Journal of the American Society of Hypertension 10(3) (2016) 263–270

Research Article

The complexity of diagnosing postural orthostatic tachycardia syndrome: influence of the diurnal variability

Jangsup Moon, MD, PhD[a,b,c,1], Han Sang Lee, MD[a,b,1], Jung-Ick Byun, MD[a,b], Jun-Sang Sunwoo, MD[a,b], Jung-Won Shin, MD[d], Jung-Ah Lim, MD[a,b], Tae-Joon Kim, MD[a,b], Yong-Won Shin, MD[a,b], Keon-Joo Lee, MD[a,b], Daejong Jeon, PhD[a,b], Keun-Hwa Jung, MD, PhD[a,b], Soon-Tae Lee, MD, PhD[a,b], Ki-Young Jung, MD, PhD[a,b], Kon Chu, MD, PhD[a,b,**], and Sang Kun Lee, MD, PhD[a,b,*]

[a]*Department of Neurology, Laboratory for Neurotherapeutics, Comprehensive Epilepsy Center, Biomedical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea;*

[b]*Program in Neuroscience, Neuroscience Research Institute of Seoul National University Medical Research Council, Seoul National University College of Medicine, Seoul, Republic of Korea;*

[c]*Department of Neurology, EwhaWomans University School of Medicine and Ewha Medical Research Institute, Seoul, Republic of Korea; and*

[d]*Department of Neurology, CHA Bundang Medical Center, CHA University, Seoungnam, Republic of Korea*

Manuscript received October 20, 2015 and accepted January 9, 2016

Abstract

We investigated how the diagnosis of postural orthostatic tachycardia syndrome (POTS) would be changed due to diurnal variability in orthostatic tachycardia. The orthostatic vital sign test was administered to each patient twice, in the afternoon of the day of admission and the next morning (n = 113). Forty-six patients were diagnosed with POTS, and the remaining 67 patients were assigned to non-POTS group. Heart rate increments after standing were larger in the morning than in the afternoon in every group (all $P < .001$). Among the POTS patients, 82.6% fulfilled the diagnostic criteria for POTS in the morning and 52.2% in the afternoon. Most POTS group (65.2%) displayed normal result on single orthostatic vital sign test. Orthostatic intolerance symptoms were provoked in only 45.7% of the POTS patients, more frequently in the morning. In conclusion, diurnal variability in hemodynamic parameters and provoked symptoms significantly challenged the diagnosis of POTS. J Am Soc Hypertens 2016;10(3):263–270.

Keywords: Postural tachycardia syndrome; orthostatic tachycardia; diurnal variability; orthostatic intolerance; orthostatic hypotension.

Introduction

Postural orthostatic tachycardia syndrome (POTS) is a common cause of orthostatic intolerance which is characterized by an excessive heart rate (HR) increase after standing.[1,2] It predominantly affects young people and is more prevalent in women.[3] The clinical significance of POTS is increasingly being appreciated; it has recently been reported that POTS is often accompanied by many comorbidities, including depression, sleep problems, and chronic fatigue syndrome.[4–9] It is important not to miss diagnoses of POTS because it is largely a treatable disease.[1,3,10]

The core diagnostic criteria for POTS consist of an HR increment of ≥30 beats/min (bpm) (or ≥40 bpm in individuals aged 12 to 19 years) within 10 minutes of standing or

Conflict of interest: All the authors report no conflict of interest.

This study was supported by a grant from the Korean Health Technology R&D Project of the Ministry of Health and Welfare, Republic of Korea (HI13C1558).

*Corresponding author: Sang Kun Lee, MD, PhD, Department of Neurology, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 110-744, South Korea. Tel: +82-2-2072-2923; Fax: +82-2-3672-7553.

**Kon Chu, MD, PhD, Department of Neurology, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 110-744, South Korea. Tel: +82-2-2072-1878; Fax: + 82-2-2072-7424.

E-mail addresses: stemcell.snu@gmail.com, sangkun2923@gmail.com

[1] These two authors contributed equally to this work.

1933-1711/$ - see front matter
http://dx.doi.org/10.1016/j.jash.2016.01.011

head-up tilt in the absence of orthostatic hypotension (OH).[11–14] Some studies include a requirement for the appearance of provoked symptoms during orthostatic stress tests[15,16] or a history of chronic orthostatic intolerance[17] in the diagnostic criteria for POTS, but these are not universally accepted.

Recently, Brewster et al. have suggested that the diurnal variability of orthostatic tachycardia (OT) affects the diagnosis of the POTS.[18] They demonstrated greater OT on the modified (5 minutes) standing test performed in the morning than that in the evening, which resulted in increased diagnosis of POTS in the morning. However, they have not evaluated how many false-negative cases can occur with a single standing test. In the present study, we aimed to reevaluate the influence of HR diurnal variability on the diagnosis of POTS using the standard (10 minutes) orthostatic vital sign (OVS) test and focused on how the diagnosis of POTS can be missed in individual cases according to the timing of the OVS test. We also intended to evaluate the diurnal variability of the provoked symptoms during the OVS test.

Methods

Subjects

The electronic medical records of patients who were admitted to the Center for Epilepsy and Autonomic Disorders of Seoul National University Hospital between January 2014 and June 2014 were reviewed (n = 188). The main causes of admission were recurrent orthostatic dizziness, headaches, loss of consciousness, convulsive movements, or other paroxysmal symptoms requiring the exclusion of syncope or seizure disorders for the accurate diagnosis. Patients who underwent two OVS tests, on the afternoon of the day of admission and on the next morning, were selected (n = 163). Blood pressure (BP) and HR data at 10 minutes after standing were not available for 65 patients. Among these 65 patients, patients who satisfied the HR criteria for POTS within 5 minutes after standing (n = 15) were included in this study; the remainder of these patients were excluded (n = 50). Finally, a total of 113 patients were enrolled in our study. The history of symptoms that suggested orthostatic intolerance, such as dizziness, nausea, palpitations, headaches, sweating, chest discomfort, lightheadedness, loss of consciousness, and fatigue, was obtained from each patient. The present study was approved by the Institutional Review Board of Seoul National University Hospital.

OVS Test

The OVS test was performed under the supervision of a trained nurse. The patients were in a supine position for over 5 minutes, after which baseline BP and HR measurements were made using a Welch Allyn blood pressure monitor (Welch Allyn Protocol Inc, Beaverton, OR, USA). Patients then stood upright without support, and BP, HR, and symptoms of orthostatic intolerance were checked immediately and at 1, 3, 5, and 10 minutes after standing. The maximum increment in HR and maximum decrements in systolic BP (SBP) and diastolic BP (DBP) were compared with those observed in the supine position. Patients' symptoms were checked for 20 minutes after standing, and if a patient was unable to endure standing, then the reason for discontinuation was noted; the patient's vital signs were then checked at the remaining time points in a sitting or supine position. The test was performed in the afternoon (between 12:00 PM and 7:00 PM) on the day of admission and in the following morning (between 5:00 AM and 7:30 AM).

Patient Categorization: Diagnosis of POTS

Patients were assigned to the POTS group if (1) the increment in HR was $\geq$30 bpm (or $\geq$40 bpm in individuals aged 12 to 19 years) from the baseline within 10 minutes after standing, (2) there was no evidence of OH, defined as a drop in SBP $\geq$20 mm Hg or DBP $\geq$10 mm Hg during the OVS tests, (3) the orthostatic intolerance symptoms were provoked during the OVS test or suggested on history taking, and (4) there was no overt cause for tachycardia, such as acute blood loss, prolonged bed rest, hyperthyroidism, or tachycardia-promoting medications. All other patients were assigned to the non-POTS group.

Statistical Analysis

Data were collected and analyzed using SPSS 22.0.0 for Windows. Results were expressed as means $\pm$ standard error of the means unless otherwise noted. Data were analyzed using Fisher's exact test, Student's *t* test, or the Mann–Whitney *U* test, as applicable. OVSs at different times of the day were compared within groups using the paired Student's *t* test. The presence of a history suggesting orthostatic intolerance and whether such symptoms were provoked during the OVS test were compared using Fisher's exact test, and baseline vital sign measurements and changes in vital signs were compared between the POTS and non-POTS groups using Student's *t* test. Values of $P < .05$ were considered significant.

Results

Characteristics of Patients With or Without POTS

A total of 113 patients were included in the study (male: 55; mean age: 41.0 $\pm$ 1.8 years). Forty-six patients met the criteria for a diagnosis of POTS, and the remaining 67 patients were placed in the non-POTS group. None of the patients who fulfilled the HR criteria for POTS were taking any tachycardia-promoting medications. Patients with POTS were much younger than non-POTS subjects