

Research Report

The Prevalence of Constipation and Irritable Bowel Syndrome in Parkinson's Disease Patients According to Rome III Diagnostic Criteria

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Abstract.

Background: Gastrointestinal symptoms are one of the most common non-motor features of Parkinson's disease (PD). Recently, a report from Taiwan revealed that irritable bowel syndrome (IBS) may be associated with an increased risk of developing PD; however, the prevalence of IBS in PD patients has not been fully evaluated. Rome III criteria are widely assessed with a questionnaire to determine functional gastrointestinal disorders.

Objective: We assessed the prevalence of constipation and IBS in PD patients in our cohort using Rome III criteria.

Methods: Between October 2014 and April 2015, 118 patients with PD were treated at Fukuoka University Hospital and were enrolled in this study. Rome III criteria were used to diagnose constipation and IBS.

Results: Constipation and IBS were detected in 32 (27.1%) and 20 patients (17.0%), respectively. The most common symptom related to constipation was straining during defecation (77.1%). Among constipation symptoms, patients' self-awareness of constipation was mostly related to straining during defecation (odds ratio 5.27, 95% confidence interval 1.475–18.811). The number of constipation symptoms was correlated with the severity of the Hoehn-Yahr Stage ($p < 0.05$) and total levodopa equivalent dose ($p < 0.05$).

Conclusions: This is the first report to investigate the prevalence of IBS in PD patients with Rome III criteria. We found a higher prevalence of IBS compared with the general population. The prevalence of constipation based on Rome III criteria was much lower than that reported in previous studies. Further studies are warranted to evaluate gastrointestinal symptoms in PD patients using comparable questionnaires.

Keywords: Constipation, irritable bowel syndrome, Parkinson's disease, Rome III diagnostic criteria

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative movement disorder that clinically presents with motor and non-motor features [1]. The motor features mainly comprise bradykinesia, rigidity, postural

instability, and resting tremor, which are the clinical hallmarks of PD. The non-motor features include a variety of symptoms such as psychiatric abnormalities, executive dysfunction, autonomic dysfunction, sleep disturbance, sensory complaints, anosmia, and gastrointestinal symptoms [2]. Gastrointestinal symptoms are one of the most crucial problems for patients with PD, substantially affecting their quality of life [3]. Multiple causes including motor dysfunctions, autonomic dysfunctions, and adverse

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effect of antiparkinsonian medications may impair gastrointestinal functions [2]. Additionally, growing evidence suggests that widespread enteric nervous system synucleinopathy contributes to gastrointestinal dysfunction in this disease entity.

The gastrointestinal symptoms seen in patients with PD include drooling, dysphagia, malnutrition, impaired gastric emptying, and constipation. Constipation is one of the most prevalent non-motor symptoms in PD patients. Constipation may precede the onset of motor dysfunctions in PD patients by some years [4]. The diagnosis of constipation is variably defined in each research report. One study defined constipation as when patients had a bowel movement less often than three times per week [5], whereas others relied on a description from clinical records based on patients' documentation [6]. The Rome III diagnostic criteria, which were published in 2006, are the most standard criteria for diagnosis of functional gastrointestinal disorders and the most reliable measurement at the present time [7, 8]. The criteria include the following six major conditions for adults: functional esophageal disorders (category A); functional gastroduodenal disorders (category B); functional bowel disorders (category C); functional abdominal pain syndrome (category D); functional gallbladder and sphincter of Oddi disorders (category E); functional anorectal disorders (category F). Each category is divided into several subcategories, and each subcategory has an individual diagnostic criterion. The functional bowel disorders (category C) include irritable bowel syndrome (IBS) (C1); functional bloating (C2); functional constipation (C3); functional diarrhea (C4); unspecified functional bowel disorder (C5).

IBS is associated with an increased risk of developing PD in the Taiwanese population [9]; however, the prevalence of IBS in PD patients has not been evaluated. Decreased bowel movements are the most recognized symptom in PD patients [10]; however, few studies have investigated the other type of gastrointestinal dysfunction. In addition, no study has evaluated the prevalence of IBS by using authorized criteria. In this study, therefore, we assessed the prevalence of constipation and IBS in PD patients using Rome III diagnostic criteria.

MATERIALS AND METHODS

We designed a cross-sectional analysis at Fukuoka University Hospital. A total of 118 patients who visited our department between October 2014 and

April 2015 were consecutively enrolled in this study. All participants were clinically diagnosed as having PD by certified neurologists (TM, JF, SF, and YT) according to the UK PD Society Brain Bank clinical diagnostic criteria [11]. Demographics and clinical data including the age, disease duration at the time of enrollment in the study, gender, neurological examination, Hoehn-Yahr stage, and dopaminergic medications of the patients were prospectively collected. Questionnaires were completed in a face-to-face survey. Cognitive assessments were performed utilizing the Mini-Mental State Examination (MMSE), and we excluded patients with PD who had cognitive impairment with MMSE <24. Patients with known gastrointestinal disorders unrelated to PD were excluded. We also excluded patients who were diagnosed as having parkinsonian disorders other than PD and patients who had undergone deep brain stimulation surgery. The daily dosage of anti-parkinsonian drugs was converted to a total levodopa equivalent dose (LED) according to the previously reported method [12]. Use of laxatives and anti-cholinergics that may change the bowel habits of the subjects were evaluated. For assessment of IBS and constipation, we used the Japanese version of Rome III diagnostic criteria [13], utilizing category C1 for assessment of IBS and category C3 for evaluation of functional constipation. Diagnosis of functional IBS (C1) requires recurrent abdominal pain or discomfort for at least 3 days per month in the last 3 months that is associated with two or more of the following conditions: improvement with defecation; onset associated with a change in frequency of stool; onset associated with a change in form of stool. Criteria must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis. Diagnosis of functional constipation (C3) requires two or more of the following conditions: straining during at least 25% of defecations; lumpy or hard stools in at least 25% of defecations; sensation of incomplete evacuation for at least 25% of defecations; sensation of anorectal obstruction/blockage for at least 25% of defecations; manual maneuvers to facilitate at least 25% of defecations; fewer than three defecations per week. In addition, diagnosis of functional constipation requires that loose stools are rarely present without the use of laxatives; this criterion is insufficient for IBS. Criteria must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

All participants were Japanese. This study was approved by the Institutional Review Boards of

Fukuoka University, and informed consent was obtained from all the participants.

Data analysis

Fisher's exact test was used to compare the differences between the constipation group, the IBS group, and the neither constipation nor IBS group regarding demographic status. Kendall's tau correlation coefficient was used to evaluate the association between the frequency of constipation symptoms and baseline data. Multiple logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence interval (CI) to evaluate the association between self-awareness of constipation and constipation symptoms. All analyses were performed using SPSS (Version 22), and the statistical significance level was set at two-tailed $p < 0.05$.

RESULTS

Patient characteristics

Of the 118 patients, 51 (43.2%) were males. The mean age and mean disease duration at the time of examination were 67.8 ± 9.8 and 6.3 ± 4.8 years, respectively. The mean Hoehn-Yahr Stage was 2.7 ± 0.7 . The mean total MMSE score was 28.1 ± 1.8 . The average LED was 504.7 ± 252.0 mg/day. The number of patients who used laxative and anti-cholinergics uses were 41 (34.7%) and 4 (3.4%), respectively. Characteristics of the patients with and without constipation and IBS are shown in Table 1.

Prevalence of constipation and IBS

Constipation and IBS were detected in 32 (27.1%) and 20 (17.0%) patients, respectively. The most common symptom related to constipation was straining during defecation, as seen in 77.1% of patients (Table 2). The frequency of patients who had self-awareness of constipation was 81.4%. Among the patients, the self-awareness of constipation was most related to straining during defecation among symptoms related to constipation (OR 5.27, 95% CI 1.475–18.811) (Table 2). The severity of Hoehn-Yahr Stage ($p < 0.05$) and total LED ($p < 0.05$) were significantly correlated with the frequency of constipation symptoms (Table 3).

DISCUSSION

The present study investigated the prevalence of constipation and IBS in PD patients in our cohort based on Rome III diagnostic criteria. The prevalence of constipation in PD patients has been reported in multiple studies, and ranged from 28.7 to 64.9%, based on various definitions of constipation [3, 5, 14]. The prevalence of constipation in PD patients in our cohort (27.1%) was lower than that in studies using other definitions for constipation. The result suggested that Rome III diagnostic criteria may more strictly define the diagnosis of constipation. Rome III diagnostic criteria are widely used and are currently the gold standard for the diagnosis of functional gastrointestinal disorders; however, few studies have investigated functional gastrointestinal disorders in the PD population using these criteria [3, 15, 16]. Park and colleagues detailed characteristic features of gastrointestinal disorders in their cohort with parkinsonian disorders including PD, utilizing the Rome III diagnostic criteria. The mean age and disease duration at study enrollment were approximately 70 and 6 years, respectively. The mean LED in the PD cohort was about 660 mg/day. The prevalence of constipation (64.9%) reported in the study was much higher than that in our study [3]. The difference in age at study enrollment, disease duration, and anti-parkinsonian and/or constipation-inducing drugs may influence the prevalence of constipation in PD patients [3, 6].

As shown in a previous report, straining during defecation was the most frequent symptom related to constipation in patients in this study [17]. In addition, self-awareness of constipation was significantly related to straining during defecation in this study, indicating that this symptom may be closely related to the subjective complaint of constipation in PD patients. Our study also demonstrated a discrepancy between the self-awareness of constipation (81.4%) and the frequency of constipation (27.1%) in PD patients, indicating the possibility that PD patients may feel dissatisfaction with anti-constipation treatment. We evaluated the number of constipation symptoms and their relation to other factors and observed that the severity of the Hoehn-Yahr Stage ($\tau = 0.18$, $p < 0.05$) and total LED ($\tau = 0.13$, $p < 0.05$) were correlated with the number of constipation symptoms, though, to some extent, the significant correlations are weak. Rome diagnostic criteria are not for evaluating the severity of symptoms. However, our study indicated that the number

Table 1
Comparison among groups of Parkinson's disease patients with and without constipation and IBS

| | Patients without constipation or IBS (n = 66) | Patients with constipation (n = 32) | Patients with IBS (n = 20) | p-value |
|---------------------------|--|--|-------------------------------|---------|
| Age (years) | 68.2 ± 10.0 | 67.5 ± 8.8 | 66.5 ± 10.9 | 0.779 |
| Male (%) | 43.9 | 37.5 | 50.0 | 0.665 |
| Disease duration (years) | 6.3 ± 4.6 | 6.9 ± 5.4 | 5.2 ± 4.4 | 0.439 |
| Hoehn-Yahr Stage | 2.7 ± 0.8 | 2.8 ± 0.7 | 2.6 ± 0.7 | 0.535 |
| MMSE | 27.9 ± 1.9 | 28.5 ± 8.5 | 27.9 ± 1.8 | 0.328 |
| LED (mg/day) | 503.5 ± 245.7 | 561.8 ± 282.0 | 417.6 ± 203.1 | 0.133 |
| Laxative use (%) | 24.2 | 53.1 | 40.0 | 0.054 |
| Anti-cholinergics use (%) | 1.5 | 3.1 | 10.0 | 0.018 |

Data are presented as the mean ± SD. IBS = irritable bowel syndrome. LED = levodopa equivalent dose. MMSE = Mini-Mental State Examination.

Table 2

Frequency of each question item response in the Rome III diagnostic criteria and their relation to patients' awareness in our Parkinson's disease cohort (n = 118)

| Question items | Frequency | Patients' awareness of constipation | | OR | 95% CI | p-value |
|--|-----------|-------------------------------------|--------|------|--------------|---------|
| | | present | absent | | | |
| Straining (%) | 77.1 | 69.5 | 7.6 | 5.27 | 1.475–18.811 | 0.01 |
| Lumpy or hard stools (%) | 51.7 | 45.8 | 5.9 | 1.94 | 0.634–5.954 | 0.25 |
| Sensation of incomplete evacuation (%) | 49.1 | 39.8 | 9.3 | 0.55 | 0.175–1.755 | 0.32 |
| Sensation of anorectal obstruction (%) | 74.6 | 65.3 | 9.3 | 1.43 | 0.365–5.582 | 0.61 |
| Manual maneuvers (%) | 16.1 | 15.3 | 0.8 | 2.07 | 0.223–19.226 | 0.52 |
| Fewer defecations (%) | 39.0 | 35.6 | 3.4 | 2.08 | 0.576–7.539 | 0.26 |

Straining means straining during at least 25% of defecations. Lumpy or hard stools means lumpy or hard stools in at least 25% of defecations. Sensation of incomplete evacuation means sensation of incomplete evacuation for at least 25% of defecations. Sensation of anorectal obstruction means sensation of anorectal obstruction/blockage for at least 25% of defecations. Manual maneuvers means manual maneuvers to facilitate at least 25% of defecations. Fewer defecations means fewer than three defecations per week. OR = odds ratio. CI = confidence interval.

of constipation symptoms according to Rome diagnostic criteria may be useful for evaluation of the severity of constipation in PD patients [14].

Until now, the prevalence of IBS had not been evaluated in the PD population. The prevalence of IBS in our PD cohort (17.0%) was slightly higher than that in the general population in Japan as assessed with the Rome III diagnostic criteria (13.1–14.0%) [18].

Several limitations of this study need to be acknowledged. First, the current study was conducted at a single center using an uncontrolled design, short-term and the number of participants was small. Second, variables that could potentially influence stool consistency and bowel habits including coffee intake [10], smoking habits [10], water intake [19], beta-blockers [6], insoluble fiber intake [20], probiotics [16], and other constipation-inducing drugs [6] were not investigated in our study. Third, we did not perform a colonoscopy to exclude a diagnosis of gastrointestinal disorders such as inflammatory, metabolic, anatomic, or neoplastic causes [9]. Functional assessments including a colon transit time test might be useful to rule out alternative explanations, too [21]. Finally, we did not evaluate IBS subtypes.

Table 3

Correlation analysis of the number of constipation symptoms and baseline data (n = 118)

| | τ | p-value |
|--------------------------|--------|---------|
| Age (years) | 0.08 | 0.27 |
| Disease duration (years) | -0.10 | 0.88 |
| Hoehn-Yahr Stage | 0.18 | <0.05 |
| MMSE | -0.03 | 0.97 |
| LED (mg/day) | 0.13 | <0.05 |

LED = levodopa equivalent dose. MMSE = Mini-Mental State Examination.

IBS is generally subtyped as constipation predominant (IBS-C), diarrhea predominant (IBS-D), mixed (IBS-M) and unsubtyped (IBS-U) on the predominant stool pattern [13].

Not only constipation but also diarrhea has been reported as a potential prodromal symptom of PD [22]. That might explain why the prevalence of IBS in PD might be higher than that in general Japanese population.

Despite these limitations, this is the first report to evaluate the prevalence of constipation and IBS in PD patients according to the Rome III diagnostic criteria. Further multinational, multicenter and

longitudinal studies including prodromal cases are required to explore the pathophysiology of gastrointestinal symptoms in PD patients.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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