



National Hospice and Palliative Care Organization
Palliative Care Resource Series

**A PALLIATIVE CARE APPROACH
TO PARKINSON'S AND OTHER
NEURODEGENERATIVE DISEASES**

Mara Lugassy, MD
Hospice Medical Director, MJHS Hospice and Palliative Care
Assistant Professor of Family and Social Medicine
Albert Einstein College of Medicine

A PALLIATIVE CARE APPROACH TO PARKINSON'S AND OTHER NEURODEGENERATIVE DISEASES

Parkinson's disease, and related conditions known as Parkinson's plus syndromes, constitutes a group of progressive neurodegenerative disorders. These disorders are characterized by the motor syndrome of Parkinsonism as well as a range of nonmotor symptoms.

In addition to motor symptoms, nonmotor symptoms also contribute to disability and reduced quality of life. They include autonomic dysfunction, neuropsychiatric symptoms, sleep disorders, and pain. This paper will define Parkinson's disease; describe the role of the palliative care approach to Parkinson's including symptom management through a combination of pharmacologic and nonpharmacologic interventions.

PARKINSON'S DISEASE: SYMPTOMS AND NATURAL HISTORY

Parkinsonism is defined by the presence of bradykinesia along with at least one of the following: rigidity, tremor, or postural instability.

Bradykinesia, is the slowed initiation of and reduction in speed and amplitude of movements, which impacts a range of functions including:

- slowness and impairment of gait
- difficulty executing fine motor movements
- reduction in gestures and facial expressions
- micrographi
- hypophonia
- Dysphagia
- Progressive rigidity results in stiffness, pain, and contractures, and postural instability, which can then lead to an increased propensity to fall backwards, resulting in possible injury, immobility and institutionalization.

Parkinson's disease, the most common form of Parkinsonism, is a common neurodegenerative disease second only to Alzheimer's disease. It results from loss of the dopaminergic cells of the substantia nigra pars compacta. (1)

Parkinson's disease is a slow progressive disorder, with mean time of diagnosis to death of 14 years. (2) It typically presents in early stages as a unilateral resting tremor or rigidity, or as mild clumsiness or slowing of movements on one side and is generally relieved by treatment with dopaminergic medications. As the disease progresses to the middle stage, symptoms become bilateral and less responsive to dopaminergic medications, and activities of daily living become more impaired. Nonmotor symptoms, such as constipation, orthostatic hypotension, and cognitive decline, may also become apparent.

Late stage Parkinson's disease is marked by dependency in activities of daily living, increased falls, and progression to wheelchair or bedbound status. Nonmotor symptoms, including autonomic dysfunction, incontinence, dementia, and psychosis, predominate. Dysphagia may also develop, resulting in aspiration pneumonias, the leading cause of death in the disease.

PARKINSON'S PLUS DISORDERS

Parkinson's plus syndromes, like Parkinson's disease, involve Parkinsonism along with additional nonmotor symptoms. However, they differ from Parkinson's in terms of specific symptom profile, natural history, and response to treatment.

- **Multiple System Atrophy** is characterized by bilateral onset, early and severe autonomic dysfunction, poor response to treatment with levodopa, and a more rapidly progressive course than Parkinson's disease, with time to death after diagnosis of 6-10 years. (3)
- **Progressive Supranuclear Palsy** is marked by a progressive ophthalmoplegia, early postural instability and executive dysfunction, behavioral abnormalities, and poor response to levodopa. Average time of onset to death is 8 years. (4)
- **Dementia with Lewy Bodies** involves Parkinsonism along with cognitive impairment that occurs concurrently with or within one year of onset of the motor symptoms. Visual hallucinations and fluctuations in cognition and level of alertness are also characteristic. Motor symptoms can respond to levodopa. Average time of onset until death is 8 years. (5)

ROLE OF PALLIATIVE CARE

Currently, no treatments exist to cure or delay disease progression in Parkinson's or related diseases; thus all interventions are geared toward amelioration of symptoms and are essentially palliative in nature. The wide range of motor and nonmotor symptoms present in Parkinson's disease and their significant impact on quality of life necessitate an interdisciplinary approach, with physicians, nurses, social workers, occupational and physical therapist, pastoral care and other disciplines all playing a role.

In the **early stages** of disease, the palliative care focus may be on educating the patient and family about symptoms, treatment options and prognosis, identifying support resources, and facilitating advance care planning discussions, in particular appointing a health care agent, and initiating goals of care discussions regarding artificial nutrition and hydration and mechanical ventilation.

In the **middle stages** of disease, as symptoms progress, there is an increasing need for evaluation and management of both nonmotor and motor symptoms. Additionally, as patients begin to show increasing disability and care needs, palliative care providers may begin to evaluate more closely for caregiver distress, and work with patients and families to develop coping strategies for the shifting roles that may occur in the family unit. Goals of care discussions, often an ongoing process in this slowing progressive disease, are continued.

In the **late stages** of disease, dementia, debility, dysphagia, and difficulties with communication become salient issues. Along with steep decline in a patient's function, comes a need for increased care, and palliative care providers can play a significant role identifying, referring to, and organizing outside support services. For patients who can no longer be cared for at home, facilitating the transition of care, for example, to a nursing home, can be involved.

Hospice: People with end stage Parkinson's disease and related disorders can benefit significantly from the range of services and provisions available under the hospice benefit; however, hospice services remain underutilized.

Missed opportunities for a hospice referral may be related, in part, to lack of identification of Parkinson's disease as a terminal as opposed to a chronic condition. Additionally, absence of specific criteria for hospice eligibility for Parkinson's disease may also play a role. When considering hospice eligibility, practitioners may consider eligibility criteria for dementia, as well as more general markers of advanced disease include weight loss, declining functional status, frequent infections and hospitalizations, skin breakdown and evidence of malnutrition.

SYMPTOMATIC MANAGEMENT OF PARKINSON'S

A wide range of pharmacologic and nonpharmacologic interventions can be used to palliate both the motor and nonmotor symptoms of Parkinson's disease.

Pharmacotherapy for Motor Symptoms:

Pharmacotherapy in Parkinson's disease can significantly improve physical symptoms and quality of life, although side effects can be problematic, and treatment of motor symptoms can potentially worsen nonmotor symptoms.

- **Levodopa**, the mainstay of Parkinson's pharmacotherapy, can be of significant benefit to the motor symptoms of tremor, rigidity, and bradykinesia, particularly in the earlier stages of disease. Postural instability is overall less responsive to medical treatment.
- **Additional categories of medication** for treatment of Parkinson's disease include dopamine agonists, monoamine Oxidase –B inhibitors, Catechol-O-Methyltransferase Inhibitors, and anticholinergic medications.

Pharmacotherapy in Parkinson's disease is complicated by two major limitations: motor fluctuations, which manifest as "on periods" during which there is a positive response to medication and "off periods" marked by a reemergence of motor symptoms, and dyskinesias, which are levodopa induced involuntary movements. (6)

As the disease progresses, pharmacotherapy becomes more challenging, as patients may have less improvement with the same dose of medication, spend more time in off periods, and can develop worsening medication induced dyskinesias. Attempts to increase medication doses with the goals of increasing medication "on periods" and clinical benefit may have the unintended results of worsening dyskinesias and other side effects instead. Thus, medication management in advancing disease becomes a delicate balance requiring continued reassessment and discussion with patients and caregivers of risk versus benefits of medication.

Medications to avoid:

Certain medications commonly used in a palliative care setting may worsen Parkinson's motor symptoms, and should be avoided, including:

- **Antipsychotics**, either typical, such as haloperidol, chlorpromazine, fluphenazine, loxepine) and atypical (risperidone, olanzapine, aripiprazole).
 - ◆ For patients with psychosis that requires pharmacotherapy, quetiapine is the preferred agent, followed by clozapine for refractory cases.
- **Antiemetics:** metoclopramide, prochlorperazine, promethazine
- **Benzodiazepines** should be used with caution, due to an increased risk of balance impairment, falls, and confusion.

Nonpharmacologic interventions for Motor Symptoms:

Nonpharmacologic interventions can also play a significant role in the management of motor symptoms, especially as the disease progresses and pharmacotherapy becomes less effective. The care team plays a significant role in educating and supporting caregivers regarding these interventions. Early in the disease process, nonpharmacologic strategies focus mainly on preservation of function, while in later stages of the disease, emphasis may shift to compensation for increasing disability.

- **Exercise** has significant benefits for persons with Parkinson's disease and related disorders improving muscle strength, helping with balance and fall reduction, improving walking performance, mood, and quality of life. Animal studies have also demonstrated possible neuroprotective effects. (7,8)
 - ◆ Beneficial activities include aerobic activity, muscle strengthening and stretching activities, tai chi, yoga, and dance. Regular physical activity should be initiated early in the disease and encouraged throughout the disease course, with activities modified to the stage of illness (9, 10).
- **Compensatory Strategies:** Parkinson's disease is marked by the loss of ability to carry out movements that are normally automatic in nature; however, strategies geared toward increasing the attention or effort directed toward a movement can compensate in part for this loss. Examples include:
 - ◆ The use of external auditory or visual cues to improve motor performance, such as stepping over a line on the floor to improve gait, walking to the rhythm of a metronome or music, or verbal commands such as "one, two, three, go" to stimulate initiation of a movement.
 - ◆ Breaking down complex movement into discrete subunits.
 - ◆ Avoiding multitasking and distractions.
 - ◆ Strategies to break a freezing episode include marching in place, stepping over an imaginary line, or initiating a verbal cue such as "step forward". *Freezing*, the temporary inability to move, is a highly distressing symptom in Parkinson's and can lead to anxiety, falls, and injury. Freezing is exacerbated by medication "off" periods, narrow spaces, and turning.
 - ◆ As disease progresses, modification of the home environment becomes more important, through interventions such as avoidance of low lying obstacles and narrow space, removal of area rugs, use of elevated toilet seats and chairs, and introduction of mobility devices and other adaptive equipment.

- **Dysphagia**, which progresses throughout disease, is commonly worse with thin liquids, can result in aspiration events, and is an important topic in goals of care discussions as it pertains to initiation of artificial nutrition and hydration.
 - ◆ Dysphagia may be ameliorated by scheduling meals during medication “on” periods, increasing focused attention on chewing and swallowing, minimizing talking and other activities while eating, and using thickener with liquids. Use of a “chin tuck” technique through which a person bends the head and neck forward while swallowing, can also help.
- **Speech deficits**, also a later stage finding in Parkinson’s, can severely limit the ability to communicate and may serve as a source of social isolation. Hypophonia, dysarthria, monotone voice, hoarseness or breathiness can all occur.
 - ◆ Deficits may be improved by avoidance of multitasking while speaking, voice exercise training programs which focus on volume and enunciation, and use of voice amplifier devices for hypophonia. (11)

Nonmotor Symptoms:

Nonmotor symptoms, including autonomic dysfunction, sleep disturbances, pain, and neuropsychiatric conditions, tend to progress, and may be more distressing than motor symptoms, particularly in late stage disease. As these nonmotor symptoms are often underreported, and can both impact quality of life and contribute to hospitalization and institutionalization, they deserve particular attention. (12,13)

- **Constipation** occurs throughout disease and may be multifactorial, exacerbated by immobility, decreased oral intake and medications. Screening and careful monitoring are essential.
 - ◆ Helpful interventions include encouraging fiber and fluid intake, maximization of physical activity even for bed bound patients through frequent positional changes, establishing fixed time of bowel movements, and introduction of a step wise bowel regimen.
- **Orthostatic hypotension** may contribute to falls and injuries, and can be exacerbated by common medications. It may present as lightheadedness, fatigue, cognitive blunting, or posterior head and neck pain.
 - ◆ Nonpharmacologic interventions for orthostatic hypotension include avoidance of lying flat, minimizing hot baths and shower which can cause vasodilation, use of compression stockings, and increasing fluid and salt intake. (14,15)
 - ◆ Pharmacotherapy for orthostatic hypotension includes midodrine and fludrocortisone.
- **Urinary Symptoms**, including urgency, frequency, incomplete bladder emptying, and incontinence are common, and may contribute to embarrassment and social isolation.
 - ◆ Avoidance of caffeine, limitation of excessive fluid before bedtime, and wearing easy to remove clothing can all help. Common medications for urinary symptoms, such as alpha blocker or anticholinergics, must be used with caution as they can worsen orthostasis and cognitive impairment, respectively. (16)
- **Pain** occurs in up to 80% of people with Parkinson’s, and correlates with both depression and decreased quality of life. (17) Pain may stem from the rigidity and immobility, or from dystonia associated with wearing off effects of Parkinson’s medications. In such cases, in addition to analgesic medications, adjustment of dopamine therapy to maximize “on” and minimize “off” periods can improve pain as well. Patients with Parkinson’s may experience neuropathic pain as well as a central type pain, related directly to the disease itself. This typically stabbing or burning pain, which is found in unusual body distributions, may be improved with antiepileptic type medications, opioids, or tricyclic antidepressants. (18)

- **Sleep Disorders** are commonly associated with Parkinson's and may affect the quality of life of both patients and families.
- **Insomnia** can result from multiple causes, including nocturia, muscle cramps, dystonia during wearing off of medications, and difficulty turning in bed. Careful evaluation for and relief of underlying factors should be the first step in management, and sleep aids used only with caution.
- **REM Behavior sleep disorder**, characterized by a loss of atonia during REM sleep, results in the person physically acting out their dreams. This can put both the patient and partner at significant risk of injury, especially in the case of violent type dreams. In addition to the implementation of safety measures, REM Behavior sleep disorder can improve with either clonazepam or melatonin. (19)
- **Dementia** associated with Parkinson's disease is marked by early impairment of executive function in areas such as planning, organization, multitasking and mental flexibility, with relatively preserved memory and language in the earlier stages. Some benefit has been shown with use of cholinesterase inhibitors or memantine.
 - ◆ Due to the possibility of dementia in later stage disease, it is particularly important to begin to clarify goals of care earlier in the disease course, due to the potential for the eventual loss of the ability to communicate and make medical decisions.
- **Hallucinations**, commonly associated with Parkinson's disease, are typically visual in nature, and frequently of animals or people. Hallucinations can be either a symptom of the disease itself or a side effect of medications used for Parkinson's.
 - ◆ Education and reassurance of patients, families, and caregivers about the nature and cause of hallucinations is important to any plan of care. Careful review of all medications should be undertaken, with stepwise removal of medications according to hallucinogenic potential.
 - ◆ If hallucinations persist and are a source of distress, a trial of an antipsychotic may be indicated. Generally, Quetiapine is the first line agent due to reduced risk of exacerbating Parkinsonian symptoms. Clozapine, which also has a relatively lower risk of exacerbating motor symptoms, is generally reserved for refractory cases due to its risk of agranulocytosis and requirements of enrollment in a monitoring program. (20)
- **Depression** is the most common psychiatric symptom in Parkinson's, and is commonly associated with anxiety. Its significant negative impact on quality of life and its underreported nature make it worthy of screening. Depression may worsen during "off" periods of medication and can be improved by maximization of dopaminergic therapy. When depression warrants additional pharmacotherapy, careful consideration of the risk versus benefits of individual medications should be considered. (21,22)

CONCLUSIONS

Parkinsonian disorders involve a wide range of motor and nonmotor symptoms. While there are currently no treatments to cure or delay disease progression, a wide range of pharmacologic and nonpharmacologic therapies can benefit functionality and quality of life. Patients, families, and caregivers can also benefit from interdisciplinary palliative care throughout the course of the disease.

REFERENCES

1. Huse DM, Schulman K, Orsini L et al. Burden of illness in Parkinson's disease. *Mov Disord.* 2005;20(11):1449-54.
2. Selikhova M, Williams D, Kempster P et al. A clinico-pathological study of subtypes in Parkinson's disease. *Brain.* 2009;132(pt11):2947-2957.
3. Tada M, Onodera O, Tada M et al. Early development of autonomic dysfunction may predict poor prognosis in patients with multiple system atrophy. *Arch Neurol* 2007;64:256.
4. O'Sullivan SS, Massey LA, Williams DR et al. Clinical outcomes of progressive supranuclear palsy and multiple system atrophy. *Brain* 2008;131(pt5):1362-1372.
5. Williams MM, Xiong C, Morris JC, Galvin JE. Survival and mortality differences between dementia with Lewy bodies vs. Alzheimer disease. *Neurology* 2006 Dec 12;67(11) 1935-41.
6. Olanow CW, Watts RL, Koller WC. An algorithm (decision tree) for the management of Parkinson's disease (2001): Treatment guidelines. *Neurology*, 2001; 56 (11 Supp 5)s1.
7. Uhrbrand A, Stenager E, Pedersen MS, Dalgas U. Parkinson's disease and intensive exercise therapy – a systematic review and meta-analysis of randomized controlled trials. *J Neurol Sci* 2015 Jun 15;353(1-2)9-19.
8. Ahlskog, JE. Does vigorous exercise have a neuroprotective effect in Parkinson's disease? *Neurology* 2011 Jul 19 77(3) 288-294.
9. Morberg, BM, Jensen J, Bode M, Wermuth L. The impact of high intensity physical training on motor and nonmotor symptoms in patients with Parkinson's disease (PIP): A preliminary study. *Neurorehabilitation* 2014 Jan1; 35 (2) 291-8.
10. Suec R, Filip P, Sheardova K, Bares M. Psychological benefits of nonpharmacological methods aimed for improving balance in Parkinson's disease: A systematic review. *Behav Neurol.* 2015. Jul 7.
11. Fox C, Ebersbach G, Ramig L, Sapir S. LSVT LOUD and LSVT BIG: Behavioral treatment programs for speech and body movement in Parkinson's disease. *Parkinsons Dis.* 2012, Mar 15.
12. Chaudhuri KR, Prieto-Juvcynska C, Naidu Y, et al. The nondeclaration of nonmotor symptoms of Parkinson's disease to health care professionals: An international survey using the NMSQuest. *Mov Disord* 2010 Apr 30;25:704-9.
13. Todorova, A, Jenner P, Chaudhuri K. Non-motor Parkinson's: Integral to managing Parkinson's yet often neglected. *Pract Neurol.* 2014 Oct;14(5)310-22.
14. Low, P, Tomalia V. Orthostatic hypotension: Mechanisms, causes, management. *J Clin Neurol.* 2015 Jul;11(3) 220-6.
15. Figueroa JJ, Basford JR, Low PA. Preventing and treating orthostatic hypotension: As easy as A, B,C. *Clev Clin J Med.* 2010 May;77(5)289-306.

16. Thaisetthawatkul P, Boeve B, Benarroch E, et al.. Autonomic dysfunction in dementia with Lewy Bodies. *Neurology*. 2004;62(10)1804.
17. Valkovic P, Minar M, Singliarova H, et al. Pain in Parkinson's Disease: A cross-sectional study of its prevalence, types, and relationship to depression and quality of life. *PLoS One* 2015; 10(8)e0136541.
18. Munazza S, Ford B. Management of pain in Parkinson's disease. *CNS Drugs* 26 (11) Nov 2012. 937-48.
19. Kunz D, Mahlberg R. A two-part, double-blind placebo controlled trial of exogenous melatonin in REM sleep behavior disorder. *J Sleep Res*. 2010 Dec;19(4):591-6.
20. Williams DR, Litvan I. Parkinsonian syndromes. 2013 Oct;19(5 *Movement Disorders*):1189-212.
21. Aarsland D, Larsen JP, Lim NG, et al. Range of psychiatric disturbances in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1999;67(4)492
22. Lökk, J Delbara, A. Clinical aspects of palliative care in advanced Parkinson's disease. *BMC Palliative Care*. 2012;11(20)1-8.