

# Management of Gastrointestinal Symptoms in Parkinson's Disease A Comprehensive Review of Clinical Presentation, Workup, and Treatment

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## ABSTRACT

One of the most common and crippling side effects of Parkinson's disease (PD) is gastrointestinal symptoms, which also pose special diagnostic and treatment difficulties. Dysphagia, nausea, bloating, and constipation are common symptoms among patients with Parkinson's disease (PD) due to pathologic involvement of the enteric nerve system. Consequently, gastrointestinal issues may affect levodopa therapy effectiveness and motor irregularities. The common gastrointestinal symptoms of Parkinson's disease (PD) will be examined in this review, with a focus on clinical presentation, workup, and therapeutic approaches.

## Keywords

Parkinson's disease, constipation, bloating, nausea, and dysphagia

## INTRODUCTION

Among the most common and severe nonmotor side effects of Parkinson's disease (PD) are gastrointestinal (GI) symptoms.<sup>1</sup> GI problems affect up to 81% of patients with Parkinson's disease (PD), with constipation, dysphagia, nausea, and vomiting being the most common symptoms (Fig. 1). The burden of GI symptoms affects quality of life more for many patients with severe Parkinson's disease (PD) than even motor symptoms do.<sup>3</sup> The association between GI symptoms and mental health in Parkinson's disease (PD) is bidirectional, similar to other illnesses of the gut-brain

connection: According to a recent study, the degree of GI symptom burden in Parkinson's disease (PD) predicted both anxiety and sadness, with worse anxiety from the Harvard Medical School in Boston, Massachusetts; the University of Vic-Central University of Catalonia in Vic, Spain; and the \*Division of Gastroenterology at the Massachusetts General Hospital.

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GI symptoms were substantially predicted by depression.<sup>4</sup> In recent years, GI symptoms that appear up to 20 years before a Parkinson's disease diagnosis have received a great deal of attention. In fact, in a case-control study of Parkinson's disease, our team found four primary prodromal GI symptoms: dysphagia, constipation, heartburn, and dry mouth, with no discernible differences between males and females. The Movement Disorder Society Task Force on the Definition of Parkinson's Disease recently added constipation to the diagnostic criteria for prodromal PD due to increased data in this area. The early onset of GI symptoms supports the gut-brain pathway theory of Parkinson's disease (PD), which was made popular by Braak's theory.

The gut-brain link that is thought to underlie Parkinson's disease (PD) is supported by the earlier start of GI symptoms, which is in line with Braak's concept.<sup>7</sup> According to a rostrocaudal theory of Parkinson's disease (PD), neurotropic triggers that start in the gut—such as environmental, viral, or involving other disruptions to the microbiome—proliferate via the vagus nerve to the dorsal motor nucleus of the vagus, where 50% of neurons eventually die in PD<sup>8</sup> and subsequently the substantia nigra. Numerous mouse models and epidemiological studies have provided evidence in favor of the gut-brain axis of Parkinson's disease (PD), with the former showing a lower incidence of the disease in those who have had truncal vagotomy.<sup>10</sup> However, the bidirectional nature of the gut-brain axis has long been

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known, and Divergent findings from mouse research have also surfaced about the effects of nigrostriatal denervation on the gastrointestinal system.<sup>11, 12</sup> Some have suggested that the pathologic alterations seen in the intestinal and central nervous systems (ENS and CNS) could indicate concomitant susceptibility to a systemic disease. Thirteen A schematic depiction of the possible interaction between the CNS and ENS in the etiology of Parkinson's disease and its associated symptoms is shown in Figure 3. Few patients with Parkinson's disease (PD) receive assistance from a gastroenterologist, despite significant progress in our understanding of the gut's mechanistic role in the disease and the high incidence of GI symptoms that significantly affect patient quality of life. Just 12% of PD patients in our tertiary care hospital were sent for consultation, according to a retrospective research.

## Dysphagia esophageal

Among the most typical GI symptoms in Parkinson's disease is dysphagia. The majority of research on the prevalence of dysphagia in this population has been done on oropharyngeal dysphagia, the whose administration has been well examined elsewhere.<sup>16</sup> Although the exact cause of esophageal dysphagia is unknown, it has long been believed that the brainstem's dorsal nuclear vagus plays a role in the deficient coordination of the esophageal musculature.<sup>17</sup> Dysphagia, however, has been observed to occur prior to motor indications of Parkinson's disease (PD), and individuals with PD exhibit distinct histopathologic abnormalities of the esophagus. Increased Lewy bodies in the mid- and especially distal esophagus at the level of the myenteric plexus have been seen in postmortem studies of Parkinson's disease patients, the dorsal nuclear vagus of the brainstem, which affects the esophageal musculature.<sup>17</sup> Dysphagia, however, has been shown to occur before to motor signs of Parkinson's disease (PD), and patients with PD exhibit distinct histopathologic abnormalities of the esophageal ENS. This is similar to other GI symptoms. Elevated Lewy bodies have been found in the mid- and especially distal esophagus at the level of the myenteric plexus in postmortem PD patients; however, there is no clear link between the severity of dysphagia symptoms and esophageal Lewy pathology, nor between esophageal manometric pattern and dysphagia symptoms.<sup>18, 19</sup> Nevertheless, esophageal dysphagia continues to be a critical condition that needs to be addressed in order to meet patients' dietary and symptomatic needs as well as lower their risk of aspiration pneumonia, which is a significant cause of death in Parkinson's disease.

## EGJOO

Manometric EGJOO When EGJOO occurs in PD patients who have dysphagia, a second confirmatory diagnostic test like endoFLIP or a timed barium swallow (with a 13 mm tablet)

should be performed. Endoscopic pneumatic dilatation, which has a response rate of 69.6%, or maybe botulinum toxin injection to the lower esophageal sphincter, which has a somewhat better response rate of 63.6%, are the two options for first-line therapy for EGJOO.<sup>38</sup> Note that the effects of botulinum toxin injections often wear off six to twelve months after the treatment, and that a patient's eligibility for a peroral endoscopic myotomy may be impacted by repeated injections. Notably, even though these statistics are based on actual interventions.

## Vomiting and nausea

In at least 70% of cases, gastroparesis is present, and nausea and vomiting are two of the most common symptoms of Parkinson's disease. Currently, stomach emptying scintigraphy is the gold standard study used to identify gastroparesis; however, this test has poor correlations with the intensity of symptoms and is not reproducible; it frequently results in a negative result when repeated on the same individual in whom the results were previously positive. Furthermore, as was previously mentioned, people with Parkinson's disease (PD) should not take the only FDA-approved medicine for gastroparesis, metoclopramide, as it is associated with a high risk of asymptomatic delayed stomach emptying in this condition. There are several theories concerning the pathophysiology of PD-related nausea and vomiting, one of which is a result of Treatment with levodopa itself, which can postpone stomach emptying.

## Bloating and fluctuation of motors

Therapy might be difficult when there is persistent bloating. Bloating affects about 1 in 4 PD patients, and in this population, it is the GI symptom most frequently linked to a referral to a GI specialist for treatment.<sup>15</sup> This is not only challenging to treat, but it may also stem from a widespread worry among neurologists who care for patients with Parkinson's disease (PD) that bloating, which is a symptom of an underlying motility disorder, exacerbates motor fluctuations. Motor fluctuations are when patients receiving levodopa therapy experience a reduction in the usual benefit from a dose of the medication.

From the standpoint of the patient, bloating is a disagreeable symptom that needs to be addressed regardless of motor fluctuations. Bloating's etiology can be broadly categorized.

## Constipation

One of the most prevalent GI complaints in Parkinson's disease (PD) is constipation, which has a history of showing up well before motor symptoms—in some cases, up to 20 years before PD is diagnosed. It is true that a higher risk of developing Parkinson's disease (PD) is linked to more severe constipation (hazard ratio: 10.47 [9.46-11.58] for severe

constipation). Similar to other GI tract segments, the colon has been the subject of multiple investigations that have reported alpha-synuclein deposition. Most of these research have focused on the submucosal plexus, however a small number have also looked at the myenteric plexus. There is still insufficient information to establish clear links between the degree of constipation symptoms and the precise location or extent of aberrant alpha-synuclein depositions, as well as between neuronal death, due to small sample sizes and heterogeneity in study designs.

## CONCLUSIONS

The care of PD's highly common gastrointestinal problems is a major factor in determining the quality of life for patients. We provide an overview of the clinical presentation, workup, and treatment protocols for the range of GI symptoms that can appear in this population in this practical review. Even though these patients can benefit from our current toolkit, especially when used in conjunction with a gastroenterologist's expertise, it is evident that much more research is required in order to better understand ENS abnormalities and develop target treatments for the particular pathogenesis of GI dysfunction in Parkinson's disease (PD). This is a major National Institutes of Health aim that was recently discussed,<sup>113</sup> and it represents a significant unmet need.

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