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PARKINSON'S DISEASE: AN OVERVIEW OF MANAGEMENT

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Abstract
Parkinson's disease is classified as a neurodegenerative condition, with the death of dopamine-producing neurons thought to be the cause. PD is now far more common than it was a decade ago. The majority of pharmaceutical treatments for Parkinson's disease (PD) target alpha-synuclein by upregulating cerebrosidase, blocking LRRK2, and lowering its elimination through immunotherapy. The most common neurodegenerative illness is Parkinson's disease, followed by Alzheimer's disease. In most cases, Parkinson's disease first manifests between the ages of 55 and 65. It affects 1 to 2 percent of people over 60, and in 3 to 5 percent of cases, it advances to the ages of 85 and 89. Motor symptoms, which include bradykinesia, tremors, rigidity, and dystonia, are uncontrollable movements brought on by severe forms of Parkinson's disease. Non-motor symptoms like hysteria, sadness, constipation, and sleeplessness are also brought on by Parkinson's disease. Science and engineering principles are combined in nano biosensors to identify Parkinson's illness. Nanotechnology can also pass the blood-brain barrier with drugs in the form of nanoparticles. However, the usage of nano biosensors in biological systems is limited due to their new nature. By altering cellular chemical profiles and potentially upsetting cell metabolism and homeostasis, nano biosensors pose a threat to the ability to discern between basic biological processes and sensor-induced aberrations.

Keywords: Parkinson's disease. Neurodegenerative disease, alpha-synuclein, Lewy bodies, pharmacological treatment, herbal treatment, therapeutic targets diagnostics.

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Introduction

Parkinson's disease (PD) is a neurodegenerative disease caused by the death of a type of neuron that plays a fundamental role in the production of dopamine in the brain .PD is the second most common neurodegenerative disease, affecting 0.2% of the global-world population, 1% of the population over 60 years old, and up to 4% of the population over 80 years old. It has an exponential growth of prevalence, especially in men .[Parkinson's disease] PD patients have a risk of dementia that is 6–8 times higher than that of aged-matched controls,with a long-term prevalence of up to 80% . The cause of PD is unknown, with both inherited and environmental factors believed to play a role. Although its origin is often of unknown aetiology, age remains the main risk factor for PD.These motor symptoms manifest when 50–70% of nigrostriatal dopaminergic function has been lost. However, in30–40% of cases the patients have no tremor, which may result in half of PD cases going undiagnosed . Moreover, it is estimated that the number of people affected will double in the next 30 years due to the increasing prevalence in an ageing population (1).

The death of dopaminergic neurons means that PD is characterized by very specific motor symptoms: tremor, rigidity, bradykinesia, inability to initiate voluntary movements,and postural instability. Although these symptoms are the most characteristic, other nonmotor features also appear in PD: There has also been a rapid expansion in thetreatment options bothin the early and in the later stages of the illness together with a greater awareness of non- motor complications (2).

1. Pathophysiology:

PD is a disorder of the extra pyramidal system, which includes motor structures of the basal ganglia, and is characterized by the loss of dopaminergic function and consequent diminished motor function, leading to clinical features of the disease.4,30 Research in the late 1950s
identified striatal dopamine depletion as the major cause

of the motor symptoms of PD, although the presence of nonmotor features supports the involvement of other neurotransmitters of the glutamatergic, cholinergic, serotonergic, and adrenergic systems, in addition to the neuromodulators adenosine and encephalin (3). Typically, patients experience the motor features of PD only after 50% to 80% of dopaminergic neurons have been lost, suggesting the involvement of a compensatory mechanism in the early stages of the disease. Two types of dopamine receptors, D1 (excitatory type) and D2 (inhibitory type), influence motor activity in the extrapyramidal system. These components are part of larger circuits located in the thalamus and the cortex (4). D2 and D1 receptor activation with dopaminergic therapies mediates clinical improvement in the motor symptoms of PD.48 In addition, dopaminergic loss results not only in reduced activation of the thalamus but also in increased cholinergic activity due to the loss of dopamine's normal inhibitory influence.

The involvement of inflammation in the pathogenesis of PD is also being studied, especially the role of cytokines and other mediators. Inflammatory responses secondary to the degeneration of dopaminergic neurons may play a role in PD and contribute to its pathogenesis. In vitro data have supported the activation of microglia and astrocytes secondary to injured dopaminergic neurons (5).

Anti-Parkinsonian activities:

Parkinson's disease treatment can be done with Mucuna pruriens (Mp). Mp is an annual and perennial legume of the Fabaceae family with a variety of medicinal properties. Although mucuna pruriens, like any other source of levodopa.Chlorogenic acid (CA) found in MPTP-Intoxicated Mouse, such as UA, has strong anti-Parkinsonism efficacy in a toxin-induced Parkinsonian mouse model (6). Via the signaling pathway, Chlorogenic acid reduces MPTP- induced apoptosis in a Parkinson's disease mouse model . Behavioral tests revealed a considerable improvement in the motor activity patterns and gripping ability of Parkinsonian mice exposed to Ws root extract. Anti-Parkinsonian activity of Mucuna pruriens, ursolic acid, and chlorogenic acid in MPTP intoxicated mouse model, as well as anti-apoptotic activity of Withania somnifera in Paraquat and Maneb induced mouse model, were reported; however, there is a strong need to test the efficacy of these anti-Parkinsonism activities in some other neurodegenerative diseases, in addition to Parkinson's disease (7).

Nanobiosensor:

A biosensor is a device that provides a surface for probe target interactions and converts the interactions into quantifiable signals. Optical, cantilever deflection, electrical, and electrochemical signals are examples of signal of Nanobiosensors can detect analytes such as cerebrospinal fluid (CSF), antibodies, and other molecules of interest . The nanostructures of nanobiosensors act as a bridge between biological agents and physicochemical or biological agents (8). Nanosensors are mechanical or chemical sensors that may be utilised for temperature monitoring or chemical imbalance detection on the nanoscale. Nanobiosensors are appealing development modalities due to a variety of benefits over traditional biosensor systems. When nano-sized components are used in the development of nanosensors, detection sensitivity may be dramatically increased. Nanobiosensor technologies are being developed for cancer diagnosis Electrochemical nanobiosensors, for example Furthermore, nanobiosensors are an effective tool against COVID-19 because they are designed to act directly on the infection, improve the efficacy of current antiviral drugs. For example, a biosensor was used to identify COVID-19 (9). The developed immunosensor had a very high sensitivity with a detection limit of 0.4 pg/mL, a much lower value, and a good linear response from 0.001 to 100 ng/mL (10). In addition, nanobiosensors, which combine the benefits of nanomaterials and biosensing technologies, have been used for sensitive, selective, and quick disease detection and have received a lot of attention in the chemical, biology, and medical fieldsA visible signal was then generated for the detection of target bacteria . To monitor the interaction between the antigen, amyloid-β derived diffusible ligands (ADDLs), and particular antiADDL antibodies, a nanoscale optical biosensor based on localised surface plasmon resonance (LSPR) spectroscopy was developed

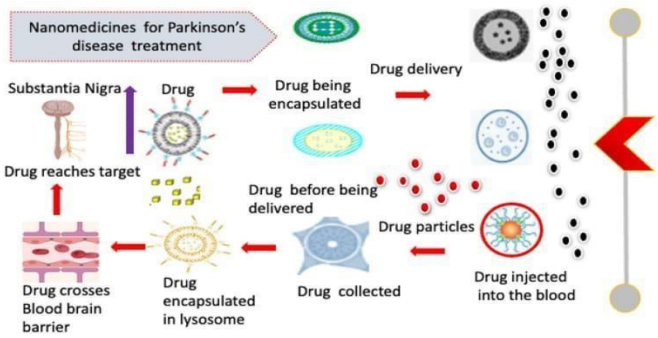


Fig 1:Nanomedicines for Parkinsons' Disease treatment

The role of surgery in PD:

The use of surgery in PD dates back over 50 years. In the early 1950s, patients particularly those with severe tremor would on occasion be referred for ablative surgery usually to the contralateral thalamus (11). With the introduction of levodopa, surgical treatment fell from vogue.This concentrated on lesion surgery usually in the form of pallidotomy which was shown to be successful particularly for levodopa-induced dyskinesias.This involved high-frequency deep brainstimulation (DBS) of discrete brain areas producing functional and reversible inhibition of the target site. A number of areas within the basal ganglia can be targeted. The procedure most commonly carried to reduce bradykinesia, tremor and rigidity and which also reduces drug-related motor complications is bilateral subthalamic stimulation. This can produce very dramatic benefit. The operation is technically difficult, but in experienced hands the risk of

adverse events is low. However, the infrastructure and support team required to asses, carry out and monitor patients limits the availability of this treatment. there is concern about the increased incidence of psychiatric side effects,particularly depression following Deep Brain Stimulation[DBS]. patients with congnitive impairment Most or significant depression (12,13).

Non-motor complications:

With the progression of the disease, there are a number of non-motorcomplications in PD thatare often seen. In many cases, these are notdirectly related to involvement of dopaminergic pathways and may therefore develop even in patients where motor symptoms are well controlled.

Cognition of PD:

Cognitive involvement in PD seems to be common. Many patients withPD develop dementia, typically 10 years or more after the onset ofmotor symptoms. The frequency of overt dementia varies from study tostudy depending on definition, methods of cognitive assessmentandpopulation differences, but is of the order of 40% for all PD patients.More subtle cognitive disturbance particularly of executive function isextremely common even in early PD (19).

Types Parkinson's 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 disorder (15).
- Multiple System Atrophy (MSA) – This progressive neurological disease triggers over- production of a brain-protein called alpha difficulties. Synuclein which causes ners.ve 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 frontotemporal dementia along with impairment of balance, speech and thought process (16).

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 indiabetes, including symptoms of urinary incontinence, loss of memory and walking (17).

Results and Discussion:

The α-syn protein is involved in synaptic maintenance: it regulates the size of dopamine vesicles in the presynaptic terminal, regulates the localization of dopamine transporters (DATs), and regulates dopamine synthesis. It is expressed in several areas of the brain: the SN, hippocampus, neocortex, hypothalamus, and cerebellum. The monomeric form of α-syn has a physiological role, but the poor folding and aggregation .Since the peripheral nervous system (PNS) is a target of α-synuclein deposition, there is a growing interest in assessing whether the intrinsic pathogenetic features of PD may predispose patients to peripheral neuropathy (PN). Recent studies have shown that PN occurs more frequently in individuals with PD compared to age-matched, healthy individuals. In this regard, there is growing evidence of pathological changes in the PNS of individuals with PD compared to age-matched, healthy individuals (18).

Dopamine:

Dopamine is a neuromodulator molecule that belongs to the catecholamine group of neurotransmitters. Dopamine is synthesized from tyrosine, which reaches the brain by an active transport mechanism. Tyrosine is generated by phenylalanine hydroxylase from

Phenylalanine in the liver.. There are two enzymes that metabolize dopamine: catechol-O- methyl transferase (COMT) and monoamine oxidase (MAO). Astrocytes contribute to dopamine metabolism as they express the MAO-B isoform, while the MAO-A isoform is present in catecholaminergic neurons. COMT is expressed mainly by glial cells. When dopamine levels are low in the brain, MAO synthesis decreases. Pharmacological targets of the dopaminergic system and/or dopamine metabolism are currently explored for treatment ofPD.

Management of motor symptoms:

This dopamine precursor was a breakthrough in the treatment of PD for reducing motor symptomatology and improving the quality of life of patients. It also led to the study of other dopaminergic therapies.Nevertheless, the administration of Levodopa has limitations due to the occurrence of adverse reactions, with dyskinesia being one of the main complications. Moreover, as the disease progresses, patients are less responsive to dopaminergic medication and require higher and more frequent doses of dopaminergic.These drugs include rasagiline, safinamide,selegiline,and monoamine oxidase B[MAOB] to increase dopamine levels.

Management of nonmotor symptoms:

As previously mentioned, cognitive impairment, depression, sleep disorders, and autonomic dysfunction are the most common non-motor problems in PD. Among the most commonly used drugs to treat cognitive impairment are acetylcholinesterase inhibitors such as Donepezil, Galantamine, and Rivastigmine . For

depression, Parkinson's patients are often treated with serotonin/norepinephrine reuptake inhibitors (SNRIs) (e.g., Duloxetine, Desvenlafaxin, Milnacipran, and venlafaxine). Other therapeutical options are benzodiazepines (e.g., Alprazolam, Clonazepam, Diazepam, and Lorazepam), selective serotonin reuptake inhibitors (SSRI) (e.g., Fluoxetine and Sertraline), tricylic compounds (e.g., Amitrytiline, Imipramine, and Nortriptyline) and additional anxiolytics (e.g., Buspirone, Propanolol, Quetiapine, and Trazodone). With respect to sleep disorders, the affected patients often use Amitriptyline, Clonazepam, Doxepin, Eszopicione, Melatonin, Mirtazapine, and Trazadone. Nevertheless, it is necessary to consider cognitive behavioural therapy as a viable option to acquire habits for sleep hygiene, as well as to reduce anxiety levels and improve the prognosis of depression.

Solifenacin, and Tolterodine; Beta-3-Agonists, with the main option being Mirabegron; Alpha-1A blockers, among which Alfuzosin, Silodosin, Tamsulosin, and Terazosin stand out; and SNRIs such as Duloxetine. On the other hand, sialorrhea in Parkinson's patients is usually due to a slowing of swallowing, which could be treated with Atropine drops, Botulinum toxins A and B, Glycopyrrolate, or a Scopolamine patch. Finally, digestive problems such as constipation are usually addressed in the first instance with non- pharmacological measures such as dietary modification (e.g., consuming high-fibre foods and plenty of fluids). However, when this does not work, drugs such as Lubiprostone and Polyethylene glycol may be administered. For other conditions such as nausea and vomiting the most commonly used treatment options are ondansetron and trimethobenzamide.

Brain Iron Deposits

Iron accumulation at the cerebral level has been described as a typical feature in the post- mortem brains of Parkinson's disease patients. Brain iron accumulation has been described as

a typical feature in the post-mortem brains of Parkinson's patients which could contribute to the loss of the substantia nigra. Therefore, iron elimination has been studied as a possible therapeutic target. The use of deferiprone in a Phase II clinical trial was shown to improve motor symptomatology and reduce iron levels in the brain. These results reinforce the need for new clinical trials to study the neuroprotective effect of this compound.

Peripheral Insulin Resistance

The discovery of Type II diabetes as a promoter of several neurodegenerative diseases, including PD, suggests an alternative in the search for a modifying treatment [109]. Oral antidiabetics, including exenatide, a glucagon-like peptide-1 (GLP-1) agonist, were administered in a Phase II clinical trial to patients with moderate PD. The Unified Parkinson'sDisease Rating Scale (UPDRS) score was found to be lower in the treatment group compared to the placebo group.

Dimethylbiguanide, better known as metformin, is an oral antidiabetic that has become highly relevant not only because of its proven efficacy in the regulation of glucose levels but also because it represents a promising approach in the treatment of neurodegenerative diseases. The latter could be explained by the fact that metformin has been shown to counteract the hypofunction of AMP-activated protein kinase (AMPK), which plays a crucial role in the

maintenance of neuronal cells, the levels of which are decreased in the development of neurodegenerative diseases, including PD.Neuroinflammation

Inflammatory processes at the brain level have been associated with PD as an important trigger of the disease. In fact, a direct relationship has been observed between the

inflammation occurring in the substantia nigra and the consequent dopaminergic neurodegeneration. In addition, the NLRP3 inflammasome has been described as a key player in the neuroinflammation observed in neurodegenerative diseases such as PD. Therefore, NLRP3 inhibitors such as Inzomelid could constitute a new therapeutic target. Among NLRP3 inhibitors, MCC950 stands out. The administration of MCC950 in murine models of PD was found to reverse inflammasome activation, leading to an improvement in motor symptoms and a reduction in dopamine degeneration and α-synuclein deposits.

9.1 Clinical diagnosis of Parkinson's disease:

Parkinson's disease is a neurological disorder that is clinically characterised as Parkinsonism (Akkaoui et al. 2020). Parkinson's disease results in the death of dopaminergic neurons in the substantia nigra pars compacta as well as the formation of intraneuronal Lewy bodies in the brain (Wal et al. 2022). Parkinson's disease is clinically diagnosed by reviewing the medical history of the patient (Peterson et al. 2020). In addition, poor sleep, a loss of smell, and constipation all play a role in the clinical diagnosis of Parkinson's disease (Mou et al. 2020). Moreover, any environmental exposure as well as a person's current and previous information are used to make a clinical diagnosis of Parkinson's disease.Early Parkinson's disease detection, for example, employing cutting-edge technology such as nanobiosensors, is critical for assisting clinicians in precisely diagnosing the disease before permanent damage occurs. Should treatment begin with levodopa, a dopa agonist or MAO-B inhibitor?

First line levodopa treatment:

For 40 years, levodopa, combined with a peripheral decarboxylase inhibitor, has been regarded as the gold standard for the treatment of PD. It still remains in many respects the most efficacious drug treatment. However, the benefits achieved often come at a price. Long-term levodopa therapy frequently leads to disabling side effects. Motor fluctuations are most strongly related to disease duration and dose of levodopa exposure, the development of drug-induced dyskinesias in PD seems to

be associated with intermittent stimulation of dopamine receptors. Levodopa has a short half-life of 60–90 min, and pulsatile levodopa supply to a denerated striatum seems to be an important aetiological factor.

A controversial issue has been whether levodopa could have a neurotoxic effect. The ELLDOPA study19 tried to address this in a large, randomized placebocontrolled clinical study of patients with early PD who had not previously received symptomatic treatment.. At the end of a 2-week washout period, the UPDRS scores of patients treated with all three doses of levodopa were better than those of the placebo group in a dose-responsive pattern. Although this may hint at a neuroprotective effect, it is possible that the 2-week washout period was insufficient. The issue regarding neuroprotection or neurotoxicity with levodopa remains unclear. However, given the risk of motor complications over time, which are dose dependent, using small doses of levodopa, tailored to the patient's needs are preferable.

First line dopamine agonist treatment

There are six orally acting dopamine agonists available in the UK. Four are ergot derivatives: bromocriptine, pergolide, cabergoline and lisuride; and two non-ergot drugs: ropinirole and pramipexole. Rotigotine is a non-ergot agonist available by transdermal patch.

The introduction of levodopa and the subsequent development of levodopa complications. Monotherapy trials have been undertaken comparing dopamine agonists with levodopa. The first such trial using bromocriptine in the 1980s showed a delay in the onset of dyskinesias with bromocriptine monotherapy compared with levodopa therapy, but no effect with regards to the onset of motor fluctuations.22 Trials of the more recently introduced dopamine agonists showed a significant reduction in the development of motor complications in patients initiated on agonist monotherapy compared with levodopa. Patient and physician assessments for the two arms were comparable. Quality of life (QoL) outcome measures over the 4 years of the CALM-PD study24 were the same for the levodopa and pramipexole groups. The side effect profile of the dopamine agonists is similar to levodopa.

First-line MAO-B inhibitors:

MAO-B inhibitors were widely used following the DATATOP study8 for their proven efficacy in symptom improvement and presumed 'neuroprotective' effect. The United Kingdom Parkinson's Disease Research Trial Group31 following over 700 patients with mildearly PD appeared to show a significant increase in mortality in patients treated withselegiline and levodopa compared with levodopa alone or bromocriptine alone.

32 A more recent meta-analysis of 17 randomized trials involving a total of 3525 patients came to the conclusion that MAO-B inhibitors reduce disability, the need for levodopa and the incidence of motor fluctuations, without substantial side effects or increased mortality.14 short duration and have not compared selegiline with initial treatment with a dopamine agonist. However, MAO-B inhibitors do have a potential role as first-line monotherapy in PD patients.

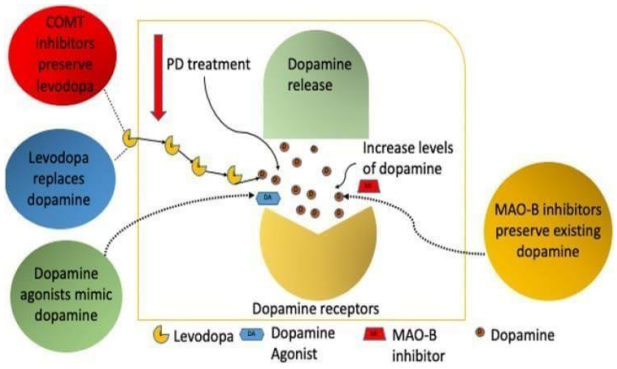
The treatment of late motor complications of PD:

After some years of stable, sustained response to levodopa therapy, most patients with PD experience fluctuations in motor performance, the effect of a single levodopa dose becoming progressively shorter (wearing-off phenomenon).Levodopa-induced dyskinesias occur with increasing duration of therapy, and more than 50% of patients will begin to develop motor fluctuations and dyskinesias between 5 and 10 years after commencing levodopa with 20– 30% developing dyskinesias after,2 years. In younger patients, the situation is worse, with almost all patients under the age of 40 developing motor complications after 6 years from the introduction of levodopa. Treatment of levodopa-induced dyskinesias remains unsatisfactory. Simply reducing the daily dose frequently renders patients rigid and immobile.

Choreic-dystonic involuntary movements appear as a concomitant of motor response to levodopa in most patients suffering from motor fluctuations. Dyskinesia is usually present during periods of maximum motor response (peak-dose dyskinesia) or the entire ON

Phase (square wave dyskinesia), but a diphasic pattern, with dyskinesias present at the beginning and end of motor response, also exists.high-plasma concentrations of levodopa and can be managed by fractionating levodopa doses. Amantidine has also been shown to reduce peak-dose dyskinesias. Long-acting dopamine agonists such as rotigotine may alsobe helpful by providing continuous dopaminergic stimulation. Biphasic dyskinesias occur when plasma levodopa levels are rising or falling. They may be difficult to control, but may respond to higher levodopa doses or a fast-acting agonist such as subcutaneous apomprphine injection.This may respond to a dispersible levodopa preparation or subcutaneous apomorphine injection. The pathophysiology of motor complications during chronic levodopa therapy (levodopa long- term syndrome) is only partially understood.

Amantadine, an NMDA receptor antagonist, was originally developed as an anti-viral agent,There is evidence that amantadine can reduce the frequency of motor complications including freezing, 'off' periods and dyskinesias,37,38 although the evidence for efficacy was felt to be insufficient in a Cochrane review.39 There is, particularly in the elderly, a relatively high incidence of side effects which include confusion, hallucinations, ankle swelling and livedo reticularis.Parenteral administration of a dopamine agonist in the form of subcutaneous apomorphine8 may be a useful adjunct to treatment by reducing 'off' time without increasing the tendency towards dyskinesias or confusion.



Deep brain stimulation treatment (DBS) is a surgical method used to treat Parkinson's disease by stimulating patients' brains . During this surgery, electrodes are implanted in particular parts of the brain to treat the symptoms of Parkinson's disease. This technique has been approved by the Food and Drug Administration as a viable therapy for severe Parkinson's disease cases (Mahajan et al. 2021). Deep brain stimulation surgery is more effective than drug therapy for Parkinson's disease.who are unresponsive to medication therapy. DBS is advantageous for dyskinesias that do not improve with medication adjustments, as well as for inconsistent and fluctuating responses to levodopa. Parkinson's disease-related involuntary movements are surgically treated in deep brain regions involved in motor regulation. A neurosurgeon may install a metal framework in the skull while under local anaesthetic in this type of surgery. This technique may aid patients with severe Parkinson's disease or those that do not respond to medication treatments. Despite DBS's effectiveness and widespread acceptance, critical problems remain, such as which brain regions should be targeted and in which patients. Supplementary Therapies for Treatment and Presentation of PD:

Diet:

A healthy diet can play a protective role against PD by delaying the onset of the symptoms that characteristics.Dieta that the rich in vegetables with a moderate inake of unsaturated fattyacids and a low intake of saturated acids have been found to protect against the onset both motor and non-motor symptoms of Parkinson's disease. This type of dietary pattern provides a large amount of antioxidant and anti-inflammatory compounds that promote the protection of the enteric and nervous system by preventing neuro inflammation,oxidative stress, and the accumulation of alpha -synuclein, which is responsible for the death of dopaminergic neurons

Clinical Presentation:

Parkinson's Disease may begin insidiously,with early symptoms presenting in upto 90% of patients .Nonmotor symptoms may be misinterpreted as related to normal aging or other comorbidities, there delaying the diagnosis . The early disease phase lats approximately four to six years on average and may include nonmotor feauters, as described previously. Although intolerance to cold is common ,thermoregulatoryabnormalities can also include profuse sweating .nociceptive[musculoskeletal] and neuroplastic pain may occur in some patients in early or later stages of the disease .

As noted in the section on diagnosis, triad of clinical mototr features in parkinson's disease patients includes tremor, rigidity,and bradykinesia. The motor presentations of [PD]parkinson's disease may correlate patient's age at onset;specifically, tremor at onset is twice as common in patients older than 64 years compared with those younger than 45 years of age. in addition , complications related to the duration of treatment .

Parkinson's disease is charecterised by both motor and nonmotor symptoms.Rigidity,sluggishness and unsteadiness are also symptoms of Parkinson's disease. Nonmotor symptoms can have a wide range of effects on the cardiovascular and genitourinarThere is substantially less diagnostic error in patients diagnosed in expert movement disorder clinics12 which strengthens the argument for early referral of patients to specialists expert in movement disorders.

A number of clinical criteria have been established.The UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria.

A loss of arm swing on one side is also an early and useful diagnostic feature. A glabellar tap does not seem to be particularly sensitive or specific.

A reduced sense of smell is, however, worth asking about since this may be one of the first symptoms in early PD.14

As the disease becomes more advanced, hypophonia, drooling of saliva (from reduced swallowing) and impairment of postural reflexes may develop.-motor complications of the disease often become more troublesome as the disease progresses. It is helpful to enquire about symptoms of depression which occurs in 40% of PD patients.suppression of the tremor with alcohol and there should be no evidence of rigidity or bradykinesia on examination. Adult onset dystonia may also present with asymmetrical

rest tremor and may explain some patients previously labelled as 'benign tremulous PD' who have scans with no evidence of dopaminergic defect.There are certain situations where investigations can prove useful. Conventional brain imaging with MRI or CT is usually not required unless an alternative diagnosis is suspected such as normal pressure hydrocephalus or vascular

Parkinsonism.Single photon emission computerized tomography (SPECT) imaging using a dopamine transporter (DAT) can be helpful in differentiating PD from a number of conditions, including essential tremor and dystonic tremor, neuroleptic-induced Parkinsonism and psychogenic Parkinsonism all of which demonstrate normal DAT scans. Uptake within the basal ganglia is reduced in PD, the Parkinsonian syndromes and DLB.19

Diagnosis:

Clinically present with less rigidity and bradykinesia, and this may result in a delayed or missed diagnosis.To avoid treating patients inappropriately and therefore necessitates a complete medication evaluation in all patients suspected of having PD. High-risk populations for DIP include elderly women, patients with multiple comorbidities, and patients taking multiple medications at high doses for extended periods. The drugs most commonly associated with DIP include those with dopamine receptor– blocking properties, such as the antipsychotic agents haloperidol, thiothixene, and risperidone.A challenge in diagnosing PD is that the disorder's clinical motor features may not present until approximately 50% to 80% of dopaminergic neurons are lost. Unfortunately, at this point significant disease progression may already exist. Adding to this problem is the need to identify subtle motor features that can easily go unrecognized, such as the absence of arm swing or jerking motions. Further complicating an early diagnosis is the presence of nonmotor comorbidities, including depression, anxiety, fatigue, constipation, anosmia, and sleep disorders.Since the onset of motor features is the point at which PD is usually diagnosed and treatment is initiated, investigators continue to search for biomarkers that may allow a more expeditious diagnosis.In the future, protein markers obtained from biopsy or other procedures, including spinal fluid, salivary gland, rectal, and colonic samples, may be used as well.

In the diagnosis of PD, imaging techniques are primarily used to rule out other neurological disorders; for example, magnetic resonance imaging (MRI) may be used to identify normal- pressure hydrocephalus.The anatomy of the substantia nigra (SN) with 7-T MRI may provide a future diagnostic option for identifying patients with PD.Dopamine transporter scans (DaT scans) may be used to differentiate LB-type dementias (PD and DLB) from non-LB dementias, such as Alzheimer's disease. Currently, the usefulness of genetic testing in diagnosing PD is debatable because of the lack of clarity on which populations to test.

Conclusion

Parkinson's disease is a chronic neurological illness that progresses over time and causes symptoms that are both motor and nonmotor. It has been established that striatal dopamine insufficiency is the main cause of the disorder's motor symptoms, which include bradykinesia, "Cogwheel" stiffness, and resting tremor. Nonmotor symptoms include depression, sleep disorders, and problems in cognition. To optimize results and enhance symptom logical control in these patients, a combination of pharmacological and nonpharmacological techniques should be employed in the therapy approach to this illness. On the other hand, these drugs only treat the condition's symptoms. There are alternative methods of treating Parkinson's disease, such as deep brain stimulation, which entails implanting electrodes in specific brain regions. By producing smaller gadgets, nanotechnology offers a practical substitute for the current Parkinson's disease detection and therapy methods. As a result, protein aggregations have been identified as biomarkers for Parkinson's disease early detection. There has been an endeavor to identify new biomarkers and therapeutic modalities. Parkinson's disease is still an unknown pathology that has a major social cost for those who suffer from it, but nanotechnology has the potential to provide new approaches for its diagnosis and treatment. Even though there is currently no known cure for Parkinson's disease (PD), there are many treatments available that aim to lessen the disease's symptoms. However, a thorough understanding of the pathophysiology underlying PD is necessary in order to provide patients with minimally harmful treatments that improve their quality of life.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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