Etiologies and Management of Postural Tachycardia Syndrome in Children

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ABSTRACT

Postural tachycardia syndrome (POTS) is a chronic condition with frequent symptoms of orthostatic intolerance or with sympathetic activation and excessive tachycardia while standing, without significant hypotension. The aim of this review was to discuss the pathogenesis and to outline the diagnosis and treatment guidelines. We conducted a literature review of articles published up to 2017, in following databases; PubMed, and Embase investigating postural tachycardia syndrome in children. We restricted our search to only English published articles with human subjects concerning children under 16 years. POTS is a disorder of the autonomic nervous system that could create considerable disability amongst previously healthy people. Patients with POTS show a HR rise of ≥ 30 bpm within 10 min of standing (or greater in kids), are typically hyperadrenergic, and tend to have a reduced blood volume. The pathophysiology of POTS is complex and the result of a variety of separate systems producing a common pattern of signs. The specific pathogenesis of POTS has yet not been completely clear. A variety of uncommon factors might be involved in the pathogenesis. Selecting the correct therapy according to the detailed pathogenesis could absolutely enhance the efficiency of medicine. Treatments targeting the hypovolemia and the excess sympathetic nervous system activation may assist eliminate symptoms. Keywords: Tachycardia, Etiology, Children.

INTRODUCTION

Postural tachycardia syndrome (POTS) is among the most common types of orthostatic intolerance in kids (¹). The main indication of POTS is sinus tachycardia pertaining to the position change. The clinical orthostatic symptoms vary, such as dizziness, headache, chest tightness, chest pain, pale skin, tiredness, presyncope, and syncope. For the medical diagnosis of POTS, previous standards, which was also related to the medical diagnosis of grown-up patients, postulated the visibility of an orthostatic heart rate (HR) increment of at least 30 beats/min or an absolute orthostatic HR of a minimum of 120 beats/min within 10 minutes of active standing or passive head-up tilt, connected with orthostatic signs and symptoms (²). Nonetheless, there have been researches recording a bigger HR changes during the orthostatic progress in adolescents than adults (³). Therefore, the orthostatic HR requirement for the medical diagnosis of adult POTS might not be appropriate for children and adolescents and need to be reviewed. Singer et al. (⁴) recommended that it appertained to use the requirements that the orthostatic HR increment ≥ 40 beats/min or absolute orthostatic HR ≥ 130 beats/min (for ages 13 years and younger), or ≥ 120 beats/min (for ages 14 years and older) within 5 min of head-up tilt, along with the symptoms of orthostatic intolerance for pediatric POTS. In a cross-sectional study, consisting of 1449 children and adolescents aged 6-18 years, Zhao et al. (⁵) suggested that POTS need to be suggested in kids and adolescents when the orthostatic HR increment ≥ 40 beats/min, or absolute orthostatic HR ≥ 130 beats/min (for ages 12 years and younger), or ≥ 125 beats/min (for ages 13 years and older) within 10 min relocating from supine to upright setting. The data of the existing prevalence of POTS in kids and adolescents at a variety of age are still doing not have; nevertheless, Lin et al. (⁶) carried out a cross-sectional investigation in Kaifeng City, Henan Province, China, where 600 Chinese children and adolescents aged 7-18 (11.9 ± 3.0) years were analyzed via questionnaires and the upright examination. Their outcomes suggested that the prevalence rate of POTS in Chinese children and adolescents was 6.8%, and there was no considerable sex difference in patients.

Postural tachycardia syndrome (POTS) is a chronic condition with frequent symptoms of orthostatic intolerance or with sympathetic activation
and excessive tachycardia while standing, without significant hypotension \(^{(2)}\). The aim of this review is to discuss the pathogenesis, and to outline the diagnosis and treatment guidelines.

**METHODOLOGY**

We conducted a literature review of articles published up to 2017, in following databases; PubMed, and Embase investigating postural tachycardia syndrome in children. We restricted our search to only English published articles with human subjects concerning children under 16 years. Search strategies used following MeSH terms in searching via these databases: “postural tachycardia syndrome”, “pediatric”, “Management”, “children”. Then we also searched the bibliographies of included studies for further relevant references to our review.

The study was done after approval of ethical board of King Khaled university.

**DISCUSSION**

- **The Pathogenesis of Postural Tachycardia Syndrome**
  
  The precise pathogenesis of POTS is not completely clear. In recent years, studies have revealed that POTS might be related to several variables consisting of hypovolemia, high catecholamine status, abnormal neighborhood vascular tension, and lowered skeletal muscle pump activity \(^{(2)}\).

- **The low blood volume**
  
  Clinical researches have shown that patients with POTS had reduced blood volume or reduced red cell volume \(^{(7)}\). Jacob et al. \(^{(8)}\) contrasted 18 patients with POTS and normal cases and, finally, located that half of patients with POTS had reduced blood volume \((16\% \text{ vs. } 2\%, \ P < 0.05)\). Twenty-four hours urinary sodium level can reflect the state of the body's volume capability \(^{(9)}\). Zhang et al. \(^{(10)}\) found that reduced 24-h urinary sodium was related to the severity of the signs of POTS in kids and teenagers. These findings also sustained the theory that reduced volume status could play a role in the pathogenesis of POTS.

- **The high catecholamine status**
  
  Jacob et al. \(^{(11)}\) found that the plasma norepinephrine and epinephrine levels were considerably increased both in supine and in upright placements. Thieben et al. \(^{(12)}\) additionally discovered a high adrenaline condition (standing plasma norepinephrine level \(\geq 2600 \text{ pg/ml} \)) in POTS patients. The impaired function of norepinephrine transporter (NET) could be one of the mechanisms. The acquired or obtained mutations may result in the disorder of NET gene; therefore, the removal of norepinephrine in the synaptic cleft suffers, causing the high adrenaline condition. There have additionally been studies revealing that patients with POTS have actually lowered expression of NET protein around the sympathetic nerve \(^{(13)}\).

- **The abnormal local vascular tension**
  
  In 1988, Streeten et al. \(^{(14)}\) researched the pathological systems underlying POTS. In a group of 34 orthostatic intolerance patients, 10 of them materialized as POTS. After identifying with sodium pertechnetate Tc-99m and infusing the erythrocytes into the body, radioscopy revealed excessive gravitational pooling of blood in the legs in patients with orthostatic tachycardia, suggesting that the uncommon local vascular tension may contribute in the start of the condition. Nitric oxide (NO), an endogenous gas signal particle which has been approved as a vasodilatation factor, could show the vascular endothelial cell function. Liao et al. \(^{(15)}\) discovered that compared with healthy children, POTS patients had raised plasma NO and NO synthase levels. The degree of brachial arterial vasodilatation in POTS kids was also raised. These searchings for sustained the theory that local vascular stress and vascular endothelial cell dysfunction could be associated with the development of POTS.

- **Decreased skeletal muscle pump activity**
  
  Stewart et al. \(^{(16)}\) researched numerous indexes of 12 cases that suffered from POTS related to low calf blood circulation (low-flow POTS). They located that the calf bone areas were decreased in these patients compared to ten controls and 7 patients that have POTS with regular calf blood flow. In addition, the decrease of calf circumferences was related to the reduced portion of calf venous capacity emptied during voluntary muscle contraction. Additionally, the blood flow was positively correlated with calf circumference. As a result, they ended that due to the reduced calf blood flow, the calf muscle size was decreased and thus the skeletal muscular tissue pump function was impaired, which better contributed to venous pooling and ultimately led to orthostatic intolerance in these patients.

- **Signs and Symptoms of POTS**
  
  POTS is connected with lots of symptoms. Patients often have trouble standing upright, resulting in a rapid heart rate with lightheadedness, nausea, tiredness, dizziness, or fainting. Due to these...
symptoms, numerous patients deal with everyday tasks and may be incapable to work, attend school or participate in recreational activities. The signs of POTS can be unforeseeable- they may come and go, show up in any kind of combination and differ in severity. Typically patients will certainly have more signs after a stressor or a physical activity, but the precise triggers that cause the beginning of POTS are unidentified. For as much as 75 percent of patients, POTS signs could improve, and even disappear, by age 21 to 25 years.

<table>
<thead>
<tr>
<th>Table 1. Symptoms of POTS.</th>
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<tbody>
<tr>
<td>Dizziness</td>
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<tr>
<td>Fainting or passing out (syncope)</td>
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<tr>
<td>Fast heart rate (tachycardia)</td>
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<tr>
<td>Chest pain</td>
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<tr>
<td>Headache</td>
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<td>Severe fatigue</td>
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<tr>
<td>Difficulty concentrating (&quot;brain fog&quot;)</td>
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<tr>
<td>Feeling worse in very hot or very cold temperatures</td>
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- **Diagnosis Testing**
  When experiencing apparent postural orthostatic tachycardia disorder, it is very important to assess and omit additional causes of orthostatism. These include yet are not limited to diabetes mellitus, chemotherapy, heavymetal poisoning, Sjogren's disorder, systemic lupus erythematosus, or symptoms of a paraneoplastic syndrome. Eating disorders with coming with volume exhaustion and weight-loss need to be taken into consideration. Furthermore, medicines that hinder venous go back to the heart may cause comparable indications. These medications consist of diuretics, anxiolytics, and vasodilators. A list of these medications is presented elsewhere. Hyperadrenergic states, anxiousness, and volume deficiency could result in postural heart-rate increases during tilt table testing. A patient can materialize one of those illness concurrently with idiopathic postural orthostatic tachycardia syndrome, which might not be uncovered till ample therapy is started for the concurrent medical diagnosis. More medical workup might be appropriate. A neurology consultation is frequently asked for these patients, to assess headaches or wooziness. An electroencephalogram is occasionally performed to leave out epilepsy. A cardiology examination is often requested to dismiss arrhythmogenic causes of syncope and dizziness. An electrocardiogram, event monitor, or Holter tracking can leave out cardiac dyshrhythmia. A gastroenterology appointment might be requested to examine grievances of abdominal pain and nausea, which might be constant yet are regularly prominent in the early morning. Serum electrolytes, a complete blood count, liver function tests, thyroid function examinations, and transmittable serologies could be carried out to rule out various other causes of dizziness, tiredness, and stomach signs and symptoms, yet these are normally normal. In symptomatic adults, postural orthostatic tachycardia disorder is specified by an increase in heart rate of > 30 beats each min on a head-up tilt table examination, or upon standing from a sitting position. Much more lately, we kept in mind that the typical rise in heart rate after 3 minutes of active standing in" typical" asymptomatic adolescent patients could be as high as 40 beats per min. This incremental rise in heart rate in upright adolescents is higher than observed in healthy and balanced adults, and stresses the have to differentiate in between active standing and the head-up tilt table examination for gauging orthostatic modifications in crucial indications, and the requirement for caution in identifying postural orthostatic tachycardia syndrome in asymptomatic adolescents. Typical distributive information for community-dwelling, asymptomatic adolescents are not yet offered, however our group is addressing this challenge.

- **Treatment Guidelines**
  Among the essential elements of managing patients with POTS is an exact medical diagnosis and elimination of additional reasons, such as medications. The available clinical evidence for therapy of POTS is based mostly on studies in grownups, with situation series and few nonrandomized, regulated trials. Pediatric POTS is a relatively new entity with heterogeneous scientific discussions, a vast spectrum of symptoms, varying degrees of disability, and premorbid comorbidities, such as migraine, attention deficit disorders, and anxiousness. Moreover, family dynamics and capability of patients and parents to manage the obstacles in treatment, and adaptation to functional
disabilities and school attendance play a crucial role in effective treatment.

- **Diet**

  Modifying diet and eating habits and increasing liquid intake aid people with POTS. Consuming small dishes has been claimed to decrease the seriousness of postprandial hypotension, due to the fact that the amount of blood needed for digestion is lowered (20). Raising electrolyte and water intake was revealed to decrease tachycardia in POTS patients with idiopathic kinds of the illness, as a result of raised blood pressure via raising blood volume (20). This is likewise believed to be helpful in POTS patients with pooling blood and/or hypovolemia (21). The research suggests a couple of litres each day; however, drinking excessive amounts of water has the prospective to disrupt electrolyte concentrations which could impact the heart rhythm (21). Enhancing salt in the diet is another option for POTS patients discovered to have damaged urinary sodium retention, which speeds up hypovolaemia episodes. The levels of renin and aldosterone in some POTS sufferers are located to be low. These hormones boost plasma quantity by promoting salt retention (22). Hence, raising salt intake by taking salt tablet computers or an electrolyte solution aids broaden blood quantity, which will certainly alleviate the hypotension some POTS patients’ experience.

- **Exercise**

  In a number of studies, exercise has been reported to be helpful both in reducing POTS symptoms, in addition to contributing in curing the condition (23). In one study, POTS patients without blood pressure fluctuations were trained slowly to relocate from lying to resting to a standing position throughout various activities, such as swimming, rowing, and cycling (23). The similar study incorporated the exercise training with raised water and salt intake to 3 ~ 4 L/d and 6 ~ 8 g/d, respectively and involved raising the head of the bed while resting at night (23). Grubb reported cardio workout 3 times a week for 20 min is likewise beneficial for patients who can tolerate it (24).

- **Sodium chloride 0.9% (Normal saline)**

  Sodium chloride 0.9% infusion has been reported very beneficial in reducing symptoms in POTS patients and boosting lifestyle. The mixture loads the POTS patient with sodium enhances blood and blood cell volume, and leads to a mild elevation in blood pressure (25). Freitas et al. (25) reported sodium chloride 0.9% mixture was one of the most reliable amongst a variety of therapies, creating a reduction in heart rate and reducing systolic blood pressure change in treated POTS patients. This appears to be a good, low-cost therapy option with couple of side effects for POTS patients who endure hypovolemia triggered by sympathetic neuropathy, which results in venous merging during upright position, or various other idiopathic reasons. Nonetheless, the problem in this research is that intravenously mixture is time consuming as the patient have to typically most likely to the hospital or to the physician's office for IV cannulation and infusion. Indwelling, peripherally put central catheters (PICC) have actually been utilized by some POTS patients to provide their infusion in your home, but there are feasible threats related to a PICC line, such as infection, occlusion or displacement.

- **Fludrocortisone**

  Fludrocortisone enhances plasma volume in patients with POTS because of salt and water retention as well as sensitizes the blood vessels to constriction (26). Some physicians combine salt tablets with fludrocortisone in order to ensure its efficiency, although this has to depend upon salt intake (27). Patients on fludrocortisone should be given magnesium and potassium supplements because of their simultaneous depletion. Likewise, fludrocortisone has the potential to increase intracranial pressure, therefore it could not be utilized in some cases, which involve the brain. Like beta-blockers, fludrocortisone reduces renin degrees and might be counterproductive for POTS patients with low renin levels (8). Some patients suffer serious adverse effects, specifically serious headache (27).

**Table2. Non-pharmacological and pharmacological interventions of management POTS** (20,23,26)

<table>
<thead>
<tr>
<th>The oral rehydration salts</th>
<th>Exercise</th>
<th>Diet</th>
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<tbody>
<tr>
<td>Sodium chloride 0.9% (Normal saline)</td>
<td>Fludrocortisone</td>
<td>Ivabradine</td>
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<tr>
<td>Beta-blockers</td>
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<td>Erythropoietin</td>
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<td></td>
<td>Pyridostigmine bromide</td>
<td>Vasoconstrictor</td>
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<td>NSAIDs</td>
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**CONCLUSION**

POTS is a disorder of the autonomic nervous system that could create considerable disability amongst previously healthy people. Patients with POTS show a HR rise of ≥ 30 bpm within 10 min of
standing (or greater in kids), are typically hyperadrenergic, and tend to have a reduced blood volume. The pathophysiology of POTS is complex and the result of a variety of separate systems producing a common pattern of signs. The specific pathogenesis of POTS has yet not been completely clear. A variety of uncommon factors might be involved in the pathogenesis. Selecting the correct therapy according to the detailed pathogenesis could absolutely enhance the efficiency of medicine. Treatments targeting the hypovolemia and the excess sympathetic nervous system activation may assist eliminate symptoms.

REFERENCE