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A Review Article On Parkinson's Disease

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Abstract:

Parkinson's disease (PD) is a complex neurodegenerative condition marked by the gradual loss of dopaminergic neurons in the substantia nigra area of the brain. Millions of people are impacted globally, and the healthcare systems, families, and patients are all heavily impacted. This study offers a thorough summary of current knowledge on Parkinson's disease, including its aetiology, clinical symptoms, diagnostic methods, and potential treatment options. In conclusion, Parkinson's disease is a very diverse and complicated sickness that has a big influence on both people and society. There is now room for more specialised and individualised management strategies thanks to improvements in our knowledge of its aetiology, clinical presentation, and available treatments. But more study is required to understand the complex pathophysiological mechanisms behind PD and create cutting-edge therapy approaches that can enhance the lives of those who are affected and finally result in a cure.

Introduction:

Parkinson's disease (PD) is a frequent synucleinopathy with an incidence of 160/100 000 in Western Europe and 4% of the population over 80. With an older population, managing PD is anticipated to become a more significant and difficult element of medical practise for neurologists and general practitioners. With the discovery of many gene mutations over the past ten years, which may provide insight into the processes

behind the pathogenesis of sporadic instances of Parkinson's disease, our understanding of the illness's aetiology has evolved. The diagnosis of Parkinson's disease (PD) is still mostly clinical, thus it's crucial to identify the early symptoms as well as any additional symptoms or indications that point to possible parkinsonism causes. Along with increased knowledge of non-motor problems, there has also been a significant development in the range of available treatments, both in the early and late phases of the illness. The National Institute for Health and Clinical Excellence (NICE) in the United Kingdom has produced guidelines for the identification and treatment of people with PD [10].

Pathology, aetiology and pathogenesis:

Cell loss inside the substantia nigra, with a focus on the ventral region of the pars compacta, is the pathological hallmark of PD. When compared to the same region in those who are not afflicted, this part of the brain has lost 50–70% of its neurones at the time of death. The medulla oblongata/pontine tegmentum and olfactory bulb have been the site of the early pathological alterations in PD [7] that have been seen. Patients are presymptomatic in the early phases, or Braak stages 1 and 2. The substantia nigra, portions of the midbrain, and the basal forebrain become affected as the illness progresses—Braak stages 3 and 4—as do other brain regions. The neocortex is the last area to show pathological alterations.

On the distribution of lewy bodies, this pathological stage is founded. The pathological defining feature of PD is lewy bodies. They are a-synuclein-immunoreactive inclusions formed up of a variety of neurofilament proteins and proteolytic enzymes. One of these is the heat shock protein ubiquitin, which is crucial in directing the breakdown of other proteins. In some family types of Parkinson's disease (PD) when lewy bodies are also present, the a-synuclein gene is mutated. In cases involving children, mutations in the parkin protein result in a parkinsonian syndrome devoid of lewy bodies, indicating that the parkin protein is crucial for the formation of the lewy body. According to research, parkin makes lewy bodies more likely to develop by facilitating the binding of ubiquitin (ubiquination) to other proteins, such the a-synuclein-interacting protein synphilin-1. [3] However, lewy bodies are not a clinical signature of any other neurodegenerative illness. They are only present in Parkinson's disease (PD) and dementia with lewy bodies (DLB).

The ubiquitin-proteasome system (UPS) has attracted attention as a potential candidate in the emergence of cell death following the finding of single gene abnormalities in PD.[6] Intracellular proteolysis and several other intracellular activities that keep cells viable depend on the UPS. By eliminating undesirable proteins that the cell no longer needs, it does this. Proteins, particularly a-synuclein, which is a key component of lewy bodies, abnormally aggregate when the UPS fails. The olfactory bulb is among the initial locations for LB deposition in early PD. It is also intriguing that a change in smell or taste is frequently one of the first clinical signs of Parkinson's disease, raising the hypothesis that LB creation may be crucial for the activation of pathways that result in neuronal malfunction and death.

The identification of mutations in multiple ubiquitin-proteasome pathway protein-coding genes in PD has reinforced the connection between UPS and neurodegeneration.

Environmental factors:

It has been difficult to pinpoint the environmental elements that increase the risk of developing PD. A association between exposure to pesticide usage and wood preservatives has been shown in certain epidemiological research, although not all have indicated that living in a rural area increases your chance of developing Parkinson's disease (PD).[7] A substantial negative link between smoking and the onset of the illness is the only environmental component that is consistently present. Furthermore, one or more environmental poisons may be the cause of mitochondrial dysfunction in PD.

Clinical diagnosis of Parkinson’s disease:

Bradykinesia, stiffness, and rest tremor are hallmark symptoms of PD. All of these might not exist. Postural instability may be a symptom, although early postural instability backwards, especially with a history of falls, is more indicative of progressive supranuclear palsy (PSP). Asymmetry is frequently present in the clinical findings in PD. Despite the fact that post-mortem investigations have shown an alternate diagnosis in up to 25% of people with Parkinson's disease (PD) who were given the diagnosis by general neurologists, it is important to note that the clinical diagnosis is frequently simple.[1] It should be noted that patients diagnosed in specialised clinics for movement disorders had significantly lower rates of diagnostic mistake [4], which supports the case for early patient referral to movement disorder experts.

It is important to note a few more clinical symptoms. With micrographia, a change in handwriting and a lack of facial expression are frequently early symptoms. Another early and helpful diagnostic sign is the lack of one side's arm swing. It doesn't look like a glabellar tap is very sensitive or precise.

However, it is important to inquire about any changes in scent as early Parkinson's disease (PD) symptoms may include this as one of the earliest signs. Hypophonia, saliva drooling (from decreased swallowing), and impairment of postural reflexes may appear as the condition progresses [2].

If a patient has symmetrical limb tremor that becomes worse with posture and is inhibited by alcohol, essential tremor should be suspected. Tremors in the head or voice are also possible. Alcohol may be used to decrease the tremor in this disease, and an examination should reveal no signs of stiffness or bradykinesia [9]. This disorder may also be inherited in an autosomal dominant manner. Investigations may be helpful in some circumstances, even if the diagnosis of Parkinson's disease is clinical. Unless a different diagnosis—like normal pressure hydrocephalus or vascular parkinsonism—is suspected, conventional brain imaging with MRI or CT is typically not necessary.

Dopamine transporter (DAT) imaging with single photon emission computer tomography (SPECT) can help distinguish Parkinson's disease (PD) from a number of conditions, such as essential and dystonic tremors, neuroleptic-induced parkinsonism, and psychogenic parkinsonism, all of which show normal DAT scans [5].

Pharmacologic management:

The major objective of PD research is to develop disease-modifying therapy that can slow or stop the neurodegenerative process. However, there is no existing definitive disease-modifying therapy to achieve this aim.

Dopaminergic therapy:

Once patients begin to experience functional impairment, the American Academy of Neurology (AAN) advises starting one of the following pharmacological regimens. Levodopa/carbidopa, dopamine agonists (ergot and non-ergot types), monoamine oxidase-B (MAO-B) inhibitors, injectable dopamine agonist (apomorphine), catechol-O-methyltransferase (COMT) inhibitors, N-methyl-D-aspartate (NMDA) receptor inhibitors, and anti-cholinergics are some of the medical treatments for motor symptoms. Using other delivery methods, such as intrajejunal infusions, subcutaneous injections, or transdermal patches, might

complement medication administration in the latter stages of Parkinson's disease (PD). The patient is a candidate for deep brain stimulation (DBS) if there are ongoing motor tics and dyskinesias. in the early stages of PD, different methods of medication administration However, monoamine MAO B inhibitors are only modestly successful in treating bradykinesia and stiffness. Levodopa and dopamine agonists slow the course of the illness and the onset of impairment. Anticholinergic medications, such as trihexyphenidyl, can reduce tremor, however dopamine replacement treatment has a poor and variable effect.

Levodopa:

Depletion of striatal dopamine as a result of dopaminergic neuron death in the SNpc is the mechanism behind the predominant motor symptoms of PD. A significant advancement in the treatment of Parkinson's disease (PD) was the use of levodopa to replace striatal dopamine. Since then, several other targets for dopaminergic treatments have been discovered. Almost all patients require this specific medication at some point throughout their disease, and levodopa is regarded as the gold standard. Motor tremors and dyskinesias make long-term levodopa usage challenging. It is yet unknown what causes these motor problems. One acknowledged explanation for this manifestation is the participation of both presynaptic and postsynaptic pathways, which finally result in non-physiological pulsatile striatal dopamine receptor activation and other maladaptive neuronal responses. Levodopa's brief half-life, its variable absorption, and the blood-brain barrier transit all contribute significantly to the emergence of motor problems.

Dopamine agonists:

The D2 receptor family is primarily the focus of dopamine receptors. Ergoline derivatives were the original medications in this class. All of the currently utilised medications, such as pramipexole, ropinirole, apomorphine, piribedil, and rotigotine, are non-ergoline medications since ergoline treatments generated safety concerns for the heart and lungs. When taken as initial monotherapy, dopamine agonists significantly lower the incidence of motor problems by inducing less pulsatile striatal dopamine receptor activation than levodopa.

MAO B inhibitors:

Synaptic dopamine concentration and symptomatic effectiveness both rise as a result of MAO B inhibition. Since the 1970s, levodopa adjuncts containing selegiline, a selective irreversible MAO B inhibitor, have demonstrated their effectiveness. Selegiline monotherapy in early-phase PD slowed the spread of the condition, according to the MONOCOMB study's findings. Selegiline was relatively well tolerated when used for a long time and demonstrated levodopa-sparing properties in advanced PD.

Catecohol-O-methyl transferase (COMT) inhibitors:

Currently available levodopa formulations incorporate carbidopa or benserazide to stop peripheral dopamine metabolism, which improves the bioavailability of the former medicine. As a result, a second route involving COMT is used for the peripheral metabolism of levodopa. Levodopa's bioavailability and half-life will rise with COMT pathway inhibition, benefiting individuals with motor irregularities. Increased ON time and decreased OFF time result with triple treatment with levodopa, carbidopa, and a COMT inhibitor, which also considerably raises quality of life. Because of its negative effects, tolcapone usage is restricted. Currently, entocapone is offered; nevertheless, it is a less effective option. Nebicapone has been demonstrated in phase II studies to be both safer and more effective than entacapone. In individuals with advanced Parkinson's disease (PD), opicapone, administered orally once daily, has also been shown to enhance ON time and decrease OFF time without causing bothersome dyskinesias [11].

Conclusion:

Parkinson's disease is one of the most prevalent neurodegenerative conditions affecting the ageing population and is linked to higher morbidity and death rates. The best case management requires knowledge of the disease's symptoms, available therapies, and its long-term progressive trajectory. Understanding the neuropathology of PD and how it spreads across the nervous system has advanced remarkably. But none of these therapies is curative. Due to the escalating severity of treatment-resistant motor issues and non-motor symptoms, PD continues to be a progressive condition that finally results in severe impairment. The primary unmet requirements that must be addressed by present and future research efforts include modifying variables that contribute to the advancement of the illness and in further postponing its impairment.

Ethical statement:

this study has no cruelty on animals. Since it was a review article, we did not tool a subjects in this study.

Conflict of interest:

The above study describes individualised management strategies thanks to improvements in our knowledge of its aetiology, clinical presentation, and available treatments, understand the complex pathophysiological mechanisms behind PD and create cutting-edge therapy approaches that can enhance the lives of those who are affected and finally result in a cure

References:

1. Hughes AJ, Daniel SE, Kilford L et al. (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases.

2. Hawkes CM (1995) Diagnosis and treatment of Parkinson's disease. Anosmia is a common finding.

3. Chung KK, Zhang Y, Lim KL et al. (2001) Parkin ubiquitinates the alpha-synuclein-interacting protein, synphilin-1: implications for Lewy-body formation in Parkinson disease.

4. Hughes AJ, Daniel SE, Ben-Shlomo Y et al. (2002) The accuracy of diagnosis of parkinsonian syndromes in a specialist movement disorder service.

5. Poewe W, Scherfler C (2003) Role of dopamine transporter imaging in investigation of parkinsonian syndromes in routine clinical practice.

6. Betarbet R, Sherer TB, Greenamyre JT (2005) Ubiquitin-proteasome system and Parkinson's diseases.

7. Braak H, Bohl JR, Mu¨ller CM et al. (2006) Stanley Fahn Lecture 2005: The staging procedure for the inclusion body pathology associated with sporadic Parkinson's disease reconsidered.

8. Dick FD (2006) Parkinson's disease and pesticide exposures.

9. Schneider SA, Edwards MJ, Mir P et al. (2007) Patients with adult-onset dystonic tremor resembling parkinsonian tremor have scans without evidence of dopaminergic deficit (SWEDDs).

10. C. A. Davie. A review of Parkinson's disease. April 8, 2008

11. Divya M Radhadakrishnan, Vinay goyal. Parkinsonism disease: A Review. 2018