CE Symptom Management Series
2.0 ANCC Contact Hours

Management of Constipation in Patients With Parkinson Disease

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Constipation management in Parkinson disease can be challenging. Physiologically, there is a slowed colonic transit time, hypokinesia of abdominal muscular due to rigidity, and central pathology as well as a functional outlet obstruction. This is because of paradoxical external anal sphincter contraction when there should be relaxation for defecation. The paradoxical contraction is likened to a focal dystonia similar to other dystonias occurring in the rest of the body. A recent study showed the effect of decreasing anal dystonia with added levadopa in de novo patients. However, more studies are needed to replicate the effect. Often, the treatment for chronic constipation is based on provider and patient experience, with more studies needed in this area as well. Complicating factors include patient age, polypharmacy, multiple comorbids, dietary factors, and limited mobility.

KEY WORDS

constipation, nonmotor symptom, Parkinson disease

PRESENTATION OF CASE STUDY

Luis is a 72-year-old Hispanic man with Parkinson disease (PD). He came onto hospice having recently moved into the home of his son's family.

Luis had been diagnosed 13 years before with PD. He has mask-like facies and a soft voice and is confused. He will stand with assistance to transfer to a bedside commode. Because of increasing rigidity, poor balance, and an exhausted caregiver, he will eventually become bedbound and dependent for all activities of daily living.

Luis has an intermittent, resting tremor of his left arm. It is becoming increasingly difficult for him to feed himself and swallow. Finger foods in a preferred high-protein diet became easier to manage than utensils. Thickened liquids are recommended, but he does not like the taste. With more difficulty in swallowing, a lidded cup is effective to slow down his efforts to swallow and manage independent intake of fluids.

Robert, the patient's son, reports Luis's history of prolonged time on the commode, with extraordinary time straining and very large hard stools. In addition, Robert reports that the stools are so large and hard that the plunging of the commode and frequent backup of stool contents occurs about 2 times a week. Luis has a firm abdomen, and it has been at least 4 days since his last bowel movement.

On admission, the medications included Carbidopa/Levodopa 25/100 immediate release 5 times daily. Carbidopa/Levodopa extended release 25/100 one-half tablet is given twice a day. Amantadine 100 mg is given 2 times daily and Amantadine 50 mg is given once daily. Entacapone 200 mg is given 5 times daily. Other medications are Escitalopram for depression and clonazepam for sleep. Docusate dosage is 50 mg once per day. Patient is also taking Ferrex (iron supplement) 150 mg daily.

Luis would increasingly have more intense hallucinations, for which Quetiapine fumarate was added to the schedule. Ativan was also available as part of a comfort kit in the home for anxiety. Because of falls, this patient would need increased supervision with 24-hour caregiving by his spouse.

PD AND CONSTIPATION

Parkinson disease is a progressive neurodegenerative disorder that results in severe disability 10 to 15 years from onset. It is characterized by 2 of 3 of the following motor symptoms: resting tremor, bradykinesia, and rigidity. Supporting features are postural instability, mask-like facies, and speech problems such as hypophonia. Patients with PD often experience nonmotor symptoms to include orthostatic hypotension, urinary urgency, sexual dysfunction, disorders of sleep, psychosis, depression, and dementia.[1]

One nonmotor symptom of PD that can be particularly disabling is constipation. The cause of constipation is slow or impaired colonic transit time (CTT), weak abdominal strain (from rigidity and reduced axial muscle contractility), and abnormal motor control of the anal sphincter.[2,3] A focal dystonic condition not unlike that which occurs in the rest of the body causes a paradoxical external anal sphincter contraction when there should be relaxation. This is described as a type of functional outlet obstruction.[4]

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During defecation, the puborectalis muscle should relax, causing a straightening of the anorectal angle. Under paradoxical circumstances, the angle is maintained with contraction of the external anal sphincter and, hence, pelvic outlet obstruction, or failed defecation.[5]

Savica et al[6] summarized several studies that suggest a long premotor phase of PD. They found that constipation may manifest as early as 10 to 20 years before the onset of motor symptoms in PD. They suggest that Lewy body neurodegenerative process may occur in a stepwise process with additional factors advancing the disease to the next level.[6]

Sung et al[7] found abnormal anorectal manometry in 12 of 19 newly diagnosed PD patients. This test measures pressure, reflex, and sensation in the rectum. The abnormality was more likely in those reporting more severe symptoms. However, 40% of patients reporting no to minimal symptoms also showed abnormal manometric testing.[7]

With advancing PD, an inadequate fluid intake, dehydration, and poor intake complicate constipation. Ignoring the urge to defecate due to poor mobility or an inattentive caregiver delays the defecation response for constipation. The inability to get to a commode or get into a sitting position additionally contributes to constipation in the palliative care setting.[8]

MEDICATIONS AS A CONTRIBUTING FACTOR

The amount of disability experienced by the patient will determine the start of dopamine therapy. A hand tremor that is disabling to an executive may not be the same experience for a retiree.[9] Once started, levadopa can be titrated to best efficacy, considering motor fluctuations and dyskinesias. The dose can be modified, the interval between dosing can be changed, or another product can be added as an adjunct. This includes catechol-*O*-methyl transferase inhibitors (entacapone, talcapone), dopamine agonists (ropinirole and pramipexole), and monoamine oxidase-b inhibitors.[10]

Antipsychotics may interact with dopamine, decreasing its effectiveness. Of the antipsychotics available, Quetiapine fumarate is preferred over clozapine because of agranulocytosis, a reduction in white blood cells.[11]

In addition to PD's physical impairments, drugs frequently prescribed to PD patients have adverse effects that can be a contributing factor for constipation. Nortryptylline is often used for depression.[12] Anticholinergics such as oxybutynin for overactive bladder and scopolamine for increased saliva can also exacerbate the symptoms of constipation.[13]

Diuretics used to treat hypertension, hypokalemia induced by diuretics, opioids, calcium to treat osteoporosis, iron supplements to treat anemia, calcium channel blockers, and nonsteroidal anti-inflammatories are all cited as confounding factors that multiply the problem of constipation.[8]

The effect of levadopa in early-stage PD gastrointestinal dysfunction was explored. Levadopa/carbidopa 200/20 mg administered 2 times a day for 3 months was found to lessen paradoxical sphincter contraction and improve anorectal constipation. There was no change in CTT. There was less resistance of paradoxical sphincter contraction (significant), lessened postdefecation residuals, and lessened amplitude of abdominal strain.[14]

PHYSICAL ASSESSMENT OF CONSTIPATION

The Rome III criteria have been developed to define both functional constipation and defecation disorders, which are both noted in PD patients (Appendix).[15]

The nurse should assess the patient's usual defecation pattern in terms of frequency and timing during the day. The patient should be asked about stool form or maneuvers to allow expulsion. Medication history should be obtained and include any herbal or over-the-counter supplements. Timing of new medications can implicate new-onset constipation. Assess diet, fluid intake, gastrointestinal diseases, and any surgery involving the genitourinary and gynecologic systems.[16,17]

Inspect and auscultate the abdomen for bowel sounds. Percuss the abdomen for dullness and palpate for masses. A distended and tender abdomen with dull percussion sounds may lead to possibility of constipation.[16,17]

RECTAL EXAMINATION ASSESSMENT

The rectal examination is performed by having the patient assume a left lateral position. Part the anal mucosa and place a gloved right index finger into the rectum, feeling for stool. The presence of stool suggests fecal impaction. As you place your left hand over the abdomen, ask the patient to bear down as if defecating. Feel for abdominal tightening and observe the right index finger movement outward from the rectum. If there is no abdominal tightening or there is a paradoxical squeeze on the right index finger, the patient may have paradoxical contraction of the anal sphincter or dyssynergistic defecation. This finding could then be confirmed by manometric testing.[18]

MANAGEMENT OF CONSTIPATION IN PD

The management of constipation in PD can be challenging. Often, recommendations are empirical and patients are advised to simply increase fluid intake. Algorithms are often developed for ease of administration, cost, physician experience, or patient choice.[8] As an example, this author

has suggested Vaseline balls for constipation in difficult cases. The balls, approximately a quarter inch in size, consist of Vaseline rolled in powdered sugar and frozen, with 2 balls taken orally. Although there is no formal evidence related to this treatment, it is known to be effective in my experience.

Treatment should start with the least invasive options such as diet and lifestyle modifications.[17] Current medications should also be reviewed. If there is a secondary contributing cause perhaps due to medication, then adjustments should be considered.

LIFESTYLE MODIFICATIONS

Patients should be provided assistance for regular toileting to maintain a regular bowel regimen. Encourage and assist patients to promote defecation in the morning especially 90 minutes after meals to respond to the gastrocolic reflex.[19]

Sikirov[20] studied defecation effort in 2 sitting (regular toilet seat and lowered toilet seat) and 1 squatting position. Time to satisfactory bowel emptying and straining in the squatting position was much less when compared with both sitting positions. The study confirmed that the squatting position necessitates much less expulsive effort owing to a straightening of the anorectal angle.[20] Whereas a squatting position is not feasible for many elderly individuals, a sitting position is still to be preferred over a supine position.

There is evidence that CTT can be decreased by physical activity.[21] Physical activity in PD also benefits improved gait, balance, posture, and energy. Stretching exercises improve rigidity as well.[12] Exercise, particularly in elderly individuals, can improve chronic constipation and certainly improve quality of life.[22]

DIETARY MODIFICATIONS

Oral iron products are known to cause constipation, even in healthy subjects. There are combination products available that contain iron and stool softeners. In addition, iron can decrease dopamine efficacy by decreasing absorption. Iron should be separated from dopamine products because of a decrease in the effectiveness of PD medications.[23,24]

It is known that protein intake interferes with levadopa therapy. Barichella et al[25] studied the effectiveness of low-protein products at breakfast and lunch. They found that these products reduced the total off time (when medication is not working) when compared with the usual balanced diet group.[25]

In a study by Coggrave et al,[26] multiple databases were searched for trials evaluating the management of constipation in neurogenic bowel disease, from January 1966 to May 2005. The study identified at least 10 trials, most of poor quality and small sample size. There was some evidence that psyllium may be of benefit, but there was not enough evidence to draw conclusions.[26]

A consensus group of gastroenterologists from the Canadian Association of Gastroenterology searched data to determine the best treatment for patients with chronic constipation. The aim was to create a guide for the health care professional. They did find some evidence that increased fluid intake is inversely related to chronic constipation severity, particularly in elderly individuals and those with PD. However, there is little evidence to support increased fluid intake in the overall chronic constipation population. They found that psyllium may be more effective than docusate in increasing stool output at least up to 8 weeks' duration. The authors believe that there may be benefit for increased fiber of more than 30 g daily with an increased fluid intake, but more studies are needed to support the data.[22]

Ford and Suares[27] conducted a systematic review of multiple databases to determine the effect of increased dietary fiber in idiopathic constipation. Soluble fiber was found to improve symptoms of straining, pain on defecation, stool consistency, and mean number of stools per week. Trials evaluating insoluble fiber (wheat bran) were conflicting. The authors concluded that dietary fiber, although frequently recommended by well-known groups, may not be scientifically based, only empirical. Furthermore, there is a paucity of quality studies on this subject.[27]

There are some data that show benefit for use of the probiotic *Bifidobacterium lactis* DN. This is a probiotic in the yogurt Activia. Few studies have been done, and there is no definitive evidence; however, Chey[28] recommends that the patient take the supplement twice daily and try a 2- to 4- week trial before deciding its effectiveness.

MEDICATION MODIFICATIONS

Zesiewicz et al[29] studied the treatment of nonmotor symptoms in PD. A literature search of databases from 1966 to August 2008 was reviewed. The study authors concluded that for constipation, polyethylene glycol (PEG) may be considered for treatment.[29]

In comparing the effects of PEG with those of lactulose, PEG was found to be more effective in terms of increased number of stools and less strain. In general, both were well tolerated, although lactulose may have produced more flatus.[30]

Pare et al[22] found insufficient evidence to recommend docusate. PEG administered daily to twice daily effectively relieved chronic constipation and has been studied up to 6 months' duration. However, studies beyond 6 months are needed.

Two prescription laxatives are Food and Drug Administration approved for chronic constipation. Lubiprostone and linaclotide act by different mechanisms to increase

intestinal chloride secretion. Lubriprostone has shown statistically significant results, with increased average of bowel movements per week.[31] Linaclotide has been studied in 2 large trials by Lembo and colleagues[32] to find statistically significant results in treatment response when compared with placebo.

PELVIC FLOOR DYSFUNCTION

Patients with pelvic floor dysfunction may not respond to typical treatments for constipation. There may be benefit from biofeedback training, with positive outcomes reported in 40% to 90% of patients with pelvic floor dysfunction. Landmann and Wexner[5] suggest a decision tree beginning with the offer of conservative management through biofeedback to botulinum toxin A injection, before surgical alternatives such as ileostomy, colostomy, or division of the puborectalis.

SUMMARY OF KEY IMPLICATIONS IN PALLIATIVE CARE

Elderly individuals (>65 years of age) often report constipation. They often come into palliative care with a myriad of comorbidities that contribute to slowed colonic motility. This includes diagnoses such as diabetes and hypothyroidism.[8] Additive to these conditions are the physiologic effects of PD causing constipation. These effects are slowed CTT, hypokinesia of abdominal musculature, and functional outlet obstruction. The paradoxical functioning of the external anal sphincter has been likened to a dystonia occurring elsewhere in the body that responds to levadopa. Constipation is a quality-of-life issue and requires vigilant attention to manage it especially under these circumstances. Nonmotor symptoms of constipation can be as debilitating as the motor dyskinesias. Although treatments are often based on experience, evidence-based recommendations exist for lifestyle, dietary, and medication modifications (Table).

TABLE Summary of Evidence-Based Recommendations Regarding Constipation

Study	Interventions	Why Helpful?
Sikirov (2003)	Sitting position	It straightens the anal rectal angle to allow defecation. It is better to be sitting than to be lying down to have a BM. Squatting may not be possible, so sitting is the closest.
Spinzi (2007)	Toileting schedule	Consider 90 min after meals for gastrocolic reflex. Assists with poor mobility and delayed defecation.
Barichella et al (2006) Campbell et al (1990)	Dopamine effectiveness	Consider decreasing protein intake and separating iron supplement dose time to decrease interaction with dopamine.
Basson and Katz (2013)	Other medications	Consider need for anticholinergics, calcium, and NSAIDs as it is a cause of constipation.
Spinzi (2007)	Diet	Assist patient with adequate fluid and food intake due to tremors.
Martine and Duda (2005)	Antipsychotics	Take clozapine or Seroquel, preferably Seroquel to avoid agranulocytosis.
Song et al (2012)	Physical activity and/or range of motion	Benefits balance, posture, and gait. Improves quality of life and ability to improve BM.
Attar et al (1999)	Polyethylene glycol	1–2 times daily for constipation. Found to be more effective than lactulose.
Chey (2012)	Probiotics	Increase friendly bacteria in colon. Trial of 2–4 weeks to determine effectiveness.
Landmann and Wexner (2008)	Pelvic floor dysfunction	Biofeedback may be helpful.
Basson and Katz (2013)	Comorbidities	Hypothyroidism, diabetes

Abbreviations: BM, bowel movement; NSAIDs, nonsteroidal anti-inflammatory drugs

CONCLUSION OF THE CASE STUDY

Luis reports that his most recent bowel movement was 4 days ago. His abdomen is firm on palpation. A bisacodyl suppository is given after manual extraction of stool. A toileting schedule is set up so that the patient is assisted to a sitting position on a bedside commode. His medications are adjusted with an increase in docusate to 100 mg twice a day. Polyethylene glycol 17 g in 8 oz of liquid twice a day is started. The patient's spouse is educated to understand that a low-protein diet will enhance the effectiveness of dopamine. When the spouse understands the constipating effects of iron, she prefers to discontinue it. Soon, Luis begins having several stools per day and the Polyethylene glycol is adjusted to once a day.

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APPENDIX. ROME III DIAGNOSTIC CRITERIA FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

C3. FUNCTIONAL CONSTIPATION

*Diagnostic criteria**

1. Must include 2 or more of the following:
   a. Straining during at least 25% of defecations
   b. Lumpy or hard stools in at least 25% of defecations
   c. Sensation of incomplete evacuation for at least 25% of defecations
   d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. Manual maneuvers to facilitate at least 25% of defecations (*e.g.*, digital evacuation, support of the pelvic floor)
   f. Fewer than 3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome

*Criteria fulfilled for the last 6 months with symptom onset at least 3 months prior to diagnosis

F3. FUNCTIONAL DEFECATION DISORDERS

*Diagnostic criteria**

1. The patient must satisfy diagnostic criteria for functional constipation.**
2. During repeated attempts to defecate must have at least 2 of the following:
   a. Evidence of impaired evacuation, based on balloon expulsion test or imaging
   b. Inappropriate contraction of the pelvic floor muscles (ie, anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
   c. Inadequate propulsive forces assessed by manometry or imaging

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

**See above diagnostic criteria for functional constipation.

F3A. DYSSYNERGIC DEFECATION

Diagnostic criterion

Inappropriate contraction of the pelvic floor or less than 20% relaxation of basal resting sphincter pressure with adequate propulsive forces during attempted defecation

F3B. INADEQUATE DEFECATORY PROPULSION

Diagnostic criterion

Inadequate propulsive forces with or without inappropriate contraction or less than 20% relaxation of the anal sphincter during attempted defecation

Abbreviation: EMG, electromyography.