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# Treatment questions in POTS with hypertension and syncope

**Case Report**

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**Abstract:** A 27-year old man experienced recurrent syncope with prodromal palpitations and resultant injury. The features of these episodes suggested a potentially neurally-mediated mechanism. Head-up tilt test revealed the postural orthostatic tachycardia syndrome (POTS). Within the first minutes of upright posture during the total head-up tilt testing, a heart rate increase of >30 beats/min and to a maximum of 150 beats/min was documented in the patient. At the end of passive tilting, the patient lost consciousness in the absence of hypotension while in sinus rhythm of 140 bpm. The 12-lead ECG and electrophysiological study showed no abnormalities. The patient received a beta-adrenergic blocker, a selective central imidazoline receptor agonist and psychiatric therapy, resulting in only a short-term improvement.

**Keywords:** *Syncope • POTS • Hypertension*



## 1.Introduction

In the postural orthostatic tachycardia syndrome (POTS), enhanced sympathetic activity causes an exaggerated heart rate response to standing. All patients with POTS suffer from symptoms of orthostatic intolerance such as dizziness, headache, blurred vision, lightheadedness, mental clouding and nausea in the absence of orthosthatic hypotension, but only one-third describe syncope. The diagnosis of POTS can be determined during head-up tilt testing [1]. We report the case of a 27-year-old man with hypertension and numerous syncopal episodes resulting in injury. POTS was diagnosed in head-up tilt testing with reproduced syncope unassociated with hypotension.

## 2. Case report

A 27-year old man experienced 6 episodes of syncope and 150 of pre-syncope during the past 14 months and was referred to our department after a negative neurological evaluation. The episodes were consistent with partially neurally-mediated syncope and in most cases they were preceded by palpitations. The patient had no family history of syncope or sudden death. Recently, labile hypertension had been diagnosed. An initial evaluation including clinical history, physical examination and baseline ECG was performed. The patient did not use medications. Blood pressure at rest was 130/90 mmHg.

The baseline ECG showed a sinus rhythm of 82 bpm, PR interval of 180 ms and normal QRS complex of 80 ms duration. A 24 h Holter ECG recording confirmed transient sinus tachycardia of 140-170 bpm. A head-up tilt test under Westminster protocol (angle of 60°, 45 min of passive tilting) was performed. Within the first minutes of upright posture a heart rate increase of >30 beats/min was observed, which persisted during the total head-up tilt testing, reaching a maximum of 150 beat/min (Figure 1). At the end of passive tilting, in the absence of hypotension (BP=140/75 mmHg), the patient lost consciousness while the heart was in sinus rhythm at 140 bpm.

Transthoracic echocardiogram showed no abnormal-

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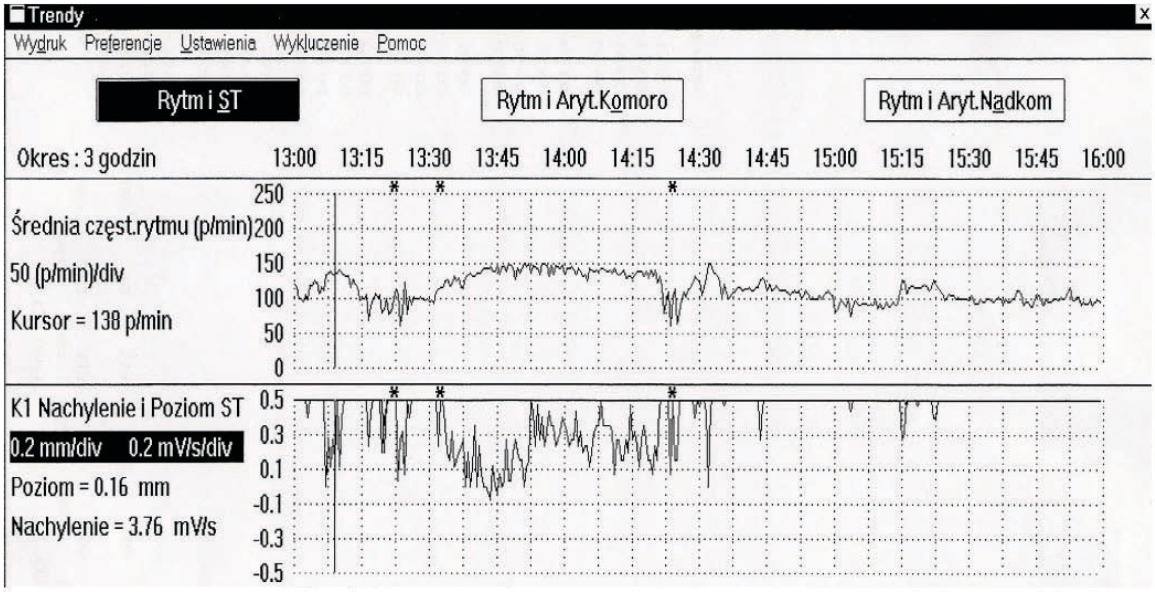
**Figure 1.** Trends of heart rate during head-up tilt testing. The points (* *) marks phases of the test: supine and tilting.




ities. To rule out syncope due to tachyarrhythmia, a transoesophageal electrophysiological study was performed. The patient gave written informed consent. Tests of sinus and atrioventricular node function were within normal ranges with an AV nodal Wenckebach conduction pattern at 170 bpm. No manifestation of ventricular pre-excitation or AVNRT /AF was observed during atrial stimulation manoeuvres. Ambulatory blood pressure monitoring showed pressures between 175/92 and 99/67 mmHg with a mean of 124/67 mmHg. Endocrinological causes of hypertension, including pheochromocytoma, were excluded.

To treat the tachycardic episodes as well as hypertension, the patient received beta blocker therapy (metopropol CR/XL). After a psychiatric evaluation an anti-anxiety treatment was introduced due to the patient's fear of injury during syncopal episodes.

In the first months after beta blocker and psychiatric therapy the frequency of symptoms decreased. However, during longer follow-up, syncope, labile hypertension and palpitations reappeared. The patient took frequent sick leave and lost his job, and his quality of life worsened in spite of changes in drug therapy to moxonidine and betaxolol. The patient did not appear for the most recent follow-up appointment.

## 3. Discussion

Orthostatic intolerance refers to a heterogeneous group of hemodynamic disorders characterized by insufficient cerebral perfusion during upright posture. As a result of autonomic dysfunction, patients with POTS demonstrate orthostatic tachycardia in the absence of orthostatic hypotension as well as increased sympathetic activity in the supine position [2-3]. POTS can be readily identified during head-up tilt-testing if a patient displays a heart rate increase of >30 beats/min and a maximum heart rate of >120 beat/min within the first minutes of upright posture in the absence of hypotension [1]. Jauregui-Renaud and cowokers [2] hypothesized that in patients with POTS tachycardia is a reflex response to inefficient cerebrovascular autoregulation after standing. They documented autonomic dysfunction in POTS patients even in the supine position, which was further accentuated by upright posture.

The etiology of POTS is still unclear. A mild form of idiopathic peripheral autonomic neuropathy [4] or beta-receptor hypersensitivity has been suggested for the pathophysiology of this disorder [5]. A single nucleotide point mutation in the norepinephrine transporter has been identified in a kindred with POTS [6]. This hypofunctional mutation of the norepinephrine transporter produces a state of excessive sympathetic activation in response to a variety of stimuli. Goldstein *et al.* described cardiac sympathetic dysautonomia in POTS and neurocardiogenic syncope, with differences in tonic cardiac sympathetic function. Increased cardiac norepinephrine release was seen in POTS and decreased release in the latter syndrome [7].

In our patient a diagnosis of POTS was readily established but therapy was very problematic. It is well-known that in most patients, the symptoms of POTS generally remain despite of therapy. In this

patient coexisting hypertension complicated the circumstances since some non-pharmacological methods of treatment (sodium intake, hydration) and medications (alpha-adrenergic agents, fludrocortisone) were cotraindicated.

Education, elastic stockings and exercise have been shown to be beneficial in treatment of POTS [8]. Central sympatholytics (methyldopa, clonidine) or peripheral beta-adrenergic blockade can be used [8], although care must be used in administering beta-blockers to patients affected with mast cell activation disorders [9]. Ewan *et al.* describe a case of POTS in which symptomatic improvement was seen after administration of the sinus node blocker ivabradine [10], although the potential usefulness of ivabradine in POTS is not yet proved.

Selective central imidazoline receptor agonists decreasing sympathetic nervous system activity, e.g. moxonidine, may prove effective. We have reported successful treatment with moxonidine therapy in the other type of orthostatic reflex-mediated intolerance – vasovagal patients - with coexisting hypertension [11]. Stimulation of selective imidazoline receptors $I_1$ localized in the cephalad abdominolateral part of the medulla results in central inhibition of sympathetic nervous system activity and reduction of catecholamine secretion from nerve boutons [12].

The clinical course of POTS is characterised by repeated instances of remission and relapse. In severely affected patients such as the patient described here, the impairment may be severe enough to decrease quality of life by resulting in inability to work, psychosocial dysfunction, and possible depression [13]. Grubb *et al.* found the selective serotonin reuptake inhibitors useful in these patients [14].

In conclusions, our observations in this patient and previous reports confirm the potential usefulness of head-up tilt testing in diagnosing POTS, but the optimal therapy in this form of orthostatic intolerance is still unknown.

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