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Review article

A practical review of gastrointestinal manifestations in Parkinson's disease

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ABSTRACT

Parkinson's disease (PD) is a chronic neurodegenerative disease with prominent motor and non-motor symptoms. Gastrointestinal (GI) dysfunction is among the most common and bothersome of non-motor symptoms that physicians will encounter while caring for their patients. Patients are subject to a wide variety of GI symptoms involving organs from the oropharynx to the anorectum. Our awareness and understanding of GI involvement in PD continues to evolve. In this review, we use a gastroenterologist's perspective to provide practical considerations for the diagnosis and symptom-based management of GI dysfunction seen in PD. Our aim is to assist neurologists and specialists as they encounter these symptoms while caring for the many neurologic manifestations of PD.

1. Introduction

Over the past few decades, there has been increasing awareness and interest in the GI manifestations of PD which appear much more commonly than in the general population [1–11]. Although historically overlooked [12,13], these GI disturbances have a high potential to impact the quality of life in PD patients, adding to the yearly costs of therapy, and often being common reasons for emergency room visits and hospitalizations [14–20]. The etiology of GI dysfunction in PD is likely multifactorial. Dysfunction of both enteric and central innervation of the gut has been described [21–24]. Alpha-synuclein deposition has been found throughout the enteric nervous system, often described in a rostro-caudal gradient, with a higher burden in the upper gut [25]. However, there has still been no neuronal loss or clear association established between such deposition and symptoms [1,21,26–29]. The central nervous system is also involved with a high level of Lewy bodies found in the dorsal motor nucleus of the vagal nerve (DMV), which has a strong influence on gastrointestinal motility [1,30]. Drugs used in the management of PD may also play a role in GI symptom induction.

PD may even arise in the gut [31,32]. With the dense innervation of the enteric nervous system connected to the vagus nerve, the DMV could serve as a conduit for alpha-synuclein to enter the CNS [1,33]. More recently there has been a search for a peripheral marker of PD. Although data has been mixed for skin and submandibular biopsies [34–36], the enteric nervous system continues to be investigated as a peripheral marker, but also with mixed results [4,37–39].

Hence it is clear that GI dysfunction needs to have a more prominent role in the PD discussion, both as a source of symptoms and as playing a role in disease pathophysiology. This review aims to provide a gastroenterologist's perspective on symptom-based management of PD patients, review the modern ancillary tests to detect abnormalities of structure and function, and discuss treatment strategies based on proper characterization of disease involvement and severity. We hope that it will help neurologists and movement disorder specialists in better managing their PD patients.

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2. Gastrointestinal symptoms

Gastrointestinal symptoms in PD are diverse and stem from involvement of different parts of the GI tract (Table 1). Although constipation is largely regarded as one of the most common symptoms [10], sialorrhea, nausea, vomiting, early satiety, dysphagia, and bloating are all quite prevalent [40]. Case-controlled series have shown these symptoms to be significantly increased in PD patients compared to controls [41]. In this section, we take a system-based approach to GI manifestations in PD while exploring the utility of various ancillary tests in identifying clinical or subclinical dysfunction at one or more gut segments and, in turn, providing therapeutic guidance.

2.1. History and physical examination in PD patients with gastrointestinal symptoms

When taking the initial history of a PD patient, a comprehensive review of systems should be performed to help localize particular segments of the GI tract affected. Symptoms of autonomic dysfunction, such as orthostasis, sexual dysfunction, bladder dysfunction and sweating should also be assessed. When evaluating for constipation, the Bristol Stool Scale, can be used to help maintain a consistent descriptor of stool form, since it has been validated and shown to correlate best with gut transit time [42]. Other defecatory symptoms, such as a sensation of rectal blockage or need for manual maneuvers, should not be ignored as they could suggest anorectal dysfunction. Once a particular GI symptom has been identified, it is useful to use a standardized scale to grade its severity and to track improvement or deterioration over time. For this, multiple validated scales are available. Although we use our own scale tracking multiple GI symptoms at once [43,44] many other scales have been validated and used widely, including the Sialorrhea Clinical Scale for PD [45], the Generic Scale for Dysphagia-Related Outcomes Quality of Life [46–48], and the Cleveland Constipation Scoring System [49].

The physical examination should be comprehensive. Orthostatic vital signs should be checked to look for autonomic dysfunction. Nutritional status should be assessed and weight should be trended at each visit. Special attention should be paid to sialorrhea or aspiration. A complete abdominal examination should be performed and if time permits a digital rectal examination can be helpful in detecting pelvic floor dyssynergia [50–52].

2.2. Ancillary tests to detect gastrointestinal dysfunction in PD patients

Table 1 highlights the various tests that are available to the gastroenterologist attending to a PD patient. Although such ancillary tests have not yet been thoroughly validated in PD, they may provide important guidance to the clinician in the recognition and management of altered GI structure and function. For example, in a PD patient with constipation, the use of the wireless motility capsule (WMC) and high-resolution anorectal manometry (HRAM) allow for further characterization of constipation into colonic inertia and defecatory dyssynergia that in turn require differential management. Given the frequent non-specificity of GI symptoms, it is quite common to perform several of these tests in order to further characterize and more accurately define specific abnormalities that may co-exist with others.

The WMC is a particularly promising new technology that is FDA approved and recommended by the American Neurogastroenterology and Motility Society as a tool to assess for GI dysmotility. It is ordered by a gastroenterologist as an ambulatory, non-invasive, non-radioactive diagnostic sensor that continuously samples intraluminal pH, temperature, and pressure as it moves through the GI tract. Patients swallow the capsule after a meal and then are given a data receiver to take home with them. Physical restrictions include no strenuous activities such as sit-ups and prolonged aerobic activity (>15 min), which could affect pressure measurements. Patients must also refrain from using gastrointestinal medication that could affect motility (ie, laxatives) or gastric pH (ie, proton pump inhibitors). They are asked to fast for 6 h after ingestion, then return to eating and a normal daily routine. They can then return the receiver to a facility in five days to have it analyzed. While it has not been evaluated extensively in the PD population, it has been in spinal cord patients and newer studies are beginning to use this technology in PD as well including a study we recently published [53].

WMC can be costly, is not covered by many private insurance plans (as it is considered experimental), but can be covered by CMS. It is hoped that with more validation in the PD population, WMC will find its important niche and be used more widely. There are no known adverse effects. WMC may be contraindicated in patients who are suspected to have esophageal, gastric, or bowel obstruction, and in deep brain stimulation patients, due to possible interference. The pill itself is 26.8 × 11.7 mm, which is a little more than double the size of a Sinemet 25/250 mg tablet (10.32 × 4.65 mm). While it may prove difficult to swallow, anecdotally, we have not had issues with PD patients swallowing this pill. The only other adverse event to be aware of is the risk of capsule retention, which is reported in 0.33% of patients [54].

3. Acute gastrointestinal syndromes in PD patients

Most of the GI dysfunction in PD has a subacute or chronic presentation. However there are rare instances of gastroenterologic emergencies that must not be ignored.

3.1. Acute dysphagia and foreign body impaction

Dysphagia is quite prevalent amongst PD patients and although usually of gradual onset and chronic, it sometimes presents acutely. Foreign body and food bolus impaction should be always considered, particularly if the patient suddenly cannot handle their own secretions. Drug-induced esophageal injury and, rarely, levodopa

Table 1
Overview of gastrointestinal symptoms and ancillary testing in PD patients.

Symptom	Ancillary test
Dysphagia	Video-fluoroscopy; barium esophagram; endoscopy; high-resolution esophageal motility (HREM)
Nausea, early satiety	Wireless motility capsule (WMC); endoscopy; gastric emptying scintigraphy; *H.pylori* testing (breath or stool antigen)
Bloating	Wireless motility capsule (WMC); lactulose breath test
Constipation	Colonoscopy; abdominal radiography; wireless motility capsule (WMC); high-resolution anorectal manometry (HRAM); MR defecography; Sitzmarks study
Fecal incontinence	High-resolution anorectal manometry (HRAM)

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