ORIGINAL ARTICLE

24-Hour Ambulatory Blood Pressure Monitoring in SWEDDs Patients With Parkinsonism

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ABSTRACT: ***Background:*** Patients diagnosed with Parkinson's disease (PD) on clinics who subsequently turn out to have normal dopamine transporter images have been referred to as scans without evidence of dopaminergic deficits (SWEDDs) patients. Cardiovascular autonomic dysfunction has frequently been reported in PD. In this study, we determined the similarities and differences in cardiac autonomic dysfunction between SWEDDs and PD patients. This study investigated whether 24-hour ambulatory blood pressure monitoring (24-hour ABPM) can help identify possible cases with SWEDDs. ***Methods:*** We enrolled 28 SWEDDs patients, 46 patients with PD, and 30 healthy controls. To evaluate cardiac autonomic function, 24-hour ABPM was performed on all subjects. Cardiac metaiodobenzylguanidine (MIBG) scintigraphy was performed on the SWEDDs and PD subjects. ***Results:*** The percentage nocturnal decline in blood pressure differed significantly among SWEDDs patients, PD patients, and controls ($p < 0.05$). In addition to the abnormal nocturnal BP, regulation (nondipping and reverse dipping) was significantly higher in SWEDDs and PD subjects than in the control subjects ($p < 0.05$). There was no significant correlation between the % nocturnal blood pressure reduction and parameters of cardiac MIBG uptake ratio. However, orthostatic hypotension was significant correlated with the nocturnal blood pressure dip (%), nocturnal blood pressure patterns, and the cardiac MIBG uptake ratio (early and late) in combined SWEDDs and PD subjects. ***Conclusions:*** Pathologic nocturnal blood pressure regulation and nocturnal hypertension, known characteristics of PD, are also present in SWEDDs. Moreover, cardiac sympathetic denervation should not be attributed to cardiac autonomic dysfunction in SWEDDs patients. As with PD patients, the SWEDDs patients studied here tended to have cardiac autonomic dysfunction.

RÉSUMÉ: Surveillance de 24 heures de la tension artérielle ambulatoire chez les patients présentant du parkinsonisme sans évidence de déficit dopaminergique. ***Contexte :*** Les patients chez qui un diagnostic de maladie de Parkinson (MP) a été posé basé sur la présentation clinique et chez qui éventuellement l'imagerie montre une activité normale du transporteur de la dopamine sont connus comme étant des patients avec scan sans évidence de déficit dopaminergique (scans without evidence of dopaminergic deficits – SWEDDs patients). Une dystonie neurovégétative cardiovasculaire a souvent été rapportée dans la MP. Dans cette étude, nous identifions les similitudes et les différences de la dystonie neuro-végétative cardiaque entre les patients atteints de SWEDD et les patients atteints de MP. Nous avons examiné si l'enregistrement de la tension artérielle ambulatoire de 24 heures (ETAA 24 h) pouvait aider à identifier les cas possibles de SWEDD. ***Méthode :*** Nous avons recruté 28 patients atteints de SWEDD, 46 patients atteints de MP et 30 sujets témoins en bonne santé. Un ETAA 24 h a été effectué chez tous les sujets afin d'évaluer la fonction neurovégétative cardiaque. Une scintigraphie cardiaque à la métaiodobenzylguanidine (MIBG) a été effectuée chez les sujets atteints de SWEDD et de MP. ***Résultats :*** Le pourcentage de diminution nocturne de la tension artérielle était significativement différent chez les patients atteints de SWEDD, les patients atteints de MP et les sujets témoins ($p < 0,05$). En plus de la TA nocturne anormale, la régulation (absence de diminution et diminution inversée) de la TA était significativement plus élevée chez les sujets atteints de SWEDD et de MP que chez les sujets témoins ($p < 0,05$). Il n'existait pas de corrélation significative entre le % de réduction de la tension artérielle nocturne et les paramètres du ratio de captation cardiaque de MIBG. Cependant, l'hypotension orthostatique était corrélée significativement à la baisse (%) de la tension artérielle nocturne, au profil de la tension artérielle nocturne et au ratio de captation cardiaque de MIBG (précoce et tardif) chez les patients atteints de SWEED et de MP. ***Conclusions :*** La régulation nocturne pathologique de la tension artérielle et l'hypertension nocturne, des caractéristiques bien connues de la MP, sont également présentes chez les patients atteints de SWEDD. De plus, la dénervation sympathique cardiaque ne devrait pas être attribuée à une dystonie neurovégétative cardiaque chez les patients atteints de SWEDD. Comme chez les patients atteints de MP, les patients atteints de SWEDD que nous avons étudiés avaient tendance à présenter une dystonie neurovégétative cardiaque.

Keywords: 24-hour ambulatory blood pressure monitoring (ABPM), SWEDDs, non-dipping, nocturnal hypotension, orthostatic hypotension, cardiac MIBG uptake

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Introduction

The concept of scans without evidence of dopaminergic deficits (SWEDDs) originates from the clinical trial literature for Parkinson's disease (PD), in which dopamine transporter images were made to monitor disease progression; these revealed that normal scans obtained in a substantial proportion of clinically diagnosed cases of PD (4%-15%). These patients were therefore designated SWEDDs patients.[1-3] Some researchers have suggested that SWEDDs patients comprise a spectrum of diseases (idiopathic PD, essential tremor, dystonic tremor, and other parkinsonisms).[2-4]

PD is characterized by multisystem degeneration.[5,6] Traditionally, it is considered a motor disorder, but nonmotor symptoms have been established in the past decade. The usual nonmotor symptoms include cognitive dysfunctions, psychiatric problems, autonomic failures, and sleep difficulties.[7] The non-motor symptoms are important to patients and have been found to have a severe effect on quality of life. Cardiovascular autonomic dysfunction has frequently been reported in PD. One of the clinically important non-motor features of PD is altered blood pressure (BP) regulation. Loss of the circadian rhythm of BP is an early sign of dysautonomia in PD patients with orthostatic hypotension.[8] A variety of circadian abnormalities that can influence hemodynamic changes are found in patients with PD. In particular, fluctuating BP, decreased heart rate variability, nocturnal BP nondipping, and nocturnal hypertension are common.[9]

Loss of the nocturnal BP fall was previously reported in various extrapyramidal syndromes (especially in early PD, multiple system atrophy, and progressive supranuclear palsy patients),[10] and loss of or decreased nocturnal BP fall (nondipper) can be a marker of autonomic dysfunction.[5] High nocturnal BP is associated with increased cardiovascular mortality; therefore, early detection is important.[11] BP variability is influenced by sympathetic factors. In addition, there is a significant correlation between systemic BP profile and cardiac ^{123}I-metaiodobenzylguanidine (MIBG) uptake in patients with PD.[12] Therefore, we investigated this profile in SWEDDs patients.

In this study, we determined the similarities and differences in cardiac autonomic dysfunction in SWEDDs versus PD patients. In addition, to confirm whether a relationship exists between abnormal findings for cardiac MIBG uptake and quantitative BP profile data, we performed both examinations in the SWEDDs and PD patients. Additionally, 24-hour ambulatory BP (ABPM) profiles and cardiac MIBG uptake differences were compared in patients with orthostatic hypotension and without orthostatic hypotension.

Materials and Methods

Subjects

Subjects who had PD were recruited from Hanyang University Hospital from January 2010 to May 2013. The SWEDDs patients were defined by the following criteria: adult onset (age >40 years) of parkinsonian symptoms, including asymmetric resting tremor or akinetic rigidity, previous diagnosis of PD by a specialist, and normal dopamine transporter imaging (^{123}I-fluoropropyl-2-beta-carbomethoxy-3-beta[4-iodophenyl] nortropane positron emission tomography [FP-CIT PET]). The dopamine transporter scans of the patients were inspected by nuclear medicine clinicians who were not aware of the clinical information. The patients in the PD group fulfilled UK brain bank PD criteria[13] and had abnormal FP-CIT PET findings. Patients with possible secondary causes of their parkinsonism were excluded. None of the patients were administered dopaminergic drugs until the tests were completed. We excluded patients with relevant cardiac problems, medical disorders, history of neuropathy, or current medication use (central nervous system stimulants, monoamine oxidase inhibitors, opioids, selective serotonin reuptake inhibitors, and sympathomimetics), which could have influenced the FP-CIT PET or cardiac MIBG scintigraphy. All individuals in the control group were in good health as established by chart review.

Basic patient demographic and clinical data were obtained for each patient. Disease severity was evaluated according to the unified PD rating scale (UPDRS) score and Hoehn and Yahr stage. Orthostatic hypotension was measured in the SWEDDs and PD patients. According to the American Autonomic Society, the definition of orthostatic hypotension is a constant decrease of the systolic blood pressure to ≥20 mmHg and diastolic blood pressure to ≥10 mmHg within 3 minutes of a change in standing position.[14]

24-Hour ABPM

All patients underwent 24-hour ABPM using a noninvasive portable recorder (TM-2430; A&D Medical, Saitama, Japan). The subjects were free to move during the recording. BP was assessed in the upper extremities every 15 minutes during the day and every 30 minutes during the night.

The following parameters were calculated from the raw data: 24-hour mean systolic BP (SBP)/diastolic BP (DBP)/mean arterial BP (MABP), waking SBP/DBP/MABP, sleeping SBP/DBP/MABP, 24-hour heart rate (HR), daytime HR, nighttime HR, and nocturnal BP fall (dipper, nondipper, reverse dipper). The individual parameters were defined as follows: nighttime BP was defined as the average of the BP at the onset of sleep and awakening based on the activity sheet. According to the American Heart Association Council on High Blood Pressure Research, nocturnal hypertension is defined as nocturnal BP >125/75 and daytime hypertension is defined as daytime BP >140/90.[15] Mean daytime and nighttime SBP and DBP were calculated, and the nocturnal BP dip (%) was calculated as follows: (daytime SBP – nighttime SBP)/daytime SBP × 100.[15] Subjects were divided into three subgroups according to the magnitude of the fall in BP, dippers (those who showed ordinary nocturnal falls [10% ≤ nocturnal BP reductions]); nondippers (those whose BP did not fall by the usual amount [0% ≤ nocturnal BP fall <10%]); and reverse dippers (those whose BP increased during the night).

MIBG Scans

Cardiac MIBG scans were performed 20 minutes and 3 hours after intravenous injection of an average of 111 MBq (3 mCi) 123I-MIBG using a dual-head gamma camera (ECAM, Siemens Medical Systems, Chicago, IL, USA). The cardiac and mediastinal regions of interest were drawn for semiquantification of the 123I-MIBG uptake. Heart-to-mediastinum (H/M) uptake ratios and washout rates (WRs) were calculated using the following formulas: H/M ratio = mean count of heart uptake at 20 minutes/mean count of mediastinum uptake at 3 hours; WR = [mean count of heart

uptake at 20 minutes (mean count of heart uptake at 3 hours)/mean count in early scan × 100].

FP-CIT PET/Computed Tomography

FP-CIT PET/computed tomography (CT) was conducted in all SWEDDs and PD patients. The PET/CT scans were performed 2 hours after an intravenous injection of an average of 185 MBq (5 mCi) FP-CIT. All subjects underwent PET/CT imaging in a Biograph TruePoint 16 scanner (Siemens Medical Systems, Hoffman Estates, IL, USA). The emission PET data were acquired for 10 minutes, and the CT data were used for the attenuation correction. The dopamine transporter binding state was evaluated through visual analysis and semiquantitative analysis of the FP-CIT PET/CT. Semiquantitative analyses were performed using the specific to nonspecific binding ratio and the asymmetric index (AI). The regions of interest were identified and drawn on both caudate nuclei, both putamen, and the occipital cortex. Standardized uptake values were taken from each area, and three adjacent slices where the striatum was best observed were used for the analysis. The specific to nonspecific binding ratio was calculated using the following formula: (average standardized uptake value of striatum – average standardized uptake value of occipital cortex)/average standardized uptake value of occipital cortex. The AI was calculated according to (better uptake – worse uptake)/better uptake.

Statistical Analysis

The data were analyzed using SPSS 21.0. Analysis of variance and Pearson's chi-squared tests were used to compare the 24-hour ABPM profiles, H/M ratios, WRs, and clinical features of the three groups. Student's t test was used to compare 24-hour ABPM profiles, cardiac MIBG uptake, and clinical features between patients with and without orthostatic hypotension. All p values of <0.05 were considered statistically significant. Results are presented as mean values (± standard deviations).

Results

A comparison of the baseline demographic and clinical data between the PD patients, SWEDDs patients, and control group is shown in Table 1. No significant differences were observed with respect to age, sex, disease duration, or UPDRS III. However, disease severity (Hoehn and Yahr stage) was higher in the PD group (2.35 ± 1.02) than in the SWEDDs group (1.89 ± 0.74). In addition, orthostatic hypotension was more frequent in the PD group (37%) than in the SWEDDs group (14.3%) (Table 1). Table 2 presents the detailed clinical features of the 28 SWEDDs patients. All had bradykinesia with other parkinsonian symptoms, but three had not been using dopaminergic drugs because of negative responses to levodopa.

Daytime mean DBP and MABP were significantly lower in the SWEDDs patients than in controls ($p < 0.05$). Nocturnal hypertension was more frequent in the SWEDDs and PD groups than in the control group ($p < 0.05$). The percentage nocturnal BP dips were significantly different among SWEDDs patients, PD patients, and control subjects ($p < 0.05$). Nocturnal BP patterns but did not differ significantly between the SWEDDs and PD groups, but they did differ between the two patient groups and the controls ($p < 0.05$) (Table 3) (Figure 1).

A comparison of cardiac MIBG uptake in the SWEDDs and PD groups revealed that the early H/M ratio was higher in the SWEDDs (2.53 ± 0.60) patients than in the PD patients (2.00 ± 0.47) ($p < 0.05$). The late H/M ratio was also higher in the SWEDDs (2.80 ± 0.90) than the PD patients (1.94 ± 0.66) ($p < 0.05$). Finally, washout rates (%) were higher in the PD (23.42 ± 11.15) than in the SWEDDs patients (14.85 ± 12.20) ($p < 0.05$).

The results of comparisons between the combined SWEDDs and PD patients with and without orthostatic hypotension are shown in Table 4. There were significant differences in diurnal hypertension, nocturnal BP dip (%), nocturnal BP patterns (Figure 2), and cardiac MIBG uptake ratio (early and late) (Table 4).

When comparing FP-CIT PET/CT parameters, significant differences were observed in the SNBRs for both the striatum and in the AIs for the caudate and putamen between the two groups ($p < 0.001$ in all areas, $p < 0.005$ in asymmetric index, caudate). Table 5 shows the mean SNBRs for the caudate and putamen and the AI indices for the caudate and putamen in each group.

We also performed a correlation analysis, but found no correlations between the absence of a nocturnal blood pressure dip and disease duration, age, or MIBG uptake profiles.

Discussion

In this study, we demonstrated for the first time that 24-hour ABPM has an altered nocturnal 24-hour BP profile in most SWEDDs patients. Therefore, ABPM could even be useful for detecting autonomic dysfunction in SWEDDs patients. In addition,

Table 1: Dermographics of the patients with SWEDDs and PD at baseline and of the control subjects

	SWEDDs (n = 28)	PD (n = 46)	Control (n = 30)	p value
Sex: female/male	10/18	19/27	15/15	0.544*
Age	70.0 ± 8.4	66.9 ± 9.1	66.3 ± 9.3	0.241*
Disease duration (months)	33.3 ± 38.9	33.5 ± 36.8	NA	0.987†
Hoehn and Yahr staging	1.8 ± 0.7	2.3 ± 1.0	NA	0.043†
UPDRS part III	22.5 ± 15.2	27.1 ± 15.4	NA	0.208†
Orthostatic hypotension, n (%)	4 (14.3%)	17 (37%)	0 (0%)	0.036‡

Data are presented as mean ± standard deviation or number (%).

NS = not significant; NA = not applicable.

*Analysis of variance, †Student t test, and ‡Pearson χ^2 test were used to determine p values.

Table 2: Clinical features in 28 patients with SWEDDs

No	Sex	Age	Durations (years)	Used dopaminergic drugs?	Types of dopaminergic drugs	LED of dopamine agonists (last visit)	Total LED (last visit)	L-dopa response	Parkinsonian signs
1	F	72	0.5	Yes	Le, Pr	25	175	Positive	TR, TP, B, R, S
2	M	71	3.6	Yes	Le, En, Pr	75	275	Positive	TR, TP, B, R
3	F	71	2	Yes	Le, Pr	75	325	Positive	TR, B, R, S
4	F	77	0.3	Yes	Le, Ro	40	790	Positive	TR, B, R, S, A
5	F	79	7	Yes	Am		200	Positive	TR, TP, B, R, S, A
6	M	72	1	Yes	Le, Pr	150	900	Positive	TR, TP, B, R, S, A
7	F	51	0.3	No				Negative	TR, TP, B, R
8	F	76	1	Yes	Am, Pr	25	125	Positive	TR, B, R
9	F	66	0.5	Yes	Am, Le, Pr	25	275	Positive	TR, B, R
10	F	78	6	Yes	Le, En, Pr	150	950	Positive	TR, TP, B, R
11	M	72	5	Yes	Am, Le, Ro	80	380	Positive	TP, B, R, S, A
12	F	74	2	Yes	Am, Le		250	Positive	TR, TP, B, R, S, A
13	F	65	3	Yes	Am, Se		75	Positive	TR, R, B
14	F	68	2	Yes	Pr	125	125	Positive	TR, B, R,
15	F	69	0.3	Yes	Se		25	Positive	B, R, A
16	F	53	2	Yes	Am, Pr	75	275	Positive	TP, B, R, A
17	F	75	2	Yes	Le		150	Positive	TR, B, R, A
18	F	77	4	Yes	Am, Le, Ro	40	740	Positive	TR, B, R, S, A
19	M	74	0.8	Yes	Am, Le, Pr	25	525	Positive	TR, B, R
20	F	64	3	No				Negative	TR, TP, B, R
21	F	75	2	Yes	Am, Le, Pr	75	425	Positive	TR, B, R, A
22	F	75	0.3	Yes	Am, Pr	100	300	Positive	TR, TP, B, R
23	M	46	5	No			300	Negative	B, R
24	M	76	0.3	Yes	Am, Le			Positive	TP, B, R
25	M	73	0.3	Yes	Am, Le, En		733	Positive	TP, B, R
26	M	72	0.5	Yes	Le, Ro, Pr	65	815	Positive	TP, B, R
27	M	79	1	Yes	Am, Le, Pr	200	700	Positive	TR, TP, B, R, A
28	M	61	2.5	Yes	Am, Pr	187.5	287.5	Positive	TR, TP, B, R, A

A = axial involvement; Am = amantadine; B = bradykinesia; En = entacapone; Le = levodopa; LED = levodopa equivalent dose; Pr = pramipexole; R = rigidity; Ro = ropinirole; S = slowness; Se = selegiline; TP = postural tremor; TR = resting tremor.

similar patterns of cardiovascular autonomic dysfunction were seen in SWEDDs and PD patients.

Studies of nonmotor manifestations have indicated that olfactory dysfunction and cardiac sympathetic denervation could differ between SWEDDs and PD patients.[16,17] We also observed differences in cardiac sympathetic denervation between SWEDDs and PD patients as in previous reports. This finding may help to differentiate patients with SWEDDs from patients with PD. However, autonomic dysfunction, which is defined by 24-hour ABPM profiles, was observed in both the SWEDDs group and the PD group. As mentioned previously, there is a spectrum of diseases in SWEDDs patients. The difference in nonmotor symptoms between SWEDDs and PD patients might also reflect a different pathophysiology of the two groups. However, we observed similar 24-hour ABPM parameters (nocturnal hypertension, non-dipping patterns) in the two groups, suggesting that they have a similar pathophysiology. A recent study suggested that most SWEDDs cases are the result of the misdiagnosis of dystonic tremor patients;[2] another study showed that most patients presenting as SWEDDs were rediagnosed with dystonic tremor after long-term follow-up. However, recent studies using longitudinal follow-up data for patients initially diagnosed as SWEDDs patients found that they were rediagnosed to PD, atypical parkinsonism, essential tremor, dystonic tremor, and others.[3,4] We found that autonomic dysfunction, especially circadian rhythm imbalance (nondipping, nocturnal hypertension), may be a characteristic of SWEDDs patients. Nondipping can be found in various extrapyramidal syndromes (PD, MSA, PSP, CBD).[10] There is one report that nondipping is correlated with the presence of subcortical ischemic lesions and cognitive impairment.[18] In the same way, SWEDDs patients may suffer from mild to moderate subcortical vascular parkinsonism. These observations suggest that SWEDDs patients include not only dystonic tremor, but also PD and other Parkinson-plus syndromes.

Table 3: Summary of the main variables in the ambulatory recording of blood pressure

	SWEDDs (n = 28)	PD (n = 46)	Control (n = 30)	p value*	Post hoc comparison
24-h ABPM					
Daytime mean SBP (mmHg)	124.6 ± 11.5	127.3 ± 12.9	131.3 ± 9.3	0.091	SWEDDs = PD = control
Daytime mean DBP (mmHg)	74.3 ± 6.6	78.2 ± 7.6	80.4 ± 7.3	0.009	SWEDDs < control
Daytime MABP (mmHg)	91.1 ± 7.5	94.6 ± 8.7	97.3 ± 7.2	0.012	SWEDDs < control
Daytime mean HR (n/min)	74.4 ± 8.2	74.8 ± 9.2	72.5 ± 7.1	0.493	SWEDDs = PD = control
Nocturnal mean SBP (mmHg)	118.9 ± 11.8	122.7 ± 19.7	116.3 ± 10.4	0.199	SWEDDs = PD = Control
Nocturnal mean DBP (mmHg)	71.0 ± 7.2	74.2 ± 12.3	69.1 ± 6.0	0.069	SWEDDs = PD = control
Nocturnal MABP (mmHg)	86.9 ± 8.0	90.4 ± 14.1	84.8 ± 6.7	0.088	SWEDDs = PD = control
Nocturnal mean HR (n/min)	67.3 ± 10.5	66.1 ± 9.3	63.3 ± 7.8	0.231	SWEDDs = PD = control
24-h mean SBP (mmHg)	122.6 ± 10.9	126.1 ± 14.0	126.9 ± 7.6	0.328	SWEDDs = PD = control
24-h mean DBP (mmHg)	74.8 ± 9.5	77.5 ± 8.7	77.0 ± 5.4	0.378	SWEDDs = PD = control
24-h MABP (mmHg)	90.7 ± 8.7	93.7 ± 9.8	93.6 ± 5.3	0.298	SWEDDs = PD = control
24-h mean HR (n/min)	73.2 ± 11.6	72.6 ± 9.0	69.6 ± 7.1	0.271	SWEDDs = PD = control
Diurnal hypertension, n (%)	4 (14.3%)	5 (10.9%)	6 (20%)	0.549†	
Nocturnal hypertension, n (%)	14 (50%)	27 (58.7%)	9 (30%)	0.042†	
Nocturnal BP dip (%)	4.3 ± 6.9	3.7 ± 10.2	11.2 ± 8.7	0.001	SWEDDs = PD < control
Nocturnal BP profile				0.001†	
Dipping, n (%)	5 (17.9)	13 (28.3)	20 (66.7)		
Nondipping, n (%)	18 (64.3)	20 (43.5)	8 (26.7)		
Reverse dipping, n (%)	5 (17.9)	13 (28.3)	2 (6.7)		
Nocturnal pulse decrease	5.46 ± 6.24	9.83 ± 9.92	9.23 ± 6.09	0.070	SWEDDs = PD = control

Data are presented as mean ± standard deviation or number (%).
*ANOVA test were used to determine p values with Bonferroni post hoc paired comparison tests.
†Pearson χ^2 test.

The causes of nondipping and nocturnal hypertension are not understood. However, autonomic dysfunction is almost always associated with a nondipping BP profile and sometimes even with nocturnal hypertension.[19,20] Daytime inactivity and poor sleep quality may explain the nondipping phenomenon, but nondipping is also related to a number of clinical conditions that usually have no influence on daytime activity and/or sleep quality.[19] In parkinsonian syndromes, orthostatic hypotension develops as a synergistic effect of cardiovascular noradrenergic denervation and

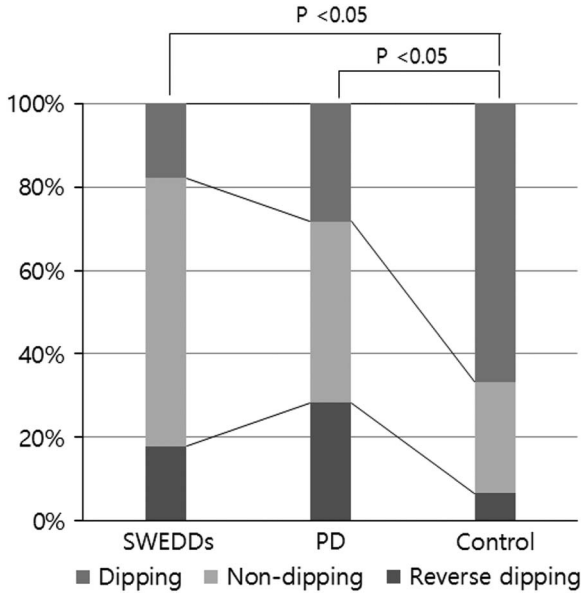

Figure 1: *24-hour blood pressure circadian patterns in SWEDDs, PD, and control.*

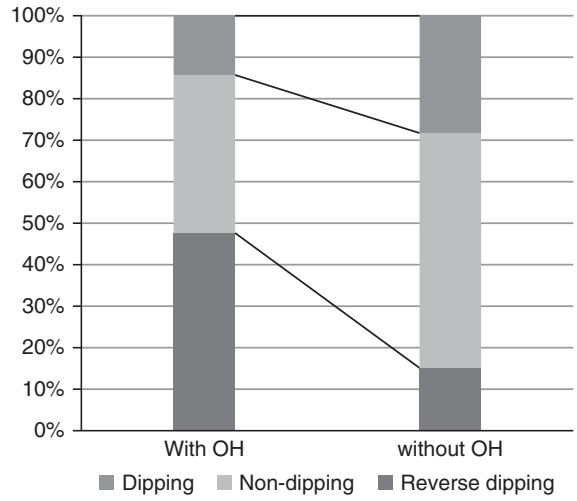

Figure 2: *24-hour blood pressure circadian patterns in with and without orthostatic hypotension. OH = orthostatic hypotension. p < 0.05.*

Table 4 : Comparisons between patients with and without orthostatic hypotension

	With OH (n = 21)	Without OH (n = 53)	p value*
Sex: female/male	9/12	20/33	0.686[b]
Age	68.1 ± 8.9	68.1 ± 9.0	0.994
Disease duration (months)	28.7 ± 33.5	35.3 ± 38.2	0.495
Hoehn and Yahr staging	2.3 ± 1.2	2.0 ± 0.7	0.336
UPDRS part III	29.1 ± 18.7	23.9 ± 13.7	0.191
Diagnosis (SWEDDs/PD)	4/17	24/29	0.037†
24-h ABPM			
Daytime mean SBP (mmHg)	122.8 ± 12.2	127.7 ± 12.3	0.128
Daytime mean DBP (mmHg)	76.5 ± 7.2	76.9 ± 7.6	0.845
Daytime MABP (mmHg)	91.9 ± 8.2	93.8 ± 8.5	0.392
Daytime mean HR (n/min)	72.9 ± 8.0	75.4 ± 9.1	0.283
Nocturnal mean SBP (mmHg)	123.8 ± 18.6	120.3 ± 16.6	0.426
Nocturnal mean DBP (mmHg)	75.4 ± 13.2	72.0 ± 9.5	0.223
Nocturnal MABP (mmHg)	91.5 ± 14.4	88.1 ± 11.2	0.277
Nocturnal mean HR (n/min)	64.2 ± 9.1	67.5 ± 9.9	0.200
24-h mean SBP (mmHg)	123.0 ± 13.1	125.4 ± 12.9	0.468
24-h mean DBP (mmHg)	76.0 ± 8.6	76.6 ± 9.3	0.774
24-h MABP (mmHg)	91.6 ± 9.5	92.9 ± 9.5	0.607
24-h mean HR (n/min)	70.8 ± 8.1	73.7 ± 10.6	0.260
Diurnal hypertension, n (%)	0 (0%)	9 (17%)	0.045†
Nocturnal hypertension, n (%)	13 (61.9%)	28 (52.8%)	0.482†
Nocturnal BP dip (%)	−0.7 ± 10.3	5.9 ± 7.8	0.002†
Nocturnal BP pattern			0.010†
Dipping, n (%)	3 (14.3%)	15 (28.3%)	
Nondipping, n (%)	8 (38.1%)	30 (56.6%)	
Reverse dipping, n (%)	10 (47.6%)	8 (15.1%)	
Nocturnal pulse decrease	8.66 ± 5.68	7.9 ± 9.9	0.768
MIBG uptake			
Early	1.9 ± 0.5	2.3 ± 0.5	0.019
Late	1.9 ± 0.6	2.4 ± 0.8	0.020
Washout	22.6 ± 11.7	19.2 ± 12.3	0.287

*Student t test.
†Pearson χ^2 test.

baroreflex failure.[21] Nondipping accompanied by nocturnal hypertension shared a common mechanism with orthostatic hypotension in PD. Autonomic dysfunction in PD has been investigated by various methodologies. Autonomic dysfunction, at least as reflected by sympathetic noradrenergic denervation, seems to occur independently of the dopaminergic lesion that produces the movement disorder in PD.[22] Therefore, nondipping and nocturnal hypertension can be observed in SWEDDs patients independently of the dopaminergic deficits.[23] However, there are significant differences in MIBG uptake between SWEDDs and PD patients that contribute to the former's lack of postganglionic cardiac sympathetic denervation. Therefore, other types of autonomic dysfunction may contribute to the nondipping in SWEDDs patients. Alternatively, SWEDDs patients could have a form of PD without evidence of postganglionic cardiac sympathetic denervation.

There have been few studies of the possible correlation between MIBG uptake and systemic BP profiles.[8,12] MIBG uptake has been reported to be correlated with nocturnal BP dips;[12] however, we could not found any correlation between MIBG uptake and systemic BP profiles in each groups. Interestingly, the nondipping patterns in the two groups (PD and SWEDDs patients) were similar. However, they differed with respect to the early and delayed H/M ratio on the MIBG scan. The SWEDDs group had nearly normal MIBG uptake, whereas the PD group had decreased MIBG uptake. This finding implies that the mechanism of nondipping in SWEDDs patients is different from that in PD. We also do not know about the mechanism of this nondipping, as other mechanisms would exist in SWEDDs.

In addition, there have been few studies of the correlation between orthostatic hypotension and autonomic dysfunction

Table 5: ^{123}I-FP-CIT PET/CT results

	SWEDDs (n = 28)	PD (n = 46)	p value	Control (n = 26) (16)
Age	70.0 ± 8.4	66.9 ± 9.1	<0.001	61.88 ± 1.88
Left caudate	3.34 ± 0.80	2.46 ± 0.90	<0.001	3.47 ± 0.38
Left putamen	3.43 ± 0.88	1.58 ± 0.77	<0.001	3.69 ± 0.40
Right caudate	3.26 ± 0.79	2.42 ± 0.89	<0.001	3.52 ± 0.65
Right putamen	3.33 ± 0.92	1.39 ± 0.70	<0.001	3.77 ± 0.38
Asymmetric index, caudate	0.05 ± 0.11	0.11 ± 0.09	0.003	0.04 ± 0.03
Asymmetric index, putamen	0.05 ± 0.04	0.24 ± 0.16	<0.001	0.05 ±0.03

Data are mean ± standard deviation.

(nocturnal BP dip, cardiac MIBG uptake).[8,23,24] In our study, we divided the SWEDDs and PD patients into two groups based on the presence of orthostatic hypotension and found a significant correlation between orthostatic hypotension/nocturnal BP pattern and cardiac MIBG uptake. This findings may be accounted for by the fact that orthostatic hypotension is a symptom of sympathetic nervous disturbance. In patients with PD and autonomic failure, orthostatic hypotension in the morning hours is caused by natriuresis and polyuria caused by nocturnal hypertension.[24,25] But not all the patients with orthostatic hypotension in our study had nocturnal hypertension. There is one report that cardiac and vasomotor sympathetic activities are present in early stage de novo PD, even without orthostatic hypotension.[26] This result could support our observation of nondipping and reverse dipping patterns in the absence of orthostatic hypotension. Conversely, SWEDDs patients may have abnormal vasomotor sympathetic activities. More studies are needed to clarify this matter. In addition, final diagnosis in patients with SWEDDs involving this study had not defined, which is a limitation of our study. We will continue follow-up studies with these subjects.

In this study, we examined the similarities and differences in cardiac autonomic dysfunction between SWEDDs and PD patients. We confirmed that cardiovascular dysautonomia can exist in SWEDDs patients. Furthermore, we concluded that 24-hour ABPM monitoring could be a useful method for detecting cardiovascular dysautonomia in SWEDDs patients.

Disclosures

None of the authors have anything to disclose.

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