

REVIEW ON PARKINSON'S DISEASE

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ABSTRACT

As the US population ages, Parkinson's disease, the second most prevalent progressive neurodegenerative illness affecting older persons in the country, is expected to become more widespread. Idiopathic Parkinson's disease, which develops from a pathophysiologic loss or degeneration of dopaminergic neurons in the substantia nigra of the midbrain and the development of neuronal Lowy bodies, is linked to risk factors such as aging, family history, exposure to pesticides, and environmental chemicals (think synthetic heroin use, for example). The cause(s) of it all are(are) unknown. Parkinson's disease (PD) patients are typically characterized by rest tremor, stiffness, bradykinesia, and stooping posture in addition to other motor and non-motor symptoms. Moreover, neurobehavioral disorders (such as anxiety and depression), dementia, and autonomic dysfunction (such as orthostatic and hyperhidrosis) have been linked to Parkinson's disease (PD). Innovative surgical procedures like deep brain stimulation (DBS) and medicinal pharmaceutical therapy have proliferated in recent decades. But there is currently a lack of a conclusive disease-modifying treatment. There has been little progress in the development and testing of experimental medicines. It is crucial for caregivers, medical professionals, and patients themselves to understand strategies that provide the best possible quality of life for people with Parkinson's disease.

Keywords: Introduction, symptoms, causes, risk factors, prevention, treatment, and pathophysiology, among other things.

1. INTRODUCTION

Parkinson's disease (PD) is an idiopathic nervous system disease that manifests in the motor and non-motor systems. This is a long-term, progressive neurodegenerative illness that primarily affects the elderly but can also affect patients much younger in life. It is the neurodegenerative disease that is most prevalent in people.[1] Since the disease's eponymous physician's first description in the early 1800s, Parkinson's disease has been known to exist. PD, sometimes known as "paralysis agate's," is uncommon in young people, particularly those under the age of 40 [2]. Up to a million Americans may be affected by Parkinson's disease (PD), and each year, around 60,000 new cases are identified. Seven to ten million people are believed to be impacted globally. PD is 1.5 times more common in men than in women [3]. The second most common neurodegenerative illness in the world is Parkinson's disease [4]. Even with all of neuroscience's advancements, the diagnosis is still clinical. James Parkinson first described it in his landmark work "An essay on the shaking palsy" two centuries ago.[5]. The critical knowledge that general neurologists and other medical professionals caring for people with Parkinson's disease need to know is compiled in this review article. Parkinson's disease is a progressive neurodegenerative condition characterized pathologically by Lewy body development in the remaining dopaminergic neurons and dopaminergic cell degeneration in the substantia nigra.[6]. Pathologic changes are accompanied by a clinical prodrome of nonspecific symptoms such as hyposmia, constipation, and exhaustion. These changes can be detected up to 20 years before the beginning of motor symptoms.[7] About 1 percent of people over 60 and up to 4 percent of people over 80 are affected by the condition.[8].

What is Parkinson's Disease?

- Parkinson's Disease (PD) is a chronic, progressive neurodegenerative disorder characterized by slowness in the initiation and execution of movement (bradykinesia), increased muscle tone (rigidity), tremor at rest, and gait Disturbance
- The exact cause of PD is unknown and although it's not considered a hereditary Condition, genetic risk factors should be evaluated for their interplay with Environmental factors – about 15% of patients with PD have a positive family History for the disease
- The pathologic process of PD involves degeneration of dopamine-producing Neurons in the substantia nigra of the midbrain which disrupts the normal Balance between dopamine and acetylcholine in the basal ganglia
Dopamine is responsible for functioning of the extrapyramidal motor system, Including control of posture, support and voluntary motion (manifestations of PD Do not occur until 80% of neurons in substantia nigra are lost.

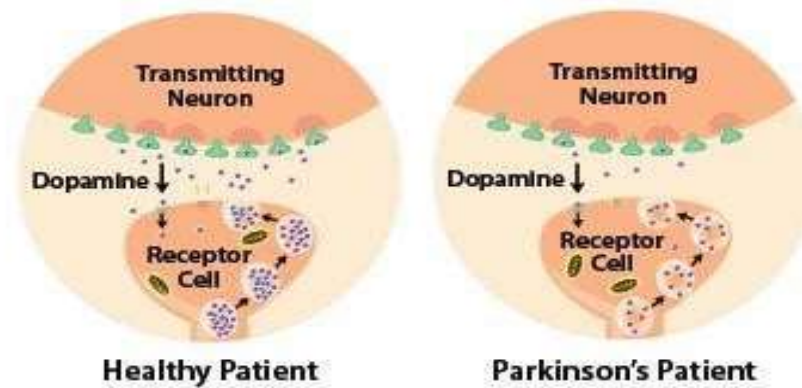


Fig .no.1

Non – motor symptoms of Parkinson’s Disease :

- Depression
- Anxiety
- Apathy
- Fatigue
- Pain
- Urinary retention
- Constipation
- Erectile dysfunction[9].

Constipation, rapid eye movement (REM), sleep behaviour disorder (RBD), anosmia, anxiety, and depression are examples of non-motor symptoms (NMS) that may appear a decade or two before motor symptoms. Particularly in the early clinical studies, which were primarily focused on controlling motor features, they were mainly overshadowed by motor features. Grading scales have been devised and integrated into therapeutic trials as a result of the recognition of NMS as a significant cause of worry for patients during the past twenty years or more [10–13]. A decade or two before PD is diagnosed, constipation may occur [14]. With delayed absorption, gastric emptying is reduced by more than 40% [15]. Oral drugs thus lose some of their effectiveness. Untreated constipation in Parkinson’s disease patients can result in bowel obstruction and death [16]. The best way to treat constipation is to increase your intake of fruits, vegetables, and water. Fiber-containing products should be avoided since their delayed stomach transit times exacerbate constipation. **Motor symptoms** : Parkinson’s disease (PD) is linked to stiffness, a shuffling gait, bradykinesia (slow movements), and postural instability. The start is subtle, and people often blame aging processes for the symptoms. Parkinson’s disease (PD) symptoms worsen over time, but motor progression rates vary widely [17]. Moreover, tremor, rigidity, or postural instability predominate in subtypes of Parkinson’s disease [18]. Other motor manifestations are noted in addition to the previously reported “classic” motor symptoms. These include stooped posture, difficulty turning in bed, dystonia, kyphosis, scoliosis, shuffling gait, masked facial expression (hypomimia), decreased eye blink rate, blurred vision, impaired upward gaze, and speech impairment, such as hypophonia (increasingly soft voice) or palilalia (repetition of word or phrase) [19].

Complications of PD :

- Dyskinesias (spontaneous, Involuntary movements)
- Weakness
- Increased neurologic problems (higher risk of dementia)
- Neuropsychiatric problems
- Depression
- Hallucinations
- Psychosis
- Dysphagia (trouble swallowing)
- Aspiration
- Urinary tract infections (UTI)
- Skin breakdown
- Orthostatic hypotension.

Sleep Disturbances and PD :

• Sleep problems are common and include difficulty staying asleep at Night, restless sleep, nightmares, and drowsiness or sudden sleep onset During the day. In particular, rapid eye movement (REM) behaviour disorder is a Preparkinsonian state that occurs in about one third of patients with PD. It is characterized by violent dreams and potentially dangerous Motor activity during REM sleep.

Current Treatment Options :

- Sinemet (Levodopa/Carbidopa)
- Requip (repinirole) / Mirapex (pramipexole)
- Neupro (rotigotine) transdermal patch
- Anticholinergic drugs (Cogentin) or antihistamines diphenhydramine)
- Exelon (rivastigmine) / Aricept (donepezil)
- Amitriptyline.

Medical Interventions :

- Deep brain stimulation (DBS) – placement of an electrode in the Thalamus, globus pallidus, or subthalami nucleus and connected To a generator placed in upper chest (now individualized)
- Ablation surgery – involves locating, targeting, and destroying an Area of the brain affected by PD
- Transplantation – transplantation of fetal neural tissue is inserted Into the basal ganglia and designed to provide dopamine Producing cells in the brain (research ongoing)

Complementary Therapies :

- Nutrition therapy
- Deep breathing
- Yoga
- Tai Chi
- Chiropracty
- Meditation/Mindfulness Massage
- Whole body vibration therapy
- Psychotherapy
- Progressive relaxation (sensory Deprivation)
- Guided imagery
- Acupuncture
- Dance
- Music
- Pet
- Theracycle (forced rate Exercise)
- Audiology consult (inner ear Issues)

Future of Treatment Options :

- Use of medical marijuana (THC / CBD)
- Dietary management (research ongoing)

Drug therapy of PD motor symptoms: Available symptomatic therapy for an early to intermediate stage of Parkinson's disease (PD) include levodopa, amantadine, dopamine agonists, anticholinergics, and MAO-B inhibitors (selegiline and rasagiline). When to begin taking a dopaminergic medication and whether to use levodopa or a dopamine agonist are the key decisions. The introduction of levodopa in 1967 transformed the field of Parkinson's disease treatment and revolutionized PD therapies [20,21]. There is no clinical evidence to justify delaying the administration of levodopa to patients in order to prevent loss of effect. Over time, all patients experience a loss of efficacy, and greater dosages will be needed to get a sufficient motor response [22]. Levodopa is more efficient than dopamine agonists and has a lower correlation with impulse control disorders (ICDs) than dopamine agonists. Excessive gambling, hypersexuality, punding, excessive shopping, compulsive eating, and dopamine dysregulation syndrome are among the ICDs [23–25]. The American Academy of Neurology stated in its 2006 assessment of its 2002 guidelines for starting treatment for Parkinson's disease (PD) that there wasn't enough data to support starting with dopamine agonists. It was determined that starting treatment with levodopa, a dopamine agonist, or an MAO-B inhibitor is feasible [26, 27]. As Parkinson's disease progresses, dopaminergic treatment side effects begin to mount. Levodopa-induced dyskinesia, ICDs, and a loss

of efficacy before the next dose is scheduled are the most prevalent adverse effects. Levodopa use over an extended period of time causes dyskinesia and motor irregularities. Levodopa dosage and duration are connected to the development of dyskinesia. Dyskinesias are more likely to occur at larger levodopa dosages and over longer periods of time [28]. Levodopa's short half-life, the requirement for frequent dosages, and the degeneration of the nigrostriatal neurons that store and release dopamine slowly are the causes of levodopa-induced dyskinesia. It is believed that delayed stomach emptying contributes significantly to dosage failure and reduces the effectiveness of oral therapy [29].

Diagnosis : Clinical markers such as bradykinesia, stiffness, tremor, and postural instability, along with progressive symptoms and a sustained response to levodopa medication, are necessary for the diagnosis of Parkinson disease.[30] However, a few of these characteristics are also present in other neurological disorders. Diseases having Parkinsonian characteristics, such as vascular Parkinsonism, progressive supranuclear palsy, and drug-induced parkinsonism, as well as nonparkinsonian tremors, including essential tremor, are frequently mistaken as Parkinson disease.[31, 32] Parkinson's disease is difficult to diagnose, and errors in diagnosis are frequent, especially in the early stages. [33, 34]. When a patient is suspected of having Parkinson disease, a physician who treats the condition seldom might think about sending them to a doctor with greater experience in order to confirm the diagnosis. [35, 36].

Treatment of Motor Symptoms :

Early medical therapy : The American Academy of Neurology advises that patients should begin therapy as soon as they experience functional impairment.[37]. Initial therapy options include levodopa, monoamine oxidase-B inhibitors, and nonergot dopamine agonists.[38,39, 40] When levodopa is given with carbidopa, which prevents levodopa from being metabolized peripherally, therapeutic doses of levodopa can reach the brain without having incapacitating side effects. For the treatment of motor symptoms, the most effective medication currently on the market is a combination of carbidopa and levodopa, known as Sinemet. On the other hand, early use is linked to an earlier onset of dyskinesias (involuntary movements that are abnormal).

Surgery : The majority of patients will experience incapacitating symptoms even after receiving the best medical care, and thus are candidates for deep brain stimulation, which targets the Globus pallidum internal or the subthalami nucleus.[41]. When it comes to severe Parkinson's disease, a favorable response to levodopa, few complications, no cognitive impairment, and no depression—or depression under control—are all indicators of positive surgical outcomes.[41] Surgery carries a number of risks, such as mortality, infection, stroke, lead migration, misplacement, or breakage, and intracranial bleeding.[41] Deep brain stimulation was compared to the best medical therapy in a recent six-month randomized multicentre experiment. Individuals undergoing deep brain stimulation showed increases in their motor function, quality of life, and timely performance. On the other hand, the surgical group experienced more unfavourable effects, such as depression, falls, and surgery site infections.[42]. Deep brain stimulation does not stop the progression of the condition, and patients eventually experience symptoms that are resistant to treatment, such as freezing their stride. [41–43].

L-Dopa Containing Foods and Herbs :

Functional foods like broad beans (*Vicia faba*) are natural Sources of L-dopa .The amount of L-dopa in the beans is Pharmacologically active in the treatment of PD. It has been suggested That *V. faba* can potentially be incorporated into dietary strategies to Manage PD motor oscillations .Other L-dopa containing herbs include

: *Vigna Aconitifolia*, *Vigna unguiculata*, *Vigna vexillata*, *Prosopis chinensis*, *Pileostigma malabarica*, *Phanera vahlis*, *Parkinsonia aculeata*, *Macaroon*, *Canvalia gladiata*, *Cassia floribunda*, *Cassia hirsute* and *Dalbergia retusa*. Besides L-dopa containing herbs, a *Ginkgo biloba* Extract showed protective effects in vivo and in vitro. An ethanolic Extract of *Plumbago zeylonica* was effective in a rat PD model .

Coffee and Tea :

The CNS stimulant caffeine is known to inhibit cyclic nucleotide Phosphodiesterase resulting in higher concentrations of c-AMP, a Key intracellular regulator. It is well known that freshly brewed coffee And tea contain polyphenols that are effective antioxidants. Recently, It has been reported that caffeine and a waxy coating on the bean may Team up to fight PD . Eicosanoyl-5-hydroxytryptamide (2), an indole derivative, has been shown to protect the brains of Mice against abnormal protein accumulation associated with PD And Lewy body dementia (due to abnormal deposits of α -synuclein). When caffeine and (2) were given together, they boosted the activity Of a catalyst that helps prevent the accumulation of harmful proteins In the brain. Further research is needed to determine the doses and Ratios of (2) and caffeine required for the protective effect in humans .Caffeine binds to brain adenosine A2a receptors that have a Neuroprotective role .

Mechanisms of Action for Traditional Chinese Medicines :

1. The inhibition of oxidative stress in the CNS.
2. The regulation of mitochondrial dysfunction.
3. The reduction of toxic excitatory amino acid Neurotransmitters (glutamate, aspartate), reflected in the activation Of corresponding receptors (NMDA-R, AMPA-R, KA-R) which Mediate acute osmotic swelling or delayed injury of nerve cells.
4. The inhibition of neuroinflammation
5. The inhibition of neuroapoptosis.
6. The inhibition of abnormal protein aggregation.

2. CONCLUSION

One of the most prevalent neurodegenerative disorders impacting the elderly population is Parkinson's disease, which is linked to higher rates of morbidity and death. For the best possible care of the cases, knowledge of the disease's symptoms, therapies, and progressive long-term course is required. Understanding the neuropathology of Parkinson's disease (PD) and how it spreads throughout the nervous system has advanced tremendously. All of these therapies are not curative, though. Parkinson's disease (PD) is still a progressive disorder that, when treatment-resistant motor difficulties and non-motor symptoms worsen, finally results in severe impairment. The primary unmet needs that must be addressed by the existing and future research efforts include modifying elements that contribute to the disease's progression and in further delaying its handicap.

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