Management of levodopa for residents with Parkinson’s disease

Date of submission: 5 May 2016; date of acceptance: 17 August 2016. doi: 10.7748/nop.2016.e833

Abstract
This article discusses the management of levodopa for older people who have Parkinson’s disease and live in nursing homes. It provides a detailed description of the diagnostic criteria and motor and non-motor clinical features. Against this clinical picture, the benefits and challenges of levodopa management are considered. A person-centred approach is championed, as it supports collaborative clinical assessment and decision making between nurses and residents.

To appreciate why a person-centred approach is important for safe and effective medication practice, the pharmacological basis of levodopa management is explained. An empowerment approach to medication management is advocated that facilitates self-medication by residents. To this end, the importance of continuing professional development for nursing home staff is discussed.

Keywords
levodopa, medication management, nursing homes, older people, Parkinson’s disease, person-centred care

PARKINSON’S DISEASE (PD) is one of the most common chronic degenerative conditions of the nervous system in Western Europe. Globally, an estimated 10 million people are living with PD (PD Foundation 2016). Under-recognition of cases is widely acknowledged because of difficulties diagnosing Parkinsonism (Weerkamp et al 2014). Studies in north east Scotland (Caslake et al 2013) and north east England (Duncan et al 2014) report an annual incidence of 17.9 and 15.9 per 100,000 people respectively.

Across the UK, the prevalence rate is reported to be 27.4 per 10,000 (Parkinson’s UK 2009), with no major geographical variations in England and Wales (Wickremaratchi et al 2009). With increasing longevity, it is expected that prevalence rates will rise. By 2020, Parkinson’s UK (2009) forecasts a 26.7% increase over its 2009 prevalence figures.

There is a marked difference in prevalence between women at 24.1 per 10,000, and men at 30.9 per 10,000 (Parkinson’s UK 2009). Risk is far greater in people over the age of 60 (Mao et al 2013), with the highest prevalence among those over 80 (Horsfall et al 2013). Onset can be early in life during the forties and fifties (Wickremaratchi et al 2009).

Despite the possible negative effect on carers’ health and well-being and the complex care required, most people with PD in the UK continue to live at home, cared for by their partner and receive varied formal support. With disease progression their support needs increase in areas such as symptom management, lifestyle adjustment, relationship change and planning for the future (Lageman et al 2015).

The annual economic effect of PD in the UK is estimated at £3.3 billion. This includes the direct costs of hospital admission and nursing home care associated with progressive disability and comorbidity (Findley 2007). Of all people with PD, 55% die in hospital and 36% die in institutional care (Porter et al 2010).

It is not known how many people affected by PD live in nursing homes in the UK, but Porter et al (2010) report the figure as 1.6%. The strongest predictors of admission to nursing home care include old age, hallucinations, dementia, physical dependence and a high falls rate (Buchanan et al 2002).

Other risk factors include living alone, impaired ability to engage in activities of daily living (ADL) and depression (Makoutonina et al 2010). This information is important to inform the clinical management of people with PD and to anticipate carers’ support needs so that people can stay at home as long as possible.
Causes
PD is caused by an imbalance between two neurotransmitters, dopamine and acetylcholine, which communicate with voluntary muscle cells to produce smooth movement. Dopamine is produced in the largest basal ganglia structure of the brain, the corpus striatum, comprising the caudate and lentiform nuclei (Figure 1).

The basal ganglia structures lie deep in the brain and control autonomic movements of skeletal muscle (Tortora and Grabowski 2003). The action of dopamine on muscle is inhibitory while that of acetylcholine is excitatory. In PD, dopamine levels are reduced, resulting in a loss of inhibitory influences on the excitatory mechanisms of acetylcholine. This produces the disordered movement of increased cholinergic activity, which is characteristic of the disease (Davie 2008).

Dopamine is not used to treat PD because it cannot cross the blood-brain barrier. Its amino-acid precursor, levodopa, can cross the blood-brain barrier and is used to replenish depleted dopamine in the brain (British National Formulary (BNF) 2016).

Diagnostic criteria
Accurate diagnosis is the starting point for optimal management of people with PD (Weerkamp et al 2014). Therefore, people with suspected PD should be referred for specialist diagnosis quickly, without treatment (National Institute for Health and Care Excellence (NICE) 2015a). This is because PD is difficult to diagnose, as there are no specific markers to identify its onset.

Cardinal diagnostic criteria are motor symptoms. They include bradykinesia and at least one clinical feature, from rigidity, tremor and postural instability (Table 1) (BMJ Best Practice 2016). Non-motor symptoms encompass multiple body systems and can affect quality of life (Table 1) (NICE 2015b). Combined with motor symptoms they can increase residents’ need for assistance with a range of ADL (NICE 2015c).

Levodopa
Levodopa is a dopaminergic drug used to stimulate dopamine production and control cholinergic excitation due to unopposed acetylcholine (Greenstein and Gould 2009).

To maintain good function and minimise motor complications, the dose of levodopa should be as low as possible (NICE 2015c). It is generally combined with a dopa-decarboxylase inhibitor, carbidopa (in co-careldopa) or benserazide (in co-beneldopa) (BNF 2016). Dopa decarboxylase is an enzyme that inhibits the metabolism of levodopa to dopamine allowing a greater percentage of levodopa to cross the blood-brain barrier. This achieves effective therapeutic dopamine concentrations in the brain. When used in combination with a dopa-decarboxylase inhibitor, levodopa is well tolerated in older or frail people, those with severe symptoms and those who have comorbidities (Reichmann 2016). However, it should be used with caution in residents who have a history of convulsions, severe pulmonary or cardiovascular disease, peptic ulcer, psychiatric illness, renal or hepatic impairment and endocrine disorders such as diabetes mellitus and osteomalacia (BNF 2016).

Knowledge of medication side effects is essential. Levodopa has complex side effects that require careful monitoring, allowing timely adjustment of medication to minimise the effect on quality of life (Box 1) (Chan et al 2008). Impulsive control disorder is reported in approximately 15-20% of people affected by PD (Weintraub et al 2010). It is commonly expressed in behaviours such as uncontrollable shopping, gambling, eating, sex and hobbies (Weiss and Marsh 2012).

Management of hallucinations and illusions is challenging, particularly when residents have dementia. Although these symptoms

![Figure 1. Frontal section of the basal ganglia nuclei](Adapted from Lecturio 2016)
may result from levodopa treatment, it is necessary to rule out causes such as delirium, pulmonary or urinary tract infections (Rabey 2009). In nursing home settings nurses should discuss these issues with the resident’s GP or consultant as soon as possible.

Side effects of levodopa also include abnormal involuntary movements (dyskinesias) that manifest as ‘chorea’ or ‘dystonic’ symptoms. Chorea symptoms range from fidgeting movements to uncontrolled movement of the arms and legs. Dystonic symptoms include sustained painful muscle contractions affecting the neck, trunk and limbs (Vernon 2009).

Dyskinesias can occur when levodopa and dopamine reach maximum dose concentrations in the brain, termed peak-dose dyskinesias.

When the dose of levodopa in the brain is very low, dystonia can occur (Calabresi et al 2010).

Although there is no recognised first-choice medication for PD (NICE 2015c), no other currently available pharmacological interventions demonstrate superior clinical benefits to levodopa (Mao et al 2013). It remains the preferred drug to control motor symptoms, particularly in people with advanced disease (Poewe et al 2010) and is the drug that physicians have most clinical experience in prescribing (Schapira et al 2009). If carefully managed, it can contribute to improved quality of life, but it does not slow, or prevent, disease progression. For these reasons it is likely that levodopa will be one of the main drugs administered in nursing home settings.

**Pharmacokinetic aspects of levodopa**

Pharmacokinetics studies the body’s influence on a drug over time during the processes of absorption, distribution, metabolism and excretion. Absorption refers to the movement of a drug from the site of administration to the bloodstream. Distribution refers to the movement of a drug from the bloodstream to the tissues. Metabolism refers to the chemical conversion of a drug into inactive metabolites. Excretion refers to the removal of a drug or its metabolites from the body.

### TABLE 1. Clinical features of Parkinson’s disease

<table>
<thead>
<tr>
<th>Motor symptoms</th>
<th>Non-motor symptoms</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor (involuntary shaking and trembling)</td>
<td>Cognitive impairment</td>
<td></td>
</tr>
<tr>
<td>Bradykinesia (slowness in movement)</td>
<td>Bradyphrenia (slowness of thought)</td>
<td></td>
</tr>
<tr>
<td>Rigidity</td>
<td>Tip-of-the-tongue phenomenon (word finding)</td>
<td></td>
</tr>
<tr>
<td>Postural instability (loss of postural reflexes)</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Hypomimia (loss of facial expression, mask-like face)</td>
<td>Apathy</td>
<td></td>
</tr>
<tr>
<td>Dysarthria</td>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Sialorrhoea (drooling)</td>
<td>Anhedonia (symptom of major depressive disorders. Loss of interest in previously rewarding enjoyable activities)</td>
<td></td>
</tr>
<tr>
<td>Decreased arm swing</td>
<td>Other behavioural /psychiatric issues</td>
<td></td>
</tr>
<tr>
<td>Shuffling gait</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Festination (gait of quickening and shortening steps)</td>
<td>Anosmia (loss of sense of smell)</td>
<td></td>
</tr>
<tr>
<td>Difficulty rising from chair or turning in bed</td>
<td>Ageusia (loss of taste functions of the tongue)</td>
<td></td>
</tr>
<tr>
<td>Micrographia (small cramped hand writing)</td>
<td>Pain (shoulder, back)</td>
<td></td>
</tr>
<tr>
<td>Difficulty in cutting food</td>
<td>Other behavioural /psychiatric issues</td>
<td></td>
</tr>
<tr>
<td>Difficulty in eating</td>
<td>Sleep disorders: rapid eye movement behaviour disorder, vivid dreams, daytime drowsiness, sleep fragmentation and restless legs syndrome</td>
<td></td>
</tr>
<tr>
<td>Difficulty maintaining hygiene</td>
<td>Sleep disorders: sleep disorders, rapid eye movement behaviour disorder, vivid dreams, daytime drowsiness, sleep fragmentation and restless legs syndrome</td>
<td></td>
</tr>
<tr>
<td>Slow activities of daily living</td>
<td>Sleep disorders: sleep disorders, rapid eye movement behaviour disorder, vivid dreams, daytime drowsiness, sleep fragmentation and restless legs syndrome</td>
<td></td>
</tr>
</tbody>
</table>

(Adapted from Jankovic 2008)
absorption, distribution, metabolism and excretion (Young 2008). This knowledge enables nurses to understand factors that influence maintenance of effective therapeutic brain-dopamine concentrations using levodopa. PD can also fluctuate from day to day even when the same dose of levodopa is administered at the right time (Parkinson’s UK 2013). Factors known to influence the pharmacokinetics of levodopa include sex and advanced age, low body weight, slowed gastric emptying and food such as fat or protein (Barichella et al 2016). Good medication management can positively or adversely influence some of these factors.

Rate of gastric emptying is described as ‘key’ to levodopa absorption (Crevoisier et al 2003). Meals provided before or concurrent with levodopa administration can delay its delivery to intestinal absorption sites. This will delay and reduce its availability to the body, termed bioavailability. Suboptimal ingestion of levodopa due to slowed gastric emptying, missed doses or irregular administration of drugs can contribute to disabling motor fluctuations and increases in non-motor symptoms, particularly as disease progresses (Magennis 2011). Levodopa should be administered at least 30 minutes before residents eat protein to prevent interference with its absorption (Parkinson’s UK 2013). A full stomach also delays drug absorption (Crevoisier et al 2003). Because protein and levodopa compete for transport across the intestinal wall and the blood-brain barrier, possible motor fluctuations after meals can be minimised by redistribution of protein intake over the course of the day (Barichella et al 2006).

Absorption of levodopa is erratic, achieving variable bioavailability even when controlled-release levodopa is used (Brooks 2008). With immediate-release levodopa, motor improvement occurs 30-90 minutes after administration. Controlled-release formulations maintain levodopa levels for longer periods, but their slower absorption increases motor improvement latency the period of time after taking a drug to its pharmacological effect (Olanow et al 2009).

**BOX 1. Side effects of levodopa**

- Alteration of libido
- Drowsiness
- Dry mouth
- Hallucinations, illusions
- Impulsive control disorder
- Mood change, depression
- Nausea and/or vomiting
- Postural hypotension
- Taste disturbances, anorexia

(Chan et al 2008)

**Figure 2. Levodopa end-of-dose ‘wearing off’**

A Typical Day

Wearing-off period

(Adapted from European Parkinson’s Disease Association 2016)

**BOX 2. Side effects of catechol-O-methyltransferase inhibitors**

- Abdominal pain, constipation, diarrhoea
- Confusion, hallucinations
- Dizziness
- Dry mouth
- Dyskinesias
- Fatigue, insomnia
- Hepatotoxicity (tolcapone)
- Nausea and/or vomiting
- Reddish brown discoloration of the urine
- Sweating

(British National Formulary 2016)

**BOX 3. Side effects of monoamine-oxidase-B inhibitors**

- Bradycardia
- Confusion
- Constipation, diarrhoea
- Depression
- Dizziness, impaired balance
- Dry mouth, stomatitis, mouth ulcers
- Fatigue
- Hair loss
- Headache
- Hypertension, hypotension
- Movement disorders, myalgia
- Nasal congestion
- Nausea
- Sweating

(British National Formulary 2016)
On this basis, controlled-release and immediate-release formulations can be administered as a morning dose, and these medications can help to maintain optimal control of motor response fluctuations (Poewe et al 2010).

Pharmacokinetic knowledge enables nurses working in long-term settings to produce person-centred care plans that support safe and effective medication management. For example, by documenting residents’ specific drug administration requirements in relation to their meals.

**Pharmacodynamic aspects of levodopa**

Pharmacodynamics is the study of how drugs act on the body (Greenstein and Gould 2009). With disease progression and long-term use, the capacity of levodopa to treat the motor symptoms of PD decreases. This is because it takes less time for levodopa medication in the body to be reduced by 50%, referred to as the drug’s half-life. Because the half-life of levodopa is shortened, the period of time for which it produces an effect is correspondingly reduced (Chan et al 2005a, 2005b). When this happens residents experience fluctuations from ‘on’ periods, when they experience motor benefit, to ‘off’ periods, when they no longer benefit from the drug (Figure 2) (Contin and Martinelli 2010, Mao et al 2013).

Adding catechol-O-methyltransferase (COMT) inhibitors (entacapone or tolcapone) to levodopa can improve fluctuating motor responses by increasing ‘on’ periods and decreasing ‘off’ periods (Stocchi and De Pandis 2006, Leegwater-Kim and Waters 2007). COMT inhibitors increase the half-life of levodopa by blocking its breakdown into dopamine before it crosses the blood-brain barrier. This is important because dopamine cannot cross the blood-brain barrier. By allowing more levodopa to reach the brain, COMT inhibitors can reduce ‘off’ periods (Vernon 2009). They have wide-ranging side effects that require careful monitoring by nurses (Box 2) (BNF 2016).

Tolcapone should only be prescribed under specialist supervision due to the risk of hepatotoxicity (BNF 2016). Monitoring liver function is therefore important and this should be clearly communicated by nurses in residents’ person-centred care plans (Grandas and Hernández 2007, Mizuno et al 2007).

Monoamine-oxidase-B (MAOB) inhibitors (selegiline and rasagiline) are licensed to use alone or in combination with levodopa to treat ‘off’ periods in PD (BNF 2016). They block the action of MAOB, an enzyme that breaks down levodopa in the brain. In this way MAOB inhibitors prolong the action of levodopa thereby supporting prescription of smaller levodopa doses (Greenstein and Gould 2009). Nurses need to monitor for their wide-ranging side effects (Box 3) (BNF 2016).

Selegiline combined with levodopa should be avoided or used with caution in residents who have postural hypotension. Its abrupt withdrawal must be avoided (BNF 2016).

Application of pharmacodynamic knowledge to person-centred monitoring and assessment enables nurses to identify specific observations they should make for each resident. For example, documentation of the need to monitor resident response and end-of-dose ‘off’ periods.

**Safe management of levodopa**

Registered nurses have a responsibility to ensure safe and reliable administration of medication, and to monitor for side effects (Nursing and Midwifery Council (NMC) 2007). Combining levodopa with decarboxylase inhibitors enables use of lower levodopa doses, which helps to limit side effects.

The therapeutic success of this combination is reflected in the rare reporting of side effects as being dose-limiting (BNF 2016). However, when combined with the exact titration requirements of levodopa medications, the possibility of adverse interactions is increased (Williams et al 2008).

Nursing documentation should reflect person-centred care from the beginning to the end of a resident’s stay (Jeffries et al 2010). It is a fundamental practice approach expected of nurses working with older people (NMC 2015) and views nurses and residents as partners in clinical decision making.

Before admission to the nursing home a comprehensive pre-admission assessment should be conducted incorporating a detailed medication history. McCormack and McCance (2006) suggest a biographical approach as this captures the person’s values, beliefs and preferences and ‘fosters a connectedness between the patient and the caregiver’ (Broderick and Coffey 2013). Thus, medication management should aim to ‘empower people with PD to participate in judgements and choices about their own care’ (NICE 2015d).

Evidence shows that incomplete or incorrect documentation, such as omission of allergy status, places residents at risk (National Patient Safety Agency 2007).
The importance of pharmacological control through administration of levodopa medication at the ‘right time’ (Parkinson’s UK 2016a, 2016b) cannot be understated. It is critical to the maintenance of uniform stimulation of the brain’s dopamine receptors so that motor symptoms are controlled.

Getting medication on time helps to maximise residents’ independence, well-being and quality of life. Whether administration is by nurses or residents, care plans should detail medication times especially if they lie outside the usual drug round times.

Medication administration requirements at mealtimes should be documented (Parkinson’s UK 2013) so that residents are protected from increased motor and non-motor symptoms due to suboptimal ingestion of levodopa (Magennis 2011). Care planning should identify any specific medication-related observations that the nurse should monitor. For levodopa, the response and end-of-dose wearing off should be noted. Revision of medication to improve residents’ motor function can produce changes in their daily energy expenditure resulting in weight loss or gain. Routine assessment of residents’ nutritional status can detect if their diet provides sufficient energy intake and ensure early identification of weight loss (Cereda et al 2010).

Medication concordance

The term ‘concordance’ embraces a consensual, person-centred approach to medication management and a consultative non-judgemental partnership between resident and nurse. In contrast the term ‘compliance’ indicates judgemental professionals and reinforces the notion of passive residents (Haynes et al 2002).

References


NICE (2015c) advises that choice of treatment should consider residents’ presenting clinical features and lifestyle. It also states that residents’ medication preferences should only be determined after the short and long-term benefits and drawbacks of their medication choices have been explained.

Medication concordance is important. It can slow disease progression, prevent complications, help achieve optimal wellbeing and improve quality of life (Williams et al 2008). ‘Suboptimal compliance’ is significant if less than 80% of medication is taken in prescribed doses and intervals. Increasing complexity of the medication regimen is strongly correlated with suboptimal compliance (Malek and Grosset 2015). Levodopa has a short plasma half-life and therefore requires multiple daily doses that can produce marked swings of therapeutic effect.

The debilitating effect of resulting motor fluctuations can lead to concordance issues. Development of individualised, simple, person-centred treatment plans can improve concordance, while complex regimens may be viewed as a burden (Fargel et al 2007).

Sensitive discussion of medication regimens with residents can help to encourage their concordance. Nurses need to spend time with residents who have depression and dementia to facilitate medication concordance (Daley et al 2012). Residents’ dignity can be maintained if nurses see their role in medication administration as acting ‘on behalf of the resident rather than to the resident’ (Centre for Policy on Ageing 2011).

Education and support

The Third World Parkinson Congress (World Parkinson Coalition 2016) championed the empowerment of people living with PD to be involved in their care. The disease is challenging because it is often characterised by changes in symptoms from one moment to the next, as in on/off syndrome, and this can result in loss of confidence and independence (Mao et al 2013). Self-help education programmes develop self-regulation skills through activities that include stress management, dealing with depression or anxiety and maintaining social competence (Macht et al 2007; A’Campo et al 2010).

Healthcare professionals who lack neurological expertise are likely to contribute to poor clinical outcomes for people who have PD (Royal College of Physicians 2011). Universal access to the expertise of PD nurse specialists by nursing home staff, residents and their families would help to address this issue, and NICE (2015d) recommends this.
Arrangement for advice, clinical monitoring and medication adjustment. Nurse specialists have been shown to relieve the negative effect of PD on the daily lives of individuals and families (Royal College of Nursing 2010, Hellqvist and Bertero 2015).

A survey of people with PD admitted to hospital, who were not self-medicating, found nearly 33% did not get their medication on time every time and 25% thought this prolonged their stay (Parkinson’s Disease Society 2008). It is vital for nurses working in long-term care to receive training on medication management specific to PD. Free resources and online courses are available for nursing home staff (Parkinson’s UK 2016c, 2016d), including a ‘Get It On Time’ training DVD (Parkinson’s UK 2016a, 2016b). This patient testimony captures the positive effect that nurse training can have: ‘Thanks to the Get It On Time campaign, staff at my local hospital now understand that I need my medication on time’ (Parkinson’s UK 2011).

Conclusion

This article has explored the pharmacokinetic and pharmacodynamic aspects of levodopa, because this knowledge underpins safe and effective person-centred medication management in nursing homes.

Discussion

Safe medication management and concordance reveal the substantial daily challenges faced by nurses caring for residents who have PD. Medication administration at the ‘right time’ is crucial to residents’ health and well-being.

Future practice should continue to develop a person-centred approach to medication management that is embedded in excellent care planning. Wherever possible, it should support residents to self-medicate.

Management of medication for residents with long-term conditions is a key nursing role in nursing homes. Ongoing professional development and updating in pharmacology and medication management relevant to residents’ conditions can equip nurses to maintain the independence of residents and enhance their quality of life.

Implications for practice

» Administration of levodopa at the ‘right time’ is crucial.

» Care home nurses can access online and face-to-face education and training offered by Parkinson’s UK, see useful resources.

» Approaches to medication management should strive to be person centred.

References


Parkinson’s UK (2016a) Get It On Time Resources. www.parkinsons.org.uk/content/get-it-time-resources (Last accessed: 5 October 2016.)


Parkinson’s UK (2016c) Carmina’s Story: Living with Advanced Parkinson’s. www.parkinsons.org.uk/content/carmina-story-keeping-advanced-parkinsons (Last accessed: 6 October 2016.)

Parkinson’s UK (2016d) Resources for Professionals. www.parkinsons.org.uk/professionals/resources-professionals (Last accessed: 5 October 2016.)


