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Characterization of gastrointestinal disorders in patients with parkinsonian syndromes

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ABSTRACT

Objectives: This study was aimed to investigate gastrointestinal (GI) dysfunction in patients with Parkinson's disease (PD) compared with those in patients with other parkinsonian disorders, and to characterize parkinsonian motor and non-motor correlates for GI dysfunction.
Methods: Consecutive patients with PD, atypical parkinsonism (P-plus) and vascular parkinsonism (VP) were enrolled in this multicenter systematic survey. Data for weight loss, appetite loss, sialorrhea, dysphagia, gastroesophageal reflux disease (GERD) and constipation were simultaneously collected using symptom-specific, structured questionnaires. For the PD group, information for onset age, PD duration, anti-parkinsonian drug dosages, unified PD rating scale, and Hoehn & Yahr stage were collected at the time of the interview.
Results: Enrolled in the study were 329 PD, 82 P-plus, and 62 VP patients. GI symptom frequencies were similar in PD and other parkinsonian groups. Among the PD patients, constipation was the most common symptom, followed by appetite loss, weight loss, dysphagia, sialorrhea, and GERD (64.9%, 45.4%, 35.7%, 19.4%, 15.0%, and 9.6%, respectively). Dysphagia, sialorrhea, and constipation became more frequent with more advanced PD stages. Cognition, sleep and mood disturbances were significantly associated with weight loss, appetite loss, and dysphagia, whereas bradykinesia, axial and postural instability with gait disturbance were associated with dysphagia.
Conclusions: GI disturbance is common in patients with non-PD parkinsonism as well as in those with PD. GI symptoms correlated with distinct parkinsonian motor and nonmotor features in PD. Further studies are warranted to reveal the pathophysiological mechanisms and prognostic features of GI disturbances in parkinsonian disorders.

1. Introduction

Gastrointestinal (GI) dysfunction is an important nonmotor feature of Parkinson disease (PD) that affects patients' quality of life from the early to late stages of PD [1]. Common symptoms include constipation, nausea and vomiting, gastric paresis, dysphagia, sialorrhea, and appetite loss [1-3]. Approximately one to three quarters of the PD population have at least one GI symptom although the reported frequencies of these GI symptoms vary widely [1,4].

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The pathophysiological mechanism of GI dysfunction in PD is generally thought to be multifactorial [5]. Lewy body pathologies are found in the enteric nervous system in PD patients, predominantly in the lower esophagus, but present throughout the gut with a rostral to caudal gradient [6]. The vagal motor nucleus at the lower brainstem is also involved in PD and can be involved during the early stages of PD [7]. Small bowel bacterial overgrowth has been recently reported in PD even in early stage patients [8]. However, there is a paucity of data regarding clinico-pathological correlations between GI dysfunction and PD [9]. GI dysfunction in PD is also related to chronic administration of dopaminergic drugs [10,11]. Aging and psychological stress from chronic illness can also affect GI function in PD patients [12].

Although studies using general nonmotor symptom questionnaires have shown that GI symptoms are prevalent in PD [1,13], the use of systematic survey questionnaires for each GI disorder in PD would allow more detailed analysis of the clinical features associated with each symptom. Moreover, it remains to be revealed how GI symptoms are inter-related during the various stages of PD, and whether there is any relationship between GI dysfunctions and parkinsonian motor and nonmotor features. Research into both those questions should provide valuable insight into the pathophysiology of GI dysfunction in PD as well as provide direction to physicians on how to manage their patients.

The aim of this cross-sectional study was to investigate six characteristic GI dysfunctions in PD patients by using a series of structured questionnaires and to characterize clinical features correlated with those dysfunctions across the stages of PD. To explore frequency of occurrence differences in GI dysfunctions among other parkinsonian disorders and PD, we also conducted a multiple questionnaire survey in patients with vascular parkinsonism (VP) and atypical parkinsonism (P-plus) syndromes.

2. Methods

This study was approved by the Institutional Review Board of Seoul National University Boramae and Bundang Hospitals and conducted according to the Declaration of Helsinki.

2.1. Subjects

A consecutive series of patients who visited movement disorders clinics at two participating centers within a defined period (February 2012 to October 2013) were enrolled in this multicenter cross-sectional survey. Subjects were assigned to one of three groups: PD, P-plus, and VP. Diagnosis of PD was based on the criteria of the UK PD brain bank society [14]. The P-plus group included patients who met the possible or probable clinical diagnostic criteria for multiple system atrophy [15], progressive supranuclear palsy [16], corticobasal degeneration [17], or dementia with Lewy bodies [18]. Diagnosis of VP was based on the criteria for bilateral akinetic-stiffness syndrome showing frequent gait impairment with structural and functional neuroimaging evidence of diffuse vascular lesions without other causes of parkinsonism [19]. Patients with isolated focal lesions in the basal ganglia were excluded from the VP group. Subjects were also excluded if they had significant cognitive dysfunction, known GI disorders unrelated to PD, or a history of GI surgery. Patients who were unable to visit an outpatient clinic due to severe motor disability or systemic illness were also excluded. At the time of a patient's survey, age, gender, age at disease onset, and Hoehn & Yahr (HY) stage data were collected and parkinsonian features in PD patients were evaluated by using the Movement Disorders Society (MDS) revised unified PD rating scale (MDS-UPDRS) [20]. For PD patients, the daily medication dosage was expressed as a levodopa equivalent dose (LED) [21].

2.2. Gastrointestinal disorder screening

Six GI symptoms were assessed in this study: weight loss, appetite loss, sialorrhea, dysphagia, gastroesophageal reflux disease (GERD), and constipation. Subjects were asked whether they had lost weight after being diagnosed with parkinsonism. Appetite, dysphagia, drooling and GERD were assessed for recent one week and constipation symptom was assessed for recent 3 months. Appetite loss was evaluated by using the Simplified Nutritional Appetite Questionnaire (SNAQ) [22], in which the cut-off value for clinical significance is 14 [22]. Sialorrhea was evaluated by using the Sialorrhea Clinical Scale for PD (SCS-PD) [23]. Dysphagia was evaluated by using the Swallowing Disturbance Questionnaire (SDQ) [24], the accuracy of which was previously validated via a video fluoroscopy swallowing study and the optimal SDQ cut-off score is 11 (sensitivity 80.5%, specificity 81.3%) [25]. GERD was evaluated by using GerdQ [26], which had a sensitivity of 65% and a specificity of 71% for the diagnosis of GERD when using a cut-off level of 8 [26]. Presence of constipation was determined by using the validated Korean Rome III Questionnaire for diagnosis of functional gastrointestinal disorders (Rome III-K) [27].

2.3. Statistical analysis

For the comparisons of the three parkinsonian groups, one-way analysis of variance (ANOVA) was used for continuous variables and in the post-hoc analysis Bonferroni method was applied. The χ^2 test was used for discrete variables. Within the PD group, correlations among the six GI dysfunctions and LED were examined by a partial correlation analysis. Comparisons between PD subjects with normal and abnormal scores for each GI symptom were conducted by using *t*-tests. To characterize clinical features associated with each GI dysfunction in PD patients, logistic regression analysis was performed with age, gender, PD duration, and LED used as covariates in each analysis. All statistical analyses were conducted by using SPSS 21.0 software with significance set at 0.05 (two-tailed).

3. Results

A total 516 patients were enrolled in the study. Of those, 17 were excluded because of the possibility of drug-induced parkinsonism, and 26 were excluded due to diagnostic uncertainty (PD versus P-plus). Within the remaining enrollees there were 329 PD, 82 P-plus, and 62 VP patients. The P-plus group included 32 patients with multiple system atrophy, 10 with progressive supranuclear palsy, 8 with corticobasal degeneration, and 32 with dementia with Lewy bodies. Clinical characteristics of the subjects are summarized in Table 1.

3.1. Comparison of six GI symptoms in PD and other parkinsonian syndromes

Each of the six GI symptoms commonly occurred in the PD, P-plus, and VP groups (Fig. 1). Constipation was the most frequent symptom, followed by loss of appetite, weight loss, dysphagia, sialorrhea, and GERD (64.9%, 45.4%, 35.7%, 19.4%, 15.0%, and 9.6%, respectively, in PD patients versus 77.6%, 51.9%, 39.2%, 29.9%, 23.5%, and 10.0%, respectively, in P-plus patients versus 52.2%, 45.2%, 30.0%, 12.1%, 18.0% and 13.3%, respectively, in VP patients). There was no significant association in the presence of GI symptoms with the use of amantadine and anticholinergics in all three groups.

Table 1
Clinical and demographic characteristics of study subjects.

Characteristics	PD (n = 329)	P-plus (n = 82)	VP (n = 62)	p-Value[a]
Age, y	70.2 ± 9.4	73.3 ± 7.8	73.4 ± 5.9	0.002
Male, n (%)	137 (41.6)	35 (42.7)	38 (61.3)	0.016
Age at onset, y	63.9 ± 10.2	69.3 ± 7.9	68.4 ± 6.5	<0.001
Disease duration, y	6.3 ± 4.8	4.3 ± 2.8	5.2 ± 3.4	0.001
Hoehn & Yahr stage, 1–5	2.1 ± 0.8	3.1 ± 0.9	3.1 ± 1.0	<0.001
LED, mg/day	660.2 ± 394.5	526.9 ± 354.4	341.3 ± 215.3	<0.001
Amantadine use, n (%)	42 (12.7)	13 (15.8)	4 (6.5)	0.230
Anticholinergics use, n (%)	25 (7.6)	3 (3.7)	0	0.042
Total UPDRS scores	49.3 ± 29.1	–	–	–
part 1 scores	10.7 ± 6.9	–	–	–
part 2 scores	12.4 ± 9.7	–	–	–
part 3 scores	28.0 ± 15.8	–	–	–

Values are shown as mean ± standard deviation unless otherwise indicated.
Abbreviations: PD = Parkinson's disease; P-plus = Parkinson-plus syndrome; VP = vascular parkinsonism; LED = daily levodopa equivalent dose; UPDRS = unified PD rating scale, the Movement Disorders Society task force-revised.
[a] Comparison of three groups by analysis of variance (ANOVA) test for continuous variables or Chi-square test for categorical variables.