Clinical Neurophysiology 125 (2014) 1248–1254

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Spectrum of autonomic dysfunction in orthostatic dizziness

Hyun-Ah Kim, Hyon-Ah Yi, Hyung Lee *

Department of Neurology, Keimyung University School of Medicine, Daegu, Republic of Korea
Brain Research Institute, Keimyung University School of Medicine, Daegu, Republic of Korea

ARTICLE INFO

Article history:
Accepted 19 October 2013
Available online 5 November 2013

Keywords:
Orthostatic dizziness
Autonomic dysfunction
Spectrum

HIGHLIGHTS

- This study investigated the frequency and detailed spectrum of autonomic dysfunction in patients with orthostatic dizziness.
- Approximately 83% (180/217) of patients showed at least one abnormal autonomic testing result. We classified orthostatic dizziness into 11 groups according to the patterns of autonomic dysfunctions.
- This study helps clinicians to understand the pattern and mechanism of autonomic dysfunction associated with orthostatic dizziness.

ABSTRACT

Objective: To investigate the frequency and detailed spectrum of autonomic dysfunction in patients with orthostatic dizziness (OD).
Methods: Over 20 months, 217 consecutive patients with OD as a presenting symptom of orthostatic intolerance were enrolled. The distribution and severity of autonomic dysfunction were measured by the composite autonomic severity score (CASS), which was derived from a standard autonomic function test including Finapres for recording of the beat-to-beat blood pressure. Sympathetic indexes (SIs) were calculated from the Valsalva maneuver (VM).
Results: Approximately 83% of patients showed at least one abnormal autonomic testing result. We classified OD into 11 groups according to the patterns of autonomic dysfunctions. The most common pattern was generalized autonomic failure of sympathetic adrenergic and parasympathetic cardiovagal functions ($n = 60$). Patients with delayed OH had larger BP increases during late phase II of the VM ($p = 0.04$), showed greater phase IV overshoot ($p = 0.04$), and had a smaller pressure recovery time increase ($p = 0.02$) than patients with classic OH. Each SI showed the strongest correlation with the CASS adrenergic subscores.
Conclusions: OD can present with a board spectrum of autonomic dysfunctions.
Significance: This investigation could be useful in understanding the pattern and mechanism of autonomic dysfunction associated with OD.

1. Introduction

Orthostatic dizziness (OD) is a common dizzy syndrome characterized by non-vertiginous light-headedness when a patient rises to standing from a sitting or supine position (Baloh and Kerber, 2011). OD is a common complaint in not only general practice and but specialized dizziness clinics. OD is believed to be one of the most common causes of non-vestibular dizziness (Baloh and Kerber, 2011; Radtke et al., 2011). A recent report showed that the one year and lifetime prevalence of OD were 10.9% and 12.5%, respectively (Radtke et al., 2011). Although OD usually results from orthostatic hypotension (OH) and is considered a representative sign of sympathetic autonomic dysfunction (Kim et al., 2013), the types of OH that may occur in patients with OD has not been described. Moreover, the frequency and pattern of other accompanying autonomic dysfunctions are not known. To study these problems, we prospectively investigated the autonomic test results of all the patients referred to our autonomic laboratory for evaluation of OD during a 20-month period.

* Corresponding author at: Department of Neurology, Keimyung University School of Medicine, 194 Dongsan dong, Daegu 700-712, Republic of Korea. Tel.: +82 53 250 7835; fax: +82 53 250 7840.
E-mail address: hlee@dsmc.or.kr (H. Lee).

1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2013.10.022

2. Methods

From July 2011 to February 2013, 300 patients with OD as a presenting symptom of orthostatic intolerance were initially included in this study. Most were referred to our autonomic laboratory for evaluation of OD. We defined OD as follows: (1) patients had non-vestibular dizziness including diffuse non-rotational dizziness, light-headedness, fogginess in the head, or a feeling of an impending black out and (2) dizziness that occurs only by postural changes, such as standing up from a sitting or supine position. After excluding 83 patients with OD, 217 patients were finally enrolled for this study. Among 83 excluded patients, 57 showed a flat top response during the Valsalva maneuver (VM) that was defined as an increase in the blood pressure (BP) response by at least 20 mmHg above baseline for at least 10 s, and 15 had significant arrhythmia with atrial fibrillation. Other had inadequate evaluations.

A standardized battery of autonomic tests, including the head-up tilt test, VM, Valsalva ratio (VR), heart rate response to deep breathing using Finometer devices (FMS, Amsterdam, The Netherlands) for recording beat-to-beat BP and heart rate (HR) response and the quantitative sudomotor axon reflex test, was performed in all the patients according to a previously validated method for the diagnosis of autonomic dysfunction (Low and Benarroch, 2008). For VM, patients were instructed to take a deep breath and blow into a syringe through a mouthpiece attached to a manometer for 15 s until expiratory pressure was reached to 40 mmHg. BP magnitude was determined for four phases, i.e., phase I, early and late phase II, phase III, and phase IV as previously described (Low, 1993; Low and Benarroch, 2008). A maximal drop in the mean blood pressure (MBP) of more than 20 mmHg during early phase II was abnormal (Novak, 2011b). Late phase II was considered abnormal if the magnitude of the end of phase II did not exceed the baseline (i.e., a negative value) (Novak, 2011b). Phase IV was considered abnormal if the magnitude of the phase IV response failed to reach the baseline (i.e., a negative value) (Novak, 2011a,b). The sympathetic indexes (SIs), including the reduction of early phase II (SI 1), magnitude of late phase II (SI 2), difference in BP between the baseline and the end of phase 2 (SI 3), magnitude of phase IV (SI 4), pressure recovery time (PRT, SI 5), and adrenergic baroreflex sensitivity index (SI 6) that have been linked to sympathetic adrenergic failure (SAF), were calculated and determined as abnormality from VM results (Novak, 2011a). The HR response was defined as the average HR difference (maximum–minimum) of the five largest consecutive responses (i.e., HR_{DB}), and expiration/inspiration (E/I) ratio during deep breathing was calculated. The VR was derived from the maximum HR divided by the lowest HR following VM. The tilt protocol included at least 10 min in the supine position and 20 min of a tilt at 70 degrees. OH was defined by a decrease in systolic blood pressure (SBP) of at least 20 mmHg or a decrease in diastolic blood pressure (DBP) of at least 10 mmHg between supine rest for 10 min and an upright posture for 20 min (The Consensus Committee of the American Autonomic Society and the American Academy of Neurology, 1996). Classic OH was defined as a decrease in systolic BP $\geqslant$ 20 mmHg or in diastolic BP $\geqslant$ 10 mmHg within 3 min of tilting. Delayed OH was defined as a slow progressive decrease in SBP that occurred after 3 min of tilting. Early OH was characterized by a decrease in SBP of 40 mmHg or more, immediately (within 30 s) after tilting, with rapid normalization of the BP response after 30 s. Transient OH was defined as an orthostatic reduction in SBP of at least 20 mmHg or a decrease in DBP of at least 10 mmHg any time during the tilting except for the initial 30 s, but decreased BP response was normalised within a few minutes after the onset of orthostatic reduction. The postural orthostatic tachycardia syndrome (POTS) was characterized by a sustained HR increment of 30 beats per minute within 10 min of the head-up tilt in the absence of OH (Thieben et al., 2007). Postganglionic sympathetic sudomotor functions were analyzed by quantitative sudomotor axonal reflex test (QSART) at the forearm, proximal leg, and distal leg using Q-Sweat machine (WR Medical Electronics, Stillwater, MN). The volume of capsules was 0.1229 cm^2, stimulation current was 2 mA, and duration of stimulation was 5 min. The sweat volume was collected for 10 min.

The pattern and severity of autonomic dysfunctions in patients with OD were determined based on the composite autonomic severity score (CASS) that consisted of each subscore evaluating the sympathetic adrenergic and cholinergic, and parasympathetic cardiovagal autonomic functions (Low, 1993; Low et al., 1995, 2013). In our study, isolated POTS was not included as a possible pattern of autonomic dysfunction because it was not recognized as an abnormality in the CASS calculation.

All patients were asked to complete the Korean version of the orthostatic grading scale (KOGS), which is known to be a reliable and valid tool for screening patients with OD in Korea(Kim et al., 2013).

We did not exclude patients who were receiving medications with potential effects on autonomic function, such as beta-blockers, anticholinergic agents, and antihypertensive drugs because medication is also a common cause of OD. No coffee, food, or nicotine was permitted for 6 h before the study.

Because this study included all consecutive patients with OD during research period, 32 patients previously reported (Kim et al., 2013) were included for completeness of the data. However, new information is added in this report.

All experiments complied with the tenets of the Declaration of the Helsinki and the study was approved by the Institutional Review Board.

We compared the clinical characteristics and autonomic test result data between patients with classic OH and patients with delayed OH using the independent-samples t-test for continuous variables and chi-squared test for categorical variables. The mean value ± standard deviation (SD) is displayed. A probability of $p < 0.05$ was considered to be statistically significant.

3. Results

Our study consisted of 217 patients with a mean age of 57.1 years (SD, 16.1 years) and an even distribution of men (52%) and women. In addition to orthostatic intolerance (100%) as a presenting symptom for inclusion to this study, patients commonly complained of blurred vision (74%) weakness or tiredness (70%), and difficulty in concentration or thinking mimicking cognitive impairments (47%). The symptoms of sympathetic hyperexcitation, including tremor and chest palpitation, were noted in approximately 40% of patients. A history of syncope was noted in approximately 15% of patients. The patients' pre-test diagnoses included 47% with hypertension, 29% with diabetes, 12% with ischemic heart disease, 11% with Parkinson's disease, 9.7% with benign prostatic hypertrophy, 5.1% with multiple system atrophy, and 4.1% with other medical illness, including thyroid disease or systemic cancer. Thirty-seven percent (81/217) of patients had no medical illness.

A total of 180 patients (83%) had at least one abnormal autonomic testing result based on an abnormality of each test in the CASS. Most (147/180, 82%) patients had abnormalities related to sympathetic adrenergic failure. If the patients with isolated POTS ($n = 7$) were included, 86% (187/217) of patients showed at least one abnormal autonomic result. We classified OD into 11 groups according to the patterns of autonomic impairment (Table 1).