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Parkinson's disease in the older patient

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ABSTRACT

Parkinson's disease (PD) is the second most commonly encountered neurodegenerative condition in clinical practice and probably offers a significantly greater variety of challenges than the management of Alzheimer's disease. As with most neurodegenerative diseases, age represents the leading risk factor for the development of PD. Current estimates would suggest that PD affects 1–2% of people over the age of 65 years and each decade sees an increasing number of cases. In addition, it is well recognised that most industrialised nations have an increasing proportion of individuals living longer. For example, recent data from Australia indicates that the prevalence of PD is anticipated to rise by 80% over the next 20 years and as such, we must all strive towards improving our clinical management of this common condition. In this article, we will attempt to highlight the issues that should be actively sought out and, where possible, addressed. We hope that an improved level of understanding will lead to better outcomes in older patients with PD.

Introduction

Our understanding of the neurobiology underlying Parkinson's disease (PD) is still in the germinal phase. A differential pattern of neuronal cell loss with a propensity towards the nigrostriatal dopaminergic projection in association with alpha-synuclein containing Lewy bodies is well appreciated and strongly correlated with a number of motor symptoms. However, other neurotransmitter systems are affected and are likely to account, at least in part, for many of the non-motor features of PD. The role of the Lewy body is hotly disputed, with recent suggestions pointing towards its possible role in a prion-like process leading to the neurodegeneration observed.[1] Despite these gaps in the knowledge base, it is clear that the rate of progression observed in PD is related to the age of disease onset with older patients having an accelerated course,[2,3] which has significant implications for those clinicians managing such cases.

Given that the majority of PD patients would be classified as being 'older', it might seem incongruous to focus on the specific considerations of managing this condition in older patients. However, this cohort does come with their own particular set of clinical challenges that have differential impacts on both the motor and non-motor features of disease. Many of these individuals will have multiple comorbidities and are likely to require polypharmacy, which can not only result in drug interactions and adverse events but also impact on the compliance to complex PD medication regimens. One of the common pitfalls in the management of PD in older patients is to ascribe all symptoms to it while failing to identify common comorbidities that can be managed. For example, most PD patients experience pain (most commonly musculoskeletal). This has obvious compounding impacts upon physical symptoms such as gait and slowness and will also be a major driver of depression, which in combination reduces quality of life and exacerbates caregiver strain.[4] In addition to such clinical factors, the older patient often exists within a different social construct. If at home, they may have limited support mechanisms and face physically challenging environments, whereas if placed in residential care there are often issues of maintaining autonomy and an understandable lack of the appropriate skills among staff.

Physical symptoms

One of the first considerations for managing PD in the older patient relates to the diagnosis itself. This can operate via two processes, namely missed diagnosis and misdiagnosis. Older people with PD may be overlooked as their parkinsonism may be mistaken for osteoarthritis, other musculoskeletal conditions and/or cardiopulmonary complaints. Furthermore, it is also this cohort

Key points

- Specific considerations are to be taken to achieve holistic care in the management of Parkinson's disease (PD) in an older person.
- Identifying non-motor symptoms, their severity, their burden on the care-giver and their management remain the hall marks of PD care in an older person.
- Input from multidisciplinary teams helps to assist this very challenging cause of improving the health-related quality of life for an older person with PD.
- Rivastigmine is the most effective drug in treating PD dementia.

KEYWORDS: Non-motor symptoms of PD, minimal cognitive impairment, PD dementia, PD psychosis, care-giver burden, holistic care ■

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who will have acquired other neurological insults, such as through cerebrovascular disease. So in essence, one must be mindful of missing the diagnosis of PD in older patients. In the absence of a diagnostic test, misdiagnosis of PD is also not uncommon and multiple mimics should be actively excluded, especially if they might be reversible like normal pressure hydrocephalus.

Reduced mobility in older PD patients should be aggressively addressed. Many patients will benefit from an active rheumatology or orthopaedic opinion, especially where pain is a significant limiting factor. Similarly, both physiotherapy and occupational therapy input can prove invaluable. Walking aids, as well as home modifications, can often improve mobility and reduce falls risk. It should be recognised that osteoporosis represents a significant comorbidity in this population and, given the increased risk of fracture from falls, should be actively screened for and treated prospectively. The conjunctive use of simple measures, such as hip pads, can also be an effective method for reducing fracture, which would necessitate a lengthy admission and commonly triggers transition into institutional care.

Improving physical symptoms in PD with dopaminergic medication should always be considered. However, such efforts are often limited by other specific non-motor issues like confusion and postural hypotension, as well as a limited absorption of prescribed medication. It is well recognised that gastric motility is reduced in PD and is even more significant in older patients. The absorption of L-dopa is restricted to the small intestine and, therefore, delayed gastric emptying will impact on the efficacy of each dose, even in patients with the most diligent compliance. A number of approaches can circumvent the issue of delayed gastric emptying, such as topical patch therapy (Rotigotine), L-dopa/carbidopa intestinal gel (Duodopa, AbbVie Ltd, Maidenhead, UK) infusion directly into the jejunem, subcutaneous apomorphine and, of course, deep brain stimulation. However, many older patients are not suitable for these approaches and clinicians are often left with the advice to use multiple low doses of L-dopa administered (ideally) on an empty stomach, while limiting protein in the diet.

Neuropsychiatric symptoms

Along with falls, problems of failing memory and the development of psychotic symptoms represent the leading causes for nursing home placement for PD patients. The natural history of PD, observed within prospective studies, would suggest that at 10 years, 70% of patients are experiencing psychotic features like hallucinations and paranoia, and after 20 years of disease, approximately 80% will have dementia.[5] However, it should be acknowledged that these rates are strongly associated with age at diagnosis, such that a patient diagnosed in their 70s will have a significantly faster progression to these neuropsychiatric complaints compared with a patient diagnosed in their 50s.[2]

It has been reported from multiple studies that at the time of the first diagnosis, approximately 20–50% of all PD patients meet criteria for mild cognitive impairment (MCI), a recognised 'at risk' state for the transition to PD dementia (PDD).[6] While a number of pharmacological trials have attempted to treat PDD and PD-MCI,[7] only rivastigmine has been shown to have any benefit in patients with PDD,[8] a finding that was not replicated in PD-MCI patients.[9] Rivastigmine has also been shown to be beneficial in the management of parkinsonian psychosis.[10]

Given that a significant proportion of PDD patients who come to postmortem have coexistent Alzheimer's disease, the mechanism of benefit from this cholinesterase inhibitor remains unclear. Non-pharmacological approaches like cognitive training hold obvious appeal in older PD patients and there is increasing evidence that such programmes can improve cognition.[11] However, there are obviously a number of difficulties in accessing such therapies and the likelihood of sustained benefit remains in doubt.

The emergence of psychotic symptoms in PD can be either gradual or abrupt in onset. A slow evolution with disease progression presumably mirroring cortical Lewy body pathology is common, passing through a number of phenomena including *ou de presence*/passage (where a shadow is seen out of the corner of the eye or passing by in the periphery), misperceptions (eg seeing figures hiding in the trees) and benign hallucinations (well formed, non-threatening images, often of people or animals). An ophthalmology review will help rule out confounders such as floaters, cataracts and macular degeneration. An abrupt onset in a previously unaffected individual usually signals a concomitant event such as infection, new medication or untreated constipation. The acute management of florid psychosis and paranoia is to identify any reversible cause and withhold dopaminergic medications. Often, medication regimens will need to be simplified to exclude adjuvant therapies and maintain the lowest possible dose of L-dopa that will facilitate management of the patient. Pervasive psychosis may require the use of atypical antipsychotic medication. Interestingly, although a number of agents, including quetiapine, olanzapine and aripiprazole, are commonly used and are efficacious in clinical practice, the only agent to have shown significant benefit in randomised controlled trials is clozapine,[12] which obviously is a difficult agent to use in this population because of the careful haematological monitoring required. As with all prescribing in these patients, lower doses should be initiated with frequent review to avoid adverse events.[13]

Affective disorder, including depression, anxiety and apathy, is common and affects approximately 40% of patients with PD. Often these symptoms coexist and are easy to miss, especially in older patients. Non-pharmacological approaches, such as counselling, are to be encouraged, especially when considering the potential for adverse events with tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors. While level 1 evidence does support the use of paroxetine, venlafaxine, amitryptiline and nortryptiline, these studies were not conducted specifically in older PD patients and obvious comorbidities may determine prescribing to avoid cardiovascular, anticholinergic or other complications. Neuropsychiatric symptoms (NPS) have been identified to be major determinants of caregiver burden in PD.[14]

Bulbar, autonomic, gastrointestinal, urological and sleep symptoms

One of the pitfalls to be avoided in the management of older patients with PD is not to ascribe every complaint to PD. Remembering that 1% of over 65-year-olds have PD, it is not surprising that such patients can develop other pathologies. For example, dysphagia may arise from motor neurone disease or myasthenia gravis; syncope as a result of arrhythmia; constipation can emerge in bowel cancer, and bladder dysfunction with prostatic issues or gynaecological prolapse.

Speech and swallowing issues are very troublesome in PD and patients should be encouraged to undertake speech therapy early in the course of their disease given its proven beneficial effect on both of these symptoms. The early involvement of a speech pathologist can also help in the assessment of swallowing, with advice on

dietary preparation to reduce aspiration. In a very small number of cases, consideration of enteral feeding via a percutaneous endoscopic gastrostomy tube is warranted. In those patients with troubling sialorrhoea, promoting deglutition with chewing gum or by sucking sweets is often less troublesome than trying to harness the benefits of pharmacological approaches such as anticholinergics (eg hyoscine skin patch, atropine eye drops applied topically, TCAs) or injectable agents (eg botulinum toxin, glycopyrrolate).

Postural hypotension calls for a review of the medication chart to discontinue agents that might be exacerbating the combined effect of disease and dopaminergic medication. Simple measures include elevating the head of the bed, increasing fluid intake, adding salt to the diet before using pharmacological approaches such as fludrocortisone, pyridostigmine, midodrine and, where available, droxidopa. Where there are concerns about overnight supine hypertension, a short acting, reversible agent such as a topical glyceryl trinitrate (GTN) patch can be an option.

Constipation is extremely common in older PD patients and presumably relates to both central and peripheral involvement of the nervous system. The sequential introduction and combination of bulking agents, softeners and lubricants, osmotics and stimulants should be titrated against the needs of the individual patient.

Urinary disorders

While patients are often very willing to increase dietary fibre, they are usually much less enthusiastic about increasing their fluid intake, presumably in view of potentially exacerbating coexistent bladder symptoms. However, increased fluids are a pre-requisite for all of the constipation treatments above. The neural mechanisms underlying bladder dysfunction in PD is complex and not well understood but then common final pathway results in instability of the detrusor muscle of the bladder, which manifests as urinary urgency and frequency. Pelvic floor exercises are worth attempting but generally do not seem very effective in clinical practice, necessitating the use of a range of strategies including anticholinergics (eg propantheline, oxybutynin, tolterodine), TCAs (eg imipramine), selective alpha-adrenergic agonists (eg mirabegron), antidiuretic hormone to promote fluid retention and, finally, intravesical injections (eg botulinum toxin). Given that the older population is often sensitive to a number of these medications, it can be worth early consideration of more invasive but locally acting injection therapy, if such services exist locally. The duration of effect for botulinum is generally estimated to be approximately 8 months, which in many cases might be seen as a reasonable trade-off.

Sleep-wake disturbances in PD are common and take a variety of forms that may coexist. The incidence of obstructive sleep apnoea (OSA) increases with ageing but case–control studies have not demonstrated higher rates amongst PD patients. However, given that OSA represents a potentially treatable cause of sleep disturbance, it should be excluded, especially in patients with excessive daytime somnolence. Increasing sleep fragmentation with difficulties entering into and remaining in the deeper stages of rapid eye movement (REM) and non-REM sleep is also associated with normal ageing and these features are further exacerbated in PD. Currently, no level 1 evidence exists for the use of hypnotics in PD (eg melatonin, eszopiclone), although improving motor PD symptoms with the rotigotine patch has been associated with an improvement in self-reported overnight sleep. Although five separate trials have shown no benefit for the use of modafanil in the treatment of excessive daytime somnolence in PD, a recent meta-analysis[15] of four of these studies did show some potential benefit of this agent, although its use would be clearly limited in the older cohort. Rapid eye movement disorder affects over half of all PD patients; they can experience violent dream enactment leading to injury to themselves and/or their bed partner. Although effective, clonazepam is probably best avoided in older patients with PD in preference to a trial of oral melatonin taken before sleep.

Conclusions

All patients with PD represent a difficult management challenge given their mixture of motor and non-motor complaints. However, these issues are compounded in older patients who need careful evaluation to identify troublesome symptoms that might benefit from treatment.■

Conflicts of interest

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