

MIBG Myocardial Scintigraphy can Predict the Occurrence of Wearing-off Phenomenon in Early-stage Parkinson's Disease

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Abstract

Background: Iodine-123 metaiodobenzylguanidine (¹²³I-MIBG) myocardial scintigraphy has been accepted as one of the most useful methods for the diagnosis of Parkinson's disease (PD). Moreover, the accumulated evidence has indicated that the heart-to-mediastinum (H/M) ratio correlates with the disease severity of hypokinesia/bradykinesia and rigidity. The present report describes the wearing-off predictions obtained from MIBG in patients with early-stage PD.

Methods: 13 males and 10 females with PD whose onset ages between 45 and 70 years were enrolled. They were separated into two groups according to their H/M ratios (less than 1.7 or 1.7 or higher). We generated Kaplan-Meier survival curves for the times of the onset of the wearing-off phenomenon, and survival differences were analyzed by the log-rank test. The onset of the wearing-off phenomenon was defined as an event during the 71-month observation.

Results: There was a significant difference in the wearing-off occurrence between the 2 groups that were divided by the H/M ratio ($P=0.016$). This result might reflect the existence of PD patients who do not show reductions in the H/M ratios at earlier stages and who do not manifest the wearing-off phenomenon later.

Conclusions: Our study suggests the possibility that patients with good prognoses represent those with almost normal H/M ratios, even though they are affected with PD. MIBG could be a valuable method for predicting prognoses as well as for diagnoses.

Keywords: Parkinson's disease; Wearing-off; MIBG Myocardial scintigraphy

Introduction

Iodine-123 metaiodobenzylguanidine (¹²³I-MIBG) myocardial scintigraphy was a useful imaging tool for differentiating Parkinson's disease (PD) from other neurodegenerative parkinsonism [1]. Moreover, the accumulated evidence has indicated that the heart-to-mediastinum (H/M) ratio correlates with the disease severity of hypokinesia/bradykinesia and rigidity [2,3,4]. To the best of our knowledge, there have been few studies about prognosis predictions, except for one paper about the effects of subthalamic stimulation [5]. The present report describes the wearing-off predictions obtained from MIBG scintigraphy in patients with early-stage PD.

Materials and Methods

Subjects were screened from consecutive patients at Tokushima University Hospital who met the criteria for diagnoses of PD according to the United Kingdom Parkinson's Disease Brain Bank. The PD onset ages of all of the patients were between 45 and 70 years. Exclusion criteria were the following: (1) no scan of MIBG scintigraphy within 5 years after the onset of motor symptoms; (2) fast decline in dopaminergic drugs effect within 5 years after onset; (3)

abnormalities in the basal ganglia or cerebellum on structural magnetic resonance imaging scans; (4) a history of treatment with antipsychotic drugs; and (5) a history of neuropathy, diabetes, previous relevant cardiac disease or any other medical condition that potentially affected the MIBG uptake. Eventually, 13 males and 10 females with PD were enrolled in our study. They were separated into two groups according to their H/M ratios (less than 1.7 or 1.7 or higher). The clinical characteristics of each group are summarized in (Table 1). Written informed consents were approved by the ethics committee of Tokushima University Hospital and were obtained from all participants. ¹²³I-MIBG (111 mBq) was injected intravenously into each subject. The early image of cardiac uptake was taken 15 minutes later and the delayed image three or four hours later. Regions of interest were placed on the whole heart and mediastinum of the front image. The ratio of ¹²³I-MIBG uptake in regions of interest of the heart to that in the mediastinum (H/M ratio) was calculated. The H/M ratios from delayed images were evaluated in this study. We generated Kaplan-Meier survival curves for the times of the onset of the wearing-off phenomenon, and survival differences were analyzed by the log-rank test. The onset of the wearing-off phenomenon was defined as an event during the 71-month observation. P values less than 0.05 were considered statistically significant. Statistical analyses were performed with R software (<http://www.r-project.org/>). To assess medication changes L-dopa equivalent units (LEU) were calculated as follows: 100mg of L-dopa=77 mg L-dopa with entacapone=1 mg pergolide=1

mg pramipexole=5 mg ropinirole=1.5 mg cabergoline=10 mg bromocriptine.

Results and Discussions

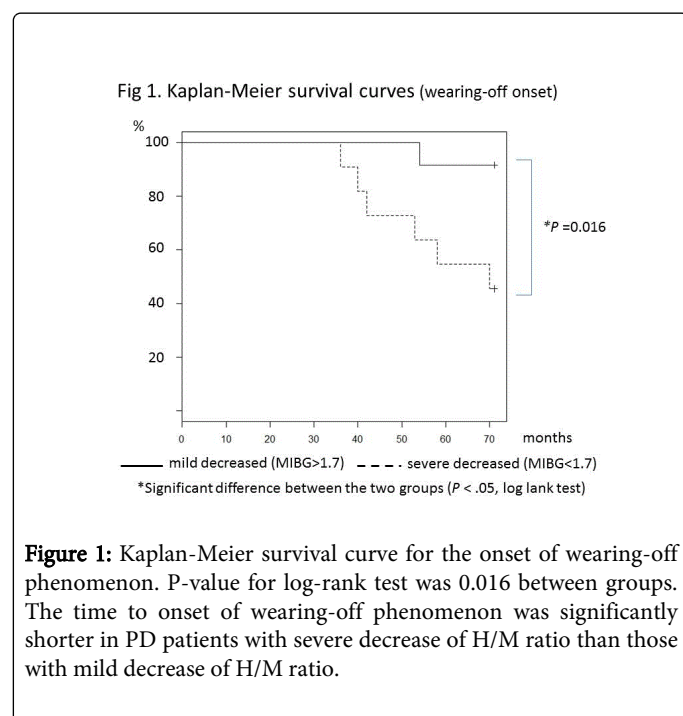
There was a significant difference in the wearing-off occurrence between the 2 groups that were divided by the H/M ratio (Figure 1;

$P=0.016$) although there were no significant differences in age, gender, disease duration, H&Y stage, and treated LEU (Table 1). This result might reflect the existence of PD patients who show reductions severely in the H/M ratios at earlier stages and who manifest the wearing-off phenomenon among a few year medications.

	Gender Male/female		Onset symptoms Tremor/Akinesia		Age onset (years)	Duration at MIBG (years)	H&Y MIBG I/II/III			LEU (mg/day)	Duration administration (years)
MIBG mildly decreased group (n=12)	7M	5F	8	4	56.6 ± 7.6	3.0 ± 1.5	1	6	5	323 ± 108	3.9 ± 1.0
MIBG severely decreased group (n=11)	6M	5F	3	8	57.4 ± 7.6	3.1 ± 1.5	2	5	4	323 ± 90.4	3.9 ± 1.2

MIBG mildly decreased group; The H/M ration from delayed images ≥ 1.70 . MIBG severely decreased group; the H/M ration < 1.70 .
H&Y: Hoehn & Yahr scale. LEU: L-dopa equivalent units

Table 1. Clinical information of subjects.



It has been reported that PD progresses more rapidly in akinetic rigid-type patients (ART) than in tremor dominant-type patients (TDT) [6], and ^{123}I -MIBG myocardial uptake was significantly higher in delayed images in TDT patients compared with ART patients at the same H&Y stage 2. However, there was another report that MIBG up take was significantly lower in delayed images in TDT patients compared with ART patients at the same disease durations [7]. In our study, we scanned of MIBG scintigraphy within 5 years after the onset of motor symptoms in all PD patients, and no differences were found in the prevalence of tremor was observed between the groups with and without low uptake ($P=0.198$; Fisher's

exact test). Which suggested that our finding was not influenced by a bias for symptoms, and the lack of impaired uptake in PD could be an independent factor that can predict the complication of the wearing-off phenomenon. Based on these findings, the patients with almost normal H/M ratios could be defined as a good-prognosis group, which could be a new subgroup with different features compared to the majority of PD patients with reductions in MIBG uptake. However, one limitation of this study was that it was small numbers trial, and another limitation of this study was short-term follow-up (71-month). This should be addressed in future studies, and longer-term follow-up (over 10 years) should also be included.

Our study suggests the possibility that patients with good prognoses represent those with almost normal H/M ratios, even though they are affected with PD. MIBG could be a valuable method for predicting prognoses as well as for diagnoses.

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