Background and Purpose: Orthostatic hypotension (OH) is known to be present even in patients with early Parkinson’s disease (PD). To affirm the presence of OH and find correlation between OH and other dysautonomic symptoms in PD, this study has done in newly-diagnosed PD patients.

Methods: Forty-five non-demented patients with no prior history of treatment for PD were recruited (17 men, 63.8 ± 10.1 years of age). All the patients were evaluated for OH before starting medications. Autonomic symptoms were evaluated with structured questionnaires. Clinical characteristics of PD were evaluated (median Hoehn and Yahr stage 2.0 (1-3), 1.3 ± 1.1 years of disease duration), and comorbid medical conditions that could affect blood pressure were also recorded. Results: OH was prevalent, and eighteen patients (40%) showed orthostatic hypotension, and twenty-seven (60%) did not (normotensive group). There was no significant difference in demographic and clinical characteristics between groups. The presence or severity of symptoms of autonomic dysfunction in the OH group also did not differ from those of the normotensive group. Conclusions: OH was prevalent even in the early stage of PD, and was not related to presence or severity of any other symptoms of autonomic dysfunction. Our findings suggest that clinicians should pay attention to OH from the early stage of disease.

Key Words: Parkinson’s disease, Orthostatic hypotension, Autonomic dysfunction.
the diagnosis was confirmed during the follow up visits for more than 6 months. Comorbid medical conditions that could affect blood pressure were also evaluated, which included hypertension, diabetes mellitus, and benign prostatic hypertrophy.

Evaluation of parkinsonian symptoms
Severity and stage of parkinsonism were rated using the unified Parkinson’s disease rating scale, the Hoehn and Yahr stage and the Modified Schwab and England activities of daily living.

Evaluation of orthostatic hypotension and autonomic dysfunction
All patients were evaluated for the presence of OH, regardless of symptoms of orthostatic dizziness or syncope. To avoid the blood pressure lowering effect of dopaminergic drugs, all patients evaluated for OH before medication. OH was measured by monitoring systolic and diastolic blood pressure and heart rate. After a 10 minute period of lying down, systolic and diastolic blood pressures were checked in the first, third, and fifth minutes after standing up. If the patient could not stand up by his or herself, a tilt table was used. OH was defined as a drop in systolic BP $\geq 20$ mmHg or diastolic BP $\geq 10$ mmHg at anytime following standing up.

Comprehensive assessment of autonomic dysfunction was also assessed using a systematized autonomic dysfunction questionnaire (ADQ). The ADQ covered gastrointestinal symptoms, urinary symptoms, sexual dysfunction, cardiovascular symptoms and thermoregulatory symptoms. The severity or frequency of each of the symptoms was expressed as scores (Table 1).

**Statistical Analysis**
SPSS version 14 for Windows was used for statistical calculations. Mann-Whitney and Chi tests were employed to analyze intergroup difference. Statistical significance was declared at the $p < 0.05$ range.

**Results**

**General and clinical characteristics of patients**
The subjects (17 men and 28 women, age of $63.8 \pm 10.1$ years) showed mild disease [median Hoehn and Yahr stage 2.0 (1-3)] with $1.3 \pm 1.1$ years of disease duration. Twenty-two patients had comorbid disease, which could affect blood pressure. Hypertension (20/45 patients) was the most common, followed by diabetes (7/45) and benign prostatic hyperplasia (1/45). Eighteen patients showed OH (OH group, 8 men, age $61.3 \pm 10.8$ years) and twenty-seven patients (normotensive group, 9

| Table 1. Autonomic dysfunction questionnaire                  |
|---------------------------------------------------------------|
| **Gastrointestinal symptoms**                                  |
| Salivation                                                     | Hesitancy                                          |
| Dysphagia                                                     | Urgency                                            |
| Nausea                                                        | Incomplete voiding                                 |
| Constipation                                                  | Weak stream                                        |
| Defecatory dysfunction (anismus)                              | Frequency                                          |
| Urinary symptoms                                              |                                                     |
| Salivation                                                     | Hesitancy                                          |
| Dysphagia                                                     | Urgency                                            |
| Nausea                                                        | Incomplete voiding                                 |
| Constipation                                                  | Weak stream                                        |
| Defecatory dysfunction (anismus)                              | Frequency                                          |
| Urinary symptoms                                              |                                                     |
| **Sexual dysfunction**                                        |
| Erectile dysfunction                                          | Ejaculation difficulty                            |
| Libido change                                                 |                                                    |
| **Cardiovascular symptoms**                                   |
| Orthostasis                                                   | Syncope                                            |
| **Thermoregulatory symptoms**                                 |
| Sweating (Face)                                               | Sweating (Trunk)                                   |
| Sweating (Limb)                                               | Heat intolerance                                   |
| Cold intolerance                                              | Oiliness & seborrhea                               |

| Table 2. Demographic & parkinsonian features in each group       |
|---------------------------------------------------------------|
| **Group**                                                     | **Patients with orthostatic hypotension (n = 18)** | **Patients without orthostatic hypotension (n = 27)** | **p** |
| Sex (M : F)                                                   | 8 : 10                                             | 9 : 18                                           | NS    |
| Age (Y)                                                       | $61.3 \pm 10.8$                                    | $65.5 \pm 9.4$                                   | NS    |
| Duration of symptoms (M)                                     | $13.8 \pm 10.1$                                   | $16.1 \pm 15.9$                                  | NS    |
| Duration of education (y)                                     | $8.0 \pm 3.9$                                     | $5.9 \pm 4.6$                                    | NS    |
| Comorbid disorders (%)                                        | 9 (50.00%)                                         | 13 (48.1%)                                       | NS    |
| UPDRS Part I                                                  | $2.7 \pm 1.5$                                     | $2.4 \pm 1.5$                                    | NS    |
| UPDRS Part II                                                 | $9.0 \pm 4.5$                                     | $9.1 \pm 3.7$                                    | NS    |
| UPDRS Part III                                                | $24.3 \pm 7.7$                                    | $26.5 \pm 8.9$                                   | NS    |
| UPDRS total                                                   | $36.7 \pm 10.5$                                   | $38.2 \pm 11.8$                                  | NS    |
| Hoehn & Yahr stage                                            | $2.0 \pm 0.6$                                     | $2.0 \pm 0.5$                                    | NS    |
| SEADL                                                         | $73.3 \pm 11.5$                                   | $75.4 \pm 11.2$                                  | NS    |

K-MMSE: Korean version of mini-mental status exam, ADL: activity of daily living, SEADL: schwab and england activity of daily living
Symptoms of autonomic dysfunctions in patients

Many dysautonomic symptoms were accompanied with OH in patients, and all the patients had more than two of those symptoms (Table 3). Urinary symptoms were most common and followed by sexual symptoms. Although urinary incontinence was more prevalence in OH group, it did not reach statistical significance. The presence of OH was not related with the presence of other symptoms.

Total score in the ADQ was slightly increased in patients with OH compared to that of patients without OH (Table 4). However, the differences did not reach statistical significance. In spite of the insignificant difference, the scores of all domains in the OH group were higher than those of the normotensive group. However, even in the questions of cardiovascular symptoms, orthostatic dizziness and history of syncope, there was no difference between groups. Only eight patients complained of orthostatic dizziness and four of those patients showed OH.

Discussion

Abnormal cardiovascular regulation, including orthostatic hypotension was frequently expressed in various stages of PD patients. The cardiovascular autonomic disturbances are following the gastrointestinal symptoms in frequency, but they have a higher impact on the quality of life in PD patients.

Lewy bodies, a pathological hallmark of Parkinson’s disease, have been found in autonomic regulatory regions of the brain or peripheral autonomic ganglia in PD patients. And, many studies have shown the evidence of cardiac sympathetic denervation in early PD patients by using cardiac sympathetic imaging.

Symptoms of autonomic dysfunction in PD patients were known to be related with older age, long disease duration, se-

Table 3. Presence of dysautonomic symptoms in each group

| Gastrointestinal symptom | Patients with orthostatic hypotension (n = 18) | Patients without orthostatic hypotension (n = 27) | p  |
|--------------------------|---------------------------------------------|-----------------------------------------------|----|
| Salivation               | 27.8% (5)                                   | 25.9% (7)                                     | NS |
| Dysphagia                | 11.1% (2)                                   | 14.8% (4)                                     | NS |
| Nausea                   | 22.2% (4)                                   | 25.9% (7)                                     | NS |
| Constipation             | 44.4% (8)                                   | 25.9% (7)                                     | NS |
| Anismus                  | 27.8% (5)                                   | 11.1% (3)                                     | NS |
| Urinary symptom          |                                             |                                              |    |
| Hesitancy                | 33.3% (6)                                   | 29.6% (8)                                     | NS |
| Urgency                  | 27.8% (5)                                   | 33.3% (9)                                     | NS |
| Incomplete voiding       | 38.9% (7)                                   | 44.4% (12)                                    | NS |
| Weak stream              | 38.9% (7)                                   | 33.3% (9)                                     | NS |
| Frequency                | 77.8% (14)                                  | 66.7% (18)                                    | NS |
| Nocturia                 | 72.2% (13)                                  | 74.1% (20)                                    | NS |
| Incontinence             | 27.8% (5)                                   | 7.4% (2)                                      | NS |
| Sexual dysfunction       |                                             |                                              |    |
| Erectile dysfunction*    | 37.5% (3/8)                                 | 22.2% (2/9)                                   | NS |
| Ejaculation difficulty*  | 37.5% (3/8)                                 | 33.3% (3/9)                                   | NS |
| Change of libido         | 50.0% (9)                                   | 40.7% (11)                                    | NS |
| Cardiovascular symptom   |                                             |                                              |    |
| Orthostasis              | 22.2% (4)                                   | 7.4% (2)                                      | NS |
| Syncope                  | 11.1% (2)                                   | 0.0% (0)                                      | NS |
| Thermoregulatory symptom |                                             |                                              |    |
| Sweat                    | 11.1% (2)                                   | 11.1% (3)                                     | NS |
| Heat intolerance         | 11.1% (2)                                   | 11.1% (3)                                     | NS |
| Cold intolerance         | 5.6% (1)                                    | 0.0% (0)                                      | NS |
| Oiliness of skin         | 11.1% (2)                                   | 0.0% (0)                                      | NS |

*Evaluated male patients only
The prevalence of OH in PD was variable according to criteria and methods. In 5 relatively large studies involving more than 80 patients each, the frequency of OH ranged from 30% to 58%. Bonuccelli et al. showed the high prevalence of OH in de novo PD patients. In our study, prevalence of OH in the drug-naive PD patients was moderate (18/45 patients, 40%), and similarly shown in the patients without comorbid disease (9/23 patient, 39.1%). Patients with OH were young and showed a short duration of disease, but those differences did not reach statistical significance, and the severity of parkinsonian symptoms was similar to those of patients without OH. The presence or severity of dysautonomic symptoms was not different between patients with or without OH, even in the cardiovascular domain. Therefore, OH did not respect the severity or distribution of other autonomic symptoms. Actually, the complaint of orthostasis was made by only six patients (13.3%), four of those patients showed OH. Most patients with OH did not complain of orthostasis, and Steven et al. showed that the majority of patients with profound orthostatic hypotension either did not show the typical symptoms (33%), or showed only atypical symptoms (24%). The unawareness of orthostatic hypotension stresses the importance of blood pressure monitoring irrelevant to complaints of patients.

Although we could not find statistical significance, patients with urinary incontinence were much higher in OH group (27.8% vs. 7.4%). This finding suggests that those patients can...
be diagnosed as multiple system atrophy (MSA). We followed all the patients more than six months and confirmed the good response to dopaminergic treatment. Because some patients with MSA show good response to treatment in early period, we could not exclude the possibility of MSA. Further studies with longer period of observation and about the change of dysautonomic symptoms along the disease course are warranted.

Although pathological implications of autonomic dysfunctions in PD patients have not been established yet, clinical implications can be significant enough to impact the daily activities of PD patients. Furthermore, most patients do not complain of noticeable symptoms, and the unawareness of patients warrants careful evaluation. Appropriate management of OH can prevent further insult and can improve daily activities of PD patients.

REFERENCES
1. Ziemssen T, Reichmann H. Non-motor dysfunction in Parkinson’s disease. Parkinsonism Relat Disord 2007;13:323-332.
2. Cheon SM, Park MJ, Kim WJ, Kim JW. Non-motor off symptoms in Parkinson’s disease. J Korean Med Sci 2009;24:311-314.
3. Siddiqui MF, Rast S, Lynn MJ, Auchas AP, Pfeiffer RF. Autonomic dysfunction in Parkinson's disease: a comprehensive symptom survey. Parkinsonism Relat Disord 2002;8:277-284.
4. Truong DD, Bhidayasiri R, Wolters E. Management of non-motor symptoms in advanced Parkinson disease. J Neurol Sci 2008;266:216-228.
5. Senard JM, Raf S, Lapeyre-Mestre M, Brefel C, Rascol O, Rascol A, et al. Prevalence of orthostatic hypotension in Parkinson’s disease. J Neurol Neurosurg Psychiatry 1997;63:584-589.
6. Goldstein DS. Orthostatic hypotension as an early finding in Parkinson’s disease. Clin Auton Res 2006;16:46-54.
7. van Dijk JG, Haan J, Zwenderman K, Kremer B, van Hilten BJ, Roos RA. Autonomic nervous system dysfunction in Parkinson’s disease: relationships with age, medication, duration, and severity. J Neurol Neurosurg Psychiatry 1993;56:1090-1095.
8. Kujawa K, Leurgans S, Raman R, Blasucci L, Goetz CG. Acute orthostatic hypotension when starting dopamine agonists in Parkinson’s disease. Arch Neurol 2000;57:1461-1463.
9. Calne DB, Brennan J, Spiers AS, Stern GM. Hypotension caused by L-dopa. Br Med J 1970;2:474-475.
10. Schoenenberger JA. Drug-induced orthostatic hypotension. Drug Saf 1991;6:402-407.
11. Montastruc JL, Chamentin B, Rostin M, Rascol O, Valet P, Gaillard G, et al. Experimental and clinical approaches to treatment of hypertension by dopamine receptor agonists. Clin Exp Hypertens A 1987;9:1069-1084.
12. Lang AE. Acute orthostatic hypotension when starting dopamine agonist therapy in Parkinson’s disease: the role of domperidone therapy. Arch Neurol 2001;58:835.
13. Allcock LM, Ulfarait K, Kenny RA, Burn DJ. Frequency of orthostatic hypotension in a community based cohort of patients with Parkinson’s disease. J Neurol Neurosurg Psychiatry 2004;75:1470-1471.
14. Asbroch B, Sandek R. Autonomic functions in the early stages of Parkinson's disease. Int Neuropsy 1994;74:9-16.
15. Hughes AJ, Daniel SE, Kifflord L, Lees AJ. Accuracy of clinical diagnosis of idiopathic parkinson’s disease: a clinical-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181-184.
16. Szil-Tő T, Kámá J, Paprika D, Dibó Rosa Z, Rudas L. Depressed baroreflex sensitivity in patients with Alzheimer’s and Parkinson’s disease. Neurobiol Aging 2001;22:435-438.
17. Ziemssen T, Reichmann H. Cardiovascular autonomic dysfunction in Parkinson’s disease. J Neurol Sci 2010;289:74-80.
18. Walter BL. Cardiovascular autonomic dysfunction in patients with movement disorders. Cleve Clin J Med 2008;75:54-58.
19. Shin DH, Lee PH, Bang OY, Joo IS, Huh K. Clinical Implications of Cardiac-MIBG SPECT in the Differentiation of Parkinsonian Syndromes. J Clin Neurol 2006;2:51-57.
20. Courbon F, Brefel-Courbon C, Thalamas C, Alibelli MJ, Berry I, Montastruc JL, et al. Cardiac MIBG scintigraphy is a sensitive tool for detecting cardiac sympathetic denervation in Parkinson’s disease. Mov Disord 2003;18:890-897.
21. Bonuccielli U, Lucreti C, Del Dotto P, Ceravolo R, Gambaccini G, Bernardini S, et al. Orthostatic hypotension in de Novo parkinson’s disease. Arch Neurol 2003;60:1400-1404.
22. Arbogast SD, Alsheikh A, Hussain Z, McNeeley K, Chelrisky TC. Hypotension unawareness in profound orthostatic hypotension. Am J Med 2009;122:574-580.