The Tomorrow: Advanced Treatments in Parkinson's Disease Does Not Necessarily Equate to Treatments in Advanced Parkinson's Disease

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Abstract

A person with Parkinson's disease (PD) can have variations in the severity of Parkinsonian symptoms; this is dependent on the stage of their medication cycle. Variations in dopamine plasma levels cause erratic changes in severity of symptoms, known as 'motor fluctuations'. Apomorphine infusion, Duodopa® and Deep brain stimulation are the three current advanced treatments for people with PD. The goal of therapy is to replicate the normal function of the neurotransmitter dopamine by providing continuous stimulation in an effort to minimise motor fluctuations. Although these advanced treatment options seem like the ideal solutions for people with PD, awareness and knowledge is relative low amongst the neuroscience community.

Advanced PD treatments have the potential to improve the quality of life in people who are battling this chronic and complex disease. The aim of the presentation is to increase awareness amongst neurosciences nurses of modern treatments available to people with PD, enabling neuroscience nurse to advocate for their patients. This presentation will also highlight the role of the Parkinson's Disease Nurse Specialist in the assessment, diagnosis, management and ongoing follow-up of these patients who require specialised expertise.

Keywords: *Parkinson's disease, tremor, deep brain stimulation, dopaminergic, movement disorders, Parkinson's disease nurse specialist, motor fluctuations, "OFF" period, "ON" period, dyskinesia.*

Traditional Thinking Versus Contemporary Thinking

Parkinson's Disease (PD) was first described by James Parkinson in 1817 in the paper 'An essay on the Shaking Palsy'. He was able to document some key features of PD which are still relevant to this day. Some of the key features he described include the chronic degenerative nature of the disease, the predominance of unilateral symptoms, tremors and the latency in tremors, akinesia and bradykinesia, rigidity, stooped posture, postural instability, gait disturbance and freezing of gait and even non-motor symptoms of the disease such as sleep disturbance, speech disturbance and constipation (Parkinson, 1817 & 2002).

The traditional understanding of the pathophysiology of PD begins with the destruction of dopamine producing neurons in the substantia nigra located in the midbrain. These structures are part of the basal ganglia which is responsible for initiation and controlling voluntary movements. The reduced production and action of dopamine lead to reduced neuro-transmission and stimulation to the motor cortex causing motor dysfunction (McCance & Heuther, 2006).

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However, the more contemporary thinking which is beginning to be more wildly accepted is known as the Braak's Hypothesis. The Braak's hypothesis proposes that there are 6 stages of PD. Stages 1 and 2 are the premotor or prodromal phase of PD which suggests the pathophysiology of PD begins in the gut causing gastrointestinal symptoms commonly manifesting as long standing constipation years before the diagnosis of PD. The progression of the pathophysiology into the medulla causes the autonomic dysfunctions such as temperature imbalance, postural hypotension, urinary and erectile dysfunction. Further progression to the pons causes the sleep disturbances such as REM sleep behaviour disorders, insomnia and day time somnolence (Braak, Del Tredici, Rüb, de Vos, Jansen Steur & Braak, 2003).

Stages 3 and 4 are classed as the motor or clinical phase of PD when the midbrain is affected causing the manifestations of the motor symptoms such as tremor, rigidity, akinesia and postural imbalance which allows for the clinical diagnosis of PD to be made (Braak et. al. 2003).

Stages 5 and 6 are caused by further progression of the pathophysiology into the forebrain and the rest of the cortex which leads to the cognitive impairments such as dementia, hallucinations and psychosis and can exacerbate pre-existing anxiety and depression (Braak et. al. 2003).

The 'OFF' & 'ON' Phenomenon and Dyskinesias

People with Parkinson's disease may have different phases that their body is in depending on the stage of their medication cycle. This is commonly known as motor fluctuations. In their "OFF" period or pre-medicated state, the person may have typical motor symptoms of PD and in their "ON" period or their medicated state, the same person may well be functioning close to the level of a normal person with minimal interruptions from their Parkinson's symptoms due to having optimised dopaminergic plasma levels. There is also a third state when the dopaminergic plasma levels peak and break through the therapeutic threshold of the "ON" state causing excessive chorea-like movements. These movements are involuntary, twisting or writhing movements which can affect any part of the body. This is known as peak-dose dyskinesia (Frabbrini, Brotchie, Grandas, Nomoto & Goetz, 2007).

Contemporary Concepts of Treatments in PD – Continuous Dopaminergic Stimulation

The control and balance of motor fluctuations within the therapeutic threshold is dependent on accurate titration of the individualised medication regimen, strict compliance and accurate timing of medication administration. However, when the symptoms are refractory to these strategies, advanced treatments in PD are considered (Hayes, Fung, Kimber, & O'Sullivan, 2010). The common misperception of advanced treatments for PD is that they are usually reserved for patients in their later or advanced stages of the disease process. However, these advanced treatments can be implemented in the earlier stages of PD and patients can benefit from earlier interventions.

The concept behind the advanced treatments in PD is referred to as 'continuous dopaminergic stimulation' where medication or stimulation is administered in a constant fashion to provide stability and continuity to prevent the sudden and pulsatile fluctuations in dopaminergic plasma levels (Nutt, 2007).

Contemporary Treatments

Despite the advancement in technology and the development of advanced treatments, some of the older treatments used in PD are still currently in use today. Oral Levodopa, in the form of Sinemet® (Levodopa/Carbidopa) or Madopar® (Levodopa/Benserazide) continue to be the gold standard treatment in PD since the 1960's (Hornykiewicz, 2010). The introduction of dopamine agonists such as Sifrol® and Cabaser® (Cabergoline) and enzyme inhibitors such as Comtan® (Entacapone) and Azilect® (Rasagiline) have assisted in maintaining and/or prolonging 'ON' periods and better management of PD symptoms (Hayes et. al. 2010).

The development of combination drugs such as Stalevo® (Levodopa/Carbidopa/Entacapone) and once daily extended release tablets such as Sifrol ER® (Pramipexole Extended Release) have enhanced simplicity and convenience in the patient's often complex medication regimen (Hayes et. al. 2010).

Delayed gastric emptying in patients with PD often leads to sporadic absorption of oral PD medications which can worsen motor fluctuations. As a result, more contemporary treatments attempt to bypass the gastrointestinal tract. The Neupro® (Rotigitine) patch, for example, is a form of dopamine agonist made into a daily 24 hour patch and is the only transdermal treatment currently available in the management of PD (Hayes et. al. 2010).

The Advanced Treatments in PD

Currently there are three advanced treatments in Parkinson's Disease based upon the concepts of providing stable and continuous dopaminergic stimulation to prevent the sudden and unexpected fluctuations in dopaminergic plasma levels. These treatments include Apomorphine, Duodopa® and Deep Brain Stimulation (DBS) (Hayes et. al. 2010).

Apomorphine is a subcutaneous injection and is the only injectable treatment available to manage PD. Apomorphine is a dopamine agonist that works to stimulate the dopamine receptors in the substantia nigra, more specifically the D1 and D2 receptors. It can be given as an intermittent rescue injection using a heparin/insulin syringe or via continuous subcutaneous infusion. Although it is derived from the morphine molecule it has no narcotic, analgesic or addictive properties. The dilution and infusion rates on the pump are pre-set and individualized to each patient

by a neurologist and commonly in conjunction with a Parkinson's Disease Nurse Specialist (PDNS) (Hayes et. al. 2010). .

Duodopa® is an intestinal gel of Levodopa/ Carbidopa (20mg/5mg/ml) enclosed in a 100 ml cassette delivered via an infusion pump for the treatment of Parkinson's Disease. The Duodopa® pump infuses the medication directly into the duodenum or jejunum via a Percutaneous Endoscopic Gastrostomy (PEG) tube with a Percutaneous Endoscopic Jejunostomy (PEJ) threaded through it. The effect is superior to oral medications because the absorption of the medication is optimal in the duodenum or jejunum. The infusion rates on the pump are also pre-set and titrated individually for each patient (Hayes et. al. 2010).

Deep brain stimulation is a neurosurgical option in the treatment of Parkinson's Disease. The treatment involves stereotactic insertion of electrodes into target sites in the brain, usually the subthalamic nucleus or globus pallidus, and connecting the electrodes to a pacemaker to control the abnormal firing of neurons by delivering steady and continuous electrical impulses to the target sites (Hayes et. al. 2010).

The Role of the Parkinson's Disease Nurse Specialist

With the development of advanced treatments in PD, there is growing complexity and subspecialisation of these treatments. Nursing assessments and interventions are vital in the initiation, implementation and ongoing management of advanced treatments in PD. Pre and post treatment assessments including the use of the Unified Parkinson's Disease Rating Scale (UPDRS), cognitive assessments, quality of life assessments and other psychosocial assessments require the expertise, detailed attention and dedicated time of a specialised PDNS. With the thoroughness of the nursing assessment, the PDNS becomes the ideal person to determine and profile which patient is appropriate for which advanced treatment based on treatment goals, lifestyle wants or needs and comorbidities.

The PDNS is also in the perfect position to be the patient's point of contact and liaison with the neurologist for medical and psychosocial support and also for follow up purposes. These may include issues such as troubleshooting device malfunctions, side effects monitoring and coordinating with other allied health professionals of the multidisciplinary team to manage the multifaceted aspects of PD.

The Future of the Parkinson's Disease Nurse Specialist Role

With the growing development of technology and advanced treatments, there is a growing need for the expertise of Parkinson's Disease Nurse Specialists. However, the majority of PDNS in New South Wales are funded only at a part time capacity and majority by pharmaceutical companies and/or research grants and therefore ongoing funding cannot always be guaranteed. Formal education programs or courses are in the development process but still in preliminary stages and there is a need for accreditation programs to ensure that PDNS are practicing according to a standardised and evidence based guidelines.

An audit performed by the World Health Organisation (WHO) in collaboration with European Parkinson's Disease Association (EPDA) and International Council of Nurses (ICN) revealed similar responses from current PDNS practicing in numerous different countries. They conclude with a consensus view that there is a lack and a need for uniformity in formal education courses and established career pathways for the development of a PDNS. A good model for the Australian PDNS to follow would be to examine the role of the PDNS in the United Kingdom of which the role was first described in the early 1990's (European Parkinson's Disease Association, 2009).

Conclusion

The field of Parkinson's Disease and Movement Disorders are growing in complexity and specialty as technology and the development of advanced treatments become more prominent and accessible. The role of the PDNS and the multidisciplinary team are a vital part of this process and there is a need for more stable government funding and accredited education programs for the development of the role of the PDNS.

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