

Understanding Parkinson's Disease: A Basic Overview

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Abstract

Parkinson's disease (PD) is a multi-system disease, with clinical features typically described across three domains: motor, non-motor, and neuropsychiatric symptoms. There is no known cause or cure for PD, and diagnosis occurs often through a process of elimination, remaining one of clinical assessment, expert opinion, and observing disease progression over time. In the absence of disease modifying therapy for PD, pharmacological treatments play a role in symptomatic relief and improving quality of life (QoL). A narrowing therapeutic window and motor fluctuations present a challenge to the pharmacological management of PD. Device assisted therapies including Duodopa, Apomorphine and deep brain stimulation are based on the concept of providing stable and continuous stimulation to minimise pulsatile sudden or unexpected fluctuations. Studies continue to demonstrate the benefit of multidisciplinary input and the impact on functional status, mood, motor abilities, cognitive performance, speech skills, independence and QoL of a person with PD. Nurses are well placed to identify complications, escalate concerns, and initiate timely referral to members of a multidisciplinary team. Understanding the clinical features of PD as well as the basic assessment and management of the disease is essential in providing holistic care and supports to maintain QoL for those with PD and their caregivers.

KEYWORDS: Parkinson's Disease, Nursing, Overview, Multidisciplinary management, Parkinson's Disease Specialist Nurse.

Introduction & history

Parkinson's disease (PD) was first documented by Dr James Parkinson in 1817 in the "Essay on the Shaking Palsy" describing a neurodegenerative disease with features of tremor, bradykinesia, rigidity, postural insta-

bility, gait disturbances and some non-motor symptoms (Lees, 2017).

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Today, PD is widely recognised as a complex multi-system disease, in which people with Parkinson's also experience a range of non-motor symptoms (NMS), autonomic dysfunction and cognitive and psychiatric symptoms (Mohamad et al., 2021). PD is considered to be the second most common neurodegenerative disease (Lee & Yankee, 2021), with the World Health Organization estimating approximately 8.5 million people live with PD worldwide (Nakmode et al., 2023). Concerningly, the rate of disability and death due to PD is increasing faster than any other neurological disorder (Nakmode et al., 2023).

Despite extensive research and technological advancements, there is currently no known cause or cure for PD. Therefore, the management of PD is targeted at symptom control and improving quality of life (QoL). Morphological and metabolic changes within the brain confirmed by medical imaging (magnetic resonance imaging, single photon emission computed tomography and positron emission tomography), may assist in the differential diagnosis between PD and atypical parkinsonism (Samson & Noseworthy, 2022). However, the diagnosis of PD is often established through a process of elimination, and remains one of clinical assessment, expert opinion and observing disease progression over time (Postuma et al., 2016).

With increasing PD prevalence, it is likely that nurses across all settings, will be required to provide care for an individual with PD at some point in their career. Additionally, in contrast to the time limited medical specialist clinic consults, nurses are often well placed to spend more time with those living with PD, are often more accessible, and nurses in specialist roles can follow an individual with PD on their journey for many

years. Despite this, to provide holistic care and maintain QoL for those living with PD, all nurses should understand the condition's clinical features, basic assessment, management including timely interventions, identification of common complications in PD, and referrals to multidisciplinary and psychosocial supports.

Aetiology

Understanding the aetiology of PD is complex, and a large portion of cases are considered to be idiopathic— meaning that the cause of the disease is unknown. Whilst a smaller portion of cases are considered to have some form of genetic component (Bhat et al., 2018), it is believed that the condition results from a complex combination of factors including hereditary variables and life-long exposure to environmental factors such as pesticides, solvents and air pollutions (Nakmode et al., 2023). Additionally, there is emerging evidence to suggest that PD may have prion-like disease traits (Kujawska & Jodanis-Liebert, 2018), with decades of other research demonstrating that oxidative stress, neuroinflammation, and apoptosis are also key elements in the development of PD (Mohamad et al., 2021). Thus, current research continues to focus on areas such as gene therapy, biological markers, neural transplantation, neuroprotection, and pharmacological treatments (Bhat et al., 2018).

Clinical features

PD is a multi-system disease, with clinical features typically described across three domains: motor, non-motor, and neuropsychiatric symptoms. Notably, from day to day, even hour to hour, PD symptoms may fluctuate,

with the degree of impairment and the rate of progression varying in each individual.

Motor Symptoms

Key motor features of PD include resting tremor (initially unilateral), bradykinesia (slow movements), rigidity, shuffling gait, and postural instability (Beitz, 2014). In addition, those with PD can experience secondary motor symptoms such as hypophonia (soft voice), dysarthria (slow, slurred speech), dysphagia (difficulty swallowing) and sialorrhea (drooling), as well as micrographia (difficulty handwriting), hypomimia (masked like facial expression), decreased blink rate, pain, dystonia and motor fluctuations (Nolden et al., 2014). Those with PD may also suffer from freezing of gait, which refers to the inability to initiate movement, or the sudden cessation of movement and this symptom can be a large contributor of falls.

Medications are a first line management for motor symptoms. As PD progresses, a narrowing therapeutic window is observed. When this happens, an individual may find their once relatively smooth symptom control begins to fluctuate between symptom improvement post medication known as the “ON” state, and a return of PD symptoms known as the “OFF” state. Motor fluctuations may involve end dose wearing off, unpredictable ON’s and OFF’s, delayed ON’s and even dose failures (Aradi & Hauser, 2020). Management of on-off phenomenon can be challenging and is reported in up to 50% of those with PD within the first three to five years of the disease, and often affecting up to 80% within 10 years of disease onset (Barrachina-Fernández et al., 2021).

In addition to motor fluctuations, dyskinesia (abnormal, involuntary, twisting, or writhing movements) can be observed and may vary in relation to the different phases of a PD medication cycle. The most common being peak dose dyskinesia which occurs during the peak of levodopa medication response (Aradi & Hauser, 2020).

Non – Motor Symptoms

While PD is primarily defined by its motor symptoms, a broad but characteristic set of NMS are present in most individuals.

Dysregulation of the autonomic nervous system leads to orthostatic hypotension, constipation, delayed gastric emptying, urinary urgency and nocturia, temperature control dysregulation (e.g., excessive sweating), sexual dysfunction (e.g., erectile dysfunction) and skin sensations (Kaiserova et al., 2021).

Additionally, sleep disturbances are among the most frequent NMS in those with PD, impacting significantly on QOL (Xu et al., 2021; Yi et al., 2022). Most commonly, insomnia, frequent awakenings, decreased sleep duration and efficacy, excessive daytime sleepiness and rapid eye movement sleep behaviour disorder (REM-SBD) (Yi et al., 2022). REM-SBD occurs due to a failure of muscle paralysis which typically occurs during the dreaming phases of normal sleep, and manifests as dream enactment behaviour including vocalisations, thrashing movements, falls out of bed and unintentional injury to a partner (Waller et al., 2021). Interestingly, the pre-motor phase of PD is now widely recognised because NMS such as REM-SBD, constipation, hyposmia, and depression often precede the development of

motor symptoms by more than a decade (Kaiserova et al., 2021).

For many with PD, the NMS are often more troublesome and have a greater negative impact on QoL than the motor symptoms (Waller et al., 2021). According to Bietz (2014), NMS can represent some of the greatest adverse effects on QoL and appropriate management is challenged when many do not respond to dopamine therapy.

Neuropsychiatric Symptoms:

Mood disorders such as depression, anxiety, and apathy occur commonly in PD, and these symptoms have been ranked among the most troublesome NMS in both early and late stages of PD (Beitz, 2014).

In the early stages of PD, an individual may suffer from mild cognitive decline, anxiety and depressive symptoms whereas in later stages, more severe neuropsychiatric symptoms such as hallucinations, depression and dementia may occur (Eichel et al., 2022). Some people with PD, may also develop a dopamine dysregulation syndrome from dopaminergic drug dependency (Grover et al., 2015). Neuropsychiatric symptoms can have a significant impact on an individual's and their caregivers QoL, leading to higher levels of caregiver stress (Eichel et al., 2022). Furthermore, they have been shown to be a predictor for early entry into residential aged care facilities (Jose et al., 2021).

Pathophysiology

The hallmark pathological finding in PD is the presence of alpha-synuclein protein aggregates (known as Lewy bodies) throughout the brain (Tysnes & Storstein, 2017). The presence of Lewy bodies and the degenera-

tion of the dopamine producing neurons in the substantia nigra pars compacta, within the basal ganglia, are responsible for the classic motor symptoms associated with PD including rigidity tremor and bradykinesia (Nolden et al., 2014). Simply explained, the basal ganglia plays an important role in the initiation and control of smooth, coordinated fine motor movements, whilst the neurotransmitter dopamine, plays a role in the transmission of messages between these neurons (Nolden et al., 2014). A recent study by Kaiserova et al. (2021) has shown that Lewy body pathology in PD not only affects the midbrain, but both the central and peripheral nervous system and is therefore, responsible for several NMS. Such evidence also contributes to the "body-first" or "brain-first" theories hypothesised in PD development (Borghammer & Van Den Berge, 2019), and lends support to Lewy body pathology being found in the olfactory and enteric nervous system (Rietdijk et al., 2017). Consequently, researchers like Hung and Schwarzschild (2014) have expressed growing interest in the non-dopaminergic neurotransmitter pathways such as glutamate, serotonin, GABA, adenosine, noradrenaline and cholinergic pathways, also being involved in PD pathophysiology. Explanations such as Braak's hypothesis, lend support by suggesting that PD may be initiated when an unknown pathogen enters the gut and/or the nasal cavity later spreading via the olfactory or vagal nerves towards the central nervous system (Rietdijk et al., 2017).

Assessment:

PD remains a clinical diagnosis, and its heterogeneity can pose diagnostic difficulties with several other conditions mimicking PD. These include essential tremor (ET), multiple

system atrophy (MSA), progressive supranuclear palsy (PSP), vascular parkinsonism and cortico-basal degeneration (CBD). Currently, a definitive diagnosis for PD is only possible post mortem (Greenland et al., 2019).

In clinical practice, medical specialists, and Parkinson's disease nurse specialists (PDNS), use many different assessment tools to assist with PD staging, measure symptoms and evaluate treatment interventions. The Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) is a popular, comprehensive and validated scale comprising of 65 questions for the assessment of symptoms across five domains including non-motor and motor experiences of daily living, and motor complications (Goetz et al., 2008). For more detailed evaluations of treatment interventions, medical specialists, PDNSs and allied health therapists may perform assessments such as; the 9-hole peg test, finger tapping tests, timed up and go and timed walking tests. The Montreal Cognitive Assessment (MOCA) and the Mini Mental State Examination (MMSE) are another two tools used for cognitive assessment (Martini et al., 2020).

For general nurses, a comprehensive head to toe assessment can identify signs of PD symptom deterioration and enable interventions to be implemented so that complications are prevented. Particular attention should be given to assessing postural blood pressures, mobility and care needs, constipation, medication management, sleep patterns, social interactions, financial management, cognitive stimulation, as well as features of impulse control disorders and hallucinations. Safety assessments such as falls

risks, and suitability for driving should also be assessed. PD symptom diaries allow for the identification of symptom trends and patterns and they can be useful in establishing the effect, duration and side effects of medications allowing for more accurate treatment adjustments (Barthel et al., 2016).

In recent times, there has been a growth in the utilisation of wearable devices for monitoring motor symptom control, identifying on-off states and providing a basis for more accurate treatment adjustments. However, Barachina-Fernández et al., (2021) report that currently the assessment of NMS through wearable devices remains inadequate.

Management

While a person with PD is likely to experience several symptoms at any one time, not all may be troublesome. Often medical specialists will identify and target the individual's most troublesome symptoms. Nurses can play a significant role in developing an individualised and holistic plan of care and are well placed to identify complications, escalate concerns for review and initiate timely referral to other members of a multidisciplinary team.

In the absence of disease modifying therapy for PD, pharmacological treatments play a role in symptomatic relief and improving quality of life (QoL) (Nakmode et al., 2023). Current available treatments include medications that either raise striatal dopamine levels or activate dopamine receptors. Unfortunately, Nakmode et al., (2023) have found with continued dopaminergic neurodegeneration over time, the effect of available treatment options become less effective and non-invasive treatments should focus on dopa-

minergic therapy optimisation by considering medication timing, dosages, delivery modes and absorption. Table 2 highlights some common medication classes, medication examples, their indications, side effects and nursing considerations.

Notably, commonly used medications such as Metoclopramide, Prochlorperazine, Haloperidol and Promethazine may worsen PD symptoms or cause acute dystonic reactions in those with PD (Grissinger, 2018). To maintain the safety of those with PD in all healthcare sectors, nurses' knowledge of contraindicated medications is paramount.

Device Assisted Therapies:

There are three device assisted therapies (DAT's) commonly used in the treatment of PD including Apomorphine, Duodopa® and Deep Brain Stimulation (DBS). Apomorphine and Duodopa® are both infusion therapies, whereas DBS involves neurosurgical intervention. All three therapies provide stable and continuous stimulation minimising pulsatile, sudden or unexpected fluctuations in PD symptoms (Hayes et al., 2010).

Apomorphine is a dopamine agonist, administered via subcutaneous injection. Apomorphine can be used as intermittent rescue subcutaneous injections or delivered through a continuous subcutaneous infusion pump. It is important to note that although Apomorphine is a derivative of morphine, it has no narcotic or analgesic properties (Tsui, 2014). The efficacy of Apomorphine absorption can depend on appropriate injection site selection, the volume of drug, skin condition and the presence of subcutaneous nodules. To prevent these issues, individuals must complete meticulous daily skin management

strategies including single use needles, rotation of injection sites and thorough skin massages (Carbone et al., 2019).

Duodopa® is a Levodopa/Carbidopa (20mg/5mg/mL) Intestinal Gel (LCIG), that comes enclosed in a 100mL cassette. The gel is administered via an infusion pump delivering continuous medication directly to the site of absorption in the intestine. This method of treatment requires the insertion of Percutaneous Endoscopic Gastrostomy (PEG) tube, with a Percutaneous Endoscopic Jejunal tube threaded through (Tsui, 2014). Daily care of the PEG-site and tube connectors is important to prevent complications such as tube blockage, buried bumper syndrome, site hyper-granulation and infection (Foltynie et al., 2013). Constipation can severely affect the absorption of LCIG. If a sudden reduction in medication response is seen, a prompt X-ray investigation must be conducted to confirm tube placement and bowel status (Taki et al., 2019). Furthermore, LCIG can reduce the absorption of Vitamin B12 and folate, increasing the risk of developing peripheral neuropathy (PN). Thus, supplementation of these micronutrients must be considered (Rispoli et al., 2017; Simioni et al., 2016).

DBS therapy is an invasive, neurosurgical procedure involving the implantation of electrodes within targeted areas of the brain, usually in the subthalamic nucleus, or globus pallidus internus to deliver calculated continuous or intermittent stimulation to yield therapeutic effects. Adverse effects of DBS therapy may include tonic muscle cramps, gaze deviation, speech disturbances, gait and postural instability (Hartmann et al., 2019). Additionally, DBS can be complicated by neuropsychiatric symptoms such as impulsivity, elevated mood, depression, and anxiety

(Mosley, 2021). Careful selection and neuropsychiatric assessments to establish suitability of patients is vital.

For the device assisted therapies, infusion rates and DBS settings are individually titrated and pre-set in consultation with the specialist.

A Multidisciplinary Approach:

To improve QoL and function in those with PD, a holistic approach to care and interprofessional collaboration is necessary. A recent study by Lo Buono et al., (2021) has demonstrated the benefit of multidisciplinary input and the impact on functional status, mood, motor abilities, cognitive performance, speech skills, independence and QoL of those with PD. Figure 1 summarises a likely set of multidisciplinary healthcare professionals and their role in the management of PD.

Multidisciplinary input may vary in relation to individual symptom presentations.

Other considerations:

Advance Care Planning (ACP) involves thinking about and documenting preferences for future health care, assisting an individual and others to prepare for a time when they can no longer communicate decisions on their own (Advance Care Planning Australia, 2021). Early and ongoing opportunities to discuss ACP should be offered to those with PD and those involved in their care.

Many people with PD are living in the community, with relatives such as partners having to provide most of the long-term care. (Spliethoff-Kamminga et al., 2003). Caregivers are required to be available 24/7, and continuously need to adapt to the unpredictable nature of the disease and the needs of those with PD. Bhasin and Bharadwaj (2021)

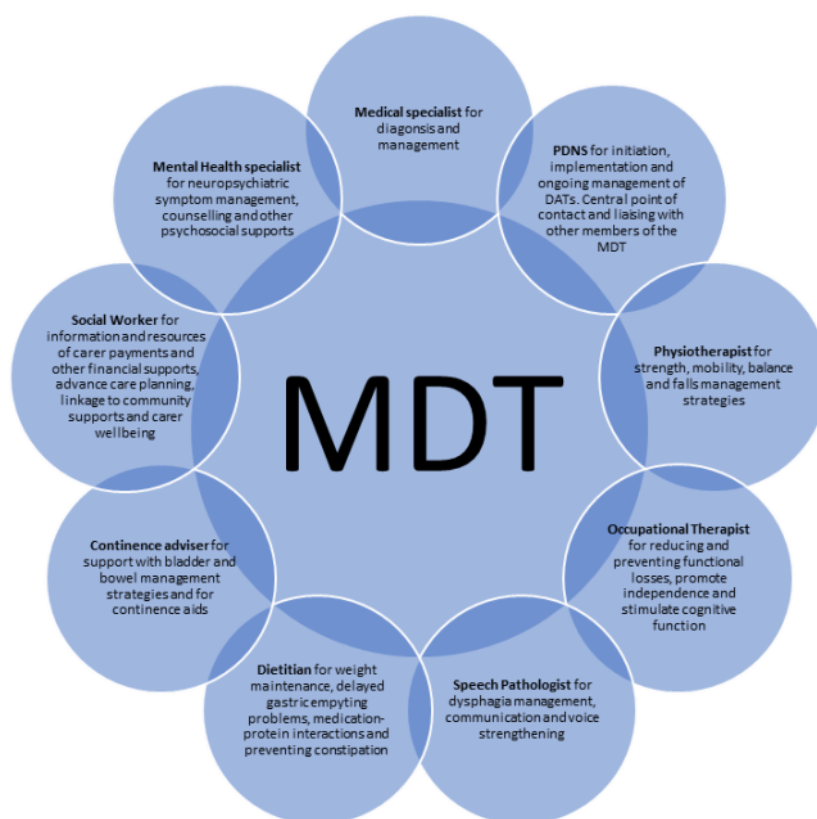


Figure 1: A multidisciplinary team and their role in the management of Parkinson's disease.

report that over time this can influence carers' QoL and frequently results in caregiver burden. Therefore, all nurses must consider the role and needs of caregivers as a critical component of comprehensive care of those living with PD.

Closing remarks:

An understanding of the clinical features and management of PD will better enable nurses across all settings to assess, monitor and facilitate timely interventions and referral to multidisciplinary members and psychosocial supports. Nurses should recognise not only their value within the multidisciplinary team, but also their advantageous position in being able to support those with PD and their caregivers to access timely and appropriate care and positively maintain QoL.

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Table 2: Parkinson's disease medications, classes, examples, indications, side effects and nursing considerations.

Class	Examples	Indication(s)	Side effects	Nursing considerations
Levodopa Therapy	Levodopa/carbidopa – Kin- son ^o , Sinemet ^o , Sinemet CR ^o , Sindopa ^o , Duodopa ^o . Levodopa/benserazide - Ma- dopar ^o , Madopar Rapid ^o , Ma- dopar HBS ^o	Remains the gold stand- ard treatment for PD and the most effective at treat- ing motor symptoms of bradykinesia, rigidity and at times tremor. As dopamine does not cross the blood-brain bar- rier, levodopa acts as the precursor to dopamine replacement, directly con- verting to dopamine in the brain and peripheral tis- sues to replace depleted striatal dopamine (Australian Medicines, 1998). Levodopa is given with a peripheral dopa decar- boxylase inhibitor (carbidopa or bense- razide) to help reduce peripheral dopamine pro- duction and reduce side effects of nausea, vomit- ing and hypotension (Levodopa benserazide/ carbidopa, (Australian Medicines, 1998))	May include nausea, vom- iting, drowsiness, mood changes, hallucinations, confusion, postural hypo- tension, dyskinesia and motor fluctuations, libido alterations, sudden sleep onset (Levodopa bense- razide/carbidopa (Australian Medicines, 1998), Dopamine dysregulation syndrome is estimated to occur in 3-4% of advanced stage PD, and can be characterised by a compul- sive overuse of levodopa causing dyskinesia's, psy- chosis, and impulse control disorders (Levodopa ben- serazide/carbidopa (Australian Medicines, 1998)).	Timely administration is crucial. Strict adherence to PD medication timing is vital to obtain optimal symptom man- agement with minimal side effects, and regime is tailored to each PwP. Nurses must be vigilant when adminis- tering PD medications, as PD medica- tions exist in a range of formulations and preparations including rapid acting, slow release, and regular release form. Recognise that protein-based foods may interact with medication. Ideally, administer 30 minutes before food or two hours after food to minimise protein/medication interactions. Never cease medications abruptly, as this can lead to life threatening neuro- leptic malignant-like syndrome which may present as hyperpyrexia, diaphore- sis, muscular rigidity, and life threatening autonomic dysfunctions. Medications should continue even if a patient is fasting for a surgical proce- dure. Contraindicated medications include Haloperidol, Metoclopramide and Pro- chlorperazine. Avoid the use of contraindicated antide- pressants, antipsychotics and some anaesthetic agents and pain medica- tions. Use alerts and warning stickers when available.

Dopamine Agonists	Pramipexole - Sifrol[®] (immediate release, extended release), Apomorphine – Movapo, Apomine Rotigotine transdermal patches - Neupro[®]).	Mimic the action of levodopa by acting as dopamine receptor activators, which in turn results in increased dopamine activity Dopamine Agonists (DA), can be used as monotherapy or in combination with medications from other classes.	Impulse control disorder (ICD) is a common side effect of DA, and can occur at any stage of PD. Features of ICD may include gambling, overspending, hypersexuality, binge eating and inappropriate internet use (Australian Medicines, 1998), Postural hypotension, nausea, vomiting, hallucinations, and confusion can be common in Apomorphine. Those with a personal or family history of bipolar disorder, substance misuse or obsessive-compulsive disorders are at higher risk of developing ICD disorders (Australian Medicines, 1998), Dopamine Agonist Withdrawal Syndrome (DAWS) has been reported in up to 20% of PwP. Symptoms can be severe and may include agitation, mood disturbance, fatigue, insomnia, sweating, orthostatic hypotension, and drug craving (Australian Medicines, 1998). Other side effects might include sudden sleep onset, abdominal pain, headache, dizziness, weakness, fatigue, nasal congestion, peripheral oedema, dyskinesia, and digital vasospasm (Australian Medicines, 1998).	Education to PwP and their caregivers is crucial in avoiding adverse outcomes and nurses should remain vigilant in monitoring for DA side effects to ensure timely review and management. DA should never be abruptly ceased; and cessation should occur over a tapering phase with close monitoring for withdrawals (Australian Medicines, 1998). Rotigotine patches should be applied to dry, non-irritated skin. Rotate patch sites daily. Firmly hold patches on skin with the palm of hand for 30 seconds to ensure the adhesive sticks to the skin.
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Catechol-O-methyl Transferase (COMT) Inhibitors	Entacapone – Comtan[®], Entacapone combinations - Stalevo[®] Carlevent[®] LECTEVA[®] Tridopa[®],	Serves as an adjunct to Levodopa. Inhibits the enzyme COMT from metabolising levodopa, prolonging the clinical response to levodopa (Australian Medicines, 1998). COMT inhibitors aim to improve the duration of 'on' time by increasing levodopa plasma levels by 10 – 30% and often the dose of levodopa may need to be reduced (Grünig, et al., 2018).	May include dizziness, dyskinesia, gastrointestinal upset, hepatotoxicity (from Tolcapone), discoloured urine (reddish/brown) and may worsen confusion, hallucinations, paranoia, dyskinesia constipation (Australian Medicines, 1998).	Entacapone should not be stopped abruptly, due to the risk of withdrawal syndrome and neuroleptic malignant syndrome.
Monoamine Oxidase Type B (MAO-B) Inhibitors	Selegiline (Selgene[®], Eldepryl[®]), Rasagiline (Azilect[®]) and Safinamide (Xadago[®])	Reduce the breakdown of dopamine and block dopamine reuptake in the brain, working to mildly enhance dopaminergic effects and lessen the degree of "wearing off." Serves as an adjunct to levodopa or might also be used as monotherapy in early PD to protect the endogenous dopamine (Australian Medicines, 1998).	Insomnia, orthostatic hypotension, headache, nausea, vomiting and confusion. Dyskinesia, vomiting, rash, arthralgia (Australian Medicines, 1998).	When used with Levodopa, MAO-B inhibitors may increase dopaminergic effects such as dyskinesia, hallucinations, nausea, and vomiting – Levodopa doses may require reduction (Australian Medicines, 1998).

Anticholinergics	Benzhexol - Artane [®] Benztropine - Benztrop [®] , Biperidine - Akineton [®]	Aim to achieve a balance between acetylcholine and dopamine. Mostly used for tremor dominant PD. Generally used infrequently given their side effect profile.	Confusion, hallucinations, blurred vision, constipation, urine retention, dry mouth, nausea, vomiting, insomnia, worsening dyskinesia, sweating. Bradyarrhythmia's, mydriasis, extrapyramidal disorders. Adverse effects may depend on dosages as well as patient factors (age, comorbidities) (Australian Medicines, 1998).	Can be used in the management of some NMS of PD, however extreme care must be taken when prescribing to the elderly as they can increase the risk of falls, delirium, cognitive impairment and worsening of some PD symptoms.
Amantadine	Symmetrel [®]	An antiviral drug with N-methyl-D-aspartate (NMDA) receptor blocker properties and is commonly used as an antidyskinetic agent in PD. (Australian Medicines, 1998).	Sleep disturbance, confusion, postural hypotension, dizziness, and blurred vision, nervousness, depression, nightmares, peripheral oedema, dry mouth, vomiting, constipation, livedo reticularis (Australian Medicines, 1998).	As Amantadine causes insomnia, it is suggested to administer no later than 4pm in the afternoon (Sawada et al., 2010). Sudden withdrawal may cause severe delirium, anxiety, and agitation.