Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2022, Volume 10, Issue 01
ISSN: 2321–3647(online)

A Review Article on Parkinson's Disease

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ABSTRACT

Parkinson's disease (PD) is neurodegenerative disorder that affects predominantly dopamine producing neurons in a specific area of the brain called substantia nigra. Parkinson's disease is associated with risk factors including aging, family history, pesticide exposure and environmental chemicals. Its ultimate causes are unknown. Characterized by both motor and non motor symptoms. Recent decades have witnessed a proliferation of medical pharmacological therapies and innovative surgical interventions like deep brain stimulation (DBS).Exercise is important for people with PD because it helps to maintain balance, mobility and the ability to perform daily routines. This review mainly highlights the etiology, clinical features, diagnosis and treatment (pharmacological and non pharmacological therapies) of peoples with Parkinson's disease.

Keywords: Parkinson's disease, Neurodegenerative disorder, Deep Brain Stimulation (DBS), Diagnosis and Treatment.

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Received 01 December 2021, Accepted 10 January 2022

Please cite this article as: Nagarjuna D *et al*., A Review Article on Parkinson's Disease. American Journal of Pharmacy & Health Research 2022.

INTRODUCTION

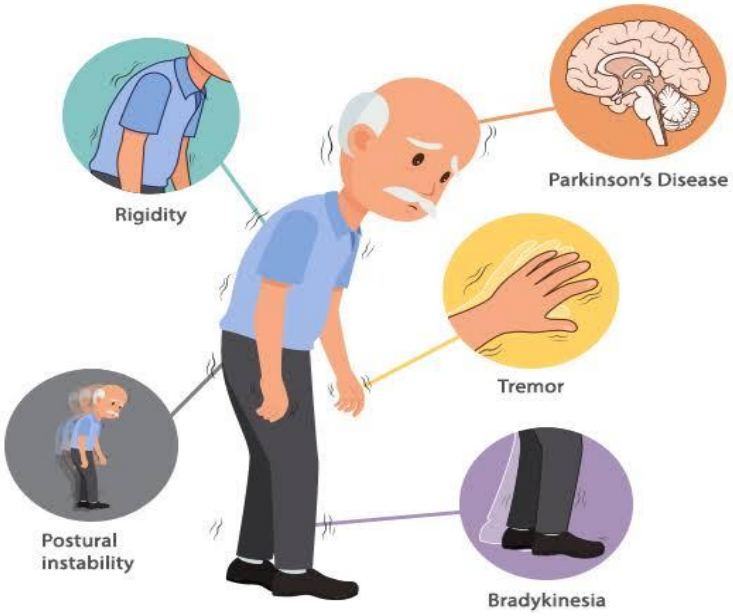
Parkinson's disease is a neurodegenerative disorder characterized by tremors, bradykinesia, rigidity and postural instability. Parkinson's disease was first described by British Physician Dr James Parkinson in 1817 published a case series describing six patients afflicted with the "shaking palsy" (paralysis agitans), a chronic and progressive neurologic disorder called Parkinsonism i.e., loss of control of movement. Parkinson's occurs when certain nerve cells in a part of the brain called the substantia nigra die or becomes impaired. Normally these cells produce a vital chemical known as Dopamine. Dopamine allows smooth, coordinated function of the body muscles and movement. When approximately 70% of the dopamine producing cells is damaged, the symptoms of Parkinson's disease appear. Then Parkinson's is recognized as one of the most common neurologic disorders, affecting approximately 1% of individuals older than 60 years it is progressive disorder marked by tremors ,rigidity ,bradykinesia.[1]

Parkinsonism is a clinical syndrome characterized by diminished facial expression, stooped posture, slowness of voluntary movement, festinating gait (progressively shortened, accelerated steps), rigidity, and a "pill-rolling" tremor. This type of motor disturbance is seen in a number of conditions that have in common damage to the nigrostriatal dopaminergic system. Parkinsonism may also be induced by drugs that affect this system, particularly dopamine antagonists and toxins. The principal diseases to be discussed here that involve the nigrostriatal system are as follows:

- Parkinson disease (PD)
- Multiple system atrophy, a disorder that may have parkinsonism as a prominent symptom as well as other symptoms (cerebellar ataxia and autonomic dysfunction)
- Post encephalitic parkinsonism, which was observed in the wake of the influenza pandemic that occurred between 1914 and 1918 and is now vanishingly rare.
- Progressive supranuclear palsy (PSP) and cortico basal degeneration (CBD), which are movement disorders that may also exhibit cognitive impairment; they share some pathologic and genetic features with each other and with other tauopathies.[2]

PD is also associated with non motor symptoms, which may precede motor symptoms by more than a decade. These non-motor symptoms become troublesome symptoms in the later stages of PD. Currently, the mainstay of PD management is pharmacological therapy; however, these symptomatic therapies have major limitations in advanced disease. Many disabling features develop later in the course of the disease including non-motor symptoms, dopamine resistant motor symptoms and motor complications of long-term dopamine therapy. Although there have

been remarkable advances in the medical and surgical treatment for PD, definitive disease modifying therapy is lacking. However, researchers are hopeful that they will be able to identify the potential targets for disease modification. In this review, we will be discussing the epidemiology, clinical features, pathophysiology, diagnosis and management (medical and surgical) of PD.[3]



Epidemiology

The incidence and prevalence of PD increases with advancing age, being present in 1% of people over the age of 65 years.[4,10] Early-onset Parkinson's disease (EOPD) is defined as the onset of parkinsonian features before the age of 40 years. It accounts for 3-5% of all PD cases. It is classified into the 'juvenile' (occurring before the age of 21 years) and 'young-onset' PD (YOPD, occurring in the age range of 21- 40 years). [5,11]

There is no homogenous and large epidemiological data on PD from India. Razdan*et al*., reported a crude prevalence rate of 14.1 per 100,000 amongst a population of 63,645 from rural Kashmir in the northern part of India. The prevalence rate over the age of 60 years was 247/100,000.[6] A low prevalence rate of 27/100,000 was reported from Bangalore, in the southern part of India, and 16.1/100,000 from rural Bengal, in the eastern part of India.[7,8] Bharucha *et al*., reported a high crude prevalence rate of 328.3/100,000 among a population of 14,010 Parsis living in colonies in Mumbai, Western India.[9]

Clinical manifestations: The clinical features historically associated with Parkinson's disease are the triad of **motor symptoms**, namely

- Tremor: shaking, which usually begins in the hand or arm and is more likely to occur when the limb is relaxed and resting

- Bradykinesia (slowness of movement): refers to slow movements with gradual loss of amplitude or speed during the rapid alteration of a body segment movements clinically bradykinesia can be tested by asking the patient to perform as rapidly and frequently as possible repetitive moments such as opening and closing the hands, tapping thumb and index fingers, or tapping the foot on the ground.
- Rigidity (muscle stiffness).stiffness and tension in the muscles , which can make it difficult to move around and make facial expressions , and can result in painful muscle cramps.[12]

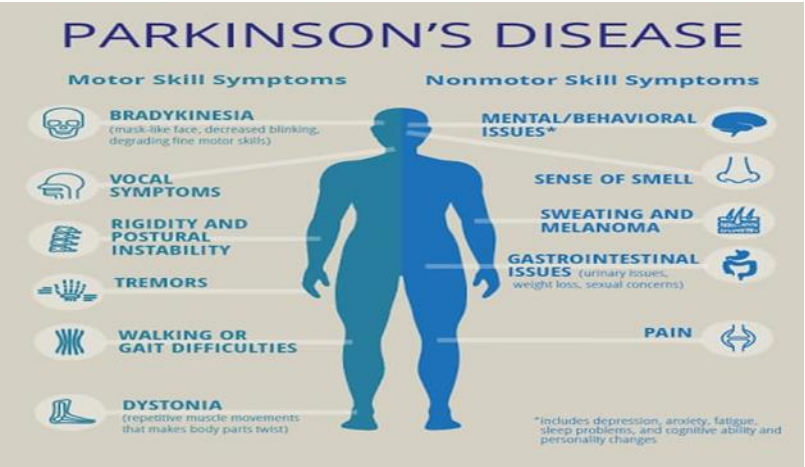
Physical symptoms:

- Loss of sense of smell (anosmia).
- Nerve pain.
- Constipation.
- Dizziness, blurred vision.
- Hyperhidrosis (excessive sweating).
- Excessive production of saliva (drooling).
- Insomnia (problems sleeping)
- Balancing problems[13]

Nonmotor symptoms

Cognitive and psychiatric symptoms:

- Depression and anxiety.
- Dementia.
- Hallucinations
- Mood disorders
- Neuro psychiatric features[13]



Etiology

PD is a multifactorial disease with both genetic and environmental factors playing a role,age is a biggest risk factors for Parkinson's Disease, with the median age of onset being 60 years of age.[14,15]Certain nerve cells in the brain gradually breakdown or die .many of the symptoms are due to loss of neurons that produce a chemical messenger in the brain called dopamine . when dopamine levels decrease, it causers abnormal brain activity, leading to impaired movement other symptoms of Parkinson's disease.

The cause of Parkinson's disease is unknown, but several factors appear to play role including

- Genetical factors
- Environmental triggers
- Cigarette smoking
- Caffeine
- Medications like antipsychotics
- Cerebrovascular diseases[16]

Risk Factors

- Past traumatic brain injury.
- Toxin exposure like pesticides, solvents, metals and other pollutants.
- Occupation.
- Age (about 1% of the people over age 60 have PD).
- gender(PD is more common in men than women).[17]

Diagnosis

The diagnosis of Parkinson's disease is usually based on clinical symptoms, history and evaluation, overtime on reaction to dopamine agents on the developments of motor fluctuations. Diagnosis of parkins disease

Step 1

Bradykinesia and at least one of the fallowing ;

- muscular rigidity
- rest termers(4 to 6 Hz)
- postural instability unrelated to primary visuals, cerebral and vestibular.

Step 2

Exclusion criteria for parkinsons disease History of

- repeated strokes with stepwise progression
- repeated head injury

- antipsychotic or dopamine drug
- more then effective related
- negative response to large doses of levodopa
- strictly unilateral features after 3 years
- exposure to known neurotoxins
- other neurological features: early sever dementia with disturbance of language, memory
- presence of cerebral tumour

Step 3

Supportive criteria for PD three or more required for diagnosis of definite PD

- unilateral onset
- rest tremor present
- progressive disorder
- persistent asymmetry affecting the side of onset most
- excellent response to levodopa
- levodopa response for over 5years
- clinical course of over 10 years

Neurological biomarkers

- Transcranial B -mode sonography (TCS)
- Magnetic resonance image (MRI)
- Single photon emission computed tomography scan (SPECT)
- Positron emission tomography scan[13,18]

Treatment

Medical therapies are the main stay of treatment for Parkinson's disease. They include pharmacotherapy and non-pharmacological treatment. Therapeutic approaches depend on patients age, disease stage, troubling symptoms, and the benefit/risk ratios of treatments.[19] Since pharmacotherapy for PD has increased substantively in its array of options, non pharmacological approaches will be discussed first.

NON PHARMACOLOGICAL TREATMENT

Non pharmacological alternative therapies include exercise, education, support groups, speech therapy and nutrition. Regular exercise and physical therapy can really assist with some of the bodily effects of PD such as joint rigidity and flexed posture. Exercises that target improved flexibility, strength, and balance should be emphasized. Patients may gain a sense of control over

some component of disease. Patient and family/ caregiver education is important but critically needed in a chronic progressive neurologic disease. Support groups are used very effectively for many chronic disease patients, and PD is no exception. Support groups can allow discussion of emotional and psychological concerns for patients and their caregivers.[20]

PHARMACOLOGICAL THERAPY

Pharmacological therapies for Parkinson's disease

Table 1: Pharmacological therapies for Parkinson's disease [20]

Group	Names	Mechanism of action
Dopamine	Carbidopa/levodopa (sinemet)	A dopamine precursor crosses the blood brain barrier (BBB) and is converted to dopamine in dopaminergic terminals by dopa-decarboxilase.
Dopamine agonists Non -Ergot	Pramipexole(mirapex) Ropinorole(requip)	Stimulates D2,D3,D4 receptors; weak stimulation of 5 -HT2 and alpha 2-adrenergic receptors
Dopamine Agonist Ergot	Bromocriptine (parlodel) Pergolide	Stimulates D2 receptors Stimulates 5HT1 and 5HT2 and NA Receptors Blockades D1 receptors
Injectable Dopamine agonists	Apomorphine(apokyn)	Stimulates D2- D5 receptors Antagonizes 5HT1 and 5HT2 receptors Antagonizes alpha 1 and alpha 2 adrenergic receptors
Monoamine oxidase-B inhibitors	Selegiline (Eldepryl) Rasagiline(Azilect)	Selective irreversible inhibition of MAO-B, inhibition of presynaptic dopamine receptors and dopamine uptake
CatecholO-Methyltransferase (COMT) inhibitors	Entacapone (Comtan) Tolcapone (Tasmar)	Reversible inhibition of COMT
N-Methyl-D-Aspartate (NMDA) receptor inhibitor	Amantadine	Increase synthesis and release of dopamine; blocks NMDA Glutamatergic receptors
Anticholinergics	Benztropine Trihexyphenidyl	Blockade of muscarinic cholinergic receptors and possible inhibition of cholinergic transmission in striatal interneurons

Surgery:

Deep brain stimulation rarely used for Parkinson's disease. This involves sending electrical impulses through a neurostimulator system to certain parts of the brain (usually SN or globus pallidus, which interacts with the SN), a brain implant known as a 'brain pacemaker'The target area of DBS is usually the subthalamic nucleus (STN). The stimulation of the dorsolateral STN border alongside the surgery can improve its efficiency.[13]

Gene Therapy:

In a recent decade, the advancement of PD gene therapy has made considerable progress. Wide loss of dopaminergic neurons is accompanied by decreasing within levels of aromatic amino acid decarboxylase (AADC), which transforms 1-DOPA to dopamine. By taking appropriate doses of levodopa, sufficient quantities of dopamine production can be managed using this tool. Another target for gene therapy in PD is glutamic acid decarboxylase (GAD) which facilitates GABA production in the subthalamic nucleus of GABA- ergic neurons. [13]

Prevention

It is not possible to prevent Parkinson's disease, but some lifestyle modification may help reduce the risk. That is

- Avoiding toxins i.e. should take precautions when using potentially toxic chemicals, such as herbicides, pesticides, and solvents. Taking precautions, such as wearing protective clothing, when it is not possible to avoid them.
- Avoid head trauma
- Exercise such as regular physical exercises may help prevent or treat Parkinson's disease.
- Dietary factors helps to reduce the risk of Parkinson's and other diseases.[17]

CONCLUSION

Parkinson's Disease represents a major clinical challenge since it is one of the most common chronic, progressive neurodegenerative disease affects primarily a population of aging individuals. Aetiology and pathogenic mechanism remain incompletelyunderstood .while a small proportion of PD patients have a monogenic cause of their disease, majority of the cases probably are not associated with specific genetic abnormality.Instead, it is likely the risk of PD is in a part, determined by combination of polygenic susceptibility factors. Knowledge of the disease manifestations, treatments and progressive long term course is essential for optimal care and enhanced quality of life for people with Parkinson's disease.

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