DOPAMINE AGONISTS ARE THE TREATMENT OF CHOICE IN EARLY PD

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There is debate relating to the treatment of early Parkinson's disease patients. Practicing clinicians have found it difficult to interpret clinical trials comparing the use of levodopa therapy with dopamine agonists. It is unclear what the clinical significance of some of the outcome measures are and how to balance side effects with efficacy.

This presentation will focus on the rationale of the different treatment options, evidence from clinical trials and incorporate the clinical experience in a large Parkinson's disease practice to aid the clinician in dealing with this controversy.

Treatment of early Parkinson's disease needs to be individualized. Many patients may not need pharmacological intervention if their symptoms do not affect quality of life. We use a multi-disciplinary team approach to support the patient and his or her family. This support is important at the time of diagnosis as well as when drug treatment is initiated.

We encourage patients to exercise and have developed a self-management program to train patients how to perform Parkinson-specific daily exercises to help them throughout the course of the disease. Social work intervention to look at psychosocial issues, help link the patient to services and help them accommodate to the diagnosis of PD is helpful. Our nursing staff provides telephone assistance to answer questions and follow up on medication implementation and dose changes. We have shown that this team approach helps improve outcomes.

Levodopa therapy has been the mainstay of pharmacological treatment for decades. It is the most efficacious of the available treatment options but is associated with – problems as the disease evolves. Many patients have a positive response with minimal side effects after treatment initiation. The long duration response provides sustained benefit for days to weeks after dosing. As the condition evolves, this long duration response declines and problems with wearing off occur. The plasma half- life of levodopa is only 90 minutes and patients experience response fluctuations more closely related to the plasma half-life. In addition, many patients develop dyskinesias in different patterns. It is unclear what the mechanism of these response fluctuations is, but it is clear that initial treatment with levodopa therapy is associated with a higher prevalence of these problems.

Dopamine agonist therapy was initially developed to treat response fluctuations. The plasma half-life of these agents is much longer than levodopa and ranges between 4-8 hours. Studies in experimental animal models of Parkinson's disease have suggested that pulsatile stimulation of dopamine receptors may be responsible for the development of response fluctuations. Levodopa therapy is pulsatile whereas dopamine agonist therapy provides more continuous stimulation of dopamine receptors.

These animal studies provided the rationale for prospective clinical trials comparing levodopa to dopamine agonist therapy when early Parkinson's disease patients require treatment. The studies identified that treatment with dopamine agonists were associated with a lower frequency of dyskinesias and wearing off. It has been controversial if these differences were clinically significant. However, the efficacy of dopamine agonist treatment was less than levodopa therapy. A number of side effects-- including sudden onset of sleep, peripheral edema and more recently impulse control problems-- have been associated with dopamine agonist therapy.