Medical and surgical care for patients with Parkinson's disease

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. It has a prevalence of 0.3% of the general population and 1.6% of people over 65 years of age (de Rijk et al, 1997). Parkinson's disease is a complex, multi-system neurodegenerative disorder (*Figure 1*) which has motor and non-motor features (*Table 1*).

Patients with Parkinson's disease are 1.5–2.6 times more likely to be admitted to hospital than age-matched controls (Martignoni et al, 2004). Patients with Parkinson's disease suffer particular challenges when they are admitted to hospital. Intercurrent illness and/or minor disruptions to the usual medication regimen of a patient with Parkinson's disease can causes an acute deterioration in motor and non-motor symptoms, hindering recovery from the presenting illness and thwarting rehabilitation (Lubomski et al, 2015). Several studies have demonstrated that patients with Parkinson's disease have longer length of stay in hospital (2–14 days) than controls (Gerlach et al, 2011). This article gives clinicians a brief guide to assessing patients with Parkinson's disease admitted to hospital and how to optimize their care.

Managing Parkinson's disease medications in hospital

Medication concordance is fundamental to managing Parkinson's disease. Maintaining a patient's usual medication regimen in hospital is essential. Missed doses can result in a drastic decline in mobility, speech and swallowing, leading to falls, aspiration and inability to administer oral medication. There are even reports of neuroleptic malignant-like syndrome being triggered by withdrawal of dopaminergic medications (Keyser and Rodnitzky, 1991).

Lack of familiarity with Parkinson's disease medications is a common cause of prescribing errors. The many different formulations of Parkinson's disease medications cause confusion. The following section gives a brief summary of each class of medication used to treat patients with Parkinson's disease, and when, why and how these medications are prescribed. *Figure 2* shows the mechanisms of action of these medications.

Medications for Parkinson's disease should only be initiated and titrated by specialists. There are no established disease-modifying or neuroprotective agents in Parkinson's disease.

Levodopa

Levodopa provides more effective motor control than any other agent and remains the mainstay of management for people with Parkinson's disease. Levodopa is usually paired with benserazide or carbidopa to prevent its peripheral breakdown, thus allowing a greater concentration of levodopa to cross

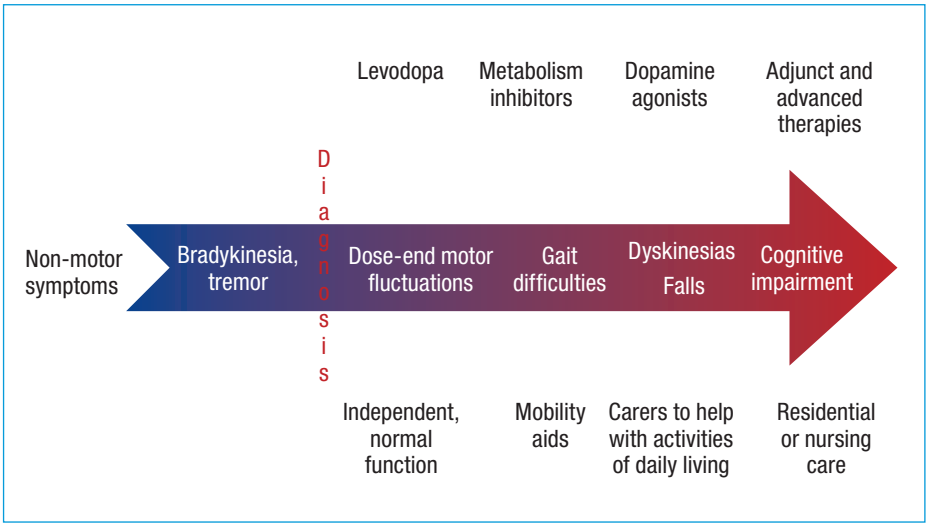

Figure 1. Progression of Parkinson's disease.

Table 1. Motor and non-motor features of Parkinson's disease

Motor features	Bradykinesia
	Rigidity
	Postural instability
	Tremor
Non-motor features	Constipation
	Urinary urgency
	Low mood
	Anxiety
	Hypotension
	Daytime somnolence
	Insomnia
	Vivid dreams
	REM-sleep behaviour disorder (acting out dreams)
	Hallucinations
	Psychosis
	Delirium
	Dysarthria
	Dysphagia (difficulty swallowing)

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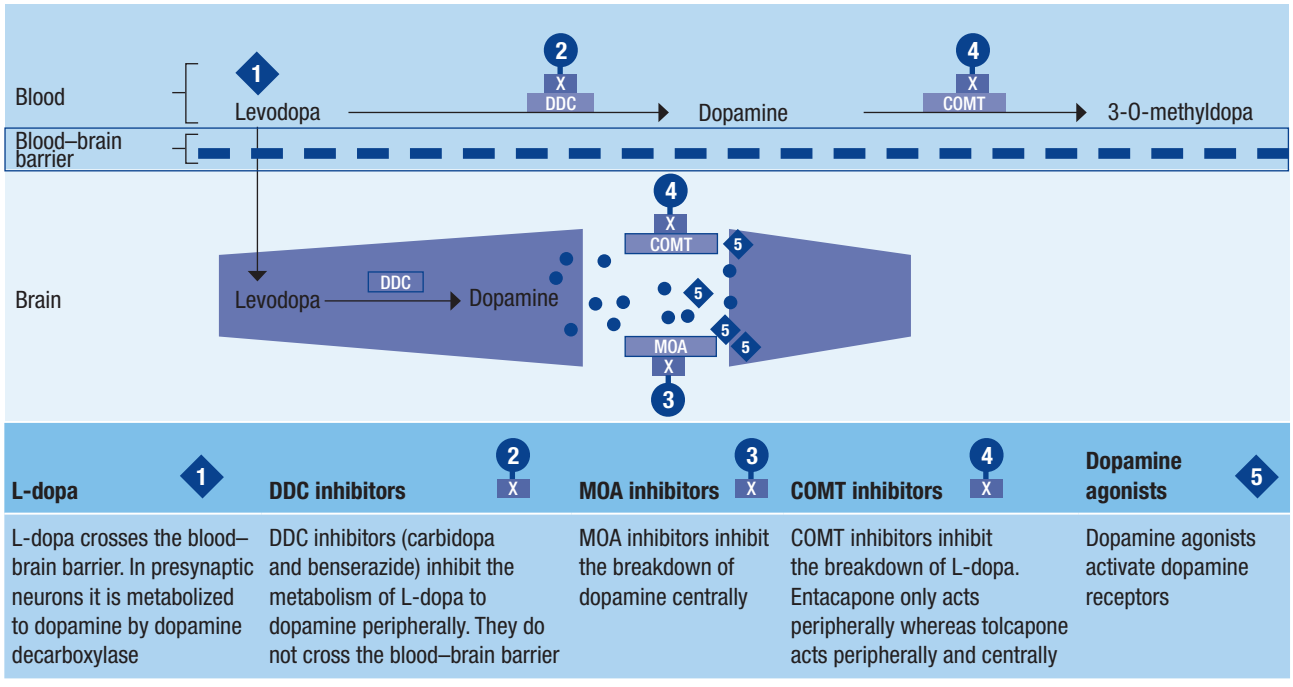

Figure 2. Mechanism of action of common dopaminergic medications. COMT = catechol-O-methyl transferase; DDC = dopa decarboxylase; MAO = monoamine oxidase.

the blood–brain barrier and preventing side effects caused by peripheral dopamine (nausea, cardiac arrhythmias).

Levodopa comes in two widely used preparations: co-beneldopa (levodopa + benserazide, trade name Madopar) and co-careldopa (levodopa + carbidopa, Sinemet). It is good practice to prescribe the decarboxylase dose and levodopa dose separately, e.g. co-beneldopa 12.5/50 mg rather than Madopar 62.5 mg, to clarify that two separate drugs are being prescribed.

Confusion also arises from the different drug preparations. Standard release preparations are used during the day and are prescribed 2–6-hourly. Controlled- or modified-release preparations are commonly used at bedtime to help prevent nocturnal akinesia, but in some cases they can be prescribed during the day. Dispersible tablets are believed to be more rapidly absorbed than standard release preparations and are therefore frequently prescribed on waking to help patients achieve an 'on' state while waiting for standard release preparations to take effect. Dispersible tablets may also be used on an as-required basis for unpredictable 'off' periods.

All dopaminergic drugs are associated with hypotension and gastrointestinal disturbances as well as dyskinesia and confusion at higher doses. Levodopa is associated with less somnolence and fewer neuropsychiatric side effects than other dopaminergic medications. It is therefore often the preferred initial treatment for older people who are more susceptible to these adverse effects.

Monoamine oxidase B inhibitors

Monoamine oxidase B inhibitors reduce the breakdown of dopamine, prolonging its action (*Figure 2*). They are taken once daily. If motor symptoms are mild but require treatment a monoamine oxidase B inhibitor may be used before moving to more potent treatments such as levodopa or dopamine agonists.

In later disease monoamine oxidase B inhibitors can be used to augment the effects of levodopa. Three monoamine oxidase B inhibitors are licensed in UK: selegiline, rasagiline and safinamide.

Catechol-O-methyl transferase inhibitors

Catechol-O-methyl transferase inhibitors also reduce the breakdown of dopamine in the synapse and are used to augment the effects of levodopa. Three catechol-O-methyl transferase inhibitors are currently licenced in the UK: entacapone, tolcapone and opicapone.

Entacapone is the most commonly used. It can be prescribed as a separate tablet alongside levodopa (useful when adjusting doses), or given in a combined tablet with levodopa and carbidopa (e.g. Stalevo, Stanek). When given in combination it should be prescribed as levodopa dose/carbidopa dose/entacapone dose, e.g. Stalevo 50/12.5/200 mg.

Tolcapone is rarely used because cases of fatal hepatotoxicity have been reported.

Dopamine agonists

Dopamine agonists are less effective than levodopa but are associated with fewer levodopa-induced dyskinesias. Dopamine agonists can also be used to augment the effects of levodopa. Dopamine agonists come in oral (pramipexole, ropinirole), transdermal (rotigotine) or subcutaneous (apomorphine) forms. Pramipexole and ropinirole come in modified release preparations.

The most important side effects of these drugs are:

- Neuropsychiatric symptoms such as cognitive impairment, hallucinations and delusions
- Daytime somnolence, which can interfere with skilled tasks such as driving and operating machinery

> In reality Parkinson's disease progresses slowly and a sudden deterioration in motor function is more likely to be caused by an intercurrent illness or change to medication.

- Impulse control disorders such as excessive gambling or shopping (often without insight into it), hypersexuality or binge eating. Impulse control disorders are uncommon but are a reason to withdraw the agonist treatment.

The older 'ergot' dopamine agonists such as bromocriptine, pergolide and cabergoline are no longer used because of their propensity to cause lung, heart valve and retroperitoneal fibrosis.

Prescribing Parkinson's disease medications when patients are admitted to hospital

A careful medication history should be recorded on admission, ensuring that the correct drug, preparation, dose and usual timings are recorded. Patients with Parkinson's disease may have complex drug regimens with medications administered at unusual times and frequencies (e.g. medication may be given at 2-hourly intervals or through the night). Medication should be prescribed in accordance with the patient's usual regimen even if this does not fit with the time of medication rounds. Nursing staff must be made aware of medications that will need to be administered outside normal medication rounds.

Patients who are able to manage their own medication should be allowed to self-administer their Parkinson's disease medications while in hospital. Patients with Parkinson's disease should be encouraged to bring their usual supply with them to hospital but accessible stocks of Parkinson's disease medications should be available out of hours so that delays obtaining medication from pharmacy are minimized.

Non-specialists should not make changes to medication without specialist advice. However, occasionally patients may be unable to take their usual oral medication as a result of impaired swallow or decreased consciousness. In this instance dispersible Madopar can be given via a nasogastric tube. Pdmedcalc.co.uk is an online calculator that will help clinicians convert a patient's usual regimen to a dispersible form (Fisher et al, 2017). Where the nasogastric route is not tolerated, contraindicated or there is impaired gastrointestinal absorption the only alternative is a rotigotine patch. Pdmedcalc.co.uk gives a conversion for rotigotine. Care should be taken when using dopamine agonists, particularly in older frailer patients who are at significant risk of delirium – for this age group a lower patch strength should be used than recommended by the above conversion. Patients whose medications have been altered should be reviewed by a specialist as soon as possible as further titration may be required.

In addition to prescribing the usual medication required by patients with Parkinson's disease, care should be taken to avoid drugs that antagonize brain dopamine receptors, e.g. first generation antipsychotics such as haloperidol, and anti-emetics such as prochlorperazine and metoclopramide. The 'drug sensitivities' box on patients' prescription charts should be used to highlight the need for caution.

Common presenting problems in patients with Parkinson's disease

Admissions to hospital may be directly related to Parkinson's disease or related to a complication of Parkinson's disease or its treatment (Gerlach et al, 2011). In patients with Parkinson's disease, reduced mobility, falls, syncope, fractures and pneumonia are among the commonest reasons for admission to hospital. However, comorbidities such as vascular diseases, cardiac disease and cancer account for over 50% of causes of admission of patients with Parkinson's disease (Temlett and Thompson, 2006).

The following section outlines the assessment and management of some common and challenging presentations.

Reduced mobility

An acute deterioration in mobility is a common presentation in Parkinson's disease. This is often attributed to 'progression of Parkinson's disease', but in reality Parkinson's disease progresses slowly and a sudden deterioration in motor function is more likely to be caused by an intercurrent illness or change to medication.

The authors strongly advocate a careful assessment of the history, from the patient and his/her family or carers, to elucidate the possible causes of reduced mobility. In patients with Parkinson's disease it is particularly important to find out if there have been recent medication changes that could have interfered with dopaminergic medications, resulting in insufficient or excessive dopaminergic activity. Examination is also important to look for limb weakness, joint problems and rigidity.

Potential causes of reduced mobility that should be explored are:

- Infection
- Dehydration or acute kidney injury
- Polypharmacy – especially sedative drugs
- Acute lower limb arthritis (e.g. gout)
- Fracture
- Oedema
- Balance problems
- Altered absorption of medication as a result of vomiting or a change in bowel habit
- Intracranial event.

Correction of the identified medical problem(s) is important, but may not fully restore mobility. Early physiotherapy and occupational therapy involvement is key to helping the patient regain his/her previous level of function.

Falls and dizziness

Falls are common among patients with Parkinson's disease. Pickering et al (2007) found that 46% of patients with Parkinson's disease fall in a typical 3-month period. Falls result from gait freezing, postural instability, non-motor features such as syncope, or cognitive impairment. Truncal stiffness and lack of arm movement when falling put patients with Parkinson's disease at particular risk of injury. Several studies have demonstrated an increased fracture risk in patients with Parkinson's disease. Patients with Parkinson's disease presenting with falls and/or dizziness should therefore have a thorough assessment including careful assessment for head injury and/or fracture, assessment of postural blood pressure, physiotherapist assessment of gait and balance, and assessment of bone health using a validated tool such as FRAX (fracture risk assessment tool).

Dizziness is experienced by up to half of patients with Parkinson's disease (van Wensen et al, 2013). Parkinson's disease causes

autonomic problems such as orthostatic hypotension, and dopaminergic medications will also exacerbate hypotension. Therefore it is very important to check lying and standing blood pressure measurements in patients with Parkinson's disease who are dizzy or who have fallen. Orthostatic hypotension may require an adjustment or reduction of Parkinson's disease medication. Furthermore, the mineralocorticoid fludrocortisone or the alpha-receptor agonist midodrine could be initiated. Expert advice should be sought if a postural drop of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure is identified. Other causes of dizziness should be explored if postural hypotension has not been demonstrated, or if the dizziness persists after adequate treatment.

Aspiration and pneumonia

Swallowing is often impaired in patients with Parkinson's disease and a patient's swallow can deteriorate in the context of an acute illness or disruption to his/her usual medication regimen. Aspiration may be silent and should be looked for in patients presenting with signs of respiratory tract infection. If aspiration is suspected the local antibiotic protocol for aspiration pneumonia should be followed. Careful consideration should be given as to whether patients are kept nil-by-mouth or Parkinson's disease medications only by mouth. If patients are kept nil-by-mouth for a suspected swallowing impairment, a nasogastric tube can be placed to allow medication to be administered as described above. Specialist speech and language therapy assessment can help minimize the risk of aspiration.

Delirium

Parkinson's disease has been noted to be an independent risk factor for delirium in observational studies (Vardy et al, 2015). Moreover, people with Parkinson's disease who do experience delirium in hospital have a worse outcome – resulting in longer hospital stays and more disability – than elderly patients without Parkinson's disease. Patients with Parkinson's disease should be screened for delirium using a validated tool such as the 4 As Test or the Abbreviated Mental Test Score.

The causes of delirium in patients with Parkinson's disease are similar to those in the general elderly population: systemic infection, polypharmacy (especially medications with high anticholinergic activity such as antidepressants, some analgesics and bladder smooth muscle relaxants), electrolyte and other metabolic disturbances, endocrine abnormalities, vitamin deficiencies and withdrawal of substances such as alcohol or other sedatives. The list is not exhaustive, but is a good checklist to initiate investigations for most patients with delirium.

In terms of specific strategies for managing delirium in Parkinson's disease, non-pharmacological measures should be initiated in all patients. In severe cases withdrawal of dopaminergic medications may be necessary. This should only be done by a Parkinson's disease specialist as there is a risk of worsening motor function and consequent immobility, falls and aspiration.

Occasionally patients with Parkinson's disease who have delirium may require an antipsychotic. First generation antipsychotics such as haloperidol are contraindicated in patients with Parkinson's disease, as they can worsen parkinsonism, but second generation antipsychotics have less effect on the motor control system. Quetiapine and clozapine are the most efficacious (Vardy et al, 2015), but as clozapine requires specialist monitoring quetiapine is the most practical pharmacological treatment for psychosis in patients with Parkinson's disease. If an antipsychotic is required expert advice regarding antipsychotic initiation should be sought from a medical consultant specializing in Parkinson's disease and an old age psychiatrist.

Pain and analgesia

Pain may be a complication of Parkinson's disease or a result of comorbidities. The analgesic ladder should be followed but prescribers should be aware of potential complications specific to patients with Parkinson's disease. Patients with Parkinson's disease often have delayed gastric emptying which may place them at greater risk of gastrointestinal complications from non-steroidal anti-inflammatory drugs. Most people with Parkinson's disease have a degree of constipation. This can be exacerbated by opioid analgesia. Care should be taken to monitor bowels and prescribe adequate laxatives.

Nausea and Parkinson's disease

Careful consideration should be given to the choice of antiemetic. Centrally acting dopamine antagonists such as metoclopramide should be avoided. Domperidone (a dopamine antagonist that does not cross the blood–brain barrier) was a popular choice of oral antiemetic in patients with Parkinson's disease. However, concerns regarding an increased risk of cardiac arrhythmia mean it is now more judiciously prescribed.

Cyclizine does have some dopamine antagonising properties and its use should be avoided if possible in patients with Parkinson's disease. However, it does still have a role in palliative care as it can be given subcutaneously and via a syringe driver.

Ondansetron does not worsen Parkinson's disease but it is associated with constipation and orthostatic hypotension (both common problem in patients with Parkinson's disease), so patients should be monitored for these side effects. Where vomiting is challenging to control, consider temporarily providing dopaminergic therapy via a rotigotine patch (as discussed above).

Constipation and pseudo-obstruction

Although constipation is virtually ubiquitous in idiopathic Parkinson's disease, it is important to be alert to physical obstruction and colonic pseudo-obstruction. Risk factors for pseudo-obstruction include neurodegenerative disease, decreased mobility, anticholinergic medication, electrolyte imbalance and infection. The

TOP TIPS

- Recognize which medications in the patient's list of drugs are dopaminergic.
- For patients being admitted to hospital, prescribe dopaminergic medications promptly.
- Change the pre-set times on the prescription system or Kardex to suit the times the patient usually takes each drug.
- Avoid dopamine antagonists such as haloperidol and metoclopramide. Domperidone can be used (be cautious in patients with heart disease).
- For patients who are 'nil-by-mouth' for swallowing problems, consider a nasogastric tube for feeding and medications.
- If patients cannot have a nasogastric tube, a transdermal rotigotine patch can be applied temporarily.

KEY POINTS

- Involve multidisciplinary and specialist teams when people with Parkinson's disease are admitted to hospital.
- Become familiar with dopaminergic medications used in people with Parkinson's disease.
- Recognize the multifactorial causes of falls, dizziness, reduced mobility and delirium in people with Parkinson's disease.
- Beware of aspiration and constipation in the unwell patient with Parkinson's disease.

features include prolonged constipation, abdominal pain and distension (Blackley et al, 2016; Su et al, 2017). If suspected, abdominal and erect chest X-rays should be requested to diagnose the pseudo-obstruction and exclude a bowel perforation. Typical radiological features include dilated bowel loops, with some patients showing the 'coffee-bean' sign. Computed tomography of the abdomen is usually required to exclude physical obstruction (Su et al, 2017).

The surgical team should be involved in the management of patients with sigmoid volvulus as the treatments include correcting the precipitating factors, decompression of the bowel, faecal disimpaction, and partial colectomy (Bruzzi et al, 2015).

Perioperative management

Patients are often kept 'nil by mouth' from the night before surgery, which can lead to morning medications being omitted. However, clear fluids and medications can safely be administered up to 2 hours before an operation. Anaesthetic and surgical teams must be informed that the patient has Parkinson's disease. Wherever possible a Parkinson's disease specialist should be involved in planning any medication changes that may be required during the intraoperative and postoperative period. Surgical teams must be informed if the patient has a deep brain stimulator as diathermy can damage the stimulator and surrounding tissue.

Conclusions

Patients with Parkinson's disease are frequently admitted to hospital. Careful assessment and attention to detail is required in order to make their hospital admission as smooth as possible. Prompt administration of dopaminergic medications, knowledge of complications of Parkinson's disease, involvement of Parkinson's disease specialists, and the multidisciplinary team are key to ensuring good care. **BJHM**

Conflict of interest: none.

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