ECRONICON OPEN ACCESS

EC NEUROLOGY
Mini Review

Parkinson's Disease, the Rationale to Start Treatment Early, Start Low and Go Slow

Roy G Beran[1,2,3]*

[1]*Conjoint Professor, South Western Clinical School, University of New South Wales, Sydney, NSW, Australia*

[2]*Professor, Medical School, Griffith University, Broadbeach, Qld, Australia*

[3]*Professor, Chair, Medical Law, Sechenov, Moscow First State University, Moscow, Russia*

***Corresponding Author:** Roy G Beran, Conjoint Professor, South Western Clinical School, University of New South Wales, Sydney, PO Box 598, Northbridge, NSW 1560, Australia.

Received: April 11, 2021; **Published:** May 27, 2021

DOI: 10.31080/ecne.2021.13.00898

Abstract

Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disease. Idiopathic PD may be more prevalent with the suggestion that PD is part of the natural progression of aging.

Background Information: The diagnosis of PD is a clinical diagnosis with no absolutely reliable, antemortem, objective test for diagnosis which remains reliant on the cardinal features of bradykinesia, rigidity and resting tremor with a basic requirement of at least two out of these three features. The neurones involved in PD are the same as those involved during aging. Progression of PD is more dependent upon advancing age, rather than duration, with the hall mark features of PD being significantly increased with age.

Discussion: The interchange of PD with aging led to an alternative approach to the management reliant on early initiation of L dopa, once PD is clinically evident, starting very low and going very slow. This was subjected to an audit confirming efficacy when compared to current regimen.

Conclusion: There is justification for the hypothesis that idiopathic PD represents aging, rather than a true pathophysiological disease, and very early introduction of dopamine replacement and supplementation, starting low and going slow is a viable alternative.

Keywords: *Parkinson's Disease; Treatment, Pathophysiology, Neuro Degeneration, Aging*

Introduction

Parkinson's disease (PD) is described as the second most common neurodegenerative disease [1-4], making it a very common neurological diagnosis, affecting approximately an estimated 0.46% (95%CI 0.23 - 0.68) prevalence of PD patients treated with medications, aged 50 years or older and a 10-year incidence of 0.84% (95%CI 0.54 - 1.33) [5]. There is an alternative view that suggests that idiopathic PD has a much higher prevalence, that has been missed in most who have it, until it is very obvious, with the argument being that PD is not, of itself, a disease but rather part of the natural progression of aging and, if sought conscientiously, will be found in many more geriatric patients [6,7].

Background Information

The diagnosis of PD is a clinical diagnosis which includes the features of bradykinesia, resting tremor, rigidity, flexed posture, "freezing," and loss of postural reflexes [8]. It is a slowly progressive syndrome which starts insidiously and usually affects one side of the body before spreading to involve the other side [8]. Pathology shows loss of neuromelanin-containing monoamine neurons, particularly dopamine (DA) neurons in the substantia nigra pars compacta [8]. DA loss in the nigrostriatal neurones accounts for many of the motor symptoms, which can be treated with DA replacement, such as levodopa. Most cases are sporadic but there are rare genetic causes [8]. Nonmotor symptoms (depression, lack of motivation, passivity, and dementia) commonly occur to add to the clinical picture [8].

James Parkinson is attributed with describing the syndrome in 1817, referring to it as Paralysis Agitans [9]. He described the classical "… resting tremor, stiffness and characteristic station and gait…" to which, in 1872, Charcot added bradykinesia as a seminal feature [10] and suggested the eponymous name of PD. References to elements of PD long predate James Parkinson and date back to ancient Chinese, Indian, Babylonian and Greek texts, thereby establishing its relatively broad-based, ubiquitous nature across cultures and societies [6,10].

There is still no absolutely reliable, antemortem, objective test to clinically diagnose PD with the diagnosis being dependent on expert opinion as the "gold standard" [11,12]. The diagnosis remains reliant on the cardinal features of bradykinesia, rigidity and resting tremor [6,13] with a basic requirement of at least two out of these three features. Various primitive reflexes, such as the glabellar tap, grasp reflexes and palmar mental/naso-palpebral reflexes, when present, assist in the clinical diagnosis of PD [6,14].

As described by Fahn [8], it is understood that PD results from degeneration of dopamine producing neurones in the mid-brain, with the resultant expression of features of PD. Proteins relevant to the pathogenesis of PD, including α-synuclein, UCH-L1, PINK1 or DJ-1 are also involved in aging [15] which led Galvan and Wickmann [15] to hypothesise that "….Present data suggests that Parkinson's Disease could be the expression of aging on a cell population with high vulnerability to aging…".

This led Beran [6] to also question if PD was little more than a simple expression of part of the aging process with those neurones, affected during the evolution of PD, being the same neurones which degenerate during the normal aging process [6] and that PD may represent a local expression of aging which impacts upon a vulnerable cell population due to an increased number of synaptic terminals, mitochondria and unmyelinated axons [16]. The clinical progression of PD is more dependant upon advancing age, as compared with disease duration [6], with a biological interaction between the disease process and aging on non-dopaminergic structures [6,17]. Parkinsonian features, the hall mark of PD, are significantly increased with age [6,17] with an artificial separation and differentiation between PD and Parkinsonism [6,18].

Discussion

Acknowledging that references to Parkinsonian features long predated James Parkinson's description [10], dating almost to the start of the history of humankind, including ancient Chinese, Indian, Babylonian and Greek texts [10], leads one to assume that PD may well be a feature of aging, with the ubiquitous nature of the picture. The above picture [6,16-18] which evaluates the interchange of PD and aging adds further to this hypothesis with the features of aging being considered as an integral component of PD [19]. This led Beran [20] to develop an alternative approach to the management of PD. This approach [20,21] relied on the initiation of L dopa, as soon as the diagnosis was clinically evident, based on the presence of at least 2 of the cardinal 3 features of PD, as described above [6,8,9-14]. This regime was maintained, at a tiny dosage of ½ L dopa/carbidopa (Sinemet®) 100/25 mg combination or L dopa/benserazide (Madopar®) also at the 100/25 strength, until reaching I bid, when other anti-Parkinsonian agents were added in sequence, including selegiline (Eldepryl®), pramipexol (Sifrol®) followed by the combination of L dopa/carbidopa with a catechol-O-methyl transferase (COMT) inhibitor (Stalevo®), also starting very low and going very slow [20].

This very early introduction of replacement therapy, based on starting early, starting low and going slow [20] was recognised as an alternative managerial paradigm for the treatment of PD. Having advocated same, it was accepted that it needed to be subjected to a rigid audit, to assess its efficacy, when compared to the accepted regimen, at the time, and as set out in the literature and was found to be superior [21]. This has been further interpreted as evidence supporting the hypothesis that PD represents a form of aging and that the introduction of dopamine replacement, as soon as there is clear evidence suggestive of PD, provides an effective and viable alternative approach to management. The argument is that it reflects the degenerative aging process and replaces the diminishing dopamine while the receptors thereof are still more sensitive and active.

Conclusion

Based on the above scenario and the response to treatment, as demonstrated in the clinical audit, there is justification for the hypothesis that idiopathic PD represents a picture of specific aging, rather than a true pathophysiological disease, and adopting an approach of very early introduction of PD remedies, with dopamine replacement and supplementation, starting low and going slow is a viable alternative.

Conflict of Interest

There are no conflicts of interest to declare.

Funding

There was no external funding associated with this paper.

Bibliography

1. Blaszczyk JW. "Parkinson's Disease and Neurodegeneration: GABA-Collapse Hypothesis". *Frontiers in Neuroscience* (2016).
2. Salari M., *et al*. "Demographic features and clinical characteristics of patients with Parkinson's disease in Isfahan". *Iranian Journal of Neurology* 17.1 (2018): 6-10.
3. Hague SM., *et al*. "Neurodegenerative disorders: Parkinson's disease and Huntington's disease". *Journal of Neurology, Neurosurgery, and Psychiatry* 76 (2005): 1058-1063.
4. Fahn S and Sulzer D. "Neurodegeneration and Neuroprotection in Parkinson Disease". *Neuro Rx* 1.1 (2004): 139-154.
5. Mehta P., *et al*. "Population prevalence and incidence of Parkinson's disease in an Australian community". *Journal of Internal Medicine* 37.12 (2007): 812-814.
6. Beran RG. "Is Parkinson's Disease truly a disease or simply an indication of a long life" (Short Communication)". *Neuro Neurosurg* 4 (2020): 1-2.
7. Galvan A and Wickmann T. "Pathophysiology of Parkinsonism". *Clinical Neurophysiology* 119.7 (2008): 1459-1474.
8. Fahn S. "Description of Parkinson's Disease as a Clinical Syndrome in Parkinson's Disease the Life Cycle of the Dopamine Neuron". Eds Howard J. Federoff HJ, Burke R E, Fahn S, and Fiskum G. The New York Academy of Sciences New York, New York (2003): 1-14.
9. Parkinson J. "An Essay on the Shaking Palsy. Sherwood, Neely, and Jones". London (1817).
10. Mulhearn RJ. "The history of James Parkinson and his disease". *Australian and New Zealand Journal of Medicine* 1 (1971): 1-6.

11. Postuma RB., *et al*. "The new definition and diagnostic criteria of Parkinson's Disease". *Lancet Neurology* 15 (2016): 546-548.

12. Marsili L., *et al*. "Diagnostic Criteria for Parkinson's Disease: From James Parkinson to the Concept of Prodromal Disease". *Frontiers in Neurology* 9 (2018): 156.

13. Postuma RB., *et al*. "MDS Clinical Diagnostic Criteria for Parkinson's Disease". *Movement Disorders* 30 (2015): 1591-1601.

14. Vreeling FW., *et al*. "Primitive reflexes in Parkinson's Disease". *Journal of Neurology, Neurosurgery, and Psychiatry* 56 (1993): 1323-1326.

15. Galvan A and Wickmann T. "Pathophysiology of Parkinsonism". *Clinical Neurophysiology* 119 (2008): 1459-1474.

16. Rodriguez M., *et al*. "The degeneration and replacement of dopamine cells in Parkinson's Disease: The role of ageing". *Frontiers in Neuroanatomy* 8 (2014): 80.

17. Rodriguez M., *et al*. "Parkinson's Disease as a result of aging". *Aging Cell* 14 (2015): 293-308.

18. Levy G. "The relationship of Parkinson's Disease with aging". *Archives of Neurology* 64 (2007): 1242-1246.

19. Buchanan AS., *et al*. "Parkinsonism in older adults and its association with adverse health outcomes and neuropathology". *Journal of Gerontology, Series A: Biological Sciences and Medical* 71 (2016): 549-556.

20. Beran RG. "Parkinson's Disease in Neurology for General Practitioners". Ed Beran RG Churchill Livingstone/Elsevier, Sydney (2012): 81-94.

21. Chow-Chuen J and Beran RG. "An independent clinical audit of an alternative treatment paradigm for the management of Parkinson's Disease". *Journal Profile Neurology Research International* 2 (2019): 180008.

Volume 13 Issue 6 June 2021