Clinical Value of Cardiac I-123 Metaiodobenzylguanidine Scintigraphy Between Parkinson's Disease and Parkinson's Disease Associated Dementia

In-Uk Song, Yong-An Chung, Sung-Woo Chung, Ryoong Huh

Neuroscience Center, Incheon St. Mary's Hospital, The Catholic University of Korea, Incheon 403-720, Korea

Received 16 July 2012; accepted 18 September 2012

ABSTRACT: It is very difficult that idiopathic Parkinson's disease (PD) patients with dementia (PDD) distinguish from PD patients, because PD patients may exhibit patterns of cognitive impairment. Recently, cardiac I-123 metaiodobenzylguanidine (MIBG) scintigraphy has been used as tools to distinguish PD from atypical parkinsonism. Thus, we performed this study to confirm significant clinical value of cardiac I-123 MIBG scintigraphy for differential diagnosis between PD and PDD. Cardiac I-123 MIBG scintigraphy was studied in 18 patients with PD, 18 patients with PDD, and 13 normal controls that were matched for age, disease duration, and severity of symptoms. The heart to mediastinum ratio (H/M ratio) was calculated. The mean value of H/M ratio of PDD and PD was significantly lower than normal controls. However, there were no differences between PDD and PD groups. Although cardiac I-123 MIBG scintigraphy did not distinguish PDD from PD, we wish to focus attention on sustained studies that are needed to differentiate other Lewy body disease from many dementia patients with PD features. © 2012 Wiley Periodicals, Inc. Int J Imaging Syst Technol, 22, 241–244, 2012; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/ima.22028

Key words: Parkinson's disease; dementia; I-123 MIBG scintigraphy; heart to mediastinum ratio

I. INTRODUCTION

Idiopathic Parkinson's disease (PD) is one of the most common neurodegenerative disorders, affecting about 1% of the population over the age of 60 (Padovani et al., 2006). Contrary to the initial assumption that cognitive dysfunction is not an essential feature of the disease, it has become increasingly apparent that patients with PD can have impairment of certain cognitive functions and develop dementia (Korczyn, 2001; Emre, 2003). The prevalence of dementia in PD was reported to range from 2% in early onset cases to 81% in an unselected patient population (Emre, 2003). Furthermore, PD is associated with a sixfold higher risk of developing dementia when compared to healthy elderly controls (Padovani et al., 2006). However, because PD patients—even those with mild disease—may exhibit patterns of cognitive impairment, it was difficult to distinguish PD patients with dementia (PDD) from PD patients without dementia.

Recently, cardiac I-123 metaiodobenzylguanidine (MIBG) scintigraphy has been used as tools to distinguish PD from atypical parkinsonism (Rascol and Schelosky, 2009). According to various contemporary investigations, authors reported that PD, diffuse Lewy body disease (LBD), and pure autonomic failure have reduced cardiac I-123 MIBG uptake (Yoshida et al., 1997; McKeith et al., 2005; Kashihara et al., 2006). And, the mean value of heart to mediastinum (H/M) ratio in patients with DLB was significantly lower than those in patients with PD, independent of the Hoehn and Yahr (H&Y) stage (Suzuki, et al., 2006).

The purpose of this study is to perform cardiac I-123 MIBG scintigraphy on PDD and nondementia PD patients and compared the results of groups to investigate the relationship between cardiac I-123 MIBG scintigraphy and these diseases.

II. MATERIALS AND METHODS

The study was approved by the local ethics committee, and each patient gave written informed consent for participation. We recruited prospectively in this study were recruited prospectively in this study 31 patients with PD and 28 patients with PDD who had visited our hospital and 13 age-matched healthy controls without neurological or cardiovascular abnormalities. There was no significant difference in age and gender among the PD, PDD, and control groups. In addition, there was no significant H&Y stage between disease groups. To evaluate severity of cognitive decline, we performed the Mini-Mental State Examination Korean-version (MMSE) and the expended version of Clinical Dementia Scale (CDR) with sum of box (SOB) of CDR (Kang et al., 1997; Choi et al., 2001).

The 18 patients with PD were diagnosed according to the United Kingdom Parkinson's disease Society Brain Bank Clinical Diagnosis Criteria and never had any history of memory impairment and other cognitive dysfunctions by dementia screening questionnaire.

Correspondence to: Ryoong Huh; e-mail: hrnsd@hanmail.net

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Table I. Demographic data and general cognitive functions in PD and PDD groups and normal controls

Variables	PD	PDD	Controls	*P* value
No. of subjects	31	28	13	
No. of man	14	13	7	0.69
Mean age (years)	64.77 ± 7.64	67.68 ± 7.49	66.94 ± 5.40	0.77
Mean education (years)	7.64 ± 2.76	4.68 ± 3.13	11.72 ± 4.34	<0.001
Mean disease duration (month)	59.76 ± 27.64	57.87 ± 26.39		0.52
MMSE	28.22 ± 1.31	21.50 ± 4.09	ND	<0.001
CDR	0.47 ± 0.13	0.82 ± 0.34	ND	<0.001
SOB	1.13 ± 0.5	4.39 ± 2.62	ND	<0.001
H&Y stage	1.92 ± 0.84	2.08 ± 0.72	ND	0.432

Values are mean ± standard deviation.
PD, Parkinson disease; PDD, Parkinson disease dementia; ND, Not done; MMSE, Minimental state examination; CDR, Clinical dementia scale; SOB, Sum of box of CDR.

The 18 patients with PDD were diagnosed according to the United Kingdom Parkinson's disease Society Brain Bank Clinical Diagnosis Criteria, and *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-IV) criteria for dementia. Those having marked fluctuating cognition with pronounced variations in attention and alertness and recurrent vivid hallucination suggesting presence of diffuse LBD, those taking medications reported to influence cognition and memory, those who had any clinical signs compatible with atypical parkinsonism, and those who fulfilled the DSM IV criteria for delirium or amnesic disorder and depressive disorders were excluded. Apart from exclusion criteria above mentioned, we also excluded secondary cause of parkinsonism, for example, Wilson's disease, neuroleptic use, and psychiatric disease that would, interfere with the safe conduct of the study, in judgment of the investigator.

We also excluded patients with a history of neuropathy or previous relevant cardiac disease, or any abnormalities on routine chest radiography and electrocardiography, and those taking medications reported to influence cardiac I-123 MIBG uptake.

I-123 MIBG scintigraphy was obtained after informed consent from each patient. Data were collected for 30 min (early) and 4 h (delayed) after injection of 111 MBq of I-123 MIBG using a dual-head camera (Simens, Germany). A static image was obtained with a 128 × 128 matrix. Regions of interest were manually drawn around the heart, mediastinum, and lung, and tracer uptake was measured within each region of interest to calculate the H/M ratio.

The results are expressed as mean values. Intergroup differences in various variances, including H/M ratio of I-123 MIBG uptake, among PD, PDD patients, and normal control subjects were examined for statistical significance using Kruskal–Wallis test, or the Mann–Whitney Test. The level of statistical significance was set at $P < 0.05$. All statistical analyses were carried out using SPSS version 18.0 software program.

III. RESULTS

Table I lists the clinical characteristics of the subjects. There were no significant differences in age and gender among all subjects groups. No significant differences between PD and PDD patients found in terms of H & Y stage and mean disease duration. But MMSE score, CDR with SOB, and length of education showed significant differences between two groups; PDD patients showed more severe cognitive impairment and shorter length of education than PD patients (Table I).

In the cardiac I-123 MIBG scintigraphy, the normal mean value of early and delayed H/M ratio obtained in 13 normal controls was 2.44 ± 0.37 and 2.47 ± 0.29, respectively. The mean value of early and delayed H/M ratio was 1.43 ± 2.27 and 1.36 ± 0.29 in patients with PD and 1.51 ± 0.30 and 1.37 ± 0.29 in patients with PDD, respectively. Thus, all mean values of the early and delayed H/M ratio in the control group were significantly higher than those in the PD and PDD patients. However, there was no significant difference between PD and PDD patients in terms of early and late H/M ratio (Fig. 1).

IV. DISCUSSION

The PD, DLB, and pure autonomic failure have Lewy bodies as a common pathologic finding and are considered to be three

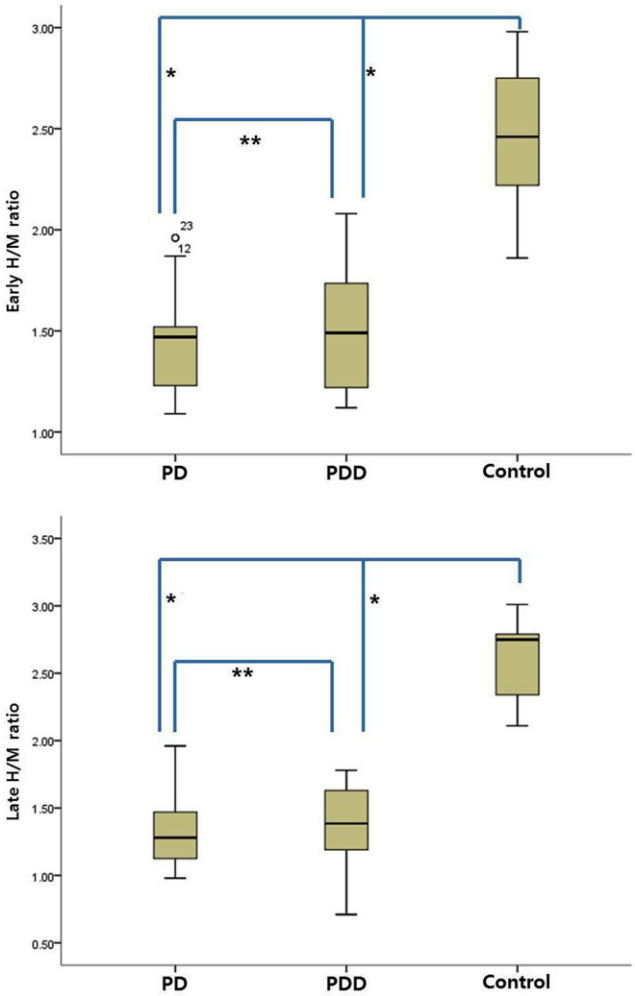

Figure 1. Comparison of the H/M ratio of I-123 MIBG uptake among patients with PD, PDD, and normal control groups. The box plot shows the median value (thick line), the 25th and 75th percentiles. Early and delay H/M ratios were compared among PD, PDD, and normal control group with Kruskal–Wallis Test ($P < 0.001$). And early and delayed H/M ratios were also compared between PD and PDD with Mann-Whitney Test. *There is difference between two groups ($P < 0.05$), **There is no difference between two groups ($P > 0.05$). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

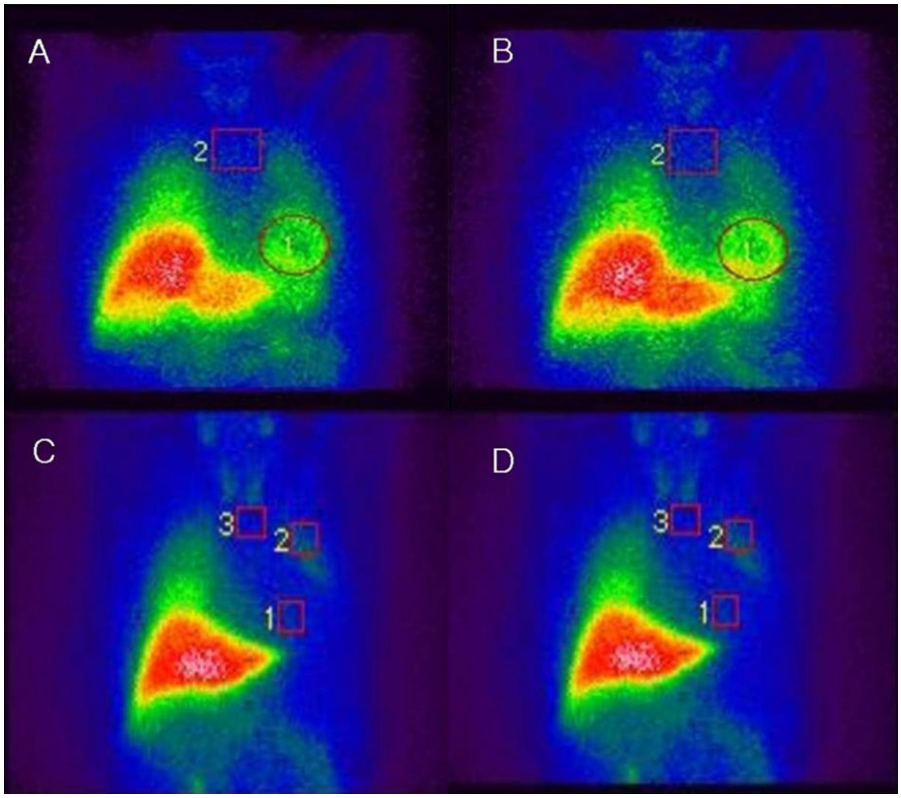

Figure 2. Cardiac I-123 MIBG scintigraphy. All of early (A) and delayed images (B) reveal normal cardiac I-123 metaiodobenzylguanidine uptake (The heart to mediastinum (H/M) ratio is 1.94 in the early image and 1.99 in the delayed image). On the other hand, early (C) and delayed (D) images reveal decreased H/M ratio (H/M ratio is 1.11 in the early and 1.10 in the delayed image), which reflect cardiac sympathetic denervation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

phenotypes of a single disorder that may be called LBD (Kashihara et al., 2006). Recent studies have indicated that cardiac I-123 MIBG scintigraphy can detect early disturbance of the sympathetic nervous system in LBD, independently of the duration of disease and autonomic failure, and provide useful diagnostic information to distinguish LBD from other neurodegenerative disorders (Hanyu et al., 2006a,b; Kashihara et al., 2006; Lee et al., 2006). The existence of the postganglionic sympathetic nerve system was involvement in LBD was estimated in recent studies. Histopathologically, Lewy neurites were detected in the cardiac plexus in all cases of incidental LBD (Rascol and Schelosky, 2009). The cardiac sympathetic nerves were dramatically depleted, independent of the presence of orthostatic hypotension in LBD patients (Orimo et al., 2005). Immunohistochemical studies also indicated that tyrosine hydroxylase-immunoreactive nerve fibers in the heart were markedly decreased in patients with PD, indicating cardiac sympathetic denervation (Orimo et al., 2001; Amino et al., 2005; Suzuki et al., 2006). Therefore, the reduced uptake of MIBG to the myocardium indicates that the capacity of MIBG to enter the neuronal tissue is weakened. Furthermore, it indicates that the ability of the sympathetic nerves to store MIBG or the amount of sympathetic nerves in the myocardium is reduced in LBD (Yoshita et al., 2006). This study also showed significant lower mean value of H/M ratio in PD and PDD patients than control.

Dementia is common and affects ~40% of PD patients during the course of the disease, and the risk for the development of dementia is six times higher than in non-PD age-matched controls (Padovani et al., 2006). But diagnosis of dementia in patient with PD may be difficult for several reasons. First, apparent impairment in certain cognitive domains may be difficult to differentiate from motor dysfunction. Second, it may be difficult to decide if impairment in activities of daily living is due to cognitive or motor dysfunction (Emre, 2003). Moreover, PDD and DLB are two common dementia of PD with overlapping clinical symptoms, suggesting that they likely represent different points on a spectrum of LBD sharing similar underlying neuropathological processes (McKeith et al., 1996; Selikhova et al., 2009). We have a very great difficulty to distinguish, PD, PDD, and DLB groups. Suzuki et al. reported that cardiac sympathetic function in DLB was severely impaired even in the early disease stage, and H/M ratio of DLB was lower value than PD, significantly (Suzuki et al., 2006). As a result of our study, we could not find significant differences in H/M ratio between PD and PDD groups. Although the previous several studies suggested that I-123 MIBG uptake of the myocardium could distinguish PD from DLB, our study did not disclose value for differential diagnosis between PD and PDD, definitely. Therefore, we could assume that occurrence of cognitive impairment in PD did not involve cardiac sympathetic nerve system. In regard to cognitive impairment, this assumption was thought that in agreement with previous reports that Alzheimer disease had normal I-123 MIBG uptake of the myocardium finding (Hanyu et al., 2006a,b). At this point, we must consider that it was itself necessary. PDD might be that only cognitive impairment was added to PD because of no difference of uptake of MIBG between PD and PDD groups. A proof will be necessary in future study.

V. CONCLUSION

As a result of many considerations, in the study, we could suggest that cardiac I-123 MIBG scintigraphy might not be used to distinguish PDD from PD and PDD might be that dementia was added to PD. We assert future studies in large numbers of subjects with LBD and attempt to obtain a new interpretation about this topic.

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