Increased odds of bladder and bowel symptoms in early Parkinson's disease

Monica Serra, Emory University
Alexus Landry, Louisiana State University
Jorge Juncos, Emory University
Alayne D. Markland, Birmingham VA Medical Center
Kathryn L. Burgio, Birmingham VA Medical Center
Patricia S. Goode, Birmingham VA Medical Center
Theodore M Johnson II, Emory University
Elizabeth Vaughan, Emory University

Journal Title: Neurourology and Urodynamics
Volume: Volume 37, Number 4
Publisher: Wiley: 12 months | 2018-04-01, Pages 1344-1348
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1002/nau.23443
Permanent URL: https://pid.emory.edu/ark:/25593/s9c8n

Final published version: http://dx.doi.org/10.1002/nau.23443

Copyright information:
© 2017 Wiley Periodicals, Inc.
Accessed April 14, 2019 2:26 AM EDT
Increased odds of bladder and bowel symptoms in early Parkinson’s disease

Monica C. Serra, PhD1,2, Alexus Landry3, Jorge L. Juncos, MD4, Alayne D. Markland, DO, MSc5,6, Kathryn L. Burgio, PhD5,6, Patricia S. Goode, MSN, MD5,6, Theodore M. Johnson II, MD, MPH1,2, and Camille P. Vaughan, MD, MS1,2

1US Department of Veterans Affairs Geriatric Research, Education and Clinical Center, Atlanta, Georgia
2Division of General Medicine and Geriatrics, Department of Medicine, Emory University, Atlanta, Georgia
3Department of Biology, Louisiana State University, Baton Rouge, Louisiana
4Department of Neurology, Emory University, Atlanta, Georgia
5Department of Veterans Affairs Geriatric Research, Education and Clinical Center, Birmingham, Alabama
6Division of Geriatrics, Gerontology, Geriatrics, and Palliative Care, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama

Abstract

Aims—To compare the prevalence of urinary and bowel symptoms in a sample of adults with early Parkinson’s disease (PD) and healthy controls (HC).

Methods—Data were obtained from the Michael J. Fox Parkinson’s Progression Markers Initiative (PPMI). Prevalent bladder (urinary incontinence (UI) and nighttime voiding) and bowel (constipation and fecal incontinence (FI)) symptoms were defined as occurring at least sometimes when queried using the Scale for Outcomes in PD for Autonomic Symptoms.

Results—The proportion of men (65% vs 64%) and the mean age (61.0 ± 9.7 vs 60.2 ± 11.2 years) was similar between early PD (n = 423) and HC (n = 195). UI and constipation were more prevalent among early PD versus HC (UI: 26.7% vs 8.2%, constipation: 32.4% vs 11.8%; P’s < 0.0001). Prevalent nighttime voiding was high among both groups, but not significantly different (82.5% vs 84.1%, P = 0.62). FI was infrequent in both. The odds of UI and constipation were significantly higher in early PD even after adjustment for age, sex, cognition, and overactive bladder (UI model only), constipation (UI and constipation models only), depression, and anxiety medication usage (UI: OR: 4.39 [95% CI: 2.92, 5.87]; constipation: 3.34 [2.20, 4.42]; P’s < 0.0001).
Conclusions—While constipation is known to precede PD diagnosis, these data suggest that the occurrence of UI is elevated in early PD compared to a well-matched HC population.

Keywords
constipation; epidemiology; fecal incontinence; Parkinson’s disease; urinary incontinence

1 INTRODUCTION
Parkinson disease (PD) is characterized by a variety of motor and non-motor symptoms. Although quality measures for PD recommend at least an annual assessment of autonomic symptoms for all stages of the disease\(^1\) and advocacy groups have recommended evaluation of treatment strategies for urinary symptoms as a top 10 priority for research in PD,\(^2\) bladder, and bowel symptoms are often not reported by patients nor recognized by providers.\(^3\)

Previous research suggests bowel symptoms such as constipation may precede the diagnosis of PD.\(^4\) Less is known about the prevalence of urinary symptoms in early PD compared to adults without PD.\(^5\) Because bladder and bowel symptoms correlate more closely with health-related quality of life in PD than motor and other non-motor symptoms,\(^3\) and PD patients with urinary symptoms experience more rapid progression of motor symptoms and disability,\(^6\) it is important to determine how frequently these occur at different stages of PD. Our aim was to evaluate the burden of bladder and bowel symptoms in early PD using data from the Parkinson’s Progression Markers Initiative (PPMI) as the identification of these symptoms could be used to aid in the diagnosis and management of PD.

2 MATERIALS AND METHODS
The PPMI is a multicenter observational clinical study conducted in the United States, Israel, Europe, and Australia to verify biomarkers important to PD progression (information and data available at www.ppmi-info.org). The study was approved by the Institutional Review Board of all participating sites, and written informed consent was obtained from each participant before inclusion in the study.

Detailed description of PPMI participant selection and recruitment procedures have been reported elsewhere.\(^7\) For this analysis, community-dwelling participants with early PD and healthy controls (HC) were included. Early PD was defined as a diagnosis of PD through physical exam and a positive dopamine transporter (DAT) scan within 2 years of the baseline PPMI evaluation. Participants were naïve to sustained dopaminergic therapy within 2 years of the baseline assessment. HC had no significant neurologic deficit, no first degree relative with PD, and a Montreal Cognitive Assessment (MoCA) of >26. Each participant’s self-reported intake of prescribed and over-the-counter medications and supplements was reviewed to categorize treatment of various chronic conditions.

2.1 Bladder and bowel symptom assessment
Prevalent bladder symptoms (urinary incontinence (UI) and nighttime voiding) and bowel symptoms (constipation and fecal incontinence (FI)) were queried during the baseline
evaluation using the Scale for Outcomes in Parkinson’s Disease for Autonomic Symptoms (SCOPA-AUT) questionnaire. The specific symptom questions utilized in this evaluation were as follows: UI—In the past month, have you had involuntary loss of urine?; Nighttime voiding—In the past month, have you had to pass urine at night?; Constipation—Constipation is the blockage of the bowel, a condition in which someone has a bowel movement twice a week or less. In the past month, have you had problems with constipation?; FI—In the past month, have you had involuntary loss of stool? For each question, response options included: Never, sometimes, regularly, often, use catheter (bladder questions only). For the purposes of this analysis, the presence of bladder or bowel symptoms was classified as a symptom occurring “sometimes,” “regularly,” or “often.”

2.2 Statistical analysis

Chi-square and t-tests were used to examine bivariable relationships between bladder and bowel symptoms and selected baseline factors. Separate multivariable logistic regression models were created to estimate the odds of reporting UI, nighttime voiding, constipation, or FI in early PD versus HC. Separate models for UI, nighttime voiding, constipation, and FI were adjusted for age, sex, cognition, and the presence of overactive bladder (UI model only), constipation (UI and constipation models only), depression, or anxiety as defined by reporting the use of a medication typically prescribed for these conditions. Analyses were conducted with SAS 9.4 (Cary, NC).

3 RESULTS

The sample for this analysis included early PD (n = 423) and HC participants (n = 195) with complete data for the SCOPA-AUT questionnaire at baseline. Groups were well-matched with regard to age (early PD vs HC: 61.0 ± 9.7 vs 60.2 ± 11.2 years; P = 0.36) and sex (65% vs 64% male; P = 0.74). Participants with early PD had a lower mean MoCA score of (27.1 ± 2.31 vs 28.1 ± 1.10; P < 0.0001), although the absolute difference in score was small. Treatment of hypercholesterolemia (early PD vs HC: 34% vs 36%), hypertension (47% vs 39%), type 2 diabetes mellitus (5% vs 3%), hypothyroidism (25% vs 21%), and sleep problems (12% vs 11%) was not different between groups, but those with early PD were more likely to be treated for depression (27% vs 18%; P < 0.01) and anxiety (17% vs 10%; P < 0.01). With regard to UI and FI, benign prostatic hyperplasia medication and supplement usage was similar between groups (14% vs 11%), but those with early PD were more likely to be treated for overactive bladder (7% vs 1%; P < 0.01) and constipation (20% vs 8%; P < 0.0001).

Early PD participants reported higher prevalence of UI (26.7% vs 8.2%) and constipation (32.4% vs 11.8%) at baseline (Figure 1). Nighttime voiding was frequent (early PD vs HC: 82.5% vs 84.1%), but not statistically different between the groups (Table 1). Of the bladder and bowel symptoms, FI was the least reported symptom in both groups (early PD vs HC: 4.3% vs 3.6%, Figure 1). The prevalence of participants reporting both UI and nighttime voiding was greater in those with PD than HC (23.6% vs 7.7%, P = 0.0001), but not different between those reporting both constipation and fecal incontinence (early PD vs HC: 2.3 vs 1.0%, P = 0.22). In both the unadjusted and the adjusted analysis, early PD
participants were >4 times as likely to report UI and >3 times as likely to report constipation compared to HC (P’s < 0.0001; Table 1). The reporting of nighttime voiding and FI was not different in the unadjusted analysis nor after multivariable adjustment (Table 1).

4 DISCUSSION

Among the motor and non-motor symptoms of PD, bladder, and bowel symptoms have the strongest association with poor QOL for persons living with PD; however, these non-motor symptoms are often overlooked by providers, and patients may not associate them with PD. Results from the PPMI study highlight the elevated prevalence of bladder and bowel symptoms in a well-defined early PD sample relative to a well-balanced non-PD population. Constipation is a common non-motor symptom in early PD, and may precede the clinical diagnosis of PD. Results from the current analysis corroborate those findings and add to the emerging literature suggesting UI is also more common in early PD.

In PPMI, UI and constipation were >3 times more prevalent in persons with early PD. Previous studies evaluating the prevalence of bowel and bladder symptoms in persons living with PD show approximately 10–15% greater prevalence for both UI and constipation than that observed in the current study; however, these participants were recruited from clinical settings or in cohorts with a wider variation in disease severity and duration. Thus, these data indicate the importance of identifying bowel and bladder symptom prevalence across the span of PD disease severity and duration.

Some studies show that urinary symptoms in PD patients are due to idiopathic detrusor (bladder muscle) overactivity leading to symptoms of urgency and urgency incontinence. Detrusor overactivity may occur secondary to increased activation of the pontine micturition center. A lack of inhibitory input caused by the degeneration of nigrostriatal dopaminergic neurons could be a contributing factor to activation of the pontine micturition center in early Parkinson disease. Several studies suggest that abnormal central nervous system processing of sensory inputs from the bladder may contribute to urinary symptoms in PD. These findings of abnormal cortical integration in response to bladder filling mirror recent findings in non-PD populations with overactive bladder. Additionally, there is some evidence that depression and anxiety, which we found are treated to a greater extent in PD patients, may precede the development of UI, implicating psychological distress as an additional risk factor that may be used in the identification of early PD patients. Behavioral therapy, including pelvic floor muscle exercises, fluid management, and bladder control strategies are recommended as first line treatment for bladder symptoms in persons without PD, and have shown promise in patients with PD. With the advent of additional drug and minimally invasive treatment options for urinary symptoms associated with overactive bladder, additional research focused on the PD population is warranted to inform clinical guidelines.

Constipation in early PD may be the result of decreased motility of the gastrointestinal tract and is associated with alpha-synuclein pathology in the enteric nervous system. The dorsal motor nucleus of the vagus nerve is susceptible to oxidative damage due to high alpha-synuclein in PD patients, indicating that other pathways of the autonomic nervous
system also may be involved. Medications commonly used to treat PD (both dopaminergic and anticholinergic) may also lead to constipation because of delayed colonic transit. These non-motor symptoms do not respond well to dopaminergic therapy. While anticholinergic drugs have been shown to decrease the frequency of bladder symptoms, they may also worsen constipation. Thus studies are needed to determine optimal treatment of constipation in PD.

The strengths of this study include a sizeable, well-defined population of early PD patients and an age and sex balanced non-PD comparison group. All PD participants were evaluated at baseline by movement disorders specialists and had a positive DaT scan, which provides greater confidence in the diagnosis of Parkinsonism.

There are limitations to this study. These data represent a cross-sectional evaluation from PPMI; therefore, no conclusions about causality can be made. While the SCOPA-AUT domains related to gastrointestinal and urinary function have high intraclass correlation for differentiating symptom clusters in PD and the individual questions for urinary incontinence and constipation have high test-retest reliability, our evaluation of urinary and bowel symptoms is limited to those queried by the SCOPA-AUT. Other questionnaires such as the International Consultation on Incontinence are validated for specific urinary symptoms of overactive bladder including urgency, frequency, nocturia, and urgency incontinence. Additionally, it has recently been noted that multiple partially complete bowel movements may occur in PD patients with constipation, which may have affected the response to the constipation question, which is defined as “a bowel movement twice a week or less” on the SCOPA-AUT. Further, the answer choices never, sometimes, regularly, and often are subjective to the participant and may not be representative of the actual number or severity of episodes. However, in other populations with similar urinary symptoms, even rare UI has an impact on health-related QOL.

5 CONCLUSIONS

UI and constipation are more prevalent even in early PD than among HC. Screening for autonomic symptoms, including bowel and bladder symptoms, is recommended at all stages of the disease. Patients and advocates have prioritized research to determine effective treatments for bladder and bowel symptoms in order to inform evidence-based guidelines for care.

Acknowledgments

Funding information

U.S. Department of Veterans Affairs, Grant numbers: 1 IK2 RX000747-01, IK2 RX000944; Michael J. Fox Foundation for Parkinson’s Research

This research was supported by the Department of Veterans Affairs Birmingham/Atlanta Geriatric Research, Education, and Clinical Center and Veterans Health Administration Career Development Awards (CDA-2) to Drs Serra (IK2 RX000944) and Vaughan (1 IK2 RX000747-01). Parkinson’s Progression Marker’s Initiative—a public-private partnership—is funded by the Michael J. Fox Foundation for Parkinson’s Research and funding partners, including: Abbvie, Avid, Biogen, Bristol-Myers Squibb, Covance, GE Healthcare, Genentech, GlaxoSmithKline, Lilly, Lundbeck, Merck, Meso Scale Discovery, Pfizer, Piramal, Roche, Servier, UCB, Golub Capital.
References


FIGURE 1.
Prevalence of bladder and bowel symptoms in early PD versus healthy controls
### TABLE 1
Odds of reporting bladder and bowel symptoms among early PD compared to healthy control participants

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Unadjusted analyses N = 618</th>
<th>Multivariable models(a) N = 618</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Urinary incontinence (UI)</td>
<td>4.08 (2.34, 7.10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nighttime voiding</td>
<td>0.89 (0.56, 1.40)</td>
<td>0.62</td>
</tr>
<tr>
<td>Constipation</td>
<td>3.58 (2.21, 5.79)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fecal incontinence (FI)</td>
<td>1.19 (0.49, 2.90)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

\(a\) Separate multivariable models for UI, nighttime voiding, constipation, and FI; All models include age, sex, cognition (MoCA), and depression and anxiety medication usage; UI model also includes overactive bladder and constipation medication usage; Constipation model also includes constipation medication usage.