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Autonomic dysfunction in chronic persistent dizziness ☆

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ABSTRACT

Objective: To investigate the autonomic dysfunction in patients with chronic persistent dizziness using standardized autonomic function tests.
Methods: We prospectively recruited 18 patients with chronic persistent dizziness after excluding other causes with extensive investigations. A standardized battery of autonomic tests including the head up tilt (HUT) test, Valsalva maneuver (VM), and heart rate (HR) response to deep breathing was performed.
Results: Approximately eighty percent of the patients showed at least one abnormality in autonomic tests. Two patterns of autonomic abnormality were identified: sympathetic failure, including abnormal decrease in blood pressure (BP) during HUT test or abnormal sympathetic indices related with the BP recovery during late phase II and phase IV during VM, and sympathetic hyperactivity, including abnormal increase in HR response during HUT test or an exaggerated phase IV response manifesting increased β-adrenergic tone during VM.
Conclusions: Autonomic dysfunction is frequently found in patients with chronic persistent dizziness after excluding other causes with extensive investigations. Sympathetic failure or hyperactivity may be postulated as one of the possible causes of chronic persistent dizziness. Clinicians should be aware of the possibility of autonomic dysfunction in patients with chronic dizziness, even if the dizziness is not orthostatic but persistent.

1. Introduction

Chronic dizziness is one of the most common and challenging complaints in general neurology and otology clinics. When patients complain chronic dizziness but without any history of true vertigo or any disequilibrium, a full clinical examination is warranted, including checking blood tests to rule out general medical conditions such as anemia, hypothyroidism or other endocrine conditions, diabetes or hypoglycemia, brain scans, and vestibular and autonomic function tests [1].

Although autonomic dysfunction is a known cause of non vertiginous dizziness, dizziness related to autonomic dysfunction is characterized by not chronic persistent but occasional recurrent non-vertiginous dizziness, light-headedness, or fogginess in the head, which is typically developed by orthostatic challenges such as arising from a recumbent posture or standing for an extended period [2]. To the best of our knowledge, there has been no systematic report on the characteristic of autonomic dysfunction in patients with chronic persistent (not orthostatic) dizziness who had no other identifiable causes using a standardized battery of autonomic function test. The aim of the present study was to investigate the frequency and pattern of autonomic abnormalities using standardized autonomic function tests in patients with chronic persistent dizziness after excluding other causes with extensive investigations.

2. Methods

From October 2011 to September 2012, we prospectively investigated patients with chronic persistent dizziness at the Dizziness Clinic of Keimyung University Dongsan Medical Center. We included patients with chronic persistent dizziness of an unknown cause as the following: (1) patients who presented with spontaneous (not positional) non-vertiginous dizziness lasting at least 3 months, (2) patients who felt dizziness continuously even if its severity can be changed, and (3) patients who had normal video-oculography results and brain MRI or CT. We excluded (1) patients with a typical history of dizziness evoked by orthostatic position because the autonomic dysfunction is easily suspected as a cause of dizziness in these patients, (2) patients who had identifiable neurological, psychiatric, cardiac, or other medical conditions that could potentially cause chronic dizziness, including Parkinson's disease, multiple system atrophy, peripheral polyneuropathy, stroke, migraine, syncope, head trauma, active psychiatric disorders, cardiac diseases, diabetes, hypertension, thyroid disease, alcoholism, or other medication history, and (3) patients with a recent history of diarrhea, vomiting, dehydration, or infection that could potentially lead to a transient deterioration of autonomic dysfunction.

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All of the patients underwent routine medical evaluations, including history taking, physical and neurological examination, routine blood sampling, detailed neurological examinations, video-oculography, and brain MRI or CT. The patients received a standardized psychiatric evaluation using semi-structured diagnostic interviews that systematically checked the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [3] and the revised version of the Symptom Check List-90 (SCL-90R) [4] to exclude any acute psychiatric disorders. The patients with T-score higher than 60 on each dimension were considered to have an appreciable level of symptoms [5] and are excluded in this study.

During the study period, 636 patients visited our dizziness clinic. Among these patients, 18 patients met our strict inclusion and exclusion criteria. A standardized battery of autonomic tests, including the head up tilt (HUT) test, Valsalva maneuver (VM), and deep breathing test using Finometer devices (FMS, Amsterdam, Netherlands) to record the beat-to-beat blood pressure (BP) and heart rate (HR) response was performed according to a previously validated method for the diagnosis of autonomic dysfunction [2,6].

Sympathetic functions were measured using the BP responses to both the VM and HUT test. VM was performed with expiratory pressure equal to 40 mmHg for 15 seconds by blowing through the mouthpiece attached to a manometer. The tilt protocol included 10 minutes in the supine position and at least 20 minutes of a tilt at 70 degrees if it was considered safe. Beat-to-beat BP and heart rate response were measured noninvasively using the Finometer device (Finapres Medical Systems BV, Amsterdam, The Netherlands). Sympathetic indices (SIs) indicating BP change during VM, including reduction of early phase II (SI1), magnitude of late phase II (SI2), difference in mean BP (MBP) between baseline and the end of phase II (SI3), magnitude of phase IV (SI4), and pressure recovery time (PRT, SI5), were also calculated from the VM results [7,8]. A "flat-top" response, which indicated that the MBP did not fall below baseline levels during phase II, was regarded as an incomplete study (Fig. 1).

The cardiovagal function was evaluated by the expiration (E): inspiration (I) ratio and the HR change to deep breathing (i.e., HR_{DB}), Valsalva ratio (VR) during VM, and HR responses during the recovery phase of VM and the 5 minutes immediately after the HUT test.

The control group consisted of 40 healthy age-matched (mean ± SD = 49.2 ± 11.2 years; range 26 to 70 years) and gender-matched (19 men, 21 women) volunteers who demonstrated no dizziness and had normal neurological examinations or medication histories that would potentially affect the autonomic nervous. None of the controls had clinically significant illness system. Autonomic data obtained from the patients were compared to control subjects. The tests were considered as abnormal if they were ±2 SDs outside of the average value (Table 1).

One-way analysis of variance (ANOVA) was used to determine the overall differences between subject groups, including controls. The post hoc Duncan test was used for pairwise comparisons if the ANOVA showed an overall significance. Independent t-test was used to compare age between patient groups. We also used chi-square test to compare sex differences between patient groups. The significance level was set to $p < 0.05$. Statistical analysis was performed using SPSS version 18.0 (SPSS, Chicago, IL) for Windows.

All of the experiments complied with the tenets of the Declaration of Helsinki, and the study protocol was also reviewed and approved by Keimyung University Institutional Review Board.

3. Results

We identified 18 patients (9 men) with chronic persistent dizziness who had no abnormal result in extensive investigations to identify the cause of chronic dizziness. These patients represented 2.8% (18/636) of all patients with dizziness who visited our dizziness clinic during the 12-month study period. The average age of the patients was 46.7 (SD = 10.0) years with a range from 32 to 73 years. The mean duration of the symptoms in our patients was 6.3 (SD = 2.9) years.

Seventy-eight percent (14/18) of the patients showed at least one abnormality in autonomic function tests: abnormal increase in HR response in the HUT test (6/18, 33%), abnormal SIs (5/18, 28%), increased VR (5/18, 28%), abnormal decrease in BP response (4/18, 22%), decreased E:I ratio and HR_{DB} (1/18, 6%), and abnormal decrease in HR during the recovery phase of VM (1/18, 6%).

In 12 (67%) patients, two patterns of autonomic abnormality were identified: decreased sympathetic responses (n = 5), including abnormal decrease in BP response during the HUT test, increase in PRT (SI5), decrease in the magnitude of late phase II (SI2), or decrease in the difference in MBP between baseline and the end of phase II (SI3) during VM (i.e., sympathetic failure group); and sympathetic hyperactivity (n = 7), including an exaggerated magnitude of phase IV (SI4) during the VM or abnormal increase in HR response during the HUT test (i.e., sympathetic hyperactivity group). Between the two groups, there was no difference in terms of gender (men, 40% vs. 43%); however, the sympathetic failure group consisted of older patients compared with the sympathetic hyperactivity group (51.8 ± 5.7 vs. 38.4 ± 4.9 years, p = 0.001). The sympathetic failure group exhibited significantly larger maximum and mean reductions in systolic BP (SBP) and diastolic BP (DBP) and a significantly larger maximum reduction in MBP in the HUT test compared to control subjects or the sympathetic hyperactivity group. In contrast, the sympathetic hyperactivity group exhibited significantly larger maximum and mean increases in HR in the HUT test compared to control subjects or the sympathetic failure group. In the VM, the SI2 and 3 were significantly lower in the sympathetic failure group compared to controls or the sympathetic hyperactivity group. In addition, the VR was increased in the sympathetic hyperactivity group compared to controls or the sympathetic failure group. Comparison of autonomic parameters between patients with sympathetic dysregulation (i.e., sympathetic failure or

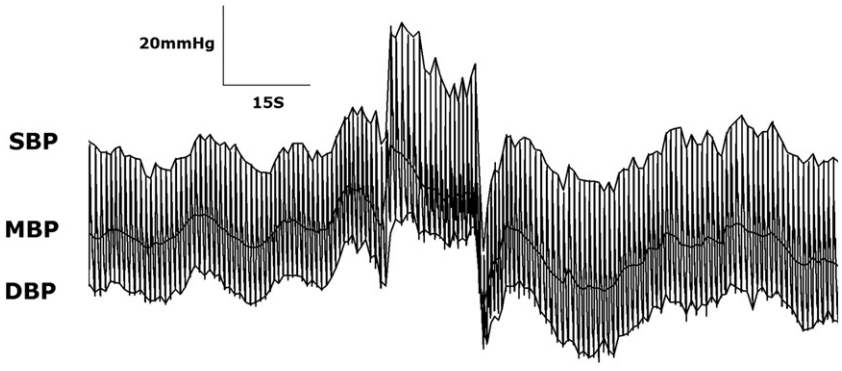

Fig. 1. Example of a "flat-top" response. Flat top response refers that the mean blood pressure does not fall below baseline levels during phase II and is regarded as an incomplete study. SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure.