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PARKINSON'S DISEASE

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Abstract:

Parkinson's disease (PD) is an advancing neurodegenerative condition characterized by the deterioration of dopaminergic neurons within the substantia nigra of the brain, resulting in a range of motor and non-motor symptoms that worsen gradually over time. The hallmark Tremors, rigidity, bradykinesia, and postural instability are among the motor symptoms, while cognitive impairment, mood disturbances, autonomic dysfunction, and sleep disturbances are considered non-motor symptoms.The diagnosis of PD relies on clinical assessment, often involving a thorough medical history, neurological examination, and supportive diagnostic tests such as neuroimaging. Despite ongoing research efforts, a definitive cure for PD remains elusive, and present interventions prioritize symptom management and enhancing quality of life."

Keywords: Parkinson's disease (PD)

Introduction

Parkinson's disease:

Parkinson's disease (PD) is an advancing neurodegenerative condition characterized by the deterioration of dopaminergic neurons within the substantia nigra of the brain, resulting in a range of motor and non-motor symptoms that worsen gradually over time. The hallmark Tremors, rigidity, bradykinesia, and postural instability are among the motor symptoms, while cognitive impairment, mood disturbances, autonomic dysfunction, and sleep disturbances are considered non-motor symptoms.The diagnosis of PD relies on clinical assessment, often involving a thorough medical history, neurological examination, and

supportive diagnostic tests such as neuroimaging. Despite ongoing research efforts, a definitive cure for PD remains elusive, and present interventions prioritize symptom management and enhancing quality of life." (1)

Cause of Parkinson's disease :

1. Hereditary Elements :

• Parkinson's disease manifests a complex genetic architecture, incorporating both rare highly penetrant mutations and common genetic variants that influence disease susceptibility.

• Familial instances of Parkinson's disease often arise from Mutations in PARKIN, SNCA, PINK1, LRRK2, and DJ-1 genes contribute to the condition, disrupting fundamental cellular processes encompassing protein aggregation, mitochondrial function, and protein degradation pathways.

• GWAS have identified many common genetic variants linked to the risk of Parkinson's disease, predominantly situated proximal to genes governing synaptic function, inflammation, and lysosomal degradation pathways. (2)

2. Environmental Exposures:

• Environmental elements constitute significant contributors to Parkinson's disease etiology, with exposure to certain toxins and pollutants being implicated in disease pathogenesis.

• Pesticides, herbicides, and insecticides have undergone extensive scrutiny for their association with Parkinson's disease, engendering disruptions in dopaminergic neurotransmission, oxidative stress induction, and facilitation of alpha-synuclein aggregation.

• Heavy metals, encompassing lead, iron, manganese, and copper, accrue within the brain, precipitating neurotoxicity through mechanisms inclusive of oxidative stress, mitochondrial dysfunction, and protein misfolding.

• Industrial chemicals such as solvents and organic pollutants have been correlated with Parkinson's disease risk, posited to exert effects via mechanisms involving neuroinflammation, mitochondrial compromise, and perturbation of cellular equilibrium.(3)

3. Oxidative Stress and Mitochondrial Dysfunction:

• Dysregulation of oxidative stress pathways and mitochondrial dysfunction represent salient features of Parkinson's disease pathology.

• Reactive oxygen species (ROS) engendered during customary cellular metabolism inflict damage upon cellular constituents, comprising lipids, proteins, and DNA, thereby eliciting neuronal compromise and demise.

- Given their principal role in cellular energetics, mitochondria are particularly susceptible to oxidative insult. Dysfunction across mitochondrial electron transport chain complexes, perturbed mitochondrial dynamics, and impaired mitophagy collectively contribute to bioenergetic collapse and neuronal susceptibilities observed in Parkinson's disease. (4)

4. Neuroinflammation:

- Neuroinflammatory processes constitute pivotal facets of Parkinson's disease pathogenesis, involving the activation of microglia, astrocytes, and infiltrating immune effectors.

- Prolonged neuroinflammation exacerbates neurodegeneration through The secretion of pro-inflammatory substances, such as chemokines , cytokines and reactive oxygen/nitrogen species.

- While activated glial elements undertake phagocytosis of neuronal detritus and misfolded proteins, they concurrently potentiate neurotoxicity by perpetuating inflammatory cascades and impairing synaptic integrity. (5)

5. Age and Other Risk Factors:

- Advanced age emerges as The primary risk factor for Parkinson's disease, being the most formidable determinant incidence demonstrating an exponential rise commensurate with chronological advancement.

- Additional risk determinants encompass male gender, genetic predisposition, traumatic head injury, rural domicile, and exposure to infectious agents or dietary constituents.

- Age-related perturbations in cellular homeostasis, spanning alterations in protein quality control mechanisms, synaptic functionality, and neuroinflammatory responses, underpin the age-associated accrual of pathological indices encountered in Parkinson disease. (6)

Manifestations of the condition:

1. Tremor:

- Tremor, characterized by involuntary shaking, often initiates in a hand but may also affect other extremities such as the foot or jaw. The tremor associated with PD exhibits a characteristic rhythmic back-and-forth motion, resembling a "pill rolling" motion, primarily involving the thumb and forefinger. This tremor is most prominent during rest or stress and typically diminishes during purposeful movements or sleep.

- Example: Sarah, a 62-year-old diagnosed with PD, experiences a tremor in her right hand that becomes more noticeable when she is relaxed or stressed, making it difficult for her to hold utensils steady during meals. (7)

2. Rigidity:

- Rigidity, or muscle stiffness, is a hallmark feature of PD, leading to a resistance to movement. Muscles remain constantly tense and contracted, resulting in aches and stiffness. When attempting to move the individual's limb, resistance is encountered, often manifesting as a "cogwheel" rigidity—a series of short, jerky movements akin to a ratchet.

- Example: John, a 58-year-old with PD, experiences rigidity in his limbs, making it challenging for his spouse to help him with tasks such as putting on a jacket due to the stiffness and lack of flexibility in his muscles. (8)

3. Bradykinesia:

- presents as a significant slowing down of spontaneous and automatic movements, posing challenges in performing routine tasks. Activities that were once executed quickly and effortlessly, such as washing or dressing, now require considerably more time and effort. Additionally, there is often a noticeable decrease in facial expressions, further contributing to the social and functional impact of this symptom.

- Example: Emily, aged 65, finds it increasingly difficult to perform daily tasks such as brushing her hair or tying her shoes due to bradykinesia, which has slowed her movements and diminished her facial expressions, leading to a loss of spontaneity and emotional expressiveness. (9)

4. Postural Instability:

- Postural instability, characterized by impaired balance and changes in posture, significantly elevates the risk of falls in individuals with PD. Maintaining equilibrium becomes challenging, particularly during dynamic activities or transitions, necessitating vigilance and precautionary measures to prevent accidents and injuries.

- Example: Tom, a 70-year-old diagnosed with PD, experiences frequent falls due to postural instability, especially when transitioning from sitting to standing, highlighting the need for assistive devices and modifications to his environment to enhance safety and stability. (10)

5. Freezing of Gait:

- Freezing of gait denotes transient episodes of locomotor arrest, characterized by an abrupt cessation or hesitation in forward progression despite the intent to ambulate. Environmental triggers and executive dysfunction are implicated in the pathophysiology of these episodes, which significantly compromise mobility and quality of life.

- Example: Lisa, aged 60, experiences freezing of gait when attempting to walk through doorways or crowded spaces, leading to a heightened fear of falling and a loss of confidence in her ability to navigate her surroundings effectively. (11)

6. Micrographia:

- Micrographia represents a characteristic trait of Parkinson's disease characterized by progressive diminution in handwriting size and fluency. This manifestation reflects deteriorating fine motor control and coordination, underscoring the intricate motor deficits inherent in the disease process.

- Example: Michael, a 55-year-old diagnosed with PD, notices a gradual decrease in size and legibility of his handwriting over time, making it increasingly challenging for him to communicate effectively in written form. (12)

7. Dysarthria:

- Dysarthria in Parkinson's disease encompasses a constellation of speech disturbances, including impaired articulation, phonation, and prosody. Disruptions in basal ganglia-thalamocortical circuits and cerebellar involvement contribute to the multifaceted speech deficits observed in affected individuals.

- Example: Susan, aged 70, experiences slurred speech and difficulty articulating words clearly due to dysarthria, leading to misunderstandings in communication and frustration in social interactions. (13)

8. Dystonia:

- Dystonia represents a diverse movement disorder characterized by sustained or intermittent muscle contractions, leading to abnormal postures or repetitive movements. Dystonic manifestations in Parkinson's disease may encompass focal or segmental dystonia, often manifesting as painful, twisting movements or abnormal posturing.

- Example: Robert, aged 65, experiences dystonic episodes characterized by involuntary twisting movements of his foot, leading to pain and discomfort, especially during periods of stress or fatigue." (14)

Methods of detecting Parkinson's disease:

1. Evaluation via Medical History and Clinical Examination :

- Medical History: A thorough review of The patient's medical background, encompassing symptom onset and development, family history of neurological conditions, and pertinent environmental exposures .

- Example: Inquiring about the patient's experience of resting tremors, muscle stiffness, or difficulties with balance over time.

- Physical Examination: Comprehensive neurological assessment to evaluate motor function, including muscle tone, tremors, coordination, gait, and balance.

- Example: Observing resting tremors in the patient's hands or assessing gait abnormalities such as festination during the physical examination. (15)

2. Movement Tests:

- Tremor Assessment: Systematic observation and evaluation of tremors at rest and during voluntary movement, assessing frequency, amplitude, and pattern.

- Example: Documenting a rhythmic, pill-rolling tremor in the patient's fingers during periods of rest.

- Gait Analysis: Detailed examination of the patient's walking pattern, posture, stride length, arm swing, and balance.

- Example: Noting a stooped posture, shuffling gait, and reduced arm swing while observing the patient walk across the room.

- Balance Tests: Performing standardized tests to assess static and dynamic balance, such as the Romberg test or tandem gait.

- Example: Administering the pull test to assess the patient's ability to recover balance after a sudden backward pull. (16)

3. Imaging Tests:

- Magnetic Resonance Imaging (MRI) employs magnetic fields and radio waves to produce detailed visuals capturing the intricate structure of the brain.

- Example: Identifying substantia nigra changes indicative of Parkinson's disease on MRI images.

- Computed Tomography (CT scan): Providing cross-sectional images of the brain to evaluate for structural abnormalities.

- Example: Ruling out other conditions mimicking Parkinsonism, such as tumors or vascular lesions, with CT scans. (17)

4. Blood Tests:

- Conducting routine blood tests to assess factors such as complete blood count, electrolyte levels, thyroid function, and liver function.

- Example: Analyzing blood samples to exclude secondary causes of Parkinsonian symptoms, such as hypothyroidism or hepatic encephalopathy. (18)

5. Treatment Response Tests:

- Levodopa Challenge Test: Administering a standardized dose of levodopa/carbidopa and monitoring for motor symptom improvement.

- Example: Documenting a significant reduction in tremors and improvement in mobility following levodopa administration, supporting a positive response indicative of Parkinson's disease. (19)

How PD Impacts the Brain:

Parkinson's disease (PD) is a complex neurodegenerative condition marked by the gradual and progressive decline of dopaminergic neurons, predominantly located within the substantia nigra pars compacta (SNpc) region of the midbrain. This pathological cascade, stemming from an intricate interplay of genetic predisposition, environmental factors, and cellular mechanisms, underlies the hallmark features of PD.

The substantia nigra serves as a pivotal hub within the basal ganglia-thalamocortical motor circuit, orchestrating the intricate modulation of voluntary movements. Dopamine, the neurotransmitter synthesized by SNpc neurons, intricately regulates the balance between excitatory and inhibitory signaling within this circuitry. The insidious loss of dopaminergic neurons and subsequent dopamine depletion precipitate a cascade of neuronal dysfunction and disrupted motor control, culminating in the characteristic range of motor and non-motor symptoms that worsen gradually over time. The hallmark Tremors, rigidity, bradykinesia, and postural instability are among the motor symptoms, while cognitive impairment, mood disturbances, autonomic dysfunction, and sleep disturbances are considered non-motor symptoms. Beyond motor dysfunction, PD manifests with a myriad of non-motor symptoms, reflecting the pervasive neurodegenerative process affecting diverse brain regions. Cognitive impairment, ranging from subtle deficits to dementia, neuropsychiatric disturbances encompassing depression, anxiety, apathy, and psychosis, autonomic dysfunction, sleep disturbances, and sensory abnormalities further compound the disease burden.

At the cellular level, PD is characterized by The buildup of anomalous protein clusters identified as Lewy bodies. These aberrant protein aggregates disrupt normal cellular physiology, precipitating neuronal dysfunction and eventual demise. In addition to dopamine depletion, disruptions in other neurotransmitter systems, notably acetylcholine and serotonin, contribute to the diverse array of symptoms observed in PD. As PD progresses, the neurodegenerative cascade extends beyond the confines of the basal ganglia to encompass widespread brain networks, including the brainstem, limbic system, and neocortex. This diffuse neuropathology underscores the heterogeneity of PD phenotypes and the intricate interplay between genetic predisposition, environmental influences, and neurobiological perturbations driving disease progression In summary, Parkinson's disease represents a complex and dynamic neurodegenerative process characterized by dopaminergic neuron loss, basal ganglia dysfunction, Lewy body pathology, neurotransmitter dysregulation, and widespread brain involvement. A comprehensive understanding of the multifaceted pathophysiology of PD is imperative for the development of targeted therapeutic interventions aimed at halting or slowing disease progression and enhancing patient outcomes. (20 ,21)

TREATMENTS:

A. Medications:

1. Levodopa:

• Mechanism of action: Levodopa, converted into dopamine by brain dopaminergic neurons after crossing the blood-brain barrier, is a precursor of dopamine. Carbidopa, a peripheral decarboxylase

inhibitor, aids in this process, is often co-administered with levodopa to prevent its conversion to dopamine in the bloodstream, increasing levodopa availability in the brain.

• Dosage forms: Available as immediate-release and extended-release formulations, often combined with carbidopa (Sinemet) or carbidopa-entacapone (Stalevo) to enhance efficacy and reduce side effects.

• Side effects: Common adverse effects consist of nausea, vomiting, dyskinesias, hallucinations, and Orthostatic hypotension can also occur, and extended use may lead to motor fluctuations and dyskinesias .(22)

2. Dopamine agonists:

• Mechanism of action: Dopamine agonists stimulate brain dopamine receptors directly, bypassing synthesis, mimicking dopamine's effects in the striatum to improve motor symptoms

• Dosage forms: Available as oral tablets, extended-release formulations, transdermal patches (rotigotine), and subcutaneous injections (apomorphine).

• Side effects: include dizziness , nausea, hallucinations, impulse control disorders, and orthostatic hypotension. Dopamine agonists may also increase the risk of compulsive behaviors, such as gambling and hypersexuality. (21)

3. MAO-B inhibitors:

• Mechanism of action: Inhibitors of monoamine oxidase type B block the enzyme responsible for dopamine metabolism in the brain.. these medications increase dopamine levels and prolong its action, improving motor symptoms.

• Dosage forms: Available as oral tablets (rasagiline, selegiline) and orally disintegrating tablets (selegiline).

• Side effects: include headache, nausea, insomnia, and orthostatic hypotension. MAO-B inhibitors may interact with certain medications and foods containing tyramine, leading to hypertensive crisis. (23)

4. COMT inhibitors:

• Mechanism of action: block the enzyme catechol-O-methyltransferase , which breaks down levodopa in the peripheral tissues. By inhibiting COMT, these medications Extending levodopa's effect in the brain, these agents diminish motor fluctuations.

• Dosage forms: Available as oral tablets (entacapone, tolcapone).

• Side effects: Common side effects include diarrhea, dyskinesias, orange discoloration of urine, and hepatotoxicity (with tolcapone). Tolcapone carries a higher risk of hepatotoxicity and requires close monitoring of liver function. (24)

5. Anticholinergics:

• Mechanism of action: Anticholinergic medications block the action of acetylcholine, a neurotransmitter that opposes dopamine in the striatum. By reducing cholinergic activity, anticholinergics help alleviate tremors and rigidity in some patients.

• Dosage forms: Available as oral tablets (trihexyphenidyl, benztropine).

• Side effects: Common side effects include dry mouth, constipation, urinary retention, blurred vision, cognitive impairment, and hallucinations. Anticholinergics are generally avoided in elderly patients due to an increased risk of cognitive impairment and falls. (25)

B. Surgical treatments:

1. Deep Brain Stimulation (DBS):

• Mechanism of action: the surgical Surgically placing electrodes in targeted brain areas, such as the subthalamic nucleus or globus pallidus. These electrodes deliver high-frequency electrical stimulation, modulating abnormal neuronal activity and restoring the balance between excitatory and inhibitory signals in the brain.

• Procedure: DBS surgery is performed under local anesthesia with sedation. Electrodes are implanted into the target brain regions, and a pulse generator (neurostimulator) is Implanted within the thoracic cavity. The neurostimulator is programmed to deliver electrical impulses to the brain, which can be adjusted as needed.

• Indications: DBS is recommended for Individuals with late-stage Parkinson's disease exhibiting motor fluctuations, dyskinesias, and medication-refractory symptoms. It is not a cure for Parkinson's disease but can significantly improve motor symptoms and quality of life. (26)

C. Physical therapy and rehabilitation:

1. Physical therapy:

• Techniques: use a variety of techniques, including stretching exercises, strength training, balance exercises, gait training, and coordination exercises, to improve motor function and mobility. They may also utilize modalities For instance, employing heat, cold, and electrical stimulation to alleviate pain and muscle stiffness

• Goal: The goal of physical therapy is to optimize physical function, prevent falls, and improve overall quality of life for patients with Parkinson's disease. Therapy is tailored to individual needs and may be provided in outpatient clinics, rehabilitation centers, or home settings. (27)

2. Occupational therapy:

• Interventions: Occupational therapists focus on improving activities of daily living (ADLs) and functional independence in patients with Parkinson's disease. They provide strategies and adaptive techniques to help patients perform self-care tasks, such as dressing, grooming, eating, and bathing. They may also address cognitive impairments, such as memory deficits and executive dysfunction, to enhance functional abilities.

• Equipment: Occupational therapists may recommend assistive devices and adaptive equipment, such as grab bars, adaptive utensils, dressing aids, and mobility aids, to facilitate independence and safety in daily activities. (28)

D. Psychological therapy:

1. Counseling:

• Modalities Include personalized individual therapy, group sessions, family counseling, and support groups designed to meet the unique requirements of patients and caregivers. Therapeutic techniques may encompass cognitive-behavioral therapy (CBT), supportive interventions, mindfulness practices, and acceptance and commitment therapy (ACT)).

• Goals: Counseling provides emotional support, coping strategies, and psychoeducation for patients and caregivers, helping them navigate the challenges of living with Parkinson's disease, address psychological symptoms such as depression and anxiety, and improve overall well-being. (29)

Medications for the Motor Symptoms of PD :

Medications represent indispensable components in the meticulous management of motor symptoms accompanying Parkinson's disease (PD). These pharmacological interventions are pivotal in ameliorating manifestations such as Tremors, stiffness, slowness of movement, and impaired balance, thereby substantially enhancing the quality of life for individuals afflicted with PD. Employing mechanisms that involve either direct replenishment of dopamine levels in the brain or augmentation of dopamine efficacy, these medications offer symptomatic relief and contribute to a deceleration in disease progression. While recognizing that medications do not provide a definitive cure for PD, their judicious administration, integrated within a comprehensive treatment framework, can effectively control symptoms and optimize patient outcomes. It is imperative for patients to engage in close collaboration with their healthcare providers to ascertain the most suitable medications and dosages tailored to their unique clinical profiles. Furthermore, the ongoing monitoring for potential side effects and the need for dosage adjustments underscore the meticulousness inherent in managing PD therapeutics. (12-13-14)

Alternative therapies:

Complementary therapies represent adjunctive modalities that, when used in conjunction with conventional pharmacological treatments, offer additional avenues for managing the multifaceted challenges of Parkinson's disease (PD). These therapies encompass a spectrum of interventions designed to address motor

and non-motor symptoms, enhance quality of life, and optimize functional independence. Below is a detailed overview of commonly utilized complementary therapies for PD:

1. Physical Therapy (PT): Physical therapy focuses on optimizing motor function, mobility, and balance through tailored exercise regimens and rehabilitation techniques. It aims to mitigate motor impairments such as rigidity, bradykinesia, and postural instability, thereby promoting functional independence and reducing the risk of falls.

2. Occupational Therapy (OT): Occupational therapy aims to facilitate engagement in activities of daily living (ADLs) and enhance functional independence by addressing fine motor skills, cognitive function, and environmental adaptations. OT interventions may involve strategies to optimize home and workplace environments, recommend assistive devices, and provide training in adaptive techniques to overcome daily challenges.

3. Speech Therapy: Speech therapy focuses on managing communication deficits, swallowing difficulties (dysphagia), and voice disorders (dysphonia) commonly encountered in PD. Therapeutic interventions encompass exercises to improve articulation, voice projection, and swallowing function, as well as strategies to enhance communication effectiveness and safety during mealtimes.

4. Tai Chi: Tai Chi, an ancient Chinese martial art characterized by slow, deliberate movements and focused breathing techniques, has emerged as a promising complementary therapy for PD. Research suggests that regular practice of Tai Chi can improve balance, gait, and functional mobility, while also reducing the risk of falls and enhancing overall well-being.

5. Yoga: Yoga encompasses a holistic mind-body practice involving physical postures (asanas), breathing exercises (pranayama), and meditation. Yoga practice offers potential benefits for individuals with PD by promoting flexibility, strength, and relaxation, while also addressing motor symptoms, reducing stress, and enhancing emotional resilience.

6. Acupuncture: Research has investigated acupuncture, a traditional Chinese medicine practice that entails inserting thin needles into precise points on the body as a complementary therapy for PD symptom management. While evidence regarding its efficacy remains inconclusive, some studies suggest potential benefits in alleviating motor symptoms, improving quality of life, and reducing medication requirements.

7. Massage Therapy: entails Manual manipulation of soft tissues aims to induce relaxation and relieve muscle tension, and enhance circulation. Massage techniques such as Swedish massage, deep tissue massage, and myofascial release may offer symptomatic relief for individuals with PD by targeting muscle stiffness, pain, and discomfort.

8. Music Therapy: Music therapy utilizes musical interventions to address physical, emotional, and cognitive goals in individuals with PD. Active participation in music-making activities, listening to music, and rhythmic exercises can improve mood, reduce anxiety, enhance motor coordination, and foster social engagement.

9. Dietary Supplements: Some individuals with PD may consider dietary supplements such as Vitamin D, omega-3 fatty acids, and Coenzyme Q10 as adjunctive therapies to conventional treatment.

10. Mindfulness and Meditation: Mindfulness-based practices and meditation techniques offer potential benefits for individuals with PD by promoting stress reduction, emotional well-being, and cognitive resilience. Mindfulness-based stress reduction (MBSR) programs, meditation practices, and mindfulness-based interventions can cultivate present-moment awareness, foster acceptance, and enhance coping strategies for managing the challenges of living with PD. (30,31)

Protection:

1. Regular Exercise: Engaging in aerobic activities like walking, jogging, or swimming promotes brain health and may reduce the risk of PD. Strive to engage in at least 150 minutes of moderate-intensity exercise weekly.

2. Healthy Diet: Consume plenty of Whole grains, lean proteins, fruits, vegetables, and healthy fats. Antioxidant-rich foods like berries and leafy greens help protect against oxidative stress, which is implicated in PD.

3. Avoidance of Toxins: Minimize exposure to environmental toxins such as pesticides and industrial chemicals, which may contribute to neurodegeneration. Practice safety measures in workplaces with potential toxin exposure.

4. Smoking Cessation: Quitting smoking reduces the risk of PD. Even former smokers can experience a decrease in risk over time, emphasizing the importance of cessation.

5. Moderate Alcohol Consumption: Keep alcohol consumption at moderate levels, as excessive intake may elevate the risk of PD. Red wine, in moderation, contains compounds like resveratrol, which may offer protective effects.

6. Caffeine Consumption: Enjoying caffeinated beverages like coffee or tea may lower the risk of PD. Aim for two to three cups of coffee per day, as caffeine has been associated with a reduced incidence of the disease.

7. Healthy Sleep Habits: Prioritize quality sleep by maintaining a regular sleep schedule, creating a comfortable sleep environment, and practicing relaxation techniques. Address any sleep disturbances promptly.

8. Brain Stimulation Activities: Engage in mentally stimulating activities like reading, puzzles, or learning new skills to promote cognitive health and reduce the risk of PD.

9. Management of Chronic Conditions: Control chronic conditions such as hypertension and diabetes through lifestyle modifications and medication adherence to lower the risk of PD-related complications. (32)

References

1. Loscalzo J, et al., eds. Parkinson's disease. In: Harrison's Principles of Internal Medicine. 21st ed. McGraw Hill; 2022.
2. Deng H, Wang P, Jankovic J. The genetics of Parkinson disease. Ageing Res Rev. 2018 Mar 1;42:72–85
3. Elbaz A, Clavel J, Rathouz PJ, Moisan F, Galanaud J-P, Delemotte B, et al. Professional exposure to pesticides and Parkinson disease. Ann Neurol. 2009 Oct;66(4):494–504.
4. Langston JW, Ballard P, Tetrud JW, Irwin I. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. Science. 1983 Feb 25;219(4587):979–80.
5. Williams-Gray CH, Wijeyekoon R, Yarnall AJ, Lawson RA, Breen DP, Evans JR, et al. Serum immune markers and disease progression in an incident Parkinson's disease cohort (ICICLE-PD). Mov Disord. 2016 Jul 1;31(7):995–1003.
6. Thomas A. Allscripts EPSi. Mayo Clinic. April 22, 2022.
7. Kumar, H., & Jog, M. (2011). A patient with tremor, part 1: making the diagnosis. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 183(13), 1507–1510.
8. Berardelli, A., Sabra, A. F., & Hallett, M. (1983). Physiological mechanisms of rigidity in Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 46(1), 45-53.
9. Berardelli, A., Rothwell, J. C., Thompson, P. D., & Hallett, M. (2001). Pathophysiology of bradykinesia in Parkinson's disease. Brain, 124(11), 2131-2146.
10. Palakurthi, B., & Burugupally, S. P. (2019). Postural instability in Parkinson's disease: a review. Brain sciences, 9(9), 239.
11. Okuma, Y. (2006). Freezing of gait in Parkinson's disease. Journal of neurology, 253, vii27-vii32.
12. McLennan, J. E., Nakano, K., Tyler, H. R., & Schwab, R. S. (1972). Micrographia in Parkinson's disease. Journal of the neurological sciences, 15(2), 141-152.
13. Moya-Galé, G., & Levy, E. S. (2019). Parkinson's disease-associated dysarthria: prevalence, impact and management strategies. Research and Reviews in Parkinsonism, 9-16.
14. Robbins JA, et al. Swallowing and speech production in Parkinson's disease. Annals of Neurology.1986
15. van der Marck, M. A., Klok, M. P. C., Okun, M. S., Giladi, N., Munneke, M., Bloem, B. R., & Force, N. F. T. (2014). Consensus-based clinical practice recommendations for the examination and management of falls in patients with Parkinson's disease. Parkinsonism & related disorders, 20(4), 360-369.
16. Guo, P. F., Bhattacharya, P., & Kharma, N. (2010). Advances in detecting Parkinson's disease. In Medical Biometrics: Second International Conference, ICMB 2010, Hong Kong, China, June 28-30, 2010. Proceedings 2 (pp. 306-314). Springer Berlin Heidelberg.
17. Chou KL. Diagnosis and differential diagnosis of Parkinson disease
18. Santiago, J. A., & Potashkin, J. A. (2014). Current challenges towards the development of a blood test for Parkinson's disease. Diagnostics, 4(4), 153-164.

19. TAYLOR, A. E., Saint-Cyr, J. A., & Lang, A. E. (1987). Parkinson's disease: Cognitive changes in relation to treatment response. Brain, 110(1), 35-51.
20. Berg D, et al. Alpha-synuclein seed amplification and its uses in Parkinson's disease. The Lancet Neurology. 2023
21. Hornykiewicz O. The discovery of dopamine deficiency in the parkinsonian brain. Journal of Neural Transmission Supplementum. 2006
22. Tambasco, N., Romoli, M., & Calabresi, P. (2018). Levodopa in Parkinson's disease: current status and future developments. Current neuropharmacology, 16(8), 1239-1252.
23. Robakis, D., & Fahn, S. (2015). Defining the role of the monoamine oxidase-B inhibitors for Parkinson's disease. CNS drugs, 29, 433-441.
24. Rivest, J., Barclay, C. L., & Suchowersky, O. (1999). COMT inhibitors in Parkinson's disease. Canadian journal of neurological sciences, 26(S2), S34-S38.
25. Brocks, D. R. (1999). Anticholinergic drugs used in Parkinson's disease: An overlooked class of drugs from a pharmacokinetic perspective. J Pharm Pharm Sci, 2(2), 39-46.
26. Fogel, W. (2003). Deep brain stimulation (DBS) in Parkinson's disease. Psychoneuro, 29(10), 454-456.
27. Kwakkel, D. G., De Goede, C. J. T., & Van Wegen, E. E. H. (2007). Impact of physical therapy for Parkinson's disease: a critical review of the literature. Parkinsonism & related disorders, 13, S478-S487.
28. Dixon, L., Duncan, D. C., Johnson, P., Kirkby, L., O'Connell, H., Taylor, H. J., & Deane, K. (2007). Occupational therapy for patients with Parkinson's disease. Cochrane Database of Systematic Reviews, (3).
29. S.A. Gunzler, D.E. Riley,Basal Ganglia, Diseases of, Michael J. Aminoff, Robert B. Daroff,Encyclopedia of the Neurological Sciences (Second Edition),Academic Press,2014,Pages 393-396
30. Isaacson SH, et al. Blinded SAPS-PD assessment after 10 weeks of pimavanserin treatment for Parkinson's disease psychosis. Journal of Parkinson's Disease. 2020
31. Ferri FF. Parkinson disease. In: Ferri's Clinical Advisor 2022. Elsevier; 2022.
32. Relaxation techniques for health. National Center for Complementary and Integrative Health.