

Orthostatic hypotension in Iranian patients with Parkinson's disease

Abmad Chitsaz, MD, Mohammad Saadatnia, MD, Masoud Etemadifar, MD, Marzieh Tajmirriabi, MD.

ABSTRACT

Objectives: To prospectively investigate the prevalence and clinical relevance of orthostatic hypotension (OH) in Parkinson's disease (PD) in Isfahan, Iran.

Methods: We investigated 150 consecutive patients with PD (42 women, 108 men) in Al-Zahra Hospital, Isfahan, Iran from January 2002 to January 2004. Blood pressure was measured first in a supine position following a rest of at least 10 minutes, and then after 3 minutes of active standing. Data concerning the age, gender, duration of disease, and drug consumption were recorded in a questionnaire.

Results: Orthostatic hypotension in PD is more frequent in women, patients taking a higher dose of levodopa, in higher age groups, and patients with longer duration of the disease, however, a statistically significant difference was seen in the female group and patients taking a higher dose of levodopa.

Conclusion: Orthostatic hypotension is mainly related to PD pathology and the clinical relevance of OH to gender, age, and disease duration may be due to the natural course for progression of human autonomic dysfunction during life. Higher doses of levodopa may increase the risk of OH.

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From the Department of Neurology (Chitsaz, Saadatnia, Etemadifar), Iranian Neurological Science Research Center, the Department of Cardiology (Tajmirriabi), and Isfahan Medical Education Research Center (Saadatnia), Isfahan University of Medical Sciences, Isfahan, Iran.

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Address correspondence and reprint request to: Mohammad Saadatnia, Assistant Professor of Neurology, Division of Neurology, Al-Zahra Hospital, Soffeh Street, Isfahan, Iran. Tél. +98 9131147179. E-mail: mosaadatnia@yahoo.com, saadatnia@med.mui.ac.ir

One of the important autonomic features of Parkinson's disease (PD) is orthostatic hypotension (OH), and despite evidence for the involvement of the sympathetic system in the autonomic dysfunction of PD, the occurrence of OH

remains controversial in the course of the disease. Some authors have reported the existence of OH,¹⁻¹⁰ whereas others did not find this.¹¹⁻¹⁵ However, recent studies showed OH was common in PD.⁸⁻¹⁰ Conversely, the clinical relevance of OH for people with PD has some controversy and is poorly understood. Senard et al⁸ determined the relation between OH and disease characteristics (duration, severity) and the use of antiparkinsonian drugs, whereas Allcock et al⁹ showed no difference in PD disease duration or severity. In the present study, we prospectively investigated the prevalence and demographic associations of OH in a series of 150 consecutive patients with PD in Isfahan, Iran.

Methods. The study was performed on patients with idiopathic PD from January 2002 to January 2004, referred to the section of Neurology of Al-Zahra Hospital, Isfahan, Iran. Only those patients meeting the United Kingdom Parkinson's Disease Society (UKPDS) Brain Bank Criteria for PD, with a clear and sustained response to levodopa and without recent modifications of their drug regimen (all treatments were stable for at least 20 days) were recruited after they had given their informed consent.¹⁶ Ethical approval was received from the local committee before this research was undertaken. We excluded patients with disease that developed OH, such as multiple system atrophy and diseases with acute or chronic peripheral neuropathy (secondary OH) such as amyloidosis, diabetes, Guillain-Barré, alcoholic-nutritional and toxic neuropathy. The sex, age, duration of the disease, and daily doses of all current hypotension-inducing medications (levodopa, anticholinergic, antihypertensive, tricyclic antidepressive, and antianxiety drugs) were recorded. We followed the American College of Neurologist's guidelines for measuring OH, which requires standing for 3 minutes, following a 10 minute supine rest period. Readings were taken at one and 2 minutes, as local experience has demonstrated that a blood pressure fall after 2 minutes is unlikely to occur. The OH was defined as a drop in systolic blood pressure greater than or equal to 20 mm Hg or to less than 90 mm Hg after standing. Postural blood pressure changes were recorded on 2 separate occasions for each patient.¹⁷ All subjects were assessed in the morning and all patients

Table 1 - Number of patients with and without orthostatic hypotension (OH) in different age groups.

Age group (years)	With (OH) n=62 n (%)	Without OH n=88 n (%)
Less than 50	6 (9.6%)	6 (6.8%)
51-60	15 (24.1%)	16 (18.18%)
61-70	18 (29%)	44 (50%)
71-80	23 (37%)	22 (25%)

took their regular morning treatment and had a regular breakfast at least one hour before measurement of blood pressure. Quantitative data are presented as means (SD) and were compared using Student's t-test. Qualitative data were compared using the χ^2 test. Data were analyzed as univariate, using SPSS Version 10 software.

Results. One hundred and fifty consecutive patients with PD (42 women, 108 men) were investigated in Al-Zahra Hospital in Isfahan, Iran. Sixty-two (41%) patients met the criteria for OH on at least one occasion. Among these, 22 (52.3%) female and 39 (36.1%) male PD patients had OH ($p=0.03$). Seven (31%) female and 10 (25.6%) male PD patients with OH had symptomatic OH ($p=0.6$). According to **Table 1** there was no difference ($p=0.08$) in age groups between those with OH and those without, but OH was most common in the >70 age group. The mean duration of PD was 3.7 ± 1.5 in patients with and 3.6 ± 1.3 in patients without OH ($p=0.7$). One hundred and twenty-eight (85.3%) patients had PD with confounding variables such as levodopa, anticholinergic, antihypertensive, tricyclic antidepressive, and antianxiety drugs. However, there was no statistically significance difference between those patients with OH taking more items of hypotension-inducing medications than those without it (3.1 ± 0.2 and 2.9 ± 0.15 , $p=0.5$). Of 62 patients with and 88 patients without OH, 58 (93.5%) were taking levodopa and 76 (86.3%) were taking levodopa or dopamine agonist, or both, as antiparkinsonian therapy. The number of patients with and without OH in different levodopa- or calculated levodopa equivalent-dose groups is shown in **Table 2**. The mean levodopa dose or calculated levodopa equivalent dose for treated patients was significantly higher in the OH group (421 ± 42 versus 223 ± 56 , $p<0.0001$).

Discussion. Gender and higher doses of levodopa were the only factors significantly higher in the OH group compared to those without OH. Sympathetic neural responses to orthostatic stress show gender differences in autonomic functions.^{18,19} Therefore,

Table 2 - Number of patients with and without orthostatic hypotension (OH) in different levodopa dose groups.

Levodopa dosage	With (OH) n=58 n (%)	Without OH n=76 n (%)
0-250 mg	27 (46.5)	56 (73.6)*
251-500 mg	10 (17.2)	18 (23.6)†
501-750 mg	15 (25.8)	2 (2.6)*
>751 mg	6 (10.3)	0*

* $p<0.05$, † $p>0.05$

female patients even in normal physiologic conditions have more autonomic sensitivity in response to orthostatic stress, and it is possible that the findings demonstrated in our study are a reflection of gender differences in autonomic function, independent of PD related pathology. In contrast, to previous reports,^{8,20} our study did not demonstrate any association of OH with disease duration and age. This is similar to recent studies documenting that OH can occur even in early PD.^{9,21} In fact, sympathetic neurocirculatory failure does not seem to be restricted to severe cases or to occur as a late consequence of the disease,²² and reduced tracer uptake on cardiac meta-iodobenzylguanidine (MIBG) scanning does not correlate with disease duration, although it is correlated with disease severity.²³ Therefore, it is probable that OH is related to PD pathology and as a result, the subgroup of PD patients with OH may have a more aggressive course of the disease, indicating that OH may be a marker to distinguish those patients who need more medical care. In our study, although patients with OH did not show a statistically significant difference with regard to taking more OH-inducing drug items, but similar to other studies,^{8,9,24} levodopa or calculated levodopa equivalent dose (for patients treated with agonists) was significantly higher in the OH group, and the dose groups with significantly higher percentage of patients with OH were groups with above 500 mg/day. Although this study had several findings relevant to the understanding of OH in PD, it has some limitations. We did not investigate severity of disease and delayed OH that reportedly occurred in 54% of patients with dysautonomia

In conclusion, 62 (41%) of patients met the criteria for OH on at least one occasion. Female gender and higher doses of levodopa were the only factors significantly higher in the OH group compared to those without OH. It seems that OH is mainly related to PD pathology and the clinical relevance of OH to gender, age, and disease duration may be due to the natural course for progression of human autonomic dysfunction during life. Higher doses of levodopa may increase the risk of OH.

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