



A Review on Parkinson's Disease: Overview and Management

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Received: 04-06-2022; Revised: 19-08-2022; Accepted: 26-08-2022; Published on: 15-09-2022.

ABSTRACT

After Alzheimer's disease, Parkinson's disease is the most prevalent neurodegenerative condition. Parkinson's disease normally appears between the ages of 55 and 65, affects 1 to 2 percent of persons over 60, and progresses to 3 to 5 percent of people between the ages of 85 and 89. The olfactory bulbs and nucleus as well as the dorsal motor nucleus of the vagus nerve are first affected, followed by the locus coeruleus and finally the substantia nigra. Later on, the brain's cortical regions are impacted. The multifaceted pathophysiologic changes that result in impairments not only of the motor system but also of the cognitive and neuropsychological systems are caused by damage to these numerous neural systems. Although there is no known cure for Parkinson's disease, drugs can frequently significantly reduce the symptoms. Since they may be taken for a long period without having serious side effects and contain antioxidant characteristics, herbal drugs do well in this category. Surgery may be indicated in select cases with more severe conditions.

Keywords: Parkinson's disease, pharmacological treatment, herbal treatment.

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DOI:
10.47583/ijpsrr.2022.v76i01.004



DOI link: <http://dx.doi.org/10.47583/ijpsrr.2022.v76i01.004>

Pathophysiology

Parkinson's disease is characterized by a loss of dopaminergic neurones in the substantia nigra of the basal ganglia.³ A decrease in dopamine production results in facilitation of the indirect pathway because of a lack of D1 facilitation of the direct pathway and of D2 inhibition of the indirect pathway. This dopamine is associated with increased activity of inhibitory nuclei in the basal ganglia (using the neurotransmitter g-aminobutyric acid (GABA)), eventually leading to excessive inhibition, and effectively to a shutdown, of the thalamic and brainstem nuclei that receive from the basal ganglia. Excessive thalamic inhibition results in suppression of the cortical motor system with akinesia, rigidity and tremor, while inhibition of brainstem locomotor areas may contribute to abnormalities of posture and gait.⁴

Oxidative stress is thought to be the common underlying mechanism that leads to cellular dysfunction and demise. In Parkinson disease, oxidative stress induced by free radicals damages neuronal membrane lipids, proteins and other components of brain tissues and may cause dopaminergic degeneration in the substantia nigra.⁵ Antioxidant helps cells to cope with oxidative stress by effectively quenching free radicals. Antioxidants are generally regarded as safe – vitamin E, beta-carotene and lipoic acid.⁶

INTRODUCTION

Parkinson's disease (PD) is a severe longer, ongoing illness in motor symptoms. PD is more common as people get older, with 1% of persons over 65 years old having the disease. In most populations, men have twice the prevalence of PD as women. Female sex hormones may to prevent or treat. This male preponderance might be identified by the ability of biological sex genetic mechanisms or/and gender-specific differences in environmental risk factor exposure.¹ Parkinson's disease is peculiarities the creation of alpha-synuclein positive cytoplasmic aggregates known as Lewy bodies in surviving neurons, involves the continual Loss of dopaminergic neurons in the mesencephalon's substantia nigra pars compacta. PD have motor symptoms such as bradykinesia, stiffness, tremor, rigidity, freezing muscle cramps. Pathologically, Parkinson disease may cause depletion of dopamine in brain due to the presence of intra cytoplasmic inclusions known as Lewy bodies. It is not clear why Lewy body formation causes neuronal cell death. These pathological changes are also seen in the locus coeruleus and parasympathetic as well as sympathetic postganglionic neurons, pedunculo pontine raphe nucleus dorsal, and dorsal motor nucleus of the vagal nerve.²



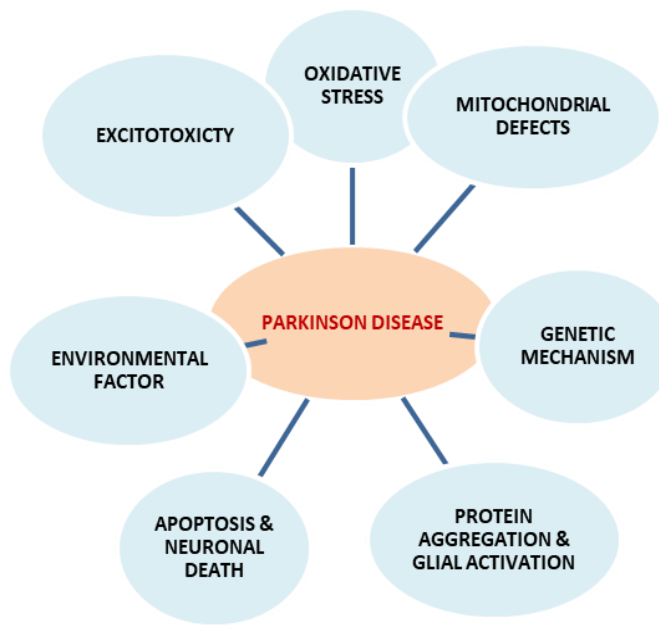


Figure 1: Pathology of Parkinson disease

Types of Parkinson’s disease

- **Primary Parkinsonism** – The majority of people around 80% suffer in this idiopathic type whose cause is unknown.
- **Corticobasal Degeneration (CBD)**– A type of Parkinsonism with progressive neuro-degenerative condition with numbness and loss of coordinated movement causing difficulties in dressing, writing, eating, etc.
- **Drug-induced Parkinsonism** – It is a form of Parkinson Disease which occurs after taking certain medicines. Some neuroleptic and antipsychotic drugs block the action of neurotransmitter dopamine causing staggering of gait and other movement disorders.
- **Multiple System Atrophy (MSA)** – This progressive neurological disease triggers over-production of a brain-protein called alpha difficulties. Synuclein which causes nerve cell degeneration and atrophy in several areas of the brain stem, cerebellum and basal ganglia. This nerve-cell degeneration can result movement disorders and other unconscious body functions.
- **Progressive Supranuclear Palsy (PSP)**– This neurodegenerative brain disease causes fronto-temporal dementia along with impairment of balance, speech and thought process.
- **Vascular Parkinsonism** – Stroke symptoms appear suddenly in this type of arteriosclerotic Parkinsonism which usually affects more in the lower extremities. Restricted blood supply to the brain is occurred in this type usually more older people who have been suffering in diabetes, including symptoms of urinary incontinence, loss of memory and walking.

Causes of Parkinson’s disease

- **Neurotransmitter Death** – The brain's substantia nigra produce dopamine. If the dopaminergic neurons that secrete dopamine begin to die rapidly, the amount of dopamine in the body declines, resulting in Parkinson's symptoms.
- **Gene Abnormality** - The much more similar inherited cause of Parkinson's disease is a single genetic mutation in the LRRK2 gene.
- **Environmental Cause** - Some chemicals and metals have been related to Parkinsonism, according to recent study. Herbicides, insecticides, and fungicides used in crops, and also metals used in factories like spur, manganese, and trichloroethylene, all could cause the disease.
- **Previous Head Injury** – If a patient had suffered a serious head injury and went into shock in the previous, he or she is more prone to developing Parkinson's cancer later in life.
- **Presence of Alpha-synuclein within Lewy Body** – Some microscopic marks remain in our brain cells as Lewy bodies, which are clumps of a specific substance. Within Lewy bodies, a crucial natural and widely spread protein called alpha-synuclein can deactivate the disease's cause.

Symptoms

Symptoms usually appear after the age of 50. The mean age at onset is 55-75 years in both sexes. The young are no except and onset before age of 30 does not preclude a diagnosis of Parkinson disease.⁷

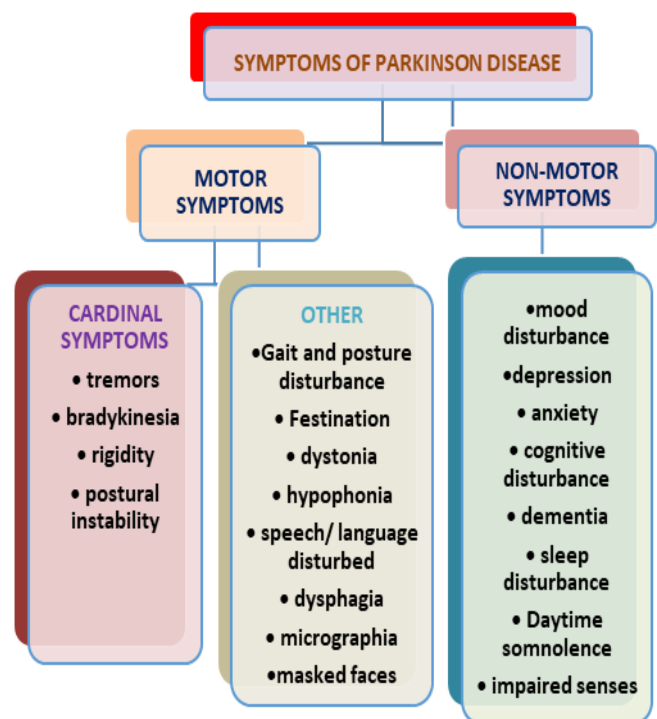


Figure 2: Symptoms of Parkinson disease

Management of Parkinson's disease

Medications are the most common therapy for PD.⁸ The goal is to correct the shortage of dopamine; it is this deficiency that causes the symptoms. Pharmacological

treatment is usually started when symptoms become disabling or disrupt daily activities. Treatments may differ according to the patient's symptoms, age, and responses to specific drugs. It often takes time to find the best combination of drugs for each patient.⁹

Table 1: Pharmacological treatment for Parkinson's disease

Drugs affecting brain dopamine systems					
S.N	Drugs	Mechanism	Therapeutic uses	Adverse effects	References
1	Levodopa	levodopa can cross the blood-brain barrier (BBB). Levodopa converts to dopamine in both the CNS and periphery. Dopamine decarboxylase inhibitors prevent the conversion of levodopa to dopamine in the periphery, allowing for more levodopa to cross the BBB. Once converted to dopamine, it activates postsynaptic dopaminergic receptors and compensates for the decrease in endogenous dopamine	as a dopamine replacement agent for the treatment of Parkinson disease control bradykinetic symptoms improve the quality of life in patients with idiopathic Parkinson disease useful for post-encephalitic parkinsonism and symptomatic parkinsonism due to carbon monoxide intoxication. Levodopa has been suggested as a reasonable treatment option for intermittent restless leg syndrome patients who do not need regular daily therapy	nausea, dizziness, headache, and somnolence confusion, hallucinations, delusions, psychosis, and agitation postural hypotension	10-15
2	Carbidopa	Carbidopa is an inhibitor of L-dopa decarboxylase and does not cross the blood-brain barrier, thus preferentially inhibiting the conversion of levodopa to dopamine outside of the brain	used with a combination levodopa/carbidopa product to treat symptoms of Parkinson's disease	Dizziness, lightheadedness, nausea, vomiting, loss of appetite, trouble sleeping, unusual dreams, or headache	16
3	Bromocriptine	Bromocriptine is a dopamine receptor agonist with selective agonist activity on D2 dopamine receptors. Bromocriptine alters monoamine neurotransmitter concentrations in the suprachiasmatic and ventromedial nuclei of the hypothalamus	Diabetes Mellitus Type II Hyperprolactinemia Acromegaly Parkinson Disease	Nausea, Vomiting Dizziness, Hypotension Headache, Fatigue Psychosis, Fibrosis (retroperitoneal, pleural, cardiac valve) Cardiovascular incidents (valvular damage, stroke, myocardial infarction)	17-18
4	Benserazide	peripheral decarboxylase inhibitor that increases the amount of levodopa crossing into the brain and its subsequent conversion to dopamine	used in conjunction with L-dopa for the treatment of Parkinson's disease	dyskinesias, nausea, vomiting, psychotic reactions, and occasionally severe hypotension	19
5	Pergolide	a dopamine agonist targeting D ₁ and D ₂ receptors	treatment of cognitive deficits of individuals with schizotypal personality disorder, a schizophrenia spectrum illness Parkinson disease	dyskinesia, hallucinations, disturbance of sleep, loss of appetite, nausea, hypotension, and tachycardia	20
6	Ropinirole	stimulates the post-synaptic dopamine receptors D2 in the central and peripheral nervous systems	used to manage and treat Parkinson's disease and restless leg syndrome (Willis-Ekbom disease)	Peripheral Edema, anterocollis, Pisa Syndrome, Reversible Dyskinesias, Dermal Eruptions	21
7	Seligiline	Monoamine oxidase B (MAO-B) inhibitors	Used to treat Parkinson disease and Alzheimer disease showed antioxidant activity and reduced the fat accumulation in the liver of rats on lipid-rich diet	Dizziness, dry mouth, constipation dry mouth, constipation.	22
8	Entacapone	Catechol-O-methyltransferase (COMT) inhibitors	entacapone used as adjuvant therapy to LD is effective in the management of later PD with fluctuation	nausea, dyskinesia, GI disorder, urine discoloration	23
9	Amantadine	blocks the early stage of viral replication	Used in the treatment of Parkinson disease, antiviral and in Covid 19.	Nausea, vomiting, decreased appetite, difficulty falling asleep or staying asleep, abnormal dreams, headache.	
Drugs affecting brain cholinergic system					
1	Trihexyphenidyl	selective M1 agonists	Used in parkinson disease and alzheimer disease	rash. fast, irregular, or pounding heartbeat. fever. confusion	25



2	Procyclidine	Procyclidine primarily antagonizes muscarinic (M) receptors M1, M2, and M4,	used in the treatment of Parkinson's disease, most commonly administered to schizophrenic patients in order to alleviate antipsychotic-induced side effects, acute administration of a clinically relevant dose of procyclidine leads to mild impairments in eye movement performance in schizophrenic patients	Drowsiness, dizziness, constipation, flushing, nausea, nervousness, blurred vision, or dry mouth	26
3	Biperiden	Its role in cleaving of acetylcholine, neurotransmitter interacting with acetylcholine muscarinic receptor (mAChR) and nicotinic receptor (nAChR)	used in Parkinson disease treatment and it serves also as an antiseizures compound in organophosphates poisoning.	dry mouth, nose or throat, blurred vision, drowsiness, euphoria, disorientation, urinary retention, dizziness, constipation	27
4	Ophenadrine	The precise mechanism of action of orphenadrine is not known, but it appears to indirectly relieve muscle pain through central atropine-like effects. The precise mechanism of action of orphenadrine is not known, but it appears to indirectly relieve muscle pain through central atropine-like effects	Orphenadrine is an anti-cholinergic drug that has been used to treat painful muscle spasms due to its potent central nervous system (CNS) and peripheral actions. ⁷ The combination of anticholinergic effects and CNS penetration make orphenadrine useful for pain of all etiologies, including pain from radiculopathy, muscles, and headaches.	Dry mouth, nausea, blurring of vision, Drowsiness, Increased intraocular pressure, Urinary retention, CNS stimulation (especially in elderly people), Constipation	28-30
5	Promethazine	Promethazine exhibits its antihistamine effects as an H1-receptor blocker.	Motion sickness, nausea, vomiting, allergic condition, sedation and Parkinson's disease	sedation, confusion, and disorientation, blurred vision, xerostomia, dry nasal passages, dilated pupils, constipation, and urinary retention	31-34

Table 1a: Herbal treatment for Parkinson's disease

S.No	Herbal treatment	Description	Mechanism	Adverse effect	Reference
1.	<i>Withania somnifera</i>	<i>Withania somnifera</i> , commonly also as winter berry or toxic gooseberry, is a Solanaceae family medicinal plant. It has protective effect in parkinson's disease.	<i>Withania somnifera</i> reduced the expression of iNOS, a measure of oxidative stress	stomach upset, diarrhea, and vomiting.	35
2	<i>Nigella sativa</i>	Thymoquinone (TQ) is the primary active ingredient of the vaporous oil from <i>Nigella sativa</i> . TQ exerts neuroprotective and anti-oxidative effects on PD.	TQ significantly increased the subsequent expression of antioxidative genes such as Heme oxygenase 1 (HO-1), quinone oxidoreductase (NQO1) and Glutathione-S-Transferase (GST)	Stomach upset, vomiting or constipation.	36
3	<i>Curcuma longa</i>	Curcumin is a polyphenol and an active component of turmeric (<i>Curcuma longa</i>). It exhibits antioxidant, anti-inflammatory and anti-cancer properties, crosses the blood-brain barrier and is neuroprotective in neurological disorders such as Parkinson disease.	Interfering with NF-B ↓ the inflammatory response of TNF-stimulated human endothelial cells.	upset stomach, acid reflux, diarrhea, dizziness and headaches.	37
4	<i>Crocus sativus</i>	Saffron- the stigma of <i>Crocus sativus</i> Linné (Iridaceae), and its constituents are crocin and crocetin.	It suppressed aggregation of α-synuclein and promoted the dissociation of α-synuclein (α-Synuclein is an aggregation-prone neural protein that plays a role in the pathogenesis of PD) fibrils.	Drowsiness, stomach problems, and nausea or vomiting.	38
5	<i>Tinospora cordifolia</i>	<i>Tinospora cordifolia</i> (Willd.) Miers. (Menispermaceae) is a large deciduous climbing shrub. It has been widely used in the traditional Indian system of medicine to treat leprosy, diabetes, asthma, anorexia,	In 6-OHDA-induced PD mice, the ethanol extract of TC has been shown to reduce oxidative stress in injured brain areas, preserve	headache or nasal pain	39

		jaundice, pyrexia, gout and diarrhea. It is also considered as a bitter tonic, astringent, diuretic, aphrodisiac and curative against skin infections.	neurons, and restore locomotor activity.		
6	<i>Ginkgo biloba</i>	EGB761 is an extract of the leaves from the <i>Ginkgo biloba</i> tree that has been reported as an antioxidant and neuroprotective agent.	The positive effect of EGB761 on Parkinson's disease is the reduction or inhibition of monoamine-oxidase activity. This enzyme metabolises dopamine, inducing the formation of free radicals, which in turn damage nigrostriatal neurons.	Headache. Dizziness. Heart palpitations. Upset stomach. Constipation	40

Table 1c: Other treatment for Parkinson's disease

S.NO	Therapy	Description	References
1	Supportive Psychotherapy	Psychotherapy techniques can help Parkinson's people with diagnosis of mental chronic depression, psychosis, poor concentration, and other higher cognitive dysfunctions.	41,42
2	Deep-Brain Stimulation (DBS)	It is a surgical practice in which electrodes are surgically implanted in a specific location of the brain. This stimulation, which sends electrical pulses to the patient's brain area, may help to reduce the symptoms of Parkinson's disease.	
3	Neuro-ablative Lesion Surgery	The destruction of the Globus pallidus internal, a part of the brain that usually causes rigidity and akinesia in Brain regions involved, can help help to reduce these symptoms	
4	MRI-guided focused ultrasound (MRgFUS)	A minimally invasive therapy called MRI-guided focused ultrasound (MRgFUS) has assisted some Parkinson's disease sufferers in controlling their tremors. An MRI directs ultrasound to the region of the brain where the tremors begin. The tremors are caused by places that are burned by the extremely hot ultrasound waves.	
4	Gait Training	Neurologists prescribe task-specific gait training for movement disorder and loss of physical balance.	
5	Physiotherapy	Physiotherapy and range-of-motion regular exercise can help people with Parkinson's disease improve their flexibility, mobility, and gait speed. Strengthening activities can help patients with primary economic muscular weakness and delayed increased mobility enhance their strength and motor functions	
6	Speech Therapy	Speech and outspoken difficulties are common in Parkinson's patients. The (LSVT) is used to repair or replace slurred speech and boost vocal total volume in patients.	
7	Occupational Therapy	This treatment is required to help patients enhance their motor skills. They are encouraged to be as active as possible in their routine activities in enhancing their health and quality of life	
8	Music Therapy	It assists patients with Parkinson's disease who have emotional instability and bradykinesia. Choral singing, speech exercise, & rhythmic free body movements can help decrease symptoms.	

CONCLUSION

PD is a long-term, progressive neurodegenerative condition with both motor and nonmotor symptoms. The primary source of the disorder's motor symptoms, which include resting tremor, "cogwheel" rigidity, and bradykinesia, has been determined to be striatal dopamine deficiency. Disorders of sleep, sadness, and cognitive abnormalities are examples of nonmotor symptoms. Treatment of the symptomatic motor and nonmotor aspects of the condition with the aim of enhancing the patient's general quality of life is the main objective in the therapy of PD. An initial evaluation and diagnosis by a multidisciplinary team made up of neurologists, general practitioners, nurses, physical therapists, social workers, and pharmacists is

necessary for appropriate management. Reactive oxygen species play a significant role, and the condition may be related to oxidative stress (ROS). Numerous medicinal herbs contain active ingredients that have been shown to have antioxidant effects. For people who prefer more natural methods, physical, occupational, and speech therapies offer non-drug alternatives that can be utilised alone or in conjunction with drugs. They can assist in managing specific symptoms as they appear. The future of PD treatment seems hopeful for patient-specific care that is more successful and has fewer side effects, but more study is still needed to explore into the under-researched medicines for PD.



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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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