

PARKINSON'S DISEASE

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Abstract- Parkinson disease, though a common neurological movement issue to practice in medicine, is not always easy to treat and diagnose. The diagnosis among the PD patients is clinical and sometimes difficult given the fact that they experience numerous motor and non-motor symptoms. The medical management of the patients with Parkinson disease is not easy as there is little medication available and levodopa is the keystone of treatment. Yet, levodopa-induced dyskinesia (LID) affects people with Parkinson disease taking levodopa quite often. This is the negative outcome that may manifest itself immediately a few days or months later, despite the fact that it is usually the case after a long period of therapy. Various surgical procedures such as as deep brain stimulation and unilateral pallidotomy have warranted great results to PD patients who are not responding to treatment.

This is a bad side that may manifest itself immediately after a few days or months of therapy, despite the fact that it is usually manifested after a long period of treatment. A number of surgical procedures such as as deep brain stimulation and unilateral pallidotomy have demonstrated great results in PD patients who cannot be treated by medicine alone.

Keywords- Besides discussing the different pharmaceutical alternatives of treating the Parkinson disease, this paper discusses epidemiology of the disease, pathophysiology, genetics, pathology, and clinicoradiological presentations of individuals with this degenerative disease.

I. INTRODUCTION

Parkinson disease (PD) is a chronic, progressive neurological condition, which is defined by the premature and extensive destruction of dopamine-producing cells in the substantia pars compacta (Plus, it is also characterized by the overall accumulation of alpha-synuclein, a protein located inside cells. This causes the typical motor symptoms of Parkinsonism such as bradykinesia, shaking, stiffness, as well as in the advanced stages, postural issues due to lack of dopamine in the basal ganglia. In addition to these motor problems, PD has several non-motor symptoms that usually appear many years before the motor symptoms start to manifest themselves, and in many cases, aggravate as the condition progresses. Although there are many methods to treat Parkinson, medication is the most used in the treatment

of the disease (PD). These treatments are however primarily symptomatic and have significant limitations especially in the later stages of the condition. With the progression of PD, patients often experience diverse debilitating complications, and these may include non-motor symptoms, non-responsive motor symptoms, and the side effects of longtime usage of dopamine therapy. Although medical and surgical solutions to Parkinson disease (PD) have been made, there is still no conclusive cure that will alter the disease. However, studies are in the process of identifying possible targets to alter the course of the disease. The review indicates epidemiology, clinical presentation, pathophysiology, diagnosis, and the current treatment methodologies medicinal and surgical of PD. The experimental treatment which has demonstrated modest efficacy has not been discussed.

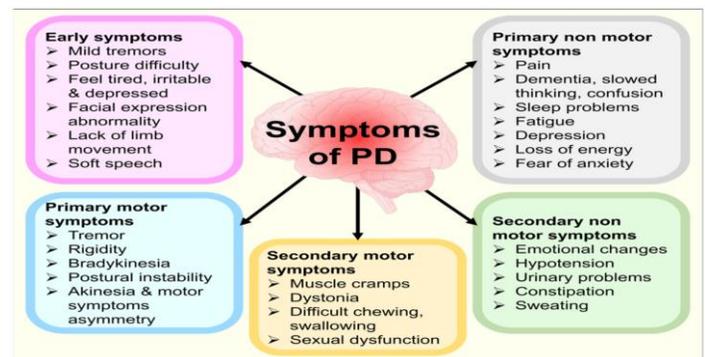


FIG NO 1

Epidemiology:

Parkinson disease (PD) is a neurodegenerative disorder of old age, and the cases as well as prevalence of the disease are related to old age. It influences about 1/000 people above 65-year old [1].

Early-onset Parkinson's disease (EOPD): PD is the occurrence of parkinsonian symptoms prior to the age of 40 and is observed in around 3-5% of all cases. EOPD is further subdivided into:

Juvenile Parkinson disease: first symptoms below the age of 21 years.

* Youthful-onset Parkinson disease (YOPD): onset age; 21-40 years old [2].

Epidemiological studies have always shown that the prevalence of Parkinson disease is two to three times higher in males, as compared to females. This superiority in males is believed to be a result of protective influence of hormones in female as well as a potential genetic peculiarity of males and females to exposure to environmental factors [3,4,5,6,7]. **Pathophysiology:**

Genetics of Parkinson's Disease

Genetic variation that leads to Parkinson disease (PD) constitutes between 5 and 10 percent of the total prevalence. [9,10]. The hereditary factor is typically assumed in individuals with a family history of the disease, those who have an early onset, and those with atypical clinical features, including the demonstration of dystonia. In young-onset PD (YOPD), over 10 percent would have a genetic origin. This number increases significantly and more than 40 percent of those who are diagnosed before the age of 30 years were found to have a genetically predetermined form of PD. [8,11,12,22].

There are some genes that have been detected as the cause of familial and early-onset PD. These include:

- * Parkin (PARK2)
- Leucine-rich repeat kinase 2 (LRRK2/PARK8).
- * Alpha-synuclein (SNCA - PARK1/PARK4)
- * PTEN-induced putative kinase 1 (PARK6)
- * DJ-1 (PARK7)
- * Ubiquitin C-terminal hydrolase L1 (UCH-L1)
- * ATPase type 13A2 (ATP13A2) [9,10,13]

These genetic changes are associated with various forms of inheritance (either autosomal dominant or recessive) and have contributed to our further understanding of the molecular mechanisms underlying PD, which include protein clustering, mitochondrial damage and oxidative damage.. [11,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46]

Genetics of PD in India:

There is a mutation report of between 1.96 to 39.1 percent among individuals with the Parkinson disease (PD) [The Parkin gene mutations are most commonly observed in the Indian population 14]. On the other hand, other genes linked to PD mutations are typically not identified, with DJ1, PINK1, and LRRK2 mutations being less frequent. [14].

These findings suggest that there is a distinct genotype of Parkinson disease in India, and Parkin gene mutations play a greater role, particularly in early-onset. The young patients with Parkinson disease with Parkin mutations and without them cannot be distinguished on the purely clinical basis only depending on their clinical features [9,10,19,24].

Neuropathology:

The etiology of the Parkinson disease (PD) is the progressive degeneration of the dopamine-producing neurons of the substantia nigra pars compacta (SNpc). Another notable phenomenon of PD is that, Lewy bodies, abnormal accumulation of proteins in cells, occurs. These aggregates primarily include alpha-synuclein (aSyn) and ubiquitin and are thought to aid the deterioration of normal neuronal functions and their survival.. [9,10,27,29].

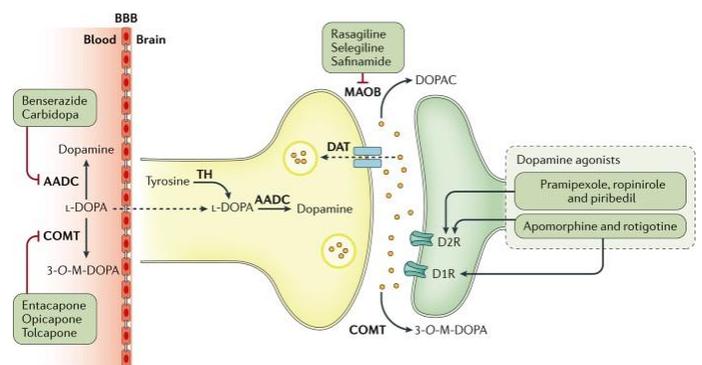


FIG NO 2

Nature Reviews | Disease Primers

Diagnosis of Parkinson's Disease (PD)

The diagnosis of Parkinson disease (PD) relies on the UK Parkinson disease society brain bank criteria [10]. According to these criteria, the person must first meet the diagnostic criteria of parkinsonism, which is the occurrence of bradykinesia (slowness in motion) and at least one out of the following crucial motor symptom attributes. [16,17,18]

- Muscular rigidity
- Resting tremor
- Postural instability

PD is subsequently identified by evaluating other supportive criteria after establishing that one has parkinsonism, as shown in Table 1 of the UK Brain Bank first publication [10,30].

Motor Symptoms

Several cardinal motor symptoms mark the Parkinson disease (PD), they include:

- Resting tremor (asymmetrical at onset)
- Bradykinesia (slowness of movements)
- Muscular rigidity
- Shuffling gait
- Postural instability

Parkinson diseases may start unobtrusively, with the initial symptoms being mistakenly interpreted as the constant changes that occur as a result of getting older. Despite the expressed fact maintained that Parkinson is an degenerative neurological disorder that progresses with age, however the rates at which motor symptoms occur sometimes vary significantly depending on an individual. [4].

Moreover, clinical types of PD exist when tremors, stiffness or balance may be considered the most predominant manifestations. [29].

Non-Motor Symptoms

A large number of non-motor symptoms is also linked to the parkinson disease (PD), and they include:

- Cognitive impairment
- Neuropsychiatric changes and behavior.
- Dysfunction of autonomic nervous system.
- Sensory disturbances
- Sleep disorders [21]

Non-motor symptoms may create significant problems of quality of life and treatment, as they are often less responsive to dopaminergic therapy than motor symptoms. [20].

Importantly, a range of non-motor features, such as constipation, the inability to smell (anosmia), or REM sleep behavior disorder, may be present many years and even decades prior to the motor manifestations. In the course of the disease development, nearly 90 percent of them experience at least one non-motor symptom. [22].

CONCLUSION

Parkinson disease (PD) is a significant clinical challenge. Owing to being among the most common neurodegenerative disorders, it primarily affects older adults, who are an age group that is increasing at a rapid pace worldwide. Despite the advancement in understanding of the disease, PD is yet to have the treatment that could alter the disease trajectory to prevent the insidious progression of the dopaminergic neurons.

Even though the consequential effect of the Parkinson disease is does not directly cause death, it is associated with increased disease and mortality due to the long-lasting consequences. Therefore, a clear understanding of its symptoms, modes of treatment as well as its progressive stages is important in providing the best care and improve the quality of life of individuals infected with Parkinson disease.

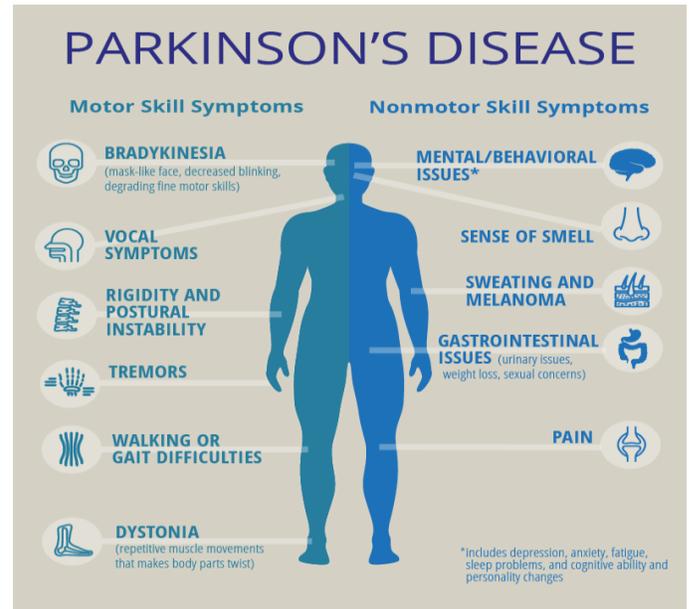


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