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Parkinson's Disease and its Management

(PD)

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I have submitted this report to finish activities requirement of 2nd year BMS

Abstract:

Parkinson's disease (PD) is a chronic progressive neurodegenerative movement disorder characterized by a profound and selective loss of nigrostriatal dopaminergic neurons. Clinical manifestations of this complex disease include motor impairments involving resting tremor, bradykinesia, postural instability, gait difficulty and rigidity. Current medications only provide symptomatic relief and fail to halt the death of dopaminergic neurons. A major hurdle in development of neuroprotective therapies are due to limited understanding of disease processes leading to death of dopaminergic neurons. Recent findings implicate mitochondrial dysfunction, oxidative damage, abnormal protein accumulation and protein phosphorylation as key molecular mechanisms compromising dopamine neuronal function and survival as the underlying cause of pathogenesis in both sporadic and familial PD. In this report provided overview of the most relevant findings the last year and discuss how these significant findings improved our understanding of how Parkinson's is being currently managed and there is debate about whether the initial treatment for patients with Parkinson's disease should be levodopa or a dopamine agonist.

Introduction:

Parkinson's disease (PD) was 1st described by Dr. James Parkinson in 1817 as a "shaking palsy." It is a chronic, progressive neurodegenerative disease characterized by both motor and non-motor features. The disease has a significant clinical effect on patients and families through its progressive degenerative effects on mobility and muscle control. The motor symptoms of PD are attributed to the loss of striatal dopaminergic neurons, although the presence of non-motor symptoms supports neuronal loss in no dopaminergic areas as well. The term Parkinsonism is a symptom complex used to describe the motor features of PD, which include resting tremor, bradykinesia, and muscular rigidity. PD is the most common cause of Parkinsonism, although a number of secondary causes also exist, including diseases that mimic PD and drug-induced causes. (1)(2)

Discussion:

PD is one of the most common neurodegenerative disorders. The Parkinson's Disease Foundation reported that approximately 1 million Americans currently have the disease The incidence of PD in the U.S. is approximately 20 cases per 100,000 people per year (60,000 per year), with the mean age of onset close to 60 years. The prevalence of PD is reported to be approximately 1% in people 60 years of age and older and increases to 1% to 3% in the 80-plus age group. Although it is primarily a disease of the elderly, individuals have developed PD in their 30s and 40s. Gender differences appearing to the incidence of PD are reflected in a 3:2 ratio of males to females, with a delayed onset in females credited to the neuroprotective effects of estrogen on the nigrostriatal dopaminergic system. (3)

PD is a disorder of the extrapyramidal system, and is characterized by the loss of dopaminergic function and consequent diminished motor function, leading to clinical

features of the disease. Research in the late 1950s identified striatal dopamine depletion as the major cause of the motor symptoms of PD, although the presence of non-motor features supports the involvement of other neurotransmitters of the glutamatergic, cholinergic, serotonergic, and adrenergic systems, in addition to the neuromodulators adenosine and encephalin. The involvement of inflammation in the pathogenesis of PD 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. (4) (5)

Management:

The primary goal in the management of PD to treat the symptomatic motor and non-motor features of the disorder, with the objective of improving the patient's overall quality of life. Comprehensive review of PD therapy is beyond, but a few basic thoughts must be set forth. Non-motor symptoms should be treated accordingly, although evidence to support most treatment decisions is scarce; Zesiewicz et al. considered Dementia symptoms are improved by cholinesterase inhibitors or memantine. An array of drugs is used to treat motor symptoms in PD (availability varies from country to country): levodopa plus peripheral dopa decarboxylase inhibitor (carbidopa or benserazide), dopamine agonists (bromocriptine, ropinirole,), monoamine oxidase B inhibitors (selegiline, rasagiline), catechol-O-methyltransferase inhibitors (entacapone, tolcapone), anticholinergics (trihexyphenidyl, benztropine), and amantadine. Currently, there is no consensus on the most adequate timing and drug of choice for therapy initiation in PD, Edwards et al. and Lang et al. agreed dopaminergic therapy is usually deferred until deteriorating quality of life demands treatment, owing to the future potential motor complications brought about by these drugs, such as peak-dose dyskinesias, wearing off, and sudden off states Levodopa seems to pose higher risks in this regard as compared with dopamine agonists, although recent data brought conflicting views on this matter Nevertheless, Katzenschlager et al.; Holloway et al. showed levodopa is the most effective drug in the control of motor symptoms, and PD patients typically show marked and sustained benefits from it for several years which Schapira et al. concluded. Antonini et al explained how Dopamine agonists may cause peripheral edema, fibrotic reactions, excessive daytime somnolence, and impulse control disorders In advanced PD, functional neurosurgery is a valuable therapeutic option, provided that patients are carefully selected. Deuschl et al. ; Follett et al. ; Moro et al. agreed Deep brain stimulation of either the subthalamic nucleus or internal globus pallidus is an effective and generally safe procedure . Weaver et al.; Williams et al. agreed advanced PD it may be more effective for the control of motor symptoms than the best medical therapy, either alone or in combination with it. (6)

Methods

In this prospective, randomized, double-blind study, we compared the safety and efficacy of the dopamine D2–receptor agonist ropinirole with that of levodopa over a period of five years in 268 patients (were enrolled at 30 centers in Europe, Israel, and Canada) with early Parkinson's disease. If symptoms were not adequately controlled by the assigned study medication, patients could receive supplementary levodopa, administered in an open-label fashion. The primary outcome measure was the occurrence of dyskinesia. (7)

Results

85 of the 179 patients in the ropinirole group (47 percent) and 45 of the 89 patients in the levodopa group (51 percent) completed all five years of the study. In the ropinirole group, 29 of the 85 patients (34 percent) received no levodopa supplementation(without open-label levodopa supplementation). At five years, the cumulative incidence of dyskinesia (excluding the three patients who had dyskinesia at base line), regardless of levodopa supplementation, was 20 percent (36 of 177 patients) in the ropinirole group and 45 percent (40 of 88 patients) in the levodopa group. Adverse events led to the early withdrawal from the study of 48 of 179 patients in the ropinirole group (27 percent) and 29 of 89 patients in the levodopa group (33 percent). the length of time until dyskinesia developed in 25 percent of the patients remaining in the study was 214 weeks among the patients in the ropinirole group and 104 weeks among the patients in the levodopa group. The risk of disabling dyskinesia was significantly lower in the ropinirole group then levodopa group. (7)

Conclusion:

1) PD is a chronic, progressive neurodegenerative disease characterized by both motor and non-motor features. Striatal dopamine depletion has been identified as the major cause of the disorder's motor symptoms, which include resting tremor, "cogwheel" rigidity, and bradykinesia. Non-motor symptoms include sleep disorders, depression, and cognitive changes.

2) The differential diagnosis of PD should include a comprehensive history and physical examination. Identifying diseases that have presentations similar to that of PD is an important component of the diagnostic process. There are no definitive tests to confirm a diagnosis of PD. The UPDRS is the most commonly used scale for assessing the clinical status of PD patients.

3) The primary goal in the management of PD is to treat the symptomatic motor and non-motor features of the disorder, with the objective of improving the patient's overall quality of life. Therapies that slow the progression of the disease or provide a neuroprotective effect have not been identified.

4) Early Parkinson's disease can be managed successfully for up to five years with a reduced risk of dyskinesia by initiating treatment with ropinirole alone and supplementing it with levodopa if necessary.

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