Diagnostic approach of orthostatic dizziness/vertigo

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This paper introduces new diagnostic criteria and differential diagnosis of orthostatic dizziness to help clinicians to diagnose hemodynamic orthostatic dizziness. Clinicians need to be able to discriminate hemodynamic orthostatic dizziness from other types of dizziness that are induced or aggravated when standing or walking. Measurements of the orthostatic blood pressure and heart rate are important when screening hemodynamic orthostatic dizziness. Detailed history-taking, a physical examination, and laboratory tests are essential for finding the cause of hemodynamic orthostatic dizziness. The differential diagnosis of hemodynamic orthostatic dizziness is crucial because it can be caused by various autonomic neuropathies.

Key words: Orthostatic intolerance, Dizziness; Hemodynamic; Diagnosis; Orthostatic hypotension; Postural orthostatic tachycardia syndrome

INTRODUCTION

Orthostatic dizziness is a common type of dizziness. The prevalence of orthostatic dizziness based on patients’ history varied from 2% to 57%.1-9 A population-based study9 found that the 1-year and lifetime prevalence rates of orthostatic dizziness were 10.9% and 12.5%, respectively. Orthostatic dizziness commonly occurs in patients with orthostatic hypotension (OH) or postural tachycardia syndrome (POTS).10 Orthostatic dizziness occurs when the cerebral perfusion is critically reduced in patients with OH. This perfusion is maintained even during changes in the systemic blood pressure (BP) until the systolic BP drops to below 80 mmHg due to cerebral autoregulation.11 However, cerebral hypoperfusion develops when cerebral autoregulation fails in the situation of a severe reduction in the systemic BP.12 Various symptoms of POTS have been attributed to reduced cerebral perfusion and sympathetic activation. However, orthostatic dizziness in patients with POTS is similar to that in patients with OH, and is also presumably due to decreased cerebral perfusion.13

Diagnosing hemodynamic orthostatic dizziness is challenging due to the high variability...
in its symptom presentation, and diagnostic tests are not sufficiently accurate. The differential diagnosis of hemodynamic orthostatic dizziness is crucial because it may be caused by various autonomic neuropathies.

TERMINOLOGY RELATED TO ORTHOSTATIC DIZZINESS

Orthostatic dizziness is a type of dizziness that develops during orthostasis; that is, when rising from a lying or sitting position to standing, or present while standing.14 If the symptom begins while supine, then the term orthostatic dizziness is not suitable. The term hemodynamic orthostatic dizziness is limited to orthostatic dizziness caused by hemodynamic changes during orthostasis. In contrast, autonomic dizziness infers a more-specific etiology and should be restricted to dizziness due to autonomic causes even though it usually occurs during orthostasis. The term presyncopal dizziness has been used with a meaning similar to orthostatic dizziness.15 However, “presyncope” indicates a prodromal symptom of syncope and may occur in any position.

The term orthostatic intolerance is loosely used to describe various symptoms that occur when standing and are relieved by lying down.16-19 The symptoms are very diverse, ranging from uneasiness, discomfort, lightheadedness (dizziness), visual symptoms (e.g., blurred vision, visual dimming, or obscurations), vertigo, palpitations, head pressure, anxious feeling, and a multitude of somatic complaints referable to sympathetic activation (i.e., shakiness, peripheral vasoconstriction, and clammy feeling), to apparent symptoms suggesting cerebral hypoperfusion, or even syncope.10,16 The most common of these symptoms is lightheadedness or dizziness.

DIAGNOSTIC CRITERIA FOR HEMODYNAMIC ORTHOSTATIC DIZZINESS

A consensus document from the Committee for the Classification of Vestibular Disorders of the Bárány Society lists the diagnostic criteria for hemodynamic orthostatic dizziness/vertigo that are included in the International Classification of Vestibular Disorders (Table 1).20 The diagnostic criteria for hemodynamic orthostatic dizziness have previously characterized dizziness symptoms due to hemodynamic insults as nonvertiginous dizziness, lightheadedness, or dizziness preceding blackout or fainting. However, OH can also induce orthostatic vertigo (i.e., spinning or other self-motion sensations). About 30-40% of patients with OH experienced orthostatic vertigo in the previous studies.21,22 Unsteadiness is classified as a postural symptom while upright (e.g., standing), rather than one related to changing the body posture with respect to gravity (e.g., standing up) in the Classification of Vestibular Symptoms.14 However, patients with OH frequently complain of unsteadiness, and new diagnostic criteria have included unsteadiness as one of the symptoms of hemodynamic orthostatic dizziness.

Table 1. Diagnostic criteria for hemodynamic orthostatic dizziness/vertigo

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<th>Hemodynamic orthostatic dizziness/vertigo</th>
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<td>Attacks fulfilling the following:</td>
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<td>A. Five or more episodes of dizziness, unsteadiness, or vertigo triggered by arising or present during upright position, which subsides by sitting or lying down.</td>
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<td>B. Orthostatic hypotension, postural tachycardia syndrome, or syncope documented when standing or during the head-up tilt test.</td>
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<td>C. Not better accounted for by another disease or disorder.</td>
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<th>Probable hemodynamic orthostatic dizziness/vertigo</th>
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<td>Attacks fulfilling the following criteria:</td>
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<tr>
<td>A. Five or more episodes of dizziness, unsteadiness, or vertigo triggered by arising or present during upright position, which subsides by sitting or lying down.</td>
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<tr>
<td>B. At least one of the following accompanying symptoms: generalized weakness/tiredness, difficulty in thinking/concentrating, blurred vision, or tachycardia/palpitations.</td>
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<td>C. Not better accounted for by another disease or disorder.</td>
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The reproducibility of OH in the head-up tilt (HUT) test is relatively low, even in well-defined patients with orthostatic symptoms and documented OH. The criteria for probable hemodynamic orthostatic dizziness might be applicable to patients with orthostatic dizziness but without evidence of OH or POTS in the HUT or standing test. Other symptoms of OH and POTS would be helpful for diagnosing hemodynamic orthostatic dizziness if OH or POTS is not found. Besides dizziness and unsteadiness, the most-common orthostatic symptoms are weakness, cognitive impairment, and blurred vision.

DIFFERENTIAL DIAGNOSIS OF ORTHOSTATIC DIZZINESS

Orthostatic dizziness should be distinguished from positional dizziness, which is triggered by a change in the head position with respect to gravity. Clinicians can discriminate positional from orthostatic dizziness by asking the patient whether the symptoms also occur when lying down or turning over in bed; if so, the symptoms are more likely to be positional than orthostatic. Positional tests for benign paroxysmal positional vertigo should be performed in patients with orthostatic dizziness even if their dizziness does not appear like the typical positional symptom.

Persistent postural-perceptual dizziness (PPPD) and chronic anxiety and depressive disorders can cause dizziness that is aggravated when upright and performing active or passive movements. PPPD is a common form of functional dizziness that manifests with one or more symptoms of dizziness, unsteadiness, or nonspinning vertigo that are present continuously for at least 3 months. In addition to an upright posture or active or passive movements, exposure to moving or complex visual stimuli may also exacerbate symptoms. Because most patients with PPPD complain that their symptom is aggravated when standing or walking, dizziness in patients with PPPD may be confused with hemodynamic orthostatic dizziness. Orthostatic and exertional dizziness tend to be more pronounced in patients with hemodynamic orthostatic dizziness than in those with PPPD. Even in the supine or sitting position, complex or moving visual stimuli can worsen the dizziness experienced by patients with PPPD. Measuring the heart rate (HR) or BP when standing and supine is important for distinguishing between hemodynamic orthostatic dizziness and PPPD; however, orthostatic dizziness can trigger or coexist with PPPD.

Lightheadedness aggravated during orthostasis can also occur in patients with chronic anxiety disorders. The detailed history about the psychological background and simple self-report questionnaires can help in detecting psychiatric morbidity. However, the presence of anxiety or depression does not exclude hemodynamic orthostatic dizziness, because psychiatric disorders often coexist. Changes in BP and HR during position changes are essential for the differential diagnosis of orthostatic dizziness.

Dizziness when upright due to bilateral vestibulopathy, peripheral neuropathy, or other clinical or subclinical gait disorders can be classified as orthostatic dizziness. Bilateral vestibulopathy is characterized by postural imbalance and/or unsteadiness of gait due to vestibular hypofunction. Standing, walking, or rapid head or body movements can cause dizziness or blurred vision in these patients. Such dizziness or unsteadiness worsens in darkness or on uneven ground in patients with bilateral vestibulopathy, but not in patients with hemodynamic orthostatic dizziness. A bilaterally reduced or absent vestibulo-ocular reflex is essential for the diagnosis of bilateral vestibulopathy.

Patients with large-fiber peripheral neuropathy can complain of unsteadiness when standing or walking if they have severe distal paresthesia, sensory impairment, and loss of ankle jerks. Nerve conduction and Romberg tests—in addition to measurements of BP and HR during position changes—can discriminate between sensory neuropathy and hemodynamic orthostatic dizziness. However, dizziness can be caused by both sensory neuropathy and hemodynamic orthostatic dizziness because peripheral neuropathy can be combined with autonomic neuropathy.

Patients with gait problems sometimes express their symptoms as dizziness during walking. On the other hand, hemodynamic orthostatic dizziness frequently causes gait and balance problems, especially in the elderly. Patients with hemodynamic orthostatic dizziness may experience sensations of veering from side to side when walking. This reduces their balance confidence, and may result in mildly slow or cautious gait. Detailed history-taking focusing on the patient’s symptoms can help to identify hemodynamic or-
thostatic dizziness. Clinicians need to ask patients if they are experiencing disequilibrium in their legs or lightheadedness during orthostasis. However, a Parkinsonian gait or cerebellar ataxia can coexist in patients with hemodynamic orthostatic dizziness, because Parkinson’s disease and multiple-system atrophy are the leading causes of neurogenic OH. Small-vessel white-matter disease is also a common cause of gait disorder and orthostatic dizziness in the elderly.36

Dizziness due to cardiac problems may occur during exertion or even when supine. In such instances the dizziness and vertigo are hemodynamic but not necessarily orthostatic. However, some patients with cardiac problems experience symptoms when standing up. Palpitation, chest discomfort, or dyspnea may also occur. Patients may have a family history of unexplained sudden death at a young age, structural heart diseases, coronary artery diseases, or arrhythmias.37

DEFINITIONS OF OH AND POTS

OH is defined as a sustained decrease in the systolic BP of at least 20 mmHg or in the diastolic BP of at least 10 mmHg within 3 minutes of standing or during the HUT test.38 POTS is characterized by a sustained increase in the HR of at least 30 bpm or by an HR of at least 120 bpm within 10 minutes of standing, or during the HUT test in the absence of OH.38 For individuals aged 12-19 years, the minimum increment in HR required for a diagnosis is 40 bpm.38

For screening, serial BP and HR measurements during supine or sitting and standing are significant bedside examinations in patients who are suspected of having hemodynamic orthostatic dizziness. The HUT test is the gold standard for detecting OH and POTS. BP and HR should be measured when tilting after resting supine for at least 5 minutes. Neurogenic OH results from sympathetic adrenergic failure and usually manifests as a decrease in the systolic BP of at least 30 mmHg or in the diastolic BP of at least 15 mmHg within 3 minutes of standing or during the HUT test.11

Because the reproducibility of the HUT test is relatively low, detecting OH may require multiple measurements on different days.79 A diary with recordings of the supine and standing BPs at different times of the day over several days may be helpful. Measurements made before breakfast, after medications, after meals, and before bed are the most useful.39

The HUT test might not be sensitive enough to detect milder forms of sympathetic adrenergic failure. The Valsalva maneuver (VM) can increase the sensitivity of the HUT test in detecting milder forms of sympathetic adrenergic failure.40,41 A diagnosis of neurogenic OH is indicated by a lack of reflex vasoconstriction shown by a reduced or absent late phase-2 and phase-4 overshoot and a prolonged BP recovery in the VM.42,43

In the absence of continuous-BP monitoring equipment, the HR response to postural change can also provide valuable clues for discriminating between neurogenic and non-neurogenic OH. A blunted HR increase during hypotension suggests a neurogenic cause. A change in the HR relative to the systolic BP of <0.5 bpm/mmHg when moving from supine to tilting is diagnostic of neurogenic OH, whereas a change of >0.5 bpm/mmHg indicates volume depletion or orthostatic intolerance.44

EVALUATING PATIENTS WITH OH

The first step in the workup of patients with documented OH is excluding potentially harmful causes such as acute bleeding and dehydration.45 Nonneurogenic causes should also be considered, including drugs, reduced cardiac output, endocrine disorders, and excessive vasodilatation. The detailed history should be obtained, focusing on medications (antihypertensives or alpha blockers for benign prostatic hyperplasia), volume losses (due to vomiting, diarrhea, or fluid restriction), and coexisting medical disorders, including heart disease. Detecting the underlying cause of OH (e.g., cardiogenic cause, thyroid disease, or malignancy) requires clinicians to ask about unexplained weight loss, chest pain, palpitation, shortness of breath, and pedal edema. Besides orthostatic intolerance, patients should be asked about other autonomic symptoms such as dry eye/mouth, cold hands/feet, urinary symptoms, constipation, sexual dysfunction, and hypohidrosis/hyperhidrosis in order to determine if autonomic dysfunction is present. The previous history about diabetes, parkinsonism, dementia, visual hallucination, REM sleep behavior disorder, alcohol abuse, cancer, and chemotherapy also need to be obtained.

A comprehensive physical examination should be per-
formed, seeking clinical clues that could explain the underlying physiological and pathological disorders. The skin turgor, conjunctiva, and a tongue examination are needed to check for dehydration or anemia. A neurologic evaluation should include a mental status examination (to identify neurodegenerative diseases such as Lewy body dementia), motor testing (Parkinson’s disease, multiple-system atrophy, and stroke), sensory testing (peripheral neuropathy), cerebellar testing (multiple-system atrophy), and pupillary size (Horner’s syndrome and Argyll Robertson pupil).

Subsequent laboratory tests should be performed based on the results of these assessments. These tests might include hemoglobin and hematocrit levels to evaluate for anemia; complete blood count for detecting infection; blood electrolytes, urea nitrogen, and creatinine to assess for dehydration or renal dysfunction; a rapid plasma reagin test for syphilis; electrocardiogram for cardiac disease; thyroid stimulation hormone for thyroid disease; cortisol for adrenal insufficiency; 24-hour urine 5-hydroxyindoleacetic acid for carcinoid syndrome; vitamin B₁₂ level for vitamin B₁₂ deficiency; and fasting glucose for diabetes. If a patient has neurogenic OH, the HR response to deep breathing, and quantitative sudomotor axon reflex tests are helpful for evaluating the extent of autonomic involvement. The norepinephrine level when supine can aid in making a diagnosis of pure autonomic failure. Neurologic antibody studies (paraneoplastic panel) to identify autoantibodies only in patients with the subacute onset of neurogenic OH in the presence of other neurologic or constitutional symptoms can suggest an autoimmune or paraneoplastic syndrome. Serum and urine protein electrophoresis can be used to identify monoclonal gammopathy in patients with features of peripheral neuropathy. Brain imaging studies should be performed if there is clinical suspicion of pathology of the central nervous system.

**EVALUATING PATIENTS WITH POTS**

The clinical history of patients with POTS should include the trigger, onset timing, and progression of orthostatic symptoms; precipitating or aggravating factors; the presence of associated nonorthostatic symptoms; fluid and caffeine intakes; the level of physical activity; sleep patterns; response to previously attempted treatments; and current drug therapy. In a physical examination, some patients will show indirect evidence of venous pooling (e.g., lower extremity edema) or excessive sympathetic activity (e.g., cold, clammy hands). The patient should undergo a comprehensive cardiac and neurologic examination in addition to measurements of BP and HR when supine and standing. The 24-hour monitoring of BP and HR could be helpful for correlating the timing of the patient’s symptoms with the presence of tachycardia in patients without orthostatic tachycardia in measurements of the BP and HR when supine and standing or the HUT test. A cardiac evaluation that includes echocardiography and Holter monitoring is needed to exclude a primary cardiac cause of inappropriate sinus tachycardia. Autonomic function tests and measurements of autoantibodies (VGKC complex and ganglionic AChR) should be performed to detect underlying autonomic neuropathy, plasma catecholamine when supine and standing to evaluate hyperadrenergic state, 24-hour urine sodium to assess the hypovolemic state, and exercise testing with measuring VO₂ max to detect physical deconditioning are necessary to identify the different pathophysiologic subtypes of POTS: neuropathic, hyperadrenergic, deconditioning, and hypovolemic. Measurements of hemoglobin, cortisol, and thyroid-stimulating hormone might be needed to assess for endocrinial or other systemic causes of POTS.

**Conflicts of Interest**

The authors declare no conflicts of interest relevant to this article.

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