Extending palliative care to patients with Parkinson's disease

Patients with Parkinson's disease have an illness which shortens their life and involves a heavy symptom burden for patient and carer. This article discusses some common palliative care issues pertinent to patients with Parkinson's disease.

Specialist palliative care services are rarely involved in the care of patients with Parkinson's disease and a palliative approach to care may not be explicit. There is a current impetus for patients to have access to palliative care and specialist palliative care services irrespective of diagnosis. Parkinson's disease progresses slowly, with increasing disability and reliance on carers. A palliative approach, with holistic, multiprofessional care, is appropriate to provide symptom control and support. The experiences and needs of patients with Parkinson's disease and their carers are similar to patients with advanced cancer, albeit over a longer time course (Hudson et al, 2006). Continuity of care is important and can be provided by the primary care team supported by a Parkinson's disease specialist nurse with appropriate access to specialist palliative care services. This article discusses how common principles of palliative care can be applied to patients with Parkinson's disease.

Pathophysiology

Parkinson's disease occurs as a result of the progressive loss of dopaminergic neurons in the substantia nigra and their projections into the neostriatum and globus pallidus. This results in central dopaminergic deficiency with a relative acetylcholinergic excess and results in a characteristic triad of clinical features (*Figure 1*). Drug therapy is directed at correcting the imbalance. The prevalence of Parkinson's disease in industrialized countries is estimated at 0.3% of the entire population. Approximately 1% of over 60-year-olds are affected (De Lau and Breteler, 2006).

Figure 1. Clinical features of Parkinson's disease.

Tremor	This is usually unilateral at onset, maximal at rest and occurs in up to 75% of patients. Combined with hypertonia, tremor results in 'pill rolling' movements in the hands. It is poorly controlled by medication and can be socially distressing
Bradykinesia	This includes slowness to initiate voluntary movements, e.g. rising from a chair, and arrest of ongoing movement, e.g. turning a corner. There is often an absence of spontaneous movements such as blinking, resulting in the characteristic 'mask-like' facial expression. Fine movements become clumsy. These features tend to respond well to medication
Rigidity	Increased muscle tone, often affecting the neck and trunk, results in a stooped, flexed posture. This contributes to a tendency to fall backwards (retropulsion) and problems with balance. Loss of balance also results from inability to make the rapid adjustments to the body's centre of gravity when changing position, e.g. from sitting to standing. Although hypertonia and stiffness can improve with medication, postural instability is much harder to treat

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Survival

The mean survival for idiopathic Parkinson's disease has been estimated at 10–15 years, with a variable rate of progression that seems to be linked to age at onset.

Different models of Parkinson's disease have been described with either four (MacMahon and Thomas, 1998) or three (Hoehn and Yahr, 1967) stages. Aims, assessment, management strategies and outcome goals are different for each stage (MacMahon and Thomas, 1998). The final 'palliative stage' aims to relieve symptoms and maintain dignity by rigorous symptom control, appropriate use and withdrawal of medication and prevention and treatment of complications. An audit of 73 patients with Parkinson's disease found that the average time spent in the palliative phase was 2.2 years (MacMahon and Thomas, 1998). However, the principles of palliative care, particularly symptom control, preserving autonomy and relieving distress, should be applied from diagnosis to bereavement, not just reserved for the end of life phase.

Prognosticating in Parkinson's disease is no easier than in many other conditions, including cancer. Palliative care physicians are often guided by the historical course of the individual's disease to provide a future estimate of disease progression. Research to identify indicators of end of life for Parkinson's disease patients might facilitate specialist palliative care referral and encourage a palliative approach (Goy et al, 2008). Death is usually from complications: falls, pneumonia, urinary sepsis or dementia. In one survey, 26% of 47 Parkinson's disease patients were tube fed in the final month of life and 30% received some form of breathing support (Goy et al, 2007). In this same survey, 53% of patients received hospice care for a median of 2.5 weeks. This contrasts with another survey which found that only 8% of 174 patients with Parkinson's disease had received input from specialist palliative care services (Kristjanson et al, 2005).

Aims of treatment

Pharmacological treatment for Parkinson's disease is symptomatic. Patients also need psychological and emotional

support to help them cope with losses of body image, mobility, social functioning and independence. Caregiver distress increases as the disease progresses. Carers need support and education through the different stages of the illness, including bereavement. A retrospective survey found that caregivers of patients dying from Parkinson's disease experience challenging physical and emotional circumstances in the final months, particularly when the patient stays at home (Goy et al, 2008). Increasing aid for or respite from physically demanding care and educating carers about what to expect were the key recommendations.

As Parkinson's disease progresses, patients become increasingly disabled, often resulting in admission to a nursing or care home. Cognitive problems tend to expedite the admission to care, whereas respite admissions can lengthen the time that patients can be maintained at home (Thomas and MacMahon, 2004a).

Common problems in palliative care of Parkinson's disease

Motor fluctuations and dyskinesias

Over time, progressively fewer dopaminergic neurons are capable of taking up exogenous l-dopa and converting it to dopamine for subsequent storage and release. Consequently, patients experience a 'wearing off response' whereby they derive an increasingly shortened period of benefit following each dose of l-dopa. This effect typically occurs 2–4 hours after a dose and may manifest as sensory (pain, paraesthesiae), psychiatric (anxiety, depression, paranoia, hallucinations) or autonomic (tachycardia, sweating, constipation, belching or breathlessness) symptoms as well as worsening parkinsonism or dystonia (Waters, 1997). Management centres around adjusting l-dopa dosage, frequency and formulation and by the balanced addition of dopamine agonists, which directly stimulate post-synaptic dopamine receptors.

Further progression of Parkinson's disease often results in the on-off effect with unpredictable shifts from over-treated (dyskinesias) to undertreated (dystonic) states, thought to be because many patients with advanced disease and a paucity of dopaminergic transmission develop enhanced sensitivity to small changes in plasma l-dopa levels. Conversely, apparent lack of response to l-dopa can be related to poor absorption or gastrointestinal dyskinesia which is ameliorated by prokinetic medication.

Dyskinesias include abnormal movements of the head, neck, trunk and limbs and can be exhausting and socially embarrassing. A good way to assess motor symptoms and identify patterns of dyskinesia is by asking patients to keep a symptom diary, recording symptoms as well as timing of medication.

Drug withdrawal

Dopaminergic drugs may cease to work in advanced Parkinson's disease and patients tend to become increasingly susceptible to side effects, especially hallucinations. The principle of 'last in first out' should be followed with specialist advice where possible. Drug withdrawal often further worsens motor function which can aggravate difficulties with turning, eating and communicating. Symptom control can sometimes be regained by adding in a dopamine agonist or other adjuncts such as clozapine.

Falls and fractures

The combination of postural instability, freezing of gait and orthostatic hypotension (as a result of autonomic dysfunction as part of the Parkinson's disease process and antiparkinsons drugs) put Parkinson's disease patients at high risk of falling (Calne and Kumar, 2003). Approximately 70% of Parkinson's disease patients fall, 13% weekly (Bunting-Perry, 2006), and this puts them at high risk of fractures, hospitalization and increased mortality. Patients may complain of dizziness or fainting and should be educated about allowing time for blood pressure to equilibrate when changing position. Dopaminergic medication should be taken with food to prevent peak dose effect and doses increased slowly. Occupational and physical therapy assessment can assist with appropriate selection of walking aids, modification of the home environment, muscle strengthening exercises and gait training.

Dysphagia

Patients with Parkinson's disease may develop dysphagia as part of the condition or secondary to co-incident conditions, e.g. gastrooesophageal malignancy. Both scenarios reduce the ability to take dopamine therapy orally and lead to consequent worsening of motor symptoms. Wherever possible, even a small dose of l-dopa should be continued. Tablets can be crushed or formulated to a liquid preparation (Calne and Kumar, 2003). Other possibilities include the use of transdermal rotigotine patches (Christie et al, 2007) or continuous subcutaneous apomorphine infusion (National Collaborating Centre for Chronic Conditions, 2006). Rotigotine is a dopamine receptor agonist acting at D1–3 dopamine receptors and is currently licensed for use as monotherapy in early Parkinson's disease to prevent the development of motor complications or in reducing the frequency of motor fluctuations in advanced Parkinson's disease when used alongside l-dopa. The patches are changed daily (see *Clinical case*).

Speech and swallowing difficulties

Bradykinesia will slow mealtimes and food should be pre-cut if this is acceptable to the patient. Frequent small meals and snacks are often easier to cope with. Adequate hydration is important to minimize constipation, hypotension and drug psychosis and patients should be prompted to drink, with assistance if required (Calne and Kumar, 2003). Dietary modification can also affect the clinical response to l-dopa because neutral amino acids compete with l-dopa for absorption and active transport across the blood–brain barrier. Consequently a diet which distributes protein evenly throughout the day, with medication at least 30 minutes before meals, can

improve motor fluctuations. The advice of an experienced dietician can be helpful in management.

Choking episodes may indicate swallowing difficulties, which may be oral or pharyngeal. Patients can also have reduced tongue movement, reduced laryngeal closure leading to aspiration, ineffective cough, pharyngeal pooling and reduced oesophageal peristalsis (Thomas and MacMahon, 2004b). Anticholinergic drugs or botulinum toxin injections can improve drooling, caused by accumulation of saliva secondary to poor swallow and posture.

Patients require speech and language therapy assessment, with texture modifications, nutritional supplements and the provision of feeding aids such as a one-way valve straw. Some patients may be eligible for gastrostomy feeding, but this has ethical implications and needs discussion with both patient and carer.

Clinical Case

The patient with Parkinson's disease who develops swallowing problems

A 64-year-old woman who had been diagnosed 6 years previously with Parkinson's disease underwent mastectomy, adjuvant radiotherapy and tamoxifen therapy for breast cancer. One year later she developed vomiting and investigations revealed gastric secondaries, with a dilated oesophagus above a thickened and stiffened gastric wall. She was admitted to the local hospice for symptom control as her vomiting meant that she was unable to take her anti-Parkinsonian medication and had consequent poor control of her motor symptoms. At the time of admission she was taking Sinemet (co-careldopa, a mixture of levo-dopa and a peripheral dopa-decarboxylase inhibitor which blocks the peripheral conversion of l-dopa to dopamine, maximizing its central effect and reducing peripheral side effects), Mirapexin (pramipexole, a dopamine receptor agonist) and benzhexol (anti-muscarinic). She was dehydrated and intravenous fluids were commenced with dexamethasone 8 mg subcutaneously to reduce oedema around her gastrointestinal tract and domperidone suppositories to try to treat her nausea (metoclopramide and cyclizine had failed to contol her vomiting and there was concern regarding worsening of her Parkinson's disease with anti-dopaminergic side effects). Vomiting initially improved, but then recurred and so her Parkinson's disease team (neurologist and specialist nurse) was contacted. They suggested the use of dispersible Madopar 100/25 instead of her usual Sinemet preparation, and a rotigotine 2 mg patch, increased by 2 mg per week according to response. They also advocated trying to continue her oral benzhexol for tremor, but suggested that this could be replaced by intravenous biperidin if the oral route became non-viable. Other therapeutic alternatives included the use of selegiline which comes in a melt formulation or a subcutaneous infusion of apomorphine (parenteral dopamine agonist) 50–120 mg via syringe driver either over the waking period or 24 hours (National Collaborating Centre for Chronic Conditions, 2006).

Discussions centred around the possibility of further oncological or interventional treatments, but it was felt that jejunostomy would be unlikely to be helpful in such advanced malignancy. The patient also underwent a barium swallow with a view to placing a gastric stent, but unfortunately this was not technically possible. The patient and her family were fully involved in discussions about her care but were happy that her symptoms were improving after the changes in medication were made and wanted the focus to be on measures to improve comfort. As the patient became weaker and approached the terminal phase, midazolam and glycopyrronium were used in a syringe driver to relieve anxiety and the distress of being unable to swallow secretions. The patient died with her family present 3 weeks after admission.

Dysphonia (a weak, quiet voice with loss of modulation) further impairs communication and social interaction. Speech therapy can help, but the amount of effort involved in engagement with exercises can be an extra burden.

Constipation

Gastrointestinal motility is impaired by Parkinson's disease, worsened by some medications and exacerbated by poor oral intake and immobility. Dietary modification, increasing fluid intake, encouraging mobilization and effective toileting should be encouraged before prescribing oral laxatives.

Bladder dysfunction

Autonomic dysfunction often leads to urinary frequency and urgency, nocturia, dribbling and incontinence. However, anticholinergic drugs can also precipitate urinary retention. Patients should be specifically asked about urinary symptoms and educated in the use of toileting schedules, pads and fluid intake. Consideration can also be given to the use of a urinary sheath or catheter if the problem is significant. Drugs to treat neurogenic bladder such as oxybutynin can be efficacious but may worsen confusion or mental state.

Pain

Pain occurs in up to 50% of Parkinson's disease patients and can have many origins (Thomas and MacMahon, 2004b) (*Table 1*). Careful adjustment of anti-parkinsonian medication is often all that is required, but simple analgesics for musculoskeletal pain and adjuvants such as gabapentin for neuropathic pain can be considered after careful evaluation of a pain history.

Pressure ulcers

These may occur in sites other than the usual bony prominences as a result of the altered body position in Parkinson's disease. Carers need to be trained about risk factors and moving and handling techniques.

Maintaining physical activity can help to prevent contractures and pain as a result of immobility. Active or

Table 1. Causes of pain in Parkinson's disease

Musculoskeletal: stiffness as a result of bradykinesia
Dystonic: cramps or spasm secondary to muscle rigidity
Related to positioning and immobility
Skin pressure areas
Dyskinetic pain (often the consequence of medication wearing off with typically early morning dystonia and pain)
Radicular (with neuropathic features)
Akasthisia (restlessness, linked to poor sleep)
Other underlying disorders, e.g. osteoarthritis
Psychological

passive movements in bed-bound patients, breathing exercises and frequent position changes can help to prevent contractures, hypostatic pneumonia and pressure ulcers respectively.

Sleep disturbance

Vivid dreams and nocturnal vocalizations can be improved by reducing the bedtime dose of l-dopa. Conversely, sleep fragmentation is often a reflection of nocturnal dystonia and cramping and can be improved by giving a dopamine agonist at bedtime. Daytime sleepiness results from disturbed sleep–wake cycles, as well as medication (particularly dopamine agonists), and can be improved by night sedation. Patients can also experience restless leg syndrome and sleep apnoea which should be investigated and appropriate management instituted.

Dementia

Subcortical dementia affects up to 80% of patients with Parkinson's disease and is related to severity of Parkinson's disease and age. Wandering, agitation, aggression and sexual disinhibition can all be features and can be difficult for families to cope with, often precipitating nursing home placement. Psychiatric adverse reactions to anti-Parkinsonian drugs are much more likely to occur in patients with dementia.

Depression

Low mood is common, affecting 40–60% of patients with Parkinson's disease, although it is unclear whether this is caused by the disease process or a psychological response to the illness. Depletion of central serotonin in addition to dopamine provides a neurochemical model for depression in Parkinson's disease. It can be difficult to distinguish symptoms of depression from the motor symptoms of Parkinson's disease so it should be specifically asked for and a psychiatric assessment obtained if uncertainty persists. Treating depression can help compliance with medication and ameliorate other non-motor symptoms. Treatment should be with serotonin-specific reuptake inhibitors or tricyclic antidepressants, although patients with Parkinson's disease are often more susceptible to anticholinergic side effects. Transitory low mood can be linked to the off state and improves with return of motor function.

The Parkinson's Disease Society provides a variety of information sheets covering many of the problems described (www.parkinsons.org.uk/advice/publications/information_sheets.aspx).

Complex symptom management issues in Parkinson's disease

Many of the drugs used to treat nausea, vomiting, hiccups and psychosis have antidopaminergic actions and are best avoided in patients with Parkinson's disease in order to avoid worsening motor functioning. Lertxundi et al (2008) carried out a systematic literature review of antidopaminergic therapies in patients with Parkinson's disease who have developed these symptoms and made recommendations regarding treatment.

Nausea and vomiting

This is often multifactorial in patients with Parkinson's disease. In addition to central neuronal loss, the pathological processes involved in Parkinson's disease result in gastroparesis as a result of loss of dopaminergic neurons in the myenteric plexus of the gastrointestinal tract. Optimizing dopamine replacement may therefore improve gastroparesis and hence nausea. However, nausea is also a common adverse effect of l-dopa and dopamine agonists and is best treated using a peripherally acting dopamine antagonist so that the central effects of l-dopa are preserved. Domperidone 10–20 mg four times daily is an antagonist at D2 receptors in the chemoreceptor trigger zone outside the blood–brain barrier (Barone, 1999) and is consequently a good anti-emetic choice in this context, although aggravation of parkinsonism cannot be completely ruled out. Because domperidone stimulates the gastrointestinal tract, it should be avoided in patients with gastrointestinal haemorrhage, mechanical obstruction or perforation.

A possible alternative to domperidone would be cyclizine 50 mg three times daily which has a central antihistaminergic action at the vomiting centre, fully within the blood–brain barrier (Twycross and Wilcock, 2002). However, the antimuscarinic side effects of this drug may be limiting in the elderly population typically suffering with Parkinson's disease, particularly confusion and psychosis. As it is an old drug, it is not certain that there is no antidopaminergic effect and careful patient monitoring is required.

Serotonin type 3 receptor (5-HT3) antagonists are useful drugs for treating emesis associated with chemotherapy and would theoretically be safe to use in patients with Parkinson's disease, although there is no evidence to corroborate their use. However, 5-HT3 antagonists are fairly specific in treating nausea and vomiting attributable to chemotherapy, damage to gut mucosa during radiotherapy or distension and their use outside of this context is less well evidenced (Twycross et al, 2007).

Hiccups

Hiccups can result from dopaminergic therapies or possibly from the Parkinson's disease itself as part of a broader gastroparesis (Wilcox et al, 2009). There is very little evidence to guide treatment but baclofen 5–20 mg three times daily is safe to use in a Parkinson's disease patient and is probably the treatment of choice (Ramirez and Graham, 1992).

Neuropsychiatric disorders

Psychotic symptoms are relatively common in patients with Parkinson's disease and are thought to reflect a side effect of dopaminergic medications as they are rarely seen

in untreated patients. Hallucinations are often visual and may involve 'delusions of presence', i.e. feeling as though someone or something is with you without actually seeing them. They are best dealt with by acknowledging that they seem very real rather than by denying them (Thomas and MacMahon, 2004b). Distraction can also help if the patient is distressed. Many patients are embarrassed or may fear they are going mad, so directly asking about hallucinations and discussing how common they are can be reassuring. Treatment should be directed at stopping anticholinergic medications and where possible considering dose reduction of dopamine agonists and l-dopa. Atypical antipsychotics, e.g. clozapine 6.25–50 mg/day, are more selective for D3–5 dopaminergic receptors and show promise in controlling parkinsonian symptoms without worsening parkinsonism (Lertxundi et al, 2008).

Ethical issues in Parkinson's disease

End-of-life decisions such as 'do not resuscitate orders', advance directives, mental capacity issues and life-prolonging treatments such as percutaneous endoscopic gastrostomy feeding are all issues that may arise in patients with Parkinson's disease. They should be raised at the appropriate time by the hospital or primary care teams, with support from specialist palliative care if required. Common dilemmas often focus around withholding or withdrawing treatments, such as antibiotic prescription for a chest infection or artificial hydration when swallowing is no longer adequate.

Advanced care planning

This should begin at diagnosis and continue throughout the course of the disease, facilitating patient autonomy in the face of chronic progressive disease (Bunting-Perry, 2006). The process is collaborative, incorporating the patient's wishes and creating contingency plans to achieve the established goals. Patients may wish to consider making an advanced decision to refuse treatment. The NHS website www.adrtnhs.co.uk gives advice on how to do this. An alternative would be to use the preferred priorities for care tool, a Department of Health document designed to facilitate discussion of key end-of-life issues, which is kept by the patient as a reference for care-givers (www.endoflifecareforadults.nhs.uk/eolc/ppc.htm). Parkinson's disease patients could also be included on the supportive care register as part of primary care's Gold Standards Framework (www.goldstandardsframework.nhs.uk).

KEY POINTS

- Many of the symptoms and problems experienced by patients with Parkinson's disease are similar to those experienced by patients with advanced cancer.
- Patients and their carers can benefit from symptom control advice in addition to the psychological and emotional support provided by palliative care services.
- Joint working between primary and secondary care and palliative care services will provide the best outcome for patients.

Bereavement support

Many caregivers have provided years of physical and emotional support to the patient with Parkinson's disease, often leading to their own social isolation so that they have few support systems to assist them through bereavement. Caregivers need support in redefining their roles and re-organizing their life; referral to a bereavement service may be needed.

Conclusions

A palliative approach is needed for the myriad problems suffered by patients and their families throughout the course of Parkinson's disease. Joint working between primary and secondary care and specialist palliative care services, with clearly defined roles to prevent duplication, appears to be the way forward. The challenge for specialist palliative care will be in identifying when to accept a referral and defining the need for specialist input to prevent existing services becoming overwhelmed. **BJHM**

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Barone JA (1999) Domperidone: a peripherally acting dopamine 2 receptor antagonist. *Ann Pharmacother* **33:** 429–44

Bunting-Perry LK (2006) Palliative care in Parkinson's disease: implications for neuroscience nursing. *J Neurosci Nurs* **38**(2): 106–13

Calne SM, Kumar S (2003) Nursing care of patients with late stage Parkinson's disease. *J Neurosci Nurs* **35**(5): 242–51

Christie J, Bentley J, Magesh R (2007) The use of transdermal rotigotine in a patient with advanced Parkinson's disease and dysphagia. *Palliat Med* **21:** 163–4

De Lau LM, Breteler MM (2006) Epidemiology of Parkinson's disease. *Lancet Neurol* **5:** 525–35

Goy ER, Carter JH, Ganzini L (2007) Parkinson's disease at the end of life: caregiver perspectives. *Neurology* **69**(6): 611–12

Goy ER, Carter JH, Ganzini L (2008) Needs and experiences of caregivers for family members. *J Palliat Care* **24**(2): 69–75

Hoehn MM, Yahr MD (1967) Parkinsonism: Onset, progression and mortality. *Neurology* **17:** 427–41

Hudson PJ, Toye C, Kristjanson LJ (2006) Would people with Parkinson's disease benefit from palliative care? *Palliat Med* **20:** 87–94

Kristjanson LJ, Aoun SM, Oldham L (2005) Palliative care and support for people with neurodegenerative conditions and their carers. *Int J Palliat Nurs* **12**(8): 368–77

Lertxundi U, Peral J, Mora O, Domingo-Echabura S, Martinez-Bengoechea MJ, Garcia-Mongo JC (2008) Antidopaminergic therapy for managing comorbidities in patients with Parkinson's disease. *Am J Health-Syst Pharm* **65:** 414–19

MacMahon DG, Thomas S (1998) Practical approach to quality of life in Parkinson's disease. *J Neurol* **245**(suppl 1): S19–22

National Collaborating Centre for Chronic Conditions (2006) Parkinson's disease: national clinical guideline for diagnosis and management in primary and secondary care. Royal College of Physicians, London (www.nice.org.uk/nicemedia/pdf/cg035fullguideline.pdf accessed 23 November 2009)

Ramirez FC, Graham DY (1992) Treatment of intractable hiccup with baclofen: results of a double-blind randomized controlled cross-over study. *Am J Gastroenterol* **87:** 1789–91

Thomas S, MacMahon D (2004a) Parkinson's disease, palliative care and older people: part 1. *Nurs Older People* **16**(1): 22–6

Thomas S, MacMahon D (2004b) Parkinson's disease, palliative care and older people: part 2. *Nurs Older People* **16**(2): 22–8

Twycross R, Wilcock A (2002) *Symptom Management in Advanced Cancer.* 4th edn. Radcliffe Medical Press, Oxon

Twycross R, Wilcock A, Charlesworth S, Dickman A (2007) *Palliative Care Formulary.* 3rd edn. Radcliffe Medical Press, Oxon

Waters C (1997) Managing the late complications of Parkinson's disease. *Neurology* **49**(suppl): S49–57

Wilcox S, Garry A, Johnson M (2009) A novel use of amantadine: to treat hiccups. *J Pain Symptom Manage* **38**(3): 460–5