



Symptomatic orthostatic hypotension in Parkinson's disease patients: Prevalence, associated factors and its impact on balance confidence

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ABSTRACT

Background: Orthostatic hypotension (OH) is a commonly reported sign of the cardiovascular autonomic dysfunctions associated with Parkinson's disease (PD). Patients might suffer from a variety of the clinical symptoms of OH, including dizziness, lightheadedness, or problems with vision and fatigue.

Objectives: To determine the prevalence of, and factors associated with, symptomatic orthostatic hypotension (OH) in Parkinson's disease (PD) and to identify any relationships between the clinical symptoms of OH and balance confidence in this patient population.

Methods: Symptomatic OH was defined as a systolic or diastolic BP fall of ≥ 20 or ≥ 10 mmHg respectively, within 3 min of standing and an Orthostatic Hypotension Questionnaire (OHQ) score of more than zero. Factors related to symptomatic OH were identified from a multivariate logistic regression analysis. Pearson's correlation test was used to reveal any relationships between the clinical symptoms of OH and a patient's confidence in their ability to balance, assessed using the Activities-specific Balance Confidence (ABC) scale.

Results: 100 Thai PD patients were consecutively recruited into this study. The prevalence of symptomatic OH was 18%, asymptomatic OH was 4%, while 78% were patients without OH. Factors associated with symptomatic OH were age (OR, 95%CI: 1.06, 1.003–1.115, $p = 0.038$) and hypertension (OR, 95%CI: 6.16, 1.171–32.440, $p = 0.032$). A significant and negative correlation ($r = -0.229$, $p = 0.022$) between OHQ composite scores and item 3 of the ABC scale (picking up slippers from floor), one of the movements in a vertical orientation, was found.

Conclusion: Elderly PD patients and with a co-morbidity of essential hypertension should be closely evaluated for the presence of symptomatic OH. In addition, they should be advised to change positions slowly, especially those in a vertical orientation.

1. Introduction

Orthostatic hypotension (OH), a sign of cardiovascular autonomic dysfunction, is one of the commonly occurring nonmotor problems in patients with PD [1], with, according to a

meta-analysis, a prevalence of 30.1% (95% CI: 22.9% to 38.4%) [2]. The consensus statement of the American Autonomic Society (AAS) and American Academy of Neurology (AAN), defines OH as a sustained fall of ≥ 20 mmHg in systolic or ≥ 10 mmHg in diastolic blood pressure (BP) within 3 min of active standing or head-up tilt to at least 60° [3]. The clinical symptoms of OH include dizziness, lightheadedness,

problems with vision, generalized weakness, fatigue, trouble concentrating, head/neck discomfort or, in worst cases, syncope [4]. OH has both neurogenic (due to failure of the autonomic nervous system (ANS) to regulate blood pressure in response to postural change, as a result of an inadequate release of norepinephrine (NE) from postganglionic sympathetic nerves) and non-neurogenic causes [5,6]. OH in PD is mostly due to postganglionic sympathetic denervation resulting in efferent baroreflex failure (i.e., neurogenic OH) [7,8]. Other non-neurogenic causes, such as intravascular volume depletion, medications, or cardiac failure, can also contribute to OH in PD [5,9], and should be identified first [5]. In addition, some studies have reported predisposing

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factors to OH in PD patients, including a more advanced disease stage, longer duration of PD [10], male gender [11–13], older age, posture and gait instability, low mini-mental state examination scores and visual hallucinations [14]. Also, the use of antiparkinson medications, including L-DOPA, dopamine agonists, and monoamine oxidase-B (MAO-B) inhibitors have been shown to reduce BP [15]. Higher doses of dopaminergic medication [16] and use of combined therapies [17] increase the risk of OH. This hypotensive effect of antiparkinson medication can be observed at the beginning of therapy and is usually tolerated [18] or can be addressed by dose adjustments [19].

OH is associated with significant morbidity and mortality in both working age adults and elderly people, with or without PD. It has been shown that OH is a predictor of ischemic stroke in middle-aged people (age range of 53–57 year olds) without a history of neurological medical problems and who did not suffer from stroke and/or heart disease at baseline assessments [20]. In addition, Ooi found that OH increased the risk of falls (RR = 2.1) in the elderly [21]. In PD, it was found that PD patients suffering with OH had an increased risk of postural sway when standing compared with those without OH [22]. Also, OH was found to be the direct cause of falls in 4.1% of PD patients [23]. Using the Activities-specific Balance Confidence (ABC) Scale, a 16-item scale used to assess balance confidence when performing activities at home or in areas external to the home environment [24], it has been shown that a lower self-perceived balance confidence level is associated with falls in the elderly [25] and in PD patients [26]. In addition, items 3, 6 and 9 of the ABC scale are predictors of falls in PD patients [27].

OH in PD can be symptomatic or asymptomatic, depending on the magnitude of the reduction in BP and an individual patient's ability to compensate for the reduction. Most people who are symptomatic for OH have a much greater fall in BP on standing and those who have an impairment of the compensatory systems in the body, including activation of the sympathetic nervous system, the renin-angiotensin system, and/or the aldosterone system are more likely to be symptomatic for OH [1]. Recently it has been shown that symptomatic OH is also associated with an impairment of activities of daily living (ADL), instrumental activities of daily living (iADL), and the Ambulatory Capacity Measure (ACM) [28]. However, little information related to symptomatic OH is available in PD and, so far, only one study has investigated its prevalence and characteristics [29]. In this study, we aimed to expand the knowledge about symptomatic OH in terms of its prevalence, associated factors and the correlation of its clinical symptoms with the level of balance confidence in PD patients.

2. Methods

2.1. Subjects

A cross-sectional study was conducted at Chulalongkorn Center of Excellence for Parkinson's disease and Related disorders, King Chulalongkorn Memorial Hospital. We consecutively recruited 100 PD patients during the period between May and August 2015. Inclusion criteria included idiopathic PD meeting the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB) diagnostic criteria; Hoehn and Yahr (H&Y) stage 1–4; and stable on drug therapy or had not received any drug modifications (dopaminergic treatment and other medications) for at least four weeks prior to enrollment. We excluded bedridden idiopathic PD patients or those in the nursing homes; patients with other neurogenic OH, including pure autonomic failure (PAF), multiple system atrophy (MSA), progressive supranuclear palsy (PSP) or an autonomic neuropathy; and patients who were treated with antihypertensive drugs (fludrocortisone, droxidopa or midodrine). Diagnosis of patients was performed by the movement disorder neurologists. The local institutional review boards approved the study, and all participants gave written informed consent prior to the study. Demographic data, medical conditions, list of medications, and the daily doses of all current medications were recorded.

2.2. Procedures

Blood pressure (BP) was recorded by autonomic sphygmomanometer (Omron® HEM-7200). BP was measured after 10 min resting in a sitting or supine position, then patients were asked to stand and, within 3 min, BP was recorded while the patient remained in a standing position. OH was defined by consensus as a fall in systolic BP (SBP) or diastolic BP (DBP) of ≥ 20 or ≥ 10 mmHg after standing within 3 min [3]. All patients took their regular morning treatment and had a regular breakfast or lunch at least 2 h before the BP measurement. The Orthostatic Hypotension Questionnaire (OHQ) was used to assess the presence of OH symptoms and the impact of OH symptoms on daily activities in the past seven days [30]. The OHQ had been translated into Thai language and used in this study (Cronbach's alpha reliability of the questionnaire was 0.759). In this study, the researcher asked the patients in Thai and recorded the scores.

The OHQ consists of two parts: OHSA (Orthostatic Hypotension Symptom Assessment) and OHDAS (Orthostatic Hypotension Daily Activities Scale). The OHSA assesses symptoms of OH using six subjective items; 1) Dizziness, lightheadedness, feeling faint, or feeling like you might black out, 2) Problems with vision (blurring, seeing spots, tunnel vision), 3) Generalized weakness, 4) Fatigue, 5) Trouble concentrating, and 6) Head/neck discomfort. The OHDAS assesses the impact of OH symptoms on daily activities and consists of four items (impact on standing for short (item 1) or long (item 2) periods of time, impact on walking for short (item 3) or long (item 4) periods of time). Each item was scored on an 11-point scale from 0 to 10, with 0 indicating no symptoms/no interference and 10 indicating the worst possible symptoms/complete interference. The composite OHQ score was calculated by averaging the OHSA and the OHDAS [30].

Using BP measurement and OHQ score, patients were categorized into 4 different groups. “symptomatic OH” was acknowledged when the subject had a BP fall according to manometric definition and composite OHQ score of more than zero, while “asymptomatic OH” was defined when the subject had a BP fall according to manometric definition, but composite OHQ score was zero. The other 2 groups were subjects who did not have BP fall according to manometric definition and their composite OHQ score can be zero or more than zero. These 2 groups were classified in this study as “patients without OH” because they did not have BP fall according to manometric definition regardless of composite OHQ score.

The self-perceived balance confidence level was measured using the Activities-specific Balance Confidence (ABC) scale [24]. The Thai validated ABC scale (Cronbach's alpha 0.952) was used in this study [27]. Patients rated their level of balance confidence from 0 (no confidence at all) to 100 (full confidence) if they were to complete each of 16 activities of daily living. Scores for each activity and collectively for all 16 activities were calculated, with a minimum score of 0 to a maximum of 100. Low ABC scores reflect a low level of balance confidence or increased fear of falling [24].

The Thammasat University Non-Motor Symptoms Questionnaire (TU-NMSQuest) was used to determine the presence of non-motor symptoms (NMS) in the PD patients. TU-NMSQuest is the Thai validated NMS questionnaire (Cronbach's alpha 0.835) consisting of 40 non-motor symptoms (items) grouped into 10 domains [31]. Patients chose the response “yes” or “no” to indicate if they do or don't experience each item of the NMS domains. The number of yes responses for each domain and for all of the domains was determined.

All measurements (BP, OHQ score, ABC score and TU-NMS score evaluations) were collected from individual patients at one point in time. Factors analyzed for an association with symptomatic OH were: age; gender; duration of PD symptoms; disease severity (Hoehn & Yahr stage); co-morbidities; antiparkinson drug use; levodopa daily dose; levodopa equivalent daily dose (LEDD); dopamine agonist levodopa equivalent daily dose (DALEDD); and polypharmacy (intake ≥ 5 medications).

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