Parkinson Disease and Its Clinical Manifestations

A Doença de Parkinson e suas Manifestações Clínicas

Raphael Lopes Olegário[1], Jerrime Bernard Fobbs[2], Bruno Sousa Lopes[3], Paulinne Junqueira Silva Andresen Strini[4], Polyanne Junqueira Silva Andresen Strini[5], Lídia Mara Aguiar Bezerra de Melo[6]

Abstract

Parkinson's disease (PD) is a neurodegenerative disorder that leads to progressive deterioration of motor function due to loss of dopamine-producing brain cells. Symptoms generally develop slowly over years. The progression of symptoms varies from person-to-person due to the diversity of the disease. Although there is no cure yet, multiple treatment options ranging from prescription dispensing, disease management and/or medication therapy management and surgery exists as a means to help patients living with this disease. Parkinson's itself is not fatal, however, complications that arise as consequence of this disorder can be serious. The diagnosis of PD within a patient is based upon its distinctive clinical features discerned from the patient's medical history and neurologic examination. At a minimum, bradykinesia coupled with either tremors or rigidity must be present in order to consider diagnosing a person with PD.

Key words: Parkinson Disease, Neurology, Parkinsonian Disorders, Neurophysiology, Neuropathology.

Resumo

A doença de Parkinson (DP) é um distúrbio neurodegenerativo que leva à deterioração progressiva da função motora devido à perda de células cerebrais produtoras de dopamina. Os sintomas geralmente se desenvolvem lentamente ao longo dos anos. A progressão dos sintomas varia de pessoa para pessoa devido à diversidade da doença. Embora ainda não exista cura, existem várias opções de tratamento, desde a dispensação de medicamentos, manejo da doença e / ou manejo da

[1] Graduate in Physical Education. Faculty of Physical Education. University of Brasilia (UNB). Brasilia, DF. Brazil. E-mail do primeiro autor: mr.raphaelolegario@gmail.com
[2] Graduate with a Bachelor of Arts in History, University of Dallas (UD). Irving, TX. United States.
[3] Doctorate in Gerontology, Catholic University of Brasília (UCB). Professor at Euro-American University Center (UNIEURO). Brasília, DF. Brazil.
[4] Doctorate in Bucodental Biology, The University of Campinas (UNICAMP). Professor of Anatomy at Federal University of Uberlandia (UFU). Uberlandia, MG. Brazil.
[5] Doctorate in Bucodental Biology, The University of Campinas (UNICAMP). Professor of Anatomy at Federal University of Goias (UFG). Jatai, GO. Brazil.
[6] Doctorate in Physical Education, Catholic University of Brasília (UCB). Professor at University of Brasília (UNB). Brasília, DF. Brazil.

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terapia medicamentosa. A cirurgia existe como meio de ajudar os pacientes que vivem com essa doença. A DP não é fatal, no entanto, as complicações que surgem como consequência deste distúrbio podem ser graves. O diagnóstico da DP dentro de um paciente é baseado em suas características clínicas distintas, discernidas do histórico médico do paciente e do exame neurológico. No mínimo, a bradicinesia associada a tremores ou rigidez deve estar presente para considerar o diagnóstico de uma pessoa com DP.

Palavras-chave: Doença de Parkinson, Neurologia, Transtornos Parkinsonianos, Neurofisiologia, Neuropatologia.

INTRODUCTION

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system.[1] The motor system is the part of the central nervous system that is involved with movement. It consists of the pyramidal tract, which starts in the motor center of the cerebral cortex and extrapyramidal system and is located in the reticular formation of the medulla. Parkinson's targets the lower motor neurons in the spinal cord that are involved in reflexive and complex locomotive, movements and postural control. [2]

PD belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells, causing a severe depletion in striatal dopamine. The motor symptoms are attributed to the loss of striatal dopaminergic neurons**;** although**,** the presence of non-motor symptoms supports neuronal loss in non-dopaminergic areas as well. Although the cause of PD is unknown, scientists believe that both genetic and environmental variables contribute to the development of this particular neurodegenerative disorder [1, 4].

The primary symptoms of PD are tremors, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination.[1] Several hypotheses have been put forth to reveal the categorical genesis of bradykinesia [5-8] According to some studies, the bradykinesia may be a compensatory response whereby patients slow down in order to improve movement accuracy.[5,6] However, it cannot be fully considered as such due to the fact that, bradykinesia still persists when spatial accuracy constraints of the task are removed. [7,9]

The motor symptoms of the disease result from the death of cells in the substantia nigra (Figure 1), a basal ganglia structure located in the midbrain that plays an important role in reward and movement.[3]

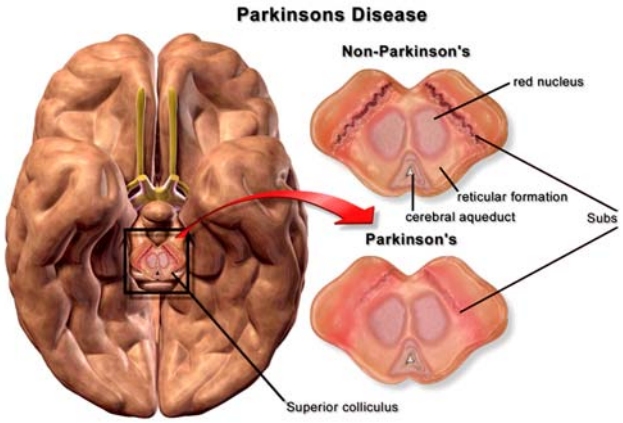

Figure1. Substantia Nigra. Source: Blausen.com staff (2014).

As these symptoms become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks. Dementia becomes common in the advanced stages of the disease.[10] As the disease progresses, the shaking, or tremor, which affects the majority of people with PD may begin to interfere with daily activities. The main risk factor is age because PD is more common in elderly persons - 50 years of age and older. Early symptoms are subtle and occur gradually. In some people the disease progresses more quickly than in others. [1-4]

The disease can be difficult to diagnose correctly. Doctors may sometimes request brain scans or laboratory tests in order to rule out other diseases. Recent brain imaging techniques are generally categorized as structural - magnetic resonance imaging, MRI; computed tomography, CT — and functional— positron emission tomography, PET; single photon emission computed tomography, SPECT. There are several studies of structural and functional imaging, but they are mainly conducted at single centers and case numbers are generally small.[11-14] Other symptoms may include depression and other emotional maladies; difficulty in swallowing, chewing, and speaking; urinary problems or intestinal constipation; skin problems; and sleep disruptions.

Therefore the diagnosis is based on medical history and a neurological examination. As the disease progresses, the shaking, or tremor, which affects the majority of people with PD may begin to interfere with daily activities [1,11,13]. The correct diagnosis of PD is important for therapeutic reasons and is essential for clinical research. Many experts use the UK Parkinson's Disease Society's Brain Bank diagnostic criteria.[15]

To understand the variances in managing PD one must understand the numerous treatment options available to each individual patient. Prescription

dispensing is widely used approach for nearly all medical maladies, including PD. According to the American College of Clinical Pharmacy prescription dispensing "focuses on a medication product, providing the right drug to the right patient with basic information on how to use the medication. As part of the dispensing process, an offer to provide counseling or education on the specific product is made to the patient" prior to beginning of this treatment regimen. Furthermore, disease management is another option for those suffering from PD whereby activities focus on specific disease in many aspects beyond medication use is the aim of this therapy.[15, 16]

Disease management provides the patient with education and tools to manage their disease(s) and includes interventions focused on medical treatments such as health screenings and wellness services and lifestyle modifications focused on improving the overall management of the specific disease (e.g., diabetes management, asthma management, Parkinson's disease management). The focus on medications within disease management programs is limited to those medications specifically used to treat the patient's disease rather than the patient's entire medication regimen. Equally beneficial is the medication therapy management approach that focuses on ongoing management of the patient's entire medication regimen with a concentration on optimizing therapeutic effectiveness, preventing adverse events and achieving optimal medication therapy goals through active involvement of patients empowering them to be full participants in their own care through better understanding and use of their medications. [16]

Clinicians delay the introduction of symptomatic treatment until symptoms interfere with functional disability, on the basis that symptomatic treatment is unlikely to be effective for mild symptoms that are not interfering with life. However, this view may change if it is found that early symptomatic treatment slows progression, as has recently been suggested. When PD diagnoses are checked by autopsy, movement disorders experts are found on average to be 79.6% accurate at initial assessment and 83.9% accurate after they have refined their diagnosis at a follow-up examination. When clinical diagnoses performed mainly by non-experts are checked by autopsy, average accuracy is 73.8%. Overall, 80.6% of PD diagnoses are accurate, and 82.7% of diagnoses using the Brain Bank criteria are accurate. [36,21]

Levodopa, also known as L-DOPA, is the most potent drug for controlling PD

symptoms, particularly those related to bradykinesia.[17] It is a dopamine precursor, effective and well-tolerated dopamine replacement agent used to treat PD. However, because levodopa therapy is frequently associated with motor complications, such as fluctuations and dyskinesias, there is ongoing debate as to when in the course of PD it is most appropriate to initiate levodopa therapy. [18,19] A majority of patients treated with levodopa experience motor fluctuations, dyskinesias or other complications after 5 years of treatment.[20] The addition of carbidopa, a peripheral dopa decarboxylase inhibitor, enhances the therapeutic benefits of it.

Treating motor symptoms with surgery was once a common practice, but since the discovery of levodopa, the number of operations has declined. [22] Surgery for PD can be divided in two main groups: lesional and deep brain stimulation (DBS). Target areas for DBS or lesions include the thalamus, the globus pallidus or the subthalamic nucleus. Other, less common, surgical therapies involve intentional formation of lesions to suppress overactivity of specific subcortical areas. For example, pallidotomy involves surgical destruction of the globus pallidus to control dyskinesia.[22]

Exercise programs are recommended in people with Parkinson's disease. [23] Regular physical exercise with or without physical therapy can be beneficial to maintain and improve mobility, flexibility, strength, gait speed, and quality of life. [24] In terms of improving flexibility and range of motion for people experiencing rigidity, generalized relaxation techniques such as gentle rocking have been found to decrease excessive muscle tension. Other effective techniques to promote relaxation include slow rotational movements of the extremities and trunk, rhythmic initiation, diaphragmatic breathing, and meditation techniques. Strengthening exercises have shown improvements in strength and motor function for people with primary muscular weakness and weakness related to inactivity with mild to moderate Parkinson's disease. However, reports show a significant interaction between strength and the time the medications was taken. Therefore, it is recommended that people with PD should perform exercises 45 minutes to one hour after medications when they are at their best. [25] Exercise may improve constipation. [26] It is unclear if exercise reduces physical fatigue in PD. [27]

One of the most widely practiced treatments for speech disorders associated with Parkinson's disease is the Lee Silverman voice treatment (LSVT). Speech therapy and specifically LSVT may improve speech. [28] There have been few studies on the effectiveness of Occupational Therapy and their quality is poor, although there is some indication that it may improve motor skills and quality of life for the duration of the therapy. [28, 29]

The life expectancy of people with PD is reduced. [30] Cognitive decline and dementia, old age at onset, a more advanced disease state and presence of swallowing problems are all mortality risk factors. On the other hand, a disease pattern mainly characterized by tremor as opposed to rigidity predicts an improved survival. Mortality ratios are around twice those of unaffected people. [31]

The costs of PD to society are high, but precise calculations are difficult due to methodological issues in research and differences between countries. The largest share of direct cost comes from inpatient care and nursing homes, while the share coming from medication is substantially lower. [32] There is little prospect of significant new PD treatments in the near future.33 Currently active research directions include the search for new animal models of the disease and studies of the potential usefulness of gene therapy, stem cell transplants and neuroprotective agents.[34]

Stem cell transplants are a recent research target, because stem cells are easy to manipulate and stem cells transplanted into the brains of rodents and monkeys have been found to survive and reduce behavioral abnormalities. Nevertheless, use of fetal stem cells is controversial. It has been proposed that effective treatments may be developed in a less controversial way by use of induced pluripotent stem cells taken from adults. [34,35]

CONCLUSION

Parkinson's disease is a complex neurodegenerative disorder which leads to progressive impairment of motor function caused by prominent loss of dopamine-secreting neurons within the substantia nigra. Parkinson's itself is not fatal, but its complications can be serious and lead to health and safety risks in those afflicted with this disorder. The goal of medical management of PD is to provide control of signs and symptoms for as long as possible while minimizing adverse effects. Knowledge regarding PD and its clinical manifestations is fundamental for the correct diagnosis of the disease and adequate treatment. It is hoped with this work to encourage future studies of the

area as well as to increase the knowledge shared by the current literature.

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