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Review article

Consensus practice recommendations for management of gastrointestinal dysfunction in Parkinson disease

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ABSTRACT

Background: Gastrointestinal (GI) dysfunction is a common non-motor feature of Parkinson disease (PD). GI symptoms may start years before the onset of motor symptoms and impair quality of life. Robust clinical trial data is lacking to guide screening, diagnosis and treatment of GI dysfunction in PD.
Objective: To develop consensus statements on screening, diagnosis, and treatment of GI dysfunction in PD.
Methods: The application of a modified Delphi panel allowed for the synthesis of expert opinions into clinical statements. Consensus was predefined as a level of agreement of 100 % for each item. Five virtual Delphi rounds were held. Two movement disorders neurologists reviewed the literature on GI dysfunction in PD and developed draft statements based on the literature review. Draft statements were distributed among the panel that included five movement disorder neurologists and two gastroenterologists, both experts in GI dysmotility and its impact on PD symptoms. All members reviewed the statements and references in advance of the virtual meetings. In the virtual meetings, each statement was discussed, edited, and a vote was conducted. If there was not 100 % consensus, further discussions and modifications ensued until there was consensus.
Results: Statements were developed for screening, diagnosis, and treatment of common GI symptoms in PD and were organized by anatomic segments: oral cavity and esophagus, stomach, small intestine, and colon and anorectum.
Conclusions: These consensus recommendations offer a practical framework for the diagnosis and treatment of GI dysfunction in PD.

1. Introduction

Gastrointestinal (GI) manifestations including drooling, swallowing dysfunction, delayed gastric emptying, bloating, constipation and defecatory dysfunction are among the most common and impactful non-motor symptoms (NMS) in PD [1]. Herein, we provide expert consensus-based guidelines for their management. Consensus guidelines are needed due to lack of high-quality clinical trial data to guide medical decision-making in this arena. The recently published Movement Disorder Society Evidence Based Medicine Review Update on Treatment of NMS of PD inspired this effort [2], as the interpretation of the scant available data on management of GI dysfunction in PD is challenging and prone to pitfalls.

2. Materials and methods

These clinical consensus statements (CCS) were developed with an a priori protocol [3]. This topic was chosen for consensus guideline

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development by the Parkinson Study Group (PSG) Other NMS Working Group (PSG ONMWG) with a target audience defined as all clinicians treating PD in any clinical setting. The movement disorders specialists participating in this modified Delphi panel are all members of the PSG ONMWG, and the gastroenterologists are recognized experts with significant contributions to the study of GI dysfunction in PD. Literature searches to identify current evidence regarding diagnosis and treatment of GI dysfunction in PD were conducted between June 2022 and October 2023, restricted to dates of publication August 1990–December 2022. Two movement disorders specialists performed systematic reviews and developed draft statements for each segment of the GI tract. Draft statements were initially reviewed and discussed by panelists via email. Five virtual meetings were held, during which draft statements were shared on screen, discussed by members, revised as needed, and ultimately vetted (agree/disagree). If a 100 % agreement was not achieved by vote, further discussion and edits ensued. The polling process was repeated until unanimous agreement was achieved. The final manuscript was drafted with participation and final review from all members.

3. Upper GI tract regions and their associated symptoms in PD

3.1. Oral cavity and esophagus

3.1.1. Consensus statements

3.1.1.1. Drooling.

1. Screening for drooling should occur at least once a year. Question 2.2 on the MDS-UPDRS can be used to screen for drooling. No objective assessments of saliva production have been shown to be clinically useful for drooling.

2. When screening for drooling, clarify whether it occurs during waking and/or sleeping hours.

3. If drooling is present, assess also for dysphagia.

4. Treatment of drooling should be considered when it impacts on quality of life.

5. Optimizing dopaminergic medications may have some positive impact on drooling.

6. Drooling that is not severe can be managed with sugar free candy or gum as needed in social situations to encourage more frequent swallowing.

7. Sublingual (atropine, ipratropium) or oral (glycopyrrolate) anticholinergics can be used with caution, when not otherwise contraindicated, for drooling that is not severe.

8. Drooling that is severe and/or refractory to the above treatments can be managed with botulinum toxin injection into the salivary glands at regular intervals.

3.1.1.2. Dysphagia.

1. Querying patients for symptoms of dysphagia should start in early stages of the disease.

2. New diagnosis of drooling and/or dysarthria should prompt reevaluation for dysphagia.

3. Reassessment is suggested in each annual comprehensive visit or more frequently as clinically indicated.

4. Patients with unexplained weight loss, aspiration pneumonia, or malnutrition, should be screened for dysphagia as one potential cause.

5. Question 2.3 on the MDS-UPDRS, which asks about difficulty swallowing pills or eating meals, can be used to screen for dysphagia.

6. Patients with clinically significant dysphagia should be referred for Speech Language Pathology (SLP) or Gastroenterology (GI) evaluation as appropriate.

7. Workup should include a modified barium swallow to evaluate oropharyngeal function. If normal, further evaluation with barium esophagogram or upper endoscopy should be considered.

8. Optimizing dopaminergic medications may help some patients with oropharyngeal dysphagia.

9. Swallow training and dietary modifications under the guidance of a Speech Language Pathologist (SLP) should be considered in patients with oropharyngeal dysphagia.

10. Referral to gastroenterology for further evaluation and management is needed for patients with esophageal dysphagia.

Drooling (excessive pooling and poor control of saliva in the oral cavity) is highly prevalent in PD. Negative sequelae include social embarrassment, poor oral hygiene, halitosis, difficulty eating and speaking, changes in oral microbiome, and increased risk of respiratory infection [4]. Saliva production is diminished in PD, which is why the term “drooling” is preferred over “sialorrhea” in PD [5]. Drooling in PD is thought to be the result of several mechanisms: infrequent and inefficient swallowing, flexed posture, and the tendency for the mouth to remain open [6]. Table 1 summarizes treatment options, doses, and side effect considerations for drooling.

Swallowing dysfunction is common in PD and is an important risk factor for aspiration pneumonia, malnutrition, hospitalization, and premature mortality. The prevalence may be as high as 95 % on objective testing but is often asymptomatic [7]. The use of modified barium swallow studies, video fluoroscopy, and esophageal manometry have identified multiple abnormalities in all three phases of swallowing (oral, pharyngeal, esophageal) including delayed swallowing reflex, pyriform sinus residues, and impaired peristalsis [8]. These abnormalities can all cause aspiration. Patients complaining of coughing or choking while eating or drinking should undergo further evaluation with SLP or gastroenterology. Workup should begin with a modified barium swallow (MBS). MBS cannot evaluate esophageal function; therefore, if the study is negative, further evaluation by gastroenterology is required to assess for and manage esophageal dysphagia. Patients with confirmed aspiration risk due to oropharyngeal dysfunction should be treated by SLP for training on compensatory and adaptive dietary strategies if warranted. Caregivers should be trained on the Heimlich maneuver.[1](Please see Footnotes) Whether optimization of dopaminergic medications improves dysphagia remains controversial, but the authors believe it can sometimes be useful for oropharyngeal dysphagia.

[1] Training on the Heimlich maneuver can be found at the following websites: https://www.mayoclinic.org/first-aid/first-aid-choking/basics/art-20056637; https://www.youtube.com/watch?v=so_HSzO6keI.

Table 1
Treatment options for drooling in PD.

Symptom	Treatment	Dose	Side effect considerations	References
Drooling	Sublingual ipratropium bromide spray	1-2 sprays (containing 21 mcg per metered dose spray) as needed up to 4x/day	Dry nasal passages, epistaxis	[70]
	Sublingual atropine ophthalmic 1 % solution	1 drop 2x/day	Delirium, hallucinations	[71]
	Glycopyrrolate	1–2 mg 2-3x/day. Maximum dose: 8 mg/day	Constipation, xerostomia, blurred vision, urinary retention, anhidrosis, palpitations, drowsiness, confusion	[72]
	Abobotulinum toxin A	75–146.2 U per parotid gland, 78.7 U per submandibular gland	Xerostomia, dysphagia	[4]
	Onabotulinum toxin A	5–50 U per parotid gland, 5 U per submandibular gland	Xerostomia, dysphagia	[73]
	Rimabotulinum toxin B	500–2000 U per parotid gland 250 U per submandibular gland	Xerostomia, dysphagia	[73]

3.2. Stomach

3.2.1. Consensus statements

1. Early satiety, nausea, bloating and bothersome after meal-related epigastric pain may be related to gastroparesis (but may be due to other causes), and can result in worse quality of life in PD.
2. Patients with these symptoms (early satiety, nausea, bloating, epigastric pain) who have associated red flags (GI bleeding, dysphagia, persistent vomiting, unintentional weight loss, iron deficiency anemia and family history of cancer), should be referred to gastroenterology for consideration of upper endoscopy and further work up.
3. H. pylori testing and treatment should be considered by PCPs and gastroenterologists in PD patients experiencing unexplained dyspepsia, with or without red flags.
4. Proton pump inhibitors can be considered as first line therapy for patients with PD and dyspepsia in the absence of red flags.
5. For persistent troublesome symptoms, referral to gastroenterology is recommended for consideration of upper endoscopy and possible gastric emptying test.
6. Gastroparesis can result in erratic responses to levodopa doses, with delayed or complete loss of benefit for individual doses.
7. Treatment of gastroparesis should start with dietary adjustments, primarily eating small frequent low-fat meals.
8. In patients with PD and delayed gastric emptying who are experiencing erratic responses to levodopa, bypassing the stomach with transdermal, subcutaneous, or jejunal drug delivery approaches may be considered.
9. For upper GI symptoms that arise during titration of anti-parkinsonian drugs, GI intolerance to these agents should be considered and addressed.
10. Successful treatment of constipation may also improve upper GI symptoms.

Nausea, bloating, early satiety, and epigastric pain are highly prevalent in PD. There are many potential causes. The authors suggest the following approach: Any patient with these symptoms and accompanying red flags (e.g. significant weight loss, low hemoglobin or signs of bleeding) should be referred to gastroenterology for urgent workup. *Helicobacter pylori* testing using a validated method (breath test, stool test, or endoscopic biopsy) and treatment should be considered by PCPs and gastroenterologists for all patients with these symptoms (with or without red flags). Randomized, placebo-controlled trials indicate that treatment of *H. pylori* does not improve motor symptoms of PD; therefore, screening for *H. pylori* solely for the purpose of improving response to PD treatment, is not recommended [9]. However, *H. pylori* infection does predispose to peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphomas. Therefore, referral for testing and eradication treatment in dyspeptic patients is important [10]. In the absence of red flags, an initial 6-week course of a proton pump inhibitor can be used as first line treatment of these symptoms in PD [11]. For persistent troublesome symptoms, referral to gastroenterology for consideration of upper gastrointestinal endoscopy and possible gastric emptying test is recommended.

Though its prevalence has not been studied systematically, gastroparesis is a common cause of these upper GI symptoms in PD and its exacerbation by dopaminergic drugs may contribute to medication intolerance. Several studies have suggested that delayed gastric emptying has the potential to contribute to motor fluctuations in PD as levodopa must reach the small intestine for absorption [12,13]. In patients with PD and delayed gastric emptying who are experiencing erratic responses to levodopa, bypassing the stomach with transdermal, subcutaneous, or jejunal drug delivery approaches may be considered. In those with suspected or confirmed gastroparesis who are suffering from bothersome GI symptoms, a gastroparesis diet should be adopted (small, frequent meals, avoidance of foods high in fat and fiber, low residue foods, taking fluids throughout meals, and remaining upright or walking for one to 2 h after meals) [8]. Pharmacologic therapies for gastroparesis in PD are limited in the United States as the only FDA-approved medication, metoclopramide, is contraindicated in PD as it worsens parkinsonism through central dopamine blockade. Patients with gastroparesis who are not adequately managed through diet should be managed by gastroenterology.

For upper GI symptoms that arise during titration of anti-parkinsonian drugs, GI intolerance to these agents should be considered and addressed. Dopamine agonists and levodopa are the most common offenders. For levodopa-induced nausea, options to mitigate nausea include adding additional carbidopa with each dose, switching from IR to CR formulations, and administering doses with meals. Use of traditional anti-emetics is not recommended as many can have extrapyramidal side effects.

4. Small intestine, colon and anorectum, and their associated symptoms in PD

4.1. Small intestine

4.1.1. Consensus statements

1. In patients with PD who have inadequate and/or unpredictable responses to levodopa (delayed time to ON, no ON, or end of dose wearing off), more detailed GI evaluation should be reserved for those with clinical symptoms suggestive of maldigestion or malabsorption (such as diarrhea and/or weight loss).
2. Although the optimal approach to the diagnosis of small intestinal bacterial overgrowth (SIBO) in PD patients remains undefined, SIBO can be evaluated by a gastroenterologist by performing endoscopic

jejunal bacterial aspiration or breath hydrogen tests with glucose or lactulose, but results of these tests need to be interpreted with caution.
3. Although data for the treatment of SIBO in PD are very limited, evidence from SIBO, in general, suggests that rifaximin is safe and effective for its treatment.
4. For patients with recurrence of symptoms suggestive of SIBO, a decision for further testing for SIBO and repetition of antibiotic treatment should be made on an individual case basis and under GI specialist supervision.

The small intestine is the least-studied part of the GI tract in patents with PD with few studies examining its motility [14]. In PD, SIBO is likely the consequence of impaired small intestinal motility and may negatively impact levodopa absorption [15]. SIBO is characterized by colonization of the small intestine with increased numbers and/or abnormal populations of (often anerobic) bacteria that normally reside in the colon [15]. Since the small intestine is the primary site of absorption for nutrients, an abnormally high density of bacteria in this segment creates competition with the host for nutrient digestion and absorption.

Common symptoms of SIBO include bloating, flatulence, malabsorption, diarrhea, and weight loss. Fat malabsorption may result in steatorrhea, fat-soluble vitamin deficiency, and, in severe cases, a protein-losing enteropathy and osteoporosis [16]. In PD, the presence of SIBO has been correlated with longer daily OFF time, and with no response or delayed response to levodopa [17]. Eradication of SIBO improved motor fluctuations in one study [17], but not others [18]. SIBO should be considered in patients with PD who have inadequate and/or unpredictable responses to levodopa along with symptoms of maldigestion or malabsorption (e.g. diarrhea and/or weight loss). In suspected SIBO, clinicians should address modifiable risk factors: consider discontinuation of PPI, aggressive control of diabetes, and consider prokinetics such as prucalopride or pyridostigmine.

Data regarding the treatment of SIBO in PD are very limited with no FDA-approved options. However, rifaximin, a non-absorbed, locally acting antibiotic, is the mainstay of treatment and is generally well tolerated [19]. The recommended dose is 550 mg three times a day for 2 weeks [20,21].

Currently, there is not enough evidence to recommend the use of probiotics, prebiotics or dietary modifications for the treatment of SIBO and there is controversy with regard to the use of fecal microbiota transplantation (FMT) [22–24].

4.2. Colon and anorectum

4.2.1. Consensus statements

1. Features of constipation include straining, hard stool, incomplete evacuation, anorectal obstruction, employment of manual maneuvers to facilitate defecation, and fewer than 3 spontaneous bowel movements (BMs)/week.
2. Screening for constipation in PD should occur at routine visits. Use of Rome questionnaire can be considered. Screening should include asking about the above clinical features and may also employ the use of the Bristol stool chart.
3. The underlying causes of constipation in PD may include defecatory dysfunction, slow colonic transit, or both.
4. In the assessment of patients with PD and constipation, risk factors such as alterations in diet, reduced activity, reduced fluid intake, depression, effects of medications (e.g., anticholinergics, opioids, antiparkinsonian drugs), and autonomic dysfunction should be considered.
5. The initial approach to the management of constipation in PD consists of adequate fluid intake, gradually increased dietary fiber and/or addition of psyllium as part of a healthy diet, and adjustment of potentially contributory medications.
6. If needed, osmotic laxatives such as polyethylene glycol-based formulations are appropriate next steps.
7. If the above fails, prescription medications such as prosecretory or prokinetic agents may be considered but the treating physician must be mindful of potential side effects in these patients.
8. For those who fail to respond adequately to the above measures, referral for functional testing, such as anorectal manometry, should be considered.
9. In managing patients with PD and severe constipation, one must maintain vigilance for silent progression to impaction, megacolon and/or perforation.
10. There is insufficient evidence to support the use of probiotics to treat constipation in patients with PD.
11. In patients with advanced PD and refractory constipation, methods such as use of suppositories, digital evacuation or enemas should be considered.

4.2.1.1. Constipation. Constipation is the most common GI symptom in PD [25]. It may be the first NMS to develop in the prodromal stage of PD and is included in the research criteria for prodromal PD diagnostics [26–28]. The definition of constipation in PD has been expanded from a focus on infrequent BMs (fewer than 3 per week), to include features such as straining, hard stool, incomplete evacuation, anorectal obstruction, and a need for manual maneuvers to facilitate defecation [29–31]. Additionally, to better capture defecatory dysfunction (DD) as a cause of the constipation together with dysmotility, the concept of complete spontaneous bowel movements (CSBM) has been introduced as a primary clinical end point in studies rather than simply the number of BMs [32].

There is some evidence that changes in microbiota can affect the absorption of levodopa [33]. Colonic involvement in PD can also contribute to motor fluctuations by further slowing gastric emptying through a colo-gastric reflex, thereby indirectly impairing levodopa absorption [34].

The two major underlying pathophysiological etiologies for constipation in PD are dysmotility and dyssynergia. Dysmotility results in a prolonged transit time and, though little studied in the context of PD, it is likely that it can affect any part of the GI tract [35,36]. The net result, in the colon, is slow transit constipation. Dyssynergia, in contrast, refers to disruption in the normal process of defecation, often due to uncoordinated relaxation of the external sphincter and pelvic floor muscles [25]. It is important that patients with PD have routine screening for constipation using review of the above-mentioned symptoms or use of Bristol stool chart [37]. Although constipation in any individual patient may be predominantly related to dyssynergia or dysmotility, in many instances it is likely multifactorial. As such, other etiologies such as autonomic dysfunction, diabetes, hypothyroidism and the effect of other medications should also be considered when evaluating PD patients with constipation. Medications with anticholinergic properties (such as amantadine) and opioids cause constipation. Some patients report that levodopa, dopamine agonists, may also contribute to constipation. Patients with PD should follow regular colon cancer screening guidelines.

4.2.1.2. Defecatory dysfunction. DD manifesting as difficulty initiating BMs, straining, incomplete evacuation, abdominal discomfort, and anal or rectal pain, can be another cause of constipation in PD [38,39]. Pelvic floor dyssynergia, rectal hyposensitivity with paradoxical anal sphincter and puborectalis contraction during defecation, as well as disorganized function of the abdominal muscles and diaphragm, collectively lead to DD [35]. Evaluation for DD should be considered in PD patients who fail to respond to initial treatment measures. Available tests for diagnosing DD, such as high-resolution anorectal manometry, balloon expulsion

test, and defecography, were compared and found to be concordant in a recent study [40].

Pelvic floor physical therapy (PT) and biofeedback, administered by specialized physical therapists and nurses, are commonly used for to treat DD [41,42]. Pelvic floor PT aims to maximize strength and coordination of muscles involved in defecation and biofeedback uses visual and/or auditory cues to identify the disordered function and improve the relaxation and contraction of the dyscoordinated muscle groups [41,43]. DD is largely the result of skeletal muscle dysfunction, in contrast to most other GI symptoms in PD, which are largely the result of smooth muscle, enteric and autonomic nervous system involvement. Studies suggest that dopamine deficiency can result in DD, and dopaminergic medications can improve it [44]. Botulinum toxin injections into the puborectalis muscle improved constipation due to obstructive defecation in 10 of 18 patients with PD in one study [45]. In another pilot study, botulinum toxin injections to the anal canal were reported to be well-tolerated and safe, with benefit persisting for several months [46]. Surgical options for chronic constipation should only be considered in refractory cases, and only after exclusion of extra colonic etiologies of constipation and failure of intensive medical treatment.

5. Evaluation of PD patients with constipation and/or defecatory dysfunction

5.1. Review of other comorbidities

First assess for other contributing factors such as medications (especially those with anticholinergic properties), reduced physical activity, dehydration, autonomic dysfunction, cognitive impairment and hypothyroidism. Depression is common in PD and can impact constipation in the elderly (see Table 2).

5.2. Lifestyle and dietary modifications

High fiber diet and increasing fluid intake, in cases where constipation is related to dehydration, may be helpful in those without significant dysphagia. Psyllium and other fiber supplements may be helpful in patients without major defecatory dysfunction [79]. The Mediterranean diet stands out for ameliorating constipation in PD [80]. Several studies have examined the effects of prebiotics, probiotics, natural biotics, and FMT on PD. Prebiotics are defined as:" a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon" [47]. Probiotics, on the other hand, are "live microorganisms which when administered in adequate amounts confer a health benefit on the host [48]. Natural prebiotics, found in fruits and vegetables, play an important role in maintaining intestinal barrier function and reducing intestinal inflammation. Evidence from a recent metanalysis suggests that probiotics can improve constipation in PD [49]. However, the use of probiotics, and their optimal formulation in the management of constipation in PD, requires further investigation [35]. While experimental evidence suggests a role for the gut microbiome in the pathogenesis of PD which may open a new therapeutic avenue for microbiome-modulating interventions, until such results are confirmed in large double-blind human studies, patients should be advised against the use of commercial pre- and probiotics, as their use may be more harmful than beneficial [50–52]. A recent randomized, controlled trial suggests that oral FMT capsules are safe and well tolerated in PD patients and can improve GI symptoms, efficacy of conventional PD medications and, therefore, motor symptoms, cognitive function, as well as quality of life in PD patients [53]. Larger double-blind and even triple-blind studies are needed to further investigate FMT before guidelines can suggest its use in PD.

Table 2
Management of constipation in PD. Adopted with modifications From Quigley E, Constipation in Parkinson's Disease, Semin Neurol 2023; 43(04): 562–571. With permission from Thieme.

	Examples	Comments
Diet	High fiber	Effective in constipation in general but dysphagia may limit use in PD
	Increase fluid intake	Effective only if dehydrated
	Mediterranean diet	Supported by RCT
Dietary supplements	Psyllium and other fiber supplements	Effective
	Probiotics	Some evidence to support
Management of PD	Dopaminergics	Some evidence that levodopa/carbidopa may help Limited but positive data for apomorphine
	Recognition and management of depression and cognitive impairment	Resolution of depression may significantly improve bowel function
	Deep brain stimulation	Impact on constipation not clear
OTC agents	polyethylene glycol, Other osmotic laxatives Stimulant laxatives Stool softeners	polyethylene glycol well tolerated; some osmotic laxatives such as lactulose may cause bloating With all agents, be cautious in the presence of fecal incontinence
Prescription drugs	Prokinetics	Best data and safety for prucalopride
	Prosecretory agents • Lubiprostone • Linaclotide • Plecanatide • Tenapanor	Effective in constipation but limited data on use in PD; be aware of diarrhea with all agents and nausea with lubiprostone
Other approaches	Botulinum toxin to the puborectalis muscle	Limited data of efficacy but beware of causing incontinence
	Abdominal Massage Functional Magnetic Stimulation Acupuncture Electroacupuncture Fecal microbiota transplantation	Limited clinical trial or just anecdotal evidence of efficacy

Abbreviations: ENS, enteric nervous system; OTC, over-the-counter; PD, Parkinson's disease; RCT, randomized controlled trial; US, United States.

5.3. Over the counter medications

When lifestyle modifications and dietary measures fail, the next step is use of over-the-counter medications. The four categories of the over-the-counter treatments for constipation include: 1. Bulking agents (e.g. psyllium), 2. Osmotic laxatives (e.g. lactulose, polyethylene glycol, magnesium citrate and magnesium hydroxide), 3. Stool softeners (e.g. docusate), 4. Stimulant laxatives (e.g. senna and bisacodyl). These agents generally perform well and are well-tolerated [25,54,55] Polyethylene glycol (Mira lax) is less likely to cause bloating than other osmotic laxatives. Advise patients to gradually increase the dose until the desired result, a regular soft bowel movement, is attained. For individuals who have not responded to dietary and lifestyle interventions, along with scheduled toileting, the subsequent step is generally the use of polyethylene glycol. If needed, subsequent treatment with stool softeners and stimulants can be considered. However, their utilization should only follow attempts with bulking and osmotic agents. Prolonged use of stimulants is not advisable.

5.4. Prescription medications

- ***Prokinetics:*** These are helpful when the primary cause of constipation is colonic hypomotility. Pyridostigmine is a cholinesterase

inhibitor that can improve chronic constipation by its promotility mechanism [56]. Newer medications in this class are serotonergic agents. Prucalopride, a selective 5-HT4 receptor agonist that has been reported in small studies to improve motility in stomach as well as colon, without imposing the cardiovascular side effects of the previous non-selective medications in its class [57–59]. Therefore, prucalopride should be considered for treatment of constipation for PD patients who have failed life style modifications and over-the-counter treatments.

- ***Prosecretory agents:*** Drugs in this class enhance intestinal secretions, lubricate stool, and facilitate stool passage. Potential side effects are diarrhea (which may lead to incontinence), and nausea (in case of lubiprostone). Hence, careful monitoring is advisable when considering these medications for PD patients, especially since they are at elevated risk for fecal incontinence and may already experience nausea associated with PD. Lubiprostone is a bicyclic fatty acid with no systemic absorption that increases water absorption in the intestinal lumen [60]. A double-blind, placebo-controlled study showed that lubiprostone is safe and well-tolerated in PD [60]. Lubiprostone is more likely to cause nausea than other medications in its class.

Another option in this class is linaclotide that, similarly to lubiprostone, has been minimally studied in PD [61]. Nausea is not a side effect of linaclotide. However due to its possible side effect of diarrhea, close monitoring is recommended in PD patients. Other prosecretory agents include plecanatide and tenapanor [35].

- **Suppositories/digital evacuations/enemas:** Use of these strategies should be considered with refractory constipation to prevent progression to fecal impaction and megacolon. Patients should be advised regarding possible side effects of enemas, such as mucosal injuries and electrolyte imbalances. Warm water enemas are safe and preferable. However, if not helpful, other options and their possible side effects are as follows: soapsuds enemas (may cause rectal mucosal damage); mineral oil enemas (may cause perianal irritation or soreness) [62]. Phosphate enemas should be avoided, due to their risk of inducing electrolyte disturbances in an elderly population [63]. Glycerin suppositories are safe and efficacious alternatives to enemas and may be considered in patients with chronic constipation [64].
- **Biofeedback:** Biofeedback (performed by pelvic floor therapists or in the GI motility laboratory) has been shown efficacious for chronic constipation in several randomized clinical trials. This technique uses neuromuscular training and visual and verbal feedback to improve DD [65–67]. It may not be feasible in PD patients with dementia [35].
- **Fecal microbiota transfer:** Not enough data exists regarding fecal microbiota transfer for treating constipation; therefore, given associated risk, it is not recommended for constipation in PD at this point [68,69].

6. Conclusion

Optimal care of the PD patient requires prompt recognition and treatment of GI symptoms. While there are many pharmacologic options to enable successful management of drooling and slow transit constipation, there still is an unmet clinical need for safe, effective, and convenient treatments for gastroparesis and DD. The area of GI dysfunction in PD lacks both adequate treatment options and adequate clinical trial data. Therefore, clinicians largely rely on data extrapolated from non-PD patients. There is an overwhelming need for research into all aspects of the pathophysiology and management of GI issues in PD. In this resource poor landscape, expert consensus guidelines are a valuable tool for clinicians until a more robust body of evidence exists to inform practice.

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Delaram Safarpour: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Conceptualization. **Natividad Stover:** Writing – review & editing, Writing – original draft, Visualization, Methodology. **David R. Shprecher:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Ali G. Hamedani:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Ronald F. Pfeiffer:** Writing – review & editing, Writing – original draft, Visualization, Validation, Conceptualization. **Henry P. Parkman:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Eamonn MM. Quigley:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Conceptualization. **Leslie J. Cloud:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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