A REVIEW ON “DIAGNOSIS AND TREATMENT OF PARKINSON’S DISEASE”

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ABSTRACT
Parkinson’s disease or Parkinson's sickness (PD) is a degenerative neurological disease. Parkinson’s disease or Parkinson's sickness (PD) is unending, dynamic, neurodegenerative turmoil with an expected predominance of 31 to 328 for every 100,000 individuals around the world. There is no accord with respect to the components and characterization of agony in PD. This paper surveys current information on the conceivable components, characterizations, assessment and potential danger variables for torment in Parkinson’s disease. L-dopa is the backbone of pharmacological treatment for Parkinson’s disease PD; be that as it may, its utilization is constrained by the advancement of engine variances and medication affected dyskinesias. Dopamine agonists (DAs) are additionally utilized, either alone or in mix with L-dopa. The conclusion is for the most part made clinically, despite the fact that up to 25 % of patients with clinical judgments of PD have gotten diverse neurotic findings at dissection.

KEYWORDS
Parkinson’s disease, Classification and Catechol O-methyl transferase (COMT) inhibitors.

INTRODUCTION
Parkinson’s disease or Parkinson's sickness (PD) is a typical neurodegenerative issue. It is also known as idiopathic Parkinsonism, and essential Parkinsonism, hypokinetic inflexible disorder i.e. HRS or Paralysis agitans. Parkinson’s disease (PD) is a perpetual, dynamic neurodegenerative infection described by loss of nigrostriatal dopaminergic pathways. It is a case of degenerative issue of the focal sensory system. It influences the engine arrangement of cerebrum1. Parkinson's infection has
been known following scriptural times, however it was just in the nineteenth century that the disorder was formally depicted by James Parkinson and termed 'the shaking paralysis'. This ailment gives engine side effects. It gives passing of dopamine creating cells in the substantianigra. Substantianigra is found in the area of the mid mind. Its pervasiveness in the all-inclusive community is 0.1 to 0.3%\(^2\), demonstrating an expansion in people matured 65 years. With a maturing populace, the administration of PD is liable to demonstrate an inexorably essential and testing part of medicinal practice for neurologists and general doctors\(^3\). The finding of PD remains basically a clinical one, and it is critical to perceive the early components together with side effects and signs recommending different reasons for Parkinsonism\(^4,5\). In 1879, Charcot noticed extra components including autonomic brokenness. The relationship between the substantianigra and Parkinson's illness was found in 1893, however it was just in the last 50% of the twentieth century that the neuropathological and neurochemical qualities of the malady were explained\(^6\). There has additionally been a fast development in the treatment alternatives both in the early and in the later phases of the ailment together with a more noteworthy attention to non-engine confusions\(^7\). Notwithstanding engine aggravations, non-engine signs and indications are likewise basic in these patients. These indications are delegated autonomic, i.e., hyperhidrosis, orthostatic hypotension, sexual-urinary brokenness, thermoregulation changes, cardiovascular unsettling influences, fringe edema, enlarged pupilae), rest aggravations, neuropsychiatric issues, i.e., disregard, weakness, anhedonia, dejection, tension, alarm assaults, dementia, psychosis, and tangible, i.e., inward tremor, eager leg disorder, deadness, par aesthesia, visual aggravations, and torment\(^8,9\). Cardinal discoveries in PD are tremor, unbending nature, gradualness of development and trouble in waking and walk\(^10\). This ailment can be grouped into two sorts like Primary Parkinson maladies and auxiliary Parkinson illnesses. Essential Parkinson's sickness is otherwise called idiopathic ailment. Treatment of this illness contains L-DOPA and dopamine agonist\(^18\). By surgery and profound mind incitement has been declines or decreases engine side effects. This infection is names after the English specialist i.e. James Parkinson in 1817.

**CLASSIFICATION AND TYPES OF PAIN IN PARKINSON’S DISEASE (PD)**

Parkinson disease is used for a motor syndrome. It can be divided into four sub type, according to their origin.

- Primary or idiopathic
- Secondary or acquired
- Hereditary Parkinson’s
- Parkinson’s plus syndrome

Classification of pain can be described by the scientist Snider et al. his Classification generally follows distinguished two main groups of sensory and pain symptoms like Primary (i.e. originating in the nervous system) and Secondary (other sources...
than the nervous system, e.g., the musculoskeletal\textsuperscript{19,20}.

Another researcher like Ford and Goetz et al. additionally gives order of torment which emerges in Parkinson sickness. It recognizes the accompanying classes\textsuperscript{21}.
1. Musculoskeletal pain
2. Radicular/Neuropathic pain
3. Dystonia-related pain
4. Akathitic discomfort/pain
5. Central parkinsonian pain

**Musculoskeletal pain**\textsuperscript{22-24}

Musculoskeletal pain or Muscle issues or snugness in patients with PD can influence any part of the body however it seems all the more commonly in the neck, arm, standard spinal or calf muscles; while joint torment happens most oftentimes in shoulder, hip, knee, and lower leg. Musculoskeletal torment covers torment emerging from solid, joint and postural etiologies, including muscle spasms. The commonness of musculoskeletal torment ranges from 45% to 74% in those patients with PD encountering torment. This pervasiveness rate is much higher than that reported in the all-inclusive community (8% to 25%).

**Radicular-neuropathic pain**\textsuperscript{25,26}

Radicular-neuropathic torment or pain shows itself with agony, deadness or shortcoming in the region of a nerve root as an outcome of nerve or root pressure. The commonness of radicular-neuropathic torment or pain in patients with PD encountering torment ranges from 5% to 20%.

**Dystonic pain or Dystonic torment**\textsuperscript{27-29}

They can be seen in the furthest points, the face and the pharyngeal muscles and are considered among the most agonizing side effects that a patient with PD may encounter. Dystonic agony or pain is spoken to by Dystonic fits which are normally paroxysmal, unconstrained, or activated by development or action. The pervasiveness of dystonia-related torment ranges from 8% to 47% in patients with PD encountering torment. Interestingly, this torment is not present in solid individuals. In the days of yore with high dosage Levodopa patients had dystonia too.

**Central pain or Focal torment**\textsuperscript{30,31}

Focal torment can happen in various zones of the body including: the mouth, rectum, vagina, guts, mid-section and testes. The pervasiveness of focal agony in patients with PD is 10% to 12%. Focal torment can be chiefly altered by dopaminergic medicine. It is by all accounts identified with an anomalous capacity of the average spinoreticulothalamic pathways.

**Akathitic discomfort (akathisia)**\textsuperscript{32,33}

Fretful leg disorder (RLS) is another wellspring of torment in patients with PD. The term akathitic uneasiness (akathisia) is utilized to portray subjective eagerness or the difficult motivation to move consistently. It is characterized as a tactile engine unsettling influence that is unmistakable during the evening and enhances with development. It appears to be clear that this agony enhances with Levodopa treatment.

### FACTORS POTENTIALLY AFFECTING PAIN IN PARKINSON’S DISEASE (PD)

The agony in PD is normally reliant of engine issues like inflexibility, tremor, akinesia, or postural irregularities. In this audit article, there are the some conceivable elements affecting the nearness of agony in PD.

**Age**\textsuperscript{34,35}

Age is major impacting conceivable variables. In the event that we consider the mean age of this patient populace, an expansion in the predominance of musculoskeletal torment with joint issues and degenerative changes somewhere else in the body would appear not out of the ordinary. Another researcher like Goetz et al. gives hypothesis about agony in age. In the study by Goetz et al. patients with agony were more youthful than those without torment. Another researcher like Defazio et al. reported that dystonia-related agony was seen at before ages. Another researcher like Nègre-Pagès et al. additionally watched that PD-related agony was seen at a before age than torment random to PD. Note that age has not methodically been considered in all studies and the relationship between the various types of agony with age has not been examined.
Gender or Sex\textsuperscript{35,36}
Sex is additionally major impacting conceivable components. Current intuition tends to support the nonattendance of sexual orientation contrasts in connection to the nearness or nonappearance of torment; be that as it may, another researcher like Beiske \textit{et al.} reported that female sexual orientation was a huge indicator of agony in PD than male. Another researcher like Scott \textit{et al.} additionally watched that male and female patients don't gripe of agony in the same areas, since ladies reported higher commonness of neck and low back torment than men. Another researcher like Vela \textit{et al.} additionally discovered lower weight torment limits in ladies. He gives the recommendation that mechanical affectability is higher in ladies.

Severity and duration or malady of the disease\textsuperscript{37-39}
The impact of seriousness and term of malady on agony is dubious. Another researcher like Nègre-Pagès \textit{et al.} watched a relationship between's PD-related agony and the seriousness and span of ailment. Additionally, a more drawn out length of infection and more noteworthy engine difficulties in patients with PD with torment has been accounted for when contrasted with agony free patients.

Depression or Sadness\textsuperscript{39,40}
Torment is a danger element in the advancement of wretchedness in the elderly and the more established age and complexities of PD patients, a connection amongst melancholy and torment appears to be likely. Side effects of sadness can be seen in PD patients, extending in force from gentle to extreme. Sorrow has been by and large assessed in investigations of torment. Another researcher like Goetz \textit{et al.} reported that torment force related with despondency, and that the last is more extreme in patients encountering torment than in those without torment. Another researcher like Stark stein \textit{et al.} was watched that torment was more successive in patients with significant gloom when contrasted with those with milder sadness. Essentially, a connection amongst torment and sadness in PD has been accounted for by another researcher like Ehrt \textit{et al.} what's more; McNamara \textit{et al.} Current confirmation proposes that gloom is a parameter to be considered in investigations of torment in patients with PD, considering the recurrence of wretchedness in PD.

Systemic disease and pre-existing disturbances\textsuperscript{41,42}
Patients with previous torment identified with systemic sicknesses, for example, diabetes, osteoporosis, rheumatic ailment, and age-subordinate, e.g., joint or circle infection or postural issues, will keep on experiencing these after judgments. Notwithstanding, new ailment related side effects, for example, unbending nature, akinesia, strong spasms, and postural flimsiness can compound these troubles. Another researcher like Beiske \textit{et al.} reported that a few patients whined of agony before the finding of PD. The outcomes reported by another researcher like Defazio \textit{et al.} demonstrated that joint torment and fringe neuropathic torment is found in controls coordinated for age with PD patients. These studies bolster the hypothesis that some torment found in patients with PD is identified with age as opposed to the ailment itself. A few studies had for the most part assessed the nearness of torment in a cross-sectional outline, without demonstrating if the grumblings began before or after the analysis of PD. The agony experienced by the patients preceding PD determination could be one explanation behind the disputable character of the discoveries with respect to the occurrence of torment in PD.

Pathology, aetiology and pathogenesis
The disorder of Parkinsonism (clinical conditions which take after idiopathic Parkinson's ailment) may have various diverse causes like arteriosclerosis; diffuse focal sensory system degenerative malady, rehashed head injury, tumor, and metabolic abandons, for example, Wilson's sickness, overwhelming metal, or carbon monoxide harming\textsuperscript{43}. The obsessive sign of PD is cell misfortune inside the substantianigra. When of death, this area of the cerebrum has lost 50–70\% of its neurons contrasted and the same locale in PD unaffected people. Loss of pigmented cells in the substantianigra is the most steady completion in Parkinson's ailment and regularly the amount of nigral cells decreases from 425 000 to 200 000 at 80
Drug-actuated Parkinsonism results from dopamine receptor obstruct by medications like Phenothiazines, Butyrophenones, and Metoclopramide. Age is the absolute most reliable danger element and it has been assessed that there is a total lifetime danger of one in 40 for building up Parkinson's malady. A plague of encephalitis lethargica in the 1920s was in charge of an episode of early onset Parkinsonism with related extreme unbending nature and respiratory entanglements. Despite the fact that the etiology of Parkinson's illness is obscure, it has for some time been guessed that neuro degeneration is affected by hereditary, ecological, or irresistible clutters. In Parkinson's ailment, the substantianigra demonstrates checked consumption of cells (<100 000) with substitution gliosis. The most punctual archived neurotic changes in PD have been seen in the medulla oblongata/pontinegmentum and olfactory globule. The recognizable proof of single quality imperfections in PD has centered enthusiasm on the Ubiquitin-Proteasome System (UPS) as one potential applicant in the improvement of cell demise. The UPS is imperative for intracellular proteolysis and countless procedures that keep up the feasibility of cells. In Parkinson's sickness, cell misfortune is dominately from the ventrolateral level of the substantianigra, however this locale is moderately saved in ordinary subjects. By and large, most instances of Parkinson's sickness are prone to come about because of a mix of hereditary and natural variables and these contrast between people. In the wake of maturing, a family history is the most grounded indicator of an expanded danger of building up the malady, in spite of the fact that the part of a typical situation should likewise be considered. It gives off an impression of being a noteworthy segment of Lewy bodies, the trademark intra cytoplasmic eosinophilia consideration bodies, and its event in Parkinson's infection recommends that this malady additionally has a place with those conditions, for example, Alzheimer's, inferable from dangerous protein conglomeration. Parkinson's illness was first depicted amid the modern upset proposing that natural poisons may assume a part in its pathogenesis. A rustic domain has been connected with an expanded danger of building up Parkinson's ailment, recommending that operators, for example, herbicides or pesticides may have an aetiological part, in spite of the fact that this is restricted to roughly 10% of patients with Parkinson's illness. Cigarette smoking has been demonstrated reliably to diminish the danger of building up Parkinson's infection. This impact has been credited to hindrance of monoamine oxidase sort B by results of tobacco ignition. Parkinson's ailment can influence the development, creating engine indications. It additionally gives some non-engine indications like autonomic brokenness neuro psychiatric issue i.e. conduct, thought modification, tangible and rest issue are most regular side effects. Engine indications like tremor, unbending nature, gradualness of development and postural precariousness. Tremor is surely understood manifestations. Hypokinesia is otherwise called gradualness of development. Unbending nature implies firmness and imperviousness to appendage development. It cause by expansions the muscles tone by over the top and persistent constriction of muscles. Postural precariousness can be seen finally phase of the sickness. Postural precariousness implies weakened equalization, optionally to bone cracks and continuous falls. Up to 40% patient may encounter falls and 10% may have falls week by week. Parkinson's ailment can likewise bring about neuro psychiatric aggravations like changes in discernment, conduct, thought and disposition. Psychological unsettling influences can see in the underlying phase of this malady. Changes in inclination and conduct modification are basic in Parkinson's malady. Another manifestation of this medication is dejection, disregard and nervousness, entirely discourse, diminishes the discourse, diminishes the outward appearance. Psychiatric side effects of this ailment are mind flight, fancies. Parkinson's ailment in a large portion of the patient is idiopathic i.e. no particular known cause. Hereditary variable is additionally primary driver of Parkinson's sickness. Different quantities of
ecological elements are in charge of Parkinson's infection. Ecological variables like pesticide introduction, bug spray, herbicides, presentation of substantial metals, head wounds, cultivating and living in nations. Overwhelming metals are gathering in the substantia nigra in mind.

Treatment of Parkinson's disease Drug therapy

The Parkinson's disease of treatment is medication treatment utilizing L-DOPA or dopamine receptor agonists. The point of treatment of Parkinson's sickness is to empower the patient to seek after an ordinary dynamic way of life. With direction, patients can more often than not adjust a regimen to suit their specific way of life. The outcome might be that they take drugs at obviously particular times.

ANTI PARKINSON’S DRUG CLASSIFICATION

Anti-Parkinson’s drug can be divided into many types like

1. Levodopa
2. Dopamine agonists

For example;

- Bromocriptine
- Pergolide
- Pramipexole
- Ropinirole
- Piribedil
- Cabergoline
- Apomorphine
- Lisuride

3. MAO-B inhibitors

For example;

- Selegiline
- Rasagiline

4. Alternative therapies like Catechol-O-methyltransferase (COMT) inhibitors:

For example;

- Tolcapone and Entacapone

Levodopa treatment

For a long time, Levodopa consolidated with a fringe decarboxylase inhibitor. L-DOPA is otherwise called L-3, 4-dihydroxyphenylalanine. It has been viewed as the highest quality level for the treatment of PD. This L-DOPA is a synthetic and it is utilized as a major aspect of the ordinary science of human. Be that as it may, the advantages accomplished frequently include some significant pitfalls. Long haul Levodopa treatment every now and again prompts handicapping reactions. L-DOPA is forerunner of neurotransmitter dopamine, norepinephrine and epinephrine i.e. adrenaline. Levodopa-incited dyskinesias create at a normal rate of 10% for each annum in the wake of starting Levodopa. They are otherwise called catecholamine. Levodopa has a short half-existence of 60–90 min. L-DOPA was blended and sold as psychoactive medication. It is utilized and sold as a part of the business sector as exchange name like Sine met, Parcopa, Atamet, Stalevo, Madopar and Prolopa. A dubious issue has been whether levodopa could have a neurotoxic impact. The objective of the study was to find out whether levodopa treatment influenced the rate of sickness movement. This medication is utilized as a part of the treatment of Parkinson's infections. This medication is likewise utilized as a part of the treatment of dopamine responsive dystonia. Levodopa is utilized generally and successfully utilized for treatment of Parkinson's infections for more than 30 years. This medication was changed over into dopamine in the dopaminergic neurons by dopa decarboxylase catalyst. An engine side effect was delivered by an absence of dopamine in the substantianigra of Central sensory system. After organization of L-DOPA, an engine side effect was lessened. Around 5-10% medication of L-DOPA can cross the blood mind hindrance i.e. BBB and afterward it changed over into dopamine. Around 90% medication was metabolized into dopamine.

Dopamine agonist treatment

The example of orally acting dopamine agonists in UK is 6 which is available in the UK. There are four ergot derivatives like Bromocriptine, Pergolide, Cabergoline and Lisuride; and two non-ergot drugs: Ropinirole and Pramipexole. These drugs all work by stimulation of the post-synaptic dopamine receptors. Bromocriptine was discovered in the 1980s. The side effect of the dopamine agonists like Bromocriptine, Pergolide, Cabergoline and Lisuride...
is similar to Levodopa, but confusion and hallucinations are more frequent than with Levodopa therapy alone. Cabergoline is an ergot derivative with a high affinity for the D$_2$ and D$_3$ receptors.

**Monoamine oxide inhibitors (MAO-B inhibitors)**

Selegilinedrug is used in the treatment of early stage of Parkinson’s disease, depression and dementia. This drug is an example of selective irreversible MAO-B inhibitor. It also inhibits the MAO-A inhibitors. Selegiline drug was discovered in Hungary by the scientist Jozsef Knoll in 1960. The type B monoamine oxidase inhibitor, Selegiline drug is also used to treat Parkinson’s disease and it prolongs the action of dopamine in the striatum. Selegiline drug improves the symptoms of Parkinson’s disease but in addition there was a suggestion in the Deprenyl and Tocopherol. Selegiline is available in the form of brand name like Anipryl, L-deprenyl, Eldepryl, Emsam and Zelapar. MAO-B inhibitors do have a potential role as first-line monotherapy in PD patients. Selegiline drug is an example of substituted phenethylamine class. Selegiline drug acts as inhibitor of MAO-A and MAO-B. These enzymes are essential for metabolism of dopamine and phenyl ethylamine.

**Uses of Selegiline**

- This drug is used in the treatment of Parkinson’s diseases. This drug is used in combination with other drug like L-DOPA.
- This drug is used in the treatment of Cushing syndrome and cognitive dysfunction in dogs.
- This drug is also used to treat ADHD.
- This drug was approved by Food and Drug Administration for the treatment of major depression.
- This drug is also acts as veterinary drug.

Rasagiline is an example of irreversible inhibitor of the monoamine oxidase. Rasagiline drug is used in the treatment of Parkinson’s diseases. Rasagiline drug acts as selective drug for MAO-B and MAO-A enzymes. Rasagiline drug is available in the form of Azilect as brand name. In human body, cell contains two type of enzyme mono amine oxidase like MAO-A and MAO-B. These are found in the brain. MAO-B is essential and responsible for the breakdown of dopamine after its reuptake. A decrease the level of dopamine level gives decreases the synaptic signal strength. Rasagiline drug inhibits the MAO enzyme. Rasagiline drug inhibits the reuptake of the neurotransmitter dopamine and norepinepherine. Rasagiline drug was discovered by Teva Pharmaceutical Company. Rasagiline drug was used in the treatment of Parkinson’s diseases in Europe.

**Uses:**

- This drug is used in the treatment of Parkinson’s diseases. This drug is used in combination with other drug like L-DOPA.
- This drug is used in the treatment of Restless Legs syndrome.

**Alternative the rapieslike Catechol-O-methyltransferase (COMT) inhibitors**

Within 5 yr of starting therapy for Parkinson’s disease, half to two-thirds of patients will experience in their motor symptoms. With continued therapy, it becomes more dependent on the plasma concentration of Levodopa. This may be achieved by changing the dosing regimen or using a controlled release preparation of L-DOPA. Alternatively, a combination of L-DOPA and a dopamine agonist may be used. Another approach is to use catechol-O-methyl transferase (COMT) inhibitors, which inhibit the breakdown of dopamine in the periphery and increase its bioavailability. The COMT inhibitors in common clinical use are Tolcapone and Entacapone. Tolcapone drug gives side effect like hepatotoxicity, so Entacapone is the preferred drug.

**CONCLUSION**

PD is a common neurodegenerative illness. Pain in PD is likely related to pathologic changes in the anatomical structures involved in nociceptive pain mechanisms. A large number of agents joined with surgical interventions are now available to treat early and late complications of PD. Increasing attention is being given to the diagnosis and treatment of non-motor complications in PD. Pain, one of the most frequent non-motor symptoms
affecting PD patients has complicated mechanisms and is influenced by several factors, e.g., age, gender, depression, severity, or duration of the disease. Future developments in PD are likely to focus on the concept of disease modifying drugs which offer neuro protection. There is a need for multicenter research with a large number of patients and controls, in which patient should be evaluated in different dimensions for measurable endpoints to acquire definitive data and open new directions for treatment.

ACKNOWLEDGMENT
The authors are thankful to Dr. V. D. Wagh, College of Pharmacy, Chincholi and Mr. Kiran Kotade for providing necessary facilities and to carry out this work.

CONFLICT OF INTEREST
We declare that we have no conflict of interest.

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