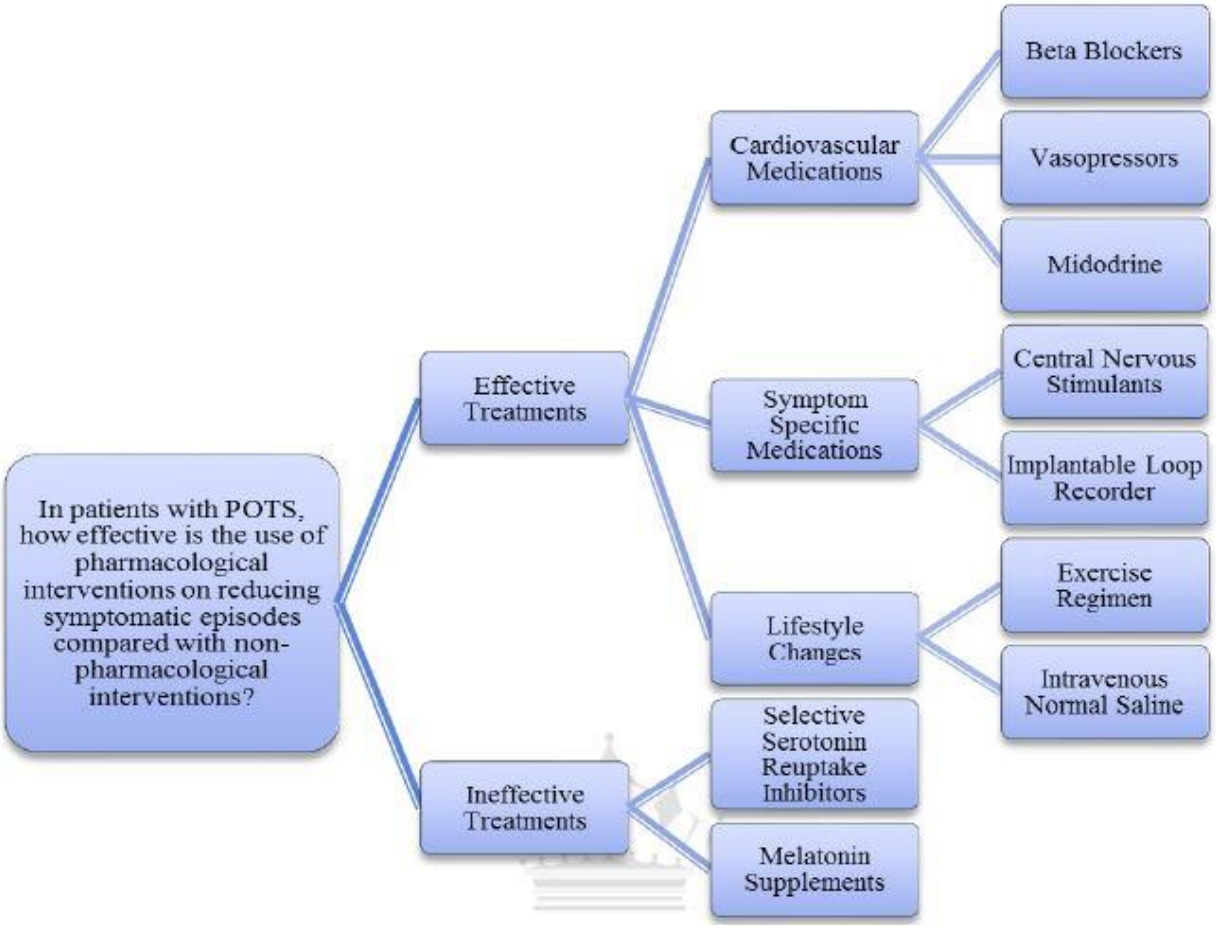

FIGURE 1: Treatment strategy for POTS [credits to IJSRM]

B.NON PHARMACOLOGICAL TREATMENT :

Reduced water consumption and shorter sleep duration are risk factors for POTS in kids and teenagers [42]. A crucial component of POTS patients' care is health education. Increasing intake of salt and water is the fundamental treatment for the illness. The majority of kids with POTS should consume up to 5.6 g of salt. The objectives are a 24-hour urinary sodium excretion of more than 200 mmol or a urine osmolality of less than 300 mmol/L [43]. Since those who slept for less than eight hours a day had a 5.9-fold higher risk of developing POTS than those who slept for more than eight hours, good sleep may also be a crucial factor to consider [42].

Researchers have discovered that patients with POTS experience reduced symptoms when participating in a consistent, brief-term progressive physical exercise program[44]. Walking on a treadmill, swimming, biking both upright and recumbent, and machine rowing are all part of this regimen. Nonetheless, a significant obstacle to effective physical therapy is patient adherence to the program regularly and consistently [45-46].

Alternative nutritional, psychological, and pharmacological therapies should be a part of a multidisciplinary treatment plan for adolescents and children with post-traumatic stress disorder (PTSD). Like other researchers, we have discovered that children with POTS have low iron storage [47-48], low levels of vitamin B12 [49], low levels of vitamin B1 [50], hypovitaminosis D [51], and high levels of homocysteine in their plasma [52]. Patients' recovery would greatly benefit from these being corrected.

VII. CONCLUSION

A significant amount of disability can be caused by POTS, an autonomic nervous system disorder, in previously healthy individuals. Patients with POTS typically have low blood volume, are frequently hyperadrenergic, and exhibit an elevated HR of ≥30 bpm with 10 minutes of standing (or higher in children). Different POTS subtypes involve various physiological and biochemical alterations and distinct clinical features. Specific biomarkers help determine the drugs used in individualized treatment plans by reflecting the pathophysiology of POTS in children. Nevertheless, more clinical research is still needed to understand the condition's pathophysiology and the available treatment options. As of right now, POTS patients' symptoms are mostly managed empirically. While orthostatic and non-orthostatic symptoms may improve with general lifestyle modifications used to treat POTS, refractory symptoms should prompt additional diagnostic testing and appropriate dietary and pharmaceutical management. When nutritional deficiencies are identified, they should be treated and monitored.

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