

Gastrointestinal Symptoms in Parkinson Disease: Clinical Aspects and Management

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ABSTRACT: Although it is now generally recognized that the clinical spectrum of Parkinson disease (PD) is broader than its defining motor aspects, its various non-motor symptoms are often not routinely assessed in the clinical setting. As most of these symptoms are amenable to treatment, improved recognition would lead to more comprehensive management of the disease, and ultimately improve the quality of life for PD patients. In an attempt to increase the general awareness of physicians caring for these patients, this article focuses on the clinical manifestations and treatment of the gastrointestinal symptoms most commonly experienced by PD patients, as well as on the gastrointestinal side effects of antiparkinsonian treatments.

RÉSUMÉ: Symptômes gastrointestinaux dans la maladie de Parkinson : aspects cliniques et traitement. Bien qu'il soit maintenant bien connu que le spectre clinique de la maladie de Parkinson (MP) soit plus large que les aspects moteurs qui le définissent, l'évaluation des symptômes non moteurs n'est souvent pas faite de routine en clinique. Comme la plupart de ces symptômes sont traitables, une recherche plus systématique de ces symptômes entraînera une prise en charge plus globale de la maladie et ainsi une meilleure qualité de vie pour les patients atteints de la MP. Cet article traite des manifestations cliniques et du traitement des symptômes gastrointestinaux les plus fréquents chez ces patients ainsi que des effets gastrointestinaux des médicaments antiparkinsoniens, afin de sensibiliser sur ce sujet les médecins qui traitent ces patients.

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Parkinson's disease (PD), which consistently accounts for over 80% of the cases of neurodegenerative parkinsonism reported in the medical literature¹⁻³, is currently diagnosed using the United Kingdom (UK) Parkinson's Disease Society Brain Bank clinical diagnostic criteria⁴. As early as 1817 James Parkinson acknowledged in his *An essay on the shaking palsy* that the clinical spectrum of PD is much broader, encompassing many non-motor symptoms⁵, among which gastrointestinal complaints are one of the most common⁶⁻⁸.

In the clinical setting gastrointestinal complaints are generally not regarded to be significant, and are often not systematically addressed^{9,10}. However, it has been well documented that gastrointestinal symptoms are prevalent, bothersome, may appear at a very early stage of the disease, and harbor a high potential to adversely impact patients' quality of life¹¹.

The purpose of this article is to review the clinical manifestations and treatment of gastrointestinal symptoms commonly experienced by patients with PD, as well as the gastrointestinal side effects of antiparkinsonian treatments. Related issues, such as the neural control of gastrointestinal function and an overview of the pathophysiology of the various gastrointestinal symptoms, lie beyond the scope of this review.

Interested readers are referred to relevant publications, where they have been extensively addressed¹²⁻¹⁸.

The clinical spectrum of gastrointestinal symptoms in PD

Drooling

Drooling is reported by 32-74% of PD patients depending on the symptom definition used, and increases with the severity of PD. A recent review by Kalf et al¹⁹ estimates an overall prevalence of 56%, with the symptom rated as frequent in 22-26% of patients. Drooling is often a source of embarrassment and may lead to the social isolation of many patients²⁰.

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In the beginning drooling tends to occur only during sleep hours and gradually extends throughout the daytime, starting in periods when the patient is fully relaxed or is about to engage in complex motor activities. In terms of severity, it is generally agreed that the amount of drooling correlates with the overall severity of the disease. For reasons that are not well understood, some reports in the literature have found gender differences, with men being more affected than women.

The output of saliva is usually normal or minimally reduced in PD. Drooling is mainly a consequence of motor impairment, mostly due to hypokinesia of the pharyngeal muscles and loss of the involuntary swallowing reflex.

The first steps in the treatment of drooling should be to explain the nature of this symptom to the patient and to optimize control of the motor aspects of the disease. Behavioral interventions and physiotherapy have been tried (although not specifically in a PD patient population), and have usually met with a low rate of success²¹. A recent study by South et al²², however, suggests that a simple intervention such as chewing gum can modify the swallowing frequency and latency, and thus may have a potential to improve drooling.

Anticholinergic drugs have been used to treat drooling in PD patients. Systemically glycopyrrolate (administered as 1 mg three times daily) is preferred by some authors due to its lower potential to cross the blood-brain barrier²³). Locally, sublingual atropine drops (0.5 mg twice daily)²⁴ or ipratropium bromide spray (one or two 21 µg puffs up to four times a day)²⁵ may be helpful. Although they should be used cautiously in PD patients, usually an aged population that may be prone to the development of cognitive and autonomic side effects, it should be noted that drugs that have anticholinergic side-effects (such as amitriptyline²⁶ or amantadine) can also be used to treat drooling. The efficacy of other drugs, such as modafinil (100 mg daily)²⁷ and clonazepam has been anecdotally reported.

If these approaches fail, injection of the parotid and/or the submandibular glands with botulinum toxin can be performed^{28,29}. Type A toxin is most often used at a starting dose of 30-100U. Its effect can be noted within 48-72 hours, peaking by the 14th day after the injection, and the benefit may last for up to 30 weeks. Subsequent injection sites and doses need to be determined according to previous results. Besides the usual side effects of botulinum toxin, attention must be paid to avoiding an excessive decrease in saliva output, as this may result in worsening of dysphagia.

Although not formally evaluated in PD patients, severe cases of drooling may be managed with aggressive strategies, such as radiotherapy³⁰, submandibular duct relocation, or transtympanic neurectomy³¹.

Dysphagia

Dysphagia is defined as the disturbance of the passage of ingested substances through the esophagus. Parkinson's disease is the most frequent neurological cause of dysphagia, affecting up to 85 % of patients with advanced disease³². In addition to patient distress³³, dysphagia may lead to weight loss and severe respiratory tract infections (odds ratios up to five times higher than age-matched healthy subjects). Aspiration pneumonia is among the most frequent causes of death of these patients.

Dysphagia can present itself either in the "on" phase, related to cervicocranial dyskinesia, or in the "off" phase, related to rigidity and hypokinesia of the muscles involved in swallowing³⁴. An additional potential cause for dysphagia is the loss of coordination of this complex activity which could result from brainstem involvement by the disease process¹².

Objective testing has shown that dysphagia can be due to malfunction of any of the structures involved in swallowing, from the mouth to the esophagus, either from direct involvement or from that of the neural centers that control them. By manometric testing, the most frequent abnormalities are decreased resting pressure of the upper esophageal sphincter, decreased peak pharyngeal contraction pressure, slow pharyngeal transport, and abnormal esophageal peristalsis (most often aperistalsis or diffuse esophageal spasm)³⁵. Videofluoroscopic assessment shows slowing of the oropharyngeal phases, abnormal tongue motion, multiple attempts to swallow after a single ingestion, delayed laryngeal elevation, incomplete esophageal transit, and abnormal esophageal peristalsis³⁶. Food residues can be seen in multiple sites (tongue, anterior and lateral sulci, valleculae, and pyriform sinuses). Electrophysiological tests disclose a prolonged swallowing reflex latency and extreme lengthening of the pharyngeal reflex time³⁷. Abnormal findings tend to correlate with the frequency of symptoms and are found in 75% of overall PD patient population, but in as many as 90% of those who have daily symptoms, irrespective of PD severity. Some of these abnormalities may be found in aging populations, so the exact relationship that they may bear to PD is hard to determine³⁸.

Patients' symptoms of dysphagia may not correlate with objective findings of abnormal deglutitive function, and vice-versa. Sung et al³⁹ recently studied the prevalence of dysphagia-associated symptoms in 54 treatment-naïve patients with early PD. The sensation of "getting stuck" (31.5%), fragmented deglutition (29.6%), choking (27.8%), globus (16.7%), and odynophagia (5.6%) were commonly reported. However, there was no statistically significant correlation between impedance/manometry testing findings and symptoms.

Due to the common finding of non-specific esophageal motility abnormalities even in healthy populations, objective testing is only recommended in symptomatic patients or those with a clinical suspicion of pulmonary aspiration. For those with predominantly oropharyngeal symptoms (such as coughing, choking, or difficulty initiating swallows) videofluoroscopic evaluation with a modified barium swallow and/or speech/language pathologist assessment is ideal. Patients with esophageal symptoms such as retrosternal dysphagia may benefit from esophageal manometry or barium esophagram.

Since dysphagia is among the non-motor symptoms that respond poorly to dopaminergic treatment⁴⁰, management is largely directed at minimizing the risk of aspiration. Standard recommendations include eating while in the "on" phase, in a sitting position and tilting the head slightly downwards. The patient should avoid foods of mixed textures, use fluid thickening preparations, take small bites, and gently cough after each swallow. However, the efficacy of these maneuvers has not been firmly established in the medical literature⁴¹, and a more comprehensive evaluation by a speech therapist may be necessary. For patients with a significant dysfunction of the upper esophageal sphincter, specific treatment with either the

injection of botulinum toxin type A (30 units in each muscle)⁴² or myotomy⁴³ have been described in small case series. However, these procedures may increase aspiration risk in PD patients with impairment of other components of their swallowing mechanism. In severe cases, feeding by nasogastric tube or a gastrostomy may be required⁴⁴.

Dyspepsia

A case-control study of 98 PD patients and 50 controls showed significantly higher reports of nausea (25% vs 8%), and a trend toward increased early satiety, bloating, vomiting and heartburn⁴⁵. These symptoms are likely multifactorial in origin due to both the disease process and the effect of dopaminergic medication.

Measurement of gastric emptying by scintigraphy has suggested slower emptying in patients with early disease on levodopa, but moderately severe PD patients in the “on” phase may have normal emptying⁴⁶. In patients with advanced disease, both erratic or impaired gastric emptying and the interference of proteins on drug absorption contribute to variable bioavailability of L-Dopa⁴⁷⁻⁴⁹. This has been linked to the development of motor complications such as the “delayed-on” and “no-on” phenomena, or dyskinesias.

Because of the lack of specificity of dyspepsia symptoms in general, the presence of “alarm” features such as persistent vomiting, evidence of gastrointestinal bleeding or anemia, abdominal mass, unexplained weight loss, or dysphagia should prompt further evaluation to rule out alternative diagnoses⁵⁰.

General dietary advice is difficult, because dietary triggers for dyspepsia vary widely and inconsistently, but identified problem foods should be avoided. However, overly restrictive diets should be discouraged due to a risk of malnourishment among PD patients. Prokinetic drugs are the mainstay of treatment for dyspepsia, with domperidone 10-20 mg orally up to four times daily being the preferred choice since it does not cross the blood-brain barrier and has minimal, if any, central antidopaminergic effects⁵¹. Aggressive treatment for severe gastric emptying, such as pyloric botulinum toxin A injection or gastric neurostimulation⁵² have not been evaluated in PD patients and should only be considered after evaluation by a gut motility specialist.

There are no specific guidelines for the management of motor complications related to the alteration of gastric emptying. Personal experiences such as that of Nyholm and Lennernäs⁴⁸ suggest that not taking the dopaminergic drugs during protein-rich meals or taking them with certain products (in their series chocolate, bananas, coffee or carbonated beverages) may be beneficial; in case these dietary measures fail, dopaminergic stimulation in any of its available modes should be tailored, according to clinical experience and local availability, to achieve maximal response with minimal side-effects.

The influence of *Helicobacter pylori* infection on the derangement of L-dopa absorption has been suggested in various studies. Decreased drug absorption and effect (which is both delayed and shortened) have been documented in infected patients⁵³, and these abnormalities can be reversed by successful eradication of the bacteria⁵⁴. Although the precise nature of this relationship remains elusive, uptake and utilization of levodopa by *Helicobacter pylori* has been proposed as an explanation for this observation⁵⁵.

Constipation

Constipation is a functional bowel disorder that presents as persistently difficult, infrequent, or seemingly incomplete defecation. Formally, it must include at least two of: straining, lumpy or hard stools, sensation of incomplete evacuation or anorectal obstruction, need for manual facilitating maneuvers, or fewer than three defecations per week⁵⁶.

Large population-based studies such as the Honolulu Asia Aging Study⁵⁷ have documented that a low frequency of bowel movements is associated with a three-fold increased risk of developing PD over a ten year follow-up period, and that, on average, constipation precedes the onset of motor symptoms by 12 years. A recent case-control study from Olmsted County (Minnesota, USA)⁵⁸ evaluated constipation in a population-based sample of incident PD cases and found that constipation was diagnosed in 36.2% of patients who subsequently developed PD but only 20.4% of the control group (odds ratio 2.48, 95% CI 1.2-3.34, p 0.008). This finding remained significant after adjustment for confounding factors such as smoking and coffee consumption, and was more robust when constipation developed over 20 years before the onset of motor symptoms. Moreover, incidental Lewy bodies or decreased cellular density in the substantia nigra at autopsy of constipated patients with no parkinsonian symptoms has been also reported^{59,60}.

Series from specialist referral clinics suggest that the prevalence of constipation among PD patients is high, with 59% of consecutive PD patients referred to a movement disorders clinic reporting the symptom vs. 21% in a control group of individuals aged over 65⁶¹. Constipation has been related to aging, so it is worth noting that this study found no significant association to the age at diagnosis of PD, suggesting that constipation and PD are not associated through the possible confounding effect of age. In a large survey study which used a validated constipation score only 7% of the patients had “severe” symptoms⁶². The nature of the symptoms, considered to be a source of dissatisfaction by as many as 45-60% of PD patients, has been evaluated by Sakakibara et al⁶³, who have made an interesting distinction between the early phase, in which mostly reduced number of bowel movements are encountered (20-81% vs. 0-33% of healthy age-matched persons), and the later stages, in which difficulty in defecation is more frequently encountered (57-67% vs. 26-28%). Parkinson disease patients typically have multiple symptoms related to constipation, among which unsuccessful defecation attempts and the sensation of incomplete emptying are associated to the severity of PD, and decreased frequency of bowel movements is associated with a longer time since diagnosis⁶².

Objective measurement of colon neuromuscular function in PD has shown decreased colonic motility, with longer mean colonic transit times as compared to healthy controls (44-130 hours vs. 20-39 hours)⁶⁴. Since an association with abnormal parasympathetic function (such as an increase in R-R variability on electrocardiogram (EKG) recordings) has been described in PD patients⁶⁵, constipation may be a manifestation of the involvement of this system by the disease process.

Anecdotal reports in the medical literature of patients with an acute dysmotility presentation (such as pseudo-obstruction, paralytic ileus, or Ogilvie’s syndrome) are likely more related to

metabolic derangements or complications of antiparkinsonian treatments than to the disease itself.

Management of constipation in PD is identical to other causes of constipation. Although their benefit has not been proven in controlled studies, the initial steps are to increase dietary fiber intake, avoid dehydration, and increase exercise. In case these initial measures fail, bulk-forming laxatives (such as psyllium⁶⁶) or osmotic laxatives (such as milk of magnesia or polyethylene glycol⁶⁷) are the mainstay of treatment. The use of stimulant laxatives such as bisacodyl or senna are common, but are not recommended for long-term use due to colonic habituation.

Domperidone, which is highly effective in the proximal gastrointestinal tract, has minimal effect on colonic function⁶⁸. Serotonergic drugs such as mosapride, tegaserod and cisapride have a prokinetic effect that can improve constipation without worsening parkinsonian symptoms, but in most countries these agents have been removed from the market due to risk of cardiac arrhythmia. Cisapride⁶⁹ is available for compassionate use through Health Canada. Refractory cases may be managed by the addition of the prostaglandin E1 analogue misoprostol (600–2400 µg daily) to a conventional therapeutic regime, although patient intolerance and loss of effectiveness over time seriously limit its long-term use⁷⁰. There have been reports on a potential benefit of other drugs, such as erythromycin or colchicine, but there is currently not enough evidence to recommend their use. Functional magnetic stimulation of the thoracic and lumbosacral nerves by placing a coil on the T9 and L3 spinal processes in 20 minute twice-daily sessions for three weeks⁷¹ has been proposed as an alternative, and found to significantly accelerate colonic transit and improve all the aspects of defecation for as long as the three month follow-up period of the study.

In a subset of patients complaining of constipation this symptom is not related to slowed intestinal transit, but to inability to expel stool due to disordered defecation. In these patients paradoxical contraction of the puborectal muscles and of the external anal sphincter during attempted defecation can be documented by electromyogram (EMG) recording, and this has been suggested to represent a focal dystonia⁷². However, a more recent report in which anal manometry was performed in a series of PD patients with lower gastrointestinal complaints, however, found that in those with a defecation disorder, a failure of anal relaxation was more common than paradoxical contraction⁷³.

An effort to relate the defecatory abnormalities to the “on” or “off” phase should be made, in order to determine the appropriate therapy. If it felt to be part of the “off” phenomenology, optimization of the dopaminergic regime is required, and apomorphine has occasionally been found to be most effective in this situation⁷⁴. Treatment with pelvic floor physiotherapy or biofeedback retraining^{75,76} has good long-term efficacy and the added benefit of being minimally invasive with no adverse effects. For refractory cases, injections of botulinum toxin A into anal sphincters or puborectalis muscles^{77,78}, trans-anal irrigation, or colostomy have been used⁷⁹.

Abdominal pain

Bouts of excruciating abdominal pain are occasionally reported by PD patients. These generally occur during the “off” phase, and are thought to be a part of a central pain syndrome, possibly related to dysfunction of the spinoreticulothalamic

pathways and their connections. Epidemiological studies on this symptom are scarce in the medical literature. Twenty-two percent of patients (as compared to 18% of controls) were found to have abdominal pain in one case-control study⁴⁵. The most useful clinical clues for its diagnosis are an intermittent course and a relation to the “off” phase.

If no other cause for the abdominal pain is found, the first step in its management should be to explain its cause to the patients and their families, and the optimization of the dopaminergic treatment. In more severe cases, symptomatic relief can be obtained by the use of analgesics, either conventional or opioid-derived agents, tricyclic antidepressants or atypical neuroleptics⁸⁰.

Fecal incontinence

Although fecal incontinence is thought to occur in less than 10% of PD patients, its impact on quality of life measures is usually marked.

In a very small series of PD patients evaluated with anal manometry, Stocchi et al⁷³ found a 5.9% prevalence of incontinence for solid feces, but reported an overall prevalence of 41% if incontinence for liquid feces (most often after laxatives had been taken to treat constipation) was included. Decreased mean resting and maximal contraction anal pressures were documented by anal manometry. Both incontinence and the manometric findings correlated with age and disease duration. No specific guidelines for therapy in PD patients are found in the literature, and given the low frequency with which it is encountered, referral to a gastroenterologist would be appropriate. Management of neurogenic fecal incontinence should start with conservative measures such as modification of stool consistency and bowel training. Pelvic floor strengthening exercises and/or biofeedback have been shown to be beneficial in the non-PD population⁸¹, and would likely be applicable to PD patients. Loperamide to slow down bowel movement frequency is another commonly-used therapy for fecal incontinence. However, as it may substantially increase the risk of constipation in the PD population, it should be used cautiously. Sacral nerve stimulation⁸² has emerged as a minimally invasive, effective and well tolerated treatment option.

Table 1: Prevalence of gastrointestinal side-effects of selected dopaminergic drugs. Adapted from Kulisevsky et al⁸³.

	L-Dopa	DA general	pramipexole	ropirinole	placebo
Nausea	27%	21%	20%	27%	14%
Vomiting	6%	6%	5%	6%	3%
Constipation	15%	7%	15%	5%	6%
Abd pain	10%	6%	8%	6%	4%

DA, dopamine agonists; Abd pain, abdominal pain

Gastrointestinal side effects of antiparkinsonian drugs

Gastrointestinal complaints are among the most frequent side effects of antiparkinsonian drugs, and can be expected in over 25% of the patients taking them. However, it should be noted that both their prevalence and severity tend to decrease over time, and are usually responsive to symptomatic therapy.

A recent meta-analysis⁸³ reported on the frequency of various gastrointestinal side effects (including nausea, vomiting, constipation, and abdominal pain) of both L-Dopa and dopamine agonists. Except for abdominal pain, all of these side effects were found to be significantly more prevalent among patients taking dopaminergic drugs compared to placebo, and are summarized in Table 1. The potential development or worsening of nausea and constipation associated with the initiation of L-Dopa therapy is worth mentioning to patients, in order to avoid the unnecessary concern that can arise if they are unaware of this possible relationship. Starting dopaminergic treatment with a low dose and titrating upwards slowly as needed (“start low, go slow”) improves the gastrointestinal tolerance of these drugs.

The addition of entacapone to an L-Dopa based treatment regime has the potential to increase the prevalence and severity of side effects, such as nausea and vomiting. In a clinical trial of

these agents, nausea was reported by 13.5% of patients taking L-Dopa/carbidopa, and by 26.6% of those taking L-Dopa/carbidopa/entacapone; however the drop-out rate for this symptom was similar in both groups⁸⁴. Diarrhea is a well known side effect of entacapone, not commonly seen with other antiparkinsonian drugs. It occurred in 8.7% of the patients in the treatment group compared to 2.8% of patients on L-Dopa/carbidopa alone, and was severe enough as to lead to the drop-out from the study in 3.9% of the patients.

Rasagiline appears to have minimal gastrointestinal side effects based on a comprehensive review by Chen et al⁸⁵. However, in the PRESTO study (in which rasagiline (0.5 mg/day or 1 mg/day) or placebo were added during 26 weeks to the levodopa/carbidopa treatment of 472 moderate to advanced PD patients with motor fluctuations) the incidence of vomiting was higher with the drug than with placebo (3.7% in patients taking 0.5 mg/day and 6.7% in patients taking 1 mg/day vs. 1.3% in the placebo group).

The gastrointestinal side-effects of amantadine are thought to be largely due to their anticholinergic properties. Nausea has been reported in 5-10%, anorexia, constipation, diarrhea, and dry mouth in 1-5%, and vomiting in up to 1% of patients taking this medication⁸⁶.

Table 2: Summary of treatment options for each gastrointestinal symptom, their level of evidence and grade of recommendation (as issued by the Quality Standards Subcommittee of the AAN⁸⁹ and the EFNS/MDS-ES Joint Task Force⁹⁰), and list of relevant references used for this review

Symptom	Treatment options	LE ⁸⁷	GR ⁸⁸	Ref
Drooling	1. Optimize dopaminergic treatment	-	-	-
	2. Behavioral and physical therapy: gum chewing and others	III	U	22
	3. Anticholinergic drugs: glycopyrrolate sublingual atropine drops	III	U	23
	ipratropium bromide puffs	IV	U	24
	4. Other pharmacological options: amitriptyline	III	U	25
	modafinil, amantadine, clonazepam	IV	U	26
5. Parotid and/or submandibular gland botulinum toxin injection	IV	U	27	
6. Radiotherapy, surgery (for resistant cases)	I	A [87]	28,29	
		IV	U	30
Dysphagia	1. Swallowing training and diet texture modification to prevent aspiration	-	-	-
	2. Cricopharyngeal botulinum toxin injection or myotomy (if UES significantly involved)	IV	U	42
	3. Tube feeding (in severe, unresponsive cases)	IV	U	43
Dyspepsia	1. Prokinetic drugs: domperidone preferred	IV	U	44
	2. Pylorus botulinum toxin A injection or gastric pacemaker implantation (for severe cases)	II	B [88]	51
	3. Consider eradication for <i>Helicobacter pylori</i> infected fluctuating patients	IV	U	52
Constipation	1. Fiber-rich diet, abundant fluid intake, increase exercise	IV	U	54
	2. Bulk-forming laxatives: psyllium, polyethylene glycol	-	-	-
	3. Prokinetic drugs: cisapride ^a	III	U	66
	4. Other pharmacological approaches: misoprostol (as add-on to conventional regime)	II	C [87]	67
	erythromycin, colchicine	III	U	69
5. Functional magnetic stimulation of thoraco-lumbar nerves	IV	U	70	
Puborectal dystonia	1. Optimize dopaminergic treatment if related to off phase (apomorphine may be especially effective)	-	-	-
	2. Biofeedback retraining	IV	U	74
	3. Puborectalis botulin toxin A injection	III	U	75,76
	4. Trans-anal or antero-grade colonic irrigation, colostomy	III	U	77
Abdominal pain	1. Optimize dopaminergic treatment	IV	U	79
	2. Symptomatic treatment: conventional or opioid-derived analgesics, tricyclic antidepressants, atypical neuroleptics	-	-	-
Fecal incontinence	1. Stool consistency modification, bowel training	IV	U	80
	2. Sacral nerve stimulation	-	-	-
	3. Trans-anal or antero-grade colonic irrigation, colostomy	IV	U	82

LE, level of evidence; GR, grade of recommendation, Ref, reference, UES, upper esophageal sphincter; A, established as effective; B, probably effective; C, possibly effective; U, current data inadequate or conflicting. ^a only available for compassionate use through Health Canada.

Anticholinergic medications are not frequently used to treat PD in North America, but they are worth mentioning because of their specific gastrointestinal side effects, among which dry mouth (which could actually be beneficial for patients with drooling) and a 30-50% chance of worsening constipation are the most significant. Worsening of constipation caused by anticholinergic treatment is almost the only circumstance in which constipation in PD can lead to serious complications, such as extreme colonic dilatation or perforation.

CONCLUSION

Parkinson's disease, the second most prevalent neurodegenerative disease, is mostly recognized by its motor manifestations. The clinical spectrum of the disease, however, is much broader and encompasses many non-motor symptoms, among which gastrointestinal complaints are a frequent source of discomfort and health risks for patients with this condition. These symptoms include drooling, dysphagia, dyspepsia, constipation, abdominal pain, and fecal incontinence.

Although the symptoms may present very early in the course of the disease, their prevalence, severity and impact on the patients' quality of life usually increase as the disease progresses.

The correlation between subjective complaints and objective findings on formal testing of the gastrointestinal tract is often poor, so the decision to undertake any ancillary testing should be guided primarily by concerns about serious complications (especially aspiration in the case of dysphagia) or alternative underlying causes for a given symptom (eg. dyspepsia in the presence of "alarm symptoms").

The management of these symptoms among PD patients does not differ significantly from what is recommended to treat them in the general population, except for the fact that drugs with a known potential to worsen extra-pyramidal signs (such as metoclopramide) or to which PD patients may be exquisitely sensitive (such as those with an anticholinergic effect) should be avoided. A summary of therapeutic options for each of the reviewed symptoms is provided in Table 2.

Gastrointestinal complaints (including nausea, vomiting, constipation, and abdominal pain) can be expected in over 25% of the patients taking antiparkinsonian drugs, although they tend to decrease over time, and are usually responsive to symptomatic therapy. Diarrhea is a potential side effect of entacapone, not commonly seen with other antiparkinsonian drugs. Drugs with an anticholinergic effect must be used cautiously, because worsening constipation in this setting may lead to serious complications, such as extreme colonic dilatation or perforation.

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APPENDIX

(selected scales for the assessment of the gastrointestinal symptoms in PD)**General scales, in which the symptoms are considered within a broad context:**

- MDS-Unified PD Rating Scale (MDS-UPDRS) part II⁹¹
- Nonmotor Symptoms Questionnaire for PD (NMSQuest)⁹²
- Nonmotor Symptoms Scale (NMSS)⁹³
- The Scales for Outcomes in PD-Autonomic (SCOPA-AUT)⁹⁴

Drizzling:

- Sialhorrea Clinical Scale for PD (SCS-PD)⁹⁵

Dysphagia:

- Generic Scale for Dysphagia-Related Outcomes Quality of Life (SWAL-QOL)^{96-98a}

Constipation:

- Cleveland Constipation Scoring System^{99a}

^ascales that have not been specifically designed or validated for PD patients.