Original Article

DOPA-sparing strategy in the treatment of young onset Parkinson's disease

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ABSTRACT

Context: Late onset Parkinson's disease (LOPD) is a neurodegenerative disorder afflicting individuals of ages 60 and older. However, 5–10% of cases can begin earlier between the ages 20 to 40, and are classified as young onset Parkinson disease (YOPD). **Aim:** In turn, this study aims to observe the trend in the choice of drug administered to patients with both YOPD and LOPD, with particular emphasis on this trend in its relation to the practice background of the neurologist. **Settings and Design:** A cross-sectional study was conducted in a community based Parkinson's disease and movement disorder clinic. **Statistical Analysis Used:** Using a retrospective chart review data was obtained and analysed. **Results:** The results showed that 83% of general neurologists prescribed levodopa to their patients with YOPD, whereas movement-disorder specialists took a different approach altogether. They opted not to use levodopa and, in its stead, prescribed a mixture of alternate drugs.

Key words: DOPA-sparing, general neurologist, late-onset Parkinson's disease, levodopa, movement disorder specialist, Parkinson's disease, young onset Parkinson's disease

Introduction

Parkinson's disease (PD) is a chronic neurodegenerative movement disorder primarily characterized by bradykinesia, resting tremor, and rigidity. Although PD is commonly diagnosed in the elderly population (>55 years of age), it is also rarely (~5%) detected in much younger populations (21–45 years of age).[1] While the former occurrence is referred to as late-onset PD (LOPD), the latter is called young onset PD (YOPD).

In the treatment of PD, levodopa is used as the gold standard, primarily administered in the late stages of the disease or when minimal risks of motor fluctuations are present.[2] In essence, levodopa is the purified form of L-DOPA which is a precursor of catecholamines. Since the catecholamines influence, a plethora of behaviors and effects, treatment with levodopa comes with many side effects including motor fluctuations and dyskinesia.[3] As a result, many physicians choose to follow a DOPA-sparing strategy in treating PD patients. The principles are simple: Avoid levodopa for as long as is practicable and limit its use whenever necessary.[4]

This notion gains its strength, in particular, from YOPD patients who present with a mild motor dysfunction; since, young patients are particularly sensitive to levodopa-induced motor fluctuations and dyskinesia.[5] However, most physicians still tend to administer levodopa due to the increased familiarity with the use of this drug in LOPD. Indeed, prescribing levodopa may be an intuitive response of many general practitioners after seeing a patient with PD, disregarding the age of the patient and the stage of

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the disease.[2] In many instances, by the time a YOPD patient has been referred to movement disorders specialist from a general practitioner, the patient had been taking levodopa and now faces irreversible dyskinesia and movement fluctuations.[2] This study seeks to investigate the prevalence of levodopa prescription among the diverse PD population. In particular, it seeks to assess the practice of DOPA sparing strategy among YOPD and LOPD individuals. Interestingly, our findings suggest that general neurologists mainly do not adhere to this practice while the majority of movement disorders specialist do. Greater efforts at raising awareness of this issue are direly needed.

Materials and Methods

A cross-sectional study was conducted, which consisted of a chart review of 26 idiopathic PD patients between 2011 and 2015 in a community-based PD and movement disorder clinic. Of these, 13 patients were found to have YOPD. By using a retrospective chart review, the choice of drug prescribed by the physician, the age of onset, stage of disease, and the presence or absence of tremor in patients was recorded. Additional data on the practice background of the prescribing physician (general neurologist vs. movement disorder specialist) was also documented. A similar methodology was also employed on 13 patients with LOPD. Efforts were made to control any confounding variables that may influence the study. As such, both groups consisted of seven females and six males, while also ensuring that all patients were at Stage II of the Hoehn and Yahr Scale.[6] The presence or absence of tremor was also taken into consideration, negating its role as a confounding variable. Furthermore, this study conforms to all rules and regulations lay out by the local research ethics board.

Results

The average age of onset in the young group was 37.7 ± 4.18 years and the mean age of diagnosis was 40.1 ± 3.64 years. The late-onset group had an average age of onset of 73.0 ± 6.83 years and 73.7 ± 6.36 years at the time of diagnosis. As patients were included in each group, efforts were made to maintain equal gender proportions (both groups had seven females and six males) to prevent any confounding bias. The average age of onset of females in the young onset group was negligibly higher than that of males (38.14 vs. 37.33 years; t(11) =0.334, P = 0.744). The average age of onset of females in the late-onset group was also slightly higher than that of males albeit nonsignificant (73.16 vs. 72.8 years; t(11) =0.068, P = 0.947). To account for PD progression, only patients at Stage II of Hoehn and Yahr scale were used in the study.[6] Finally, no trends were noted with respect to the presence or absence of tremor and the choice of medication chosen by the attending neurologist; r(24) =0.187, P = 0.359.

All LOPD patients received levodopa treatment by general neurologists as opposed to 83% of YOPD patients, who were given levodopa, initially. In contrast, patients with LOPD that were seen by movement disorder specialist were prescribed levodopa 88% of the time while YOPD patients were never prescribed levodopa. Instead, movement disorder specialists chose to prescribe drugs such as pramipexole and rasagiline to treat the Parkinsonian symptoms in these cases. In fact, a significant delineating correlation is seen for YOPD patients when comparing the type of physician with his choice of levodopa; Kendall's tau b(11) = −0.720, P = 0.013. However, the effect of this correlation disappears for LOPD patients; Kendall's tau b(11) = −0.228, P = 0.429. This suggests that movement disorders specialists constantly employ the DOPA sparing strategy for YOPD patients.

Discussion

In the treatment of LOPD, both general neurologists and movement disorder specialists prescribed levodopa. Nevertheless, neurologists still use levodopa as a first line of treatment in YOPD whereas movement disorder specialists prefer to treat PD patients with drugs other than levodopa due to their decreased risk of motor fluctuations.[2] This practice should also be employed by general neurologists and practitioners.

The use of levodopa should be delayed in YOPD patients who present with a mild motor dysfunction. This is because young patients are particularly sensitive to levodopa-induced motor fluctuations and dyskinesia.[5] It is the long-term pulsatile stimulation of dopaminergic neurons that is believed to play a role in the emergence of motor fluctuations exhibited by these patients.[5] Due to these reasons, levodopa may not be the first line of treatment in patients with YOPD, in particularly during the early stages of PD. However, most physicians still tend to administer levodopa due to the increased familiarity with the use of this drug in LOPD. Indeed, prescribing levodopa may be an automatic response of many general practitioners after seeing a patient with PD, disregarding the age of the patient and/or the stage of the disease.[2]

With the introduction of levodopa in YOPD, many young patients develop dyskinesias and movement fluctuations together, which may become so advanced that it cannot be rectified.[2] Knowing this, the movement disorder subspecialists usually prescribe alternative drugs to treat the milder symptoms of YOPD patients. These include dopamine agonists, such as pramipexole and ropinirole, or monoamine oxidase type B (MAO-B) inhibitors as rasagiline or selegiline.[7] Clinical trials with both ergot and nonergot dopamine receptor agonists, such as cabergoline, pergolide, pramipexole, and ropinirole, have shown a lower risk of motor fluctuations and dyskinesias when used as monotherapy for early PD patients.[7] Thus, the rationale for the use of these drugs is to delay or reduce the incidence of motor complications resulting from long-term levodopa therapy.

This study indicates a need in the health community to increase awareness among neurologists about the use of levodopa sparing strategy in young PD patients. Alternatively, it would be advisable for general neurologists to refer young patients with PD to movement disorder specialists to maximize treatment outcomes for patients albeit at the cost of increased wait times.[7] In addition, residents and newly trained physicians need to be conscious of these effects of levodopa early on in the course of their training.

Potentially confounding to our study, past research has shown that dopamine agonists such as pramipexole are known to have unwanted side effects such as impulsive gambling and hypersexuality.[8] Thus, general neurologists might have opted to use levodopa to prevent these undesirable outcomes, which may have further compromised the internal validity of the study. Furthermore, since levodopa is cheaper compared to dopamine agonists, affordability could potentially play a role in determining the choice of drug prescribed. However, this factor did not play a role in the patients included in this study; since, both of these drugs were covered by national health insurance at no cost to the patient.

A limitation of the study is the small sample size 13 patients per each group. However, this was due to the rare occurrence of YOPD and the necessity to maintain matched samples. Nevertheless, a strong correlation was noted between the practice background of the physician and the medication prescribed for the patients.

Conclusions

Treatment protocols for YOPD need to be re-evaluated, and more emphasis needs to be placed on individualized treatment. For instance, the therapeutic strategy for YOPD patients should include dopamine receptor agonist, MAO-B inhibitors, or amantadine, while concurrently maintaining an individually adjusted threshold of L-DOPA if more severe motor deficit is present.[9] Furthermore, interventions such as apomorphine, levodopa, or deep brain stimulation all come with their associated level of costs and complications.[10] The use of levodopa in young onset patients, in some cases, may be responsible for producing motor fluctuations and dyskinesias, which might be refractory to pharmacological treatment requiring apomorphine and deep brain stimulation.[10] Balancing this approach against the undoubted efficacy of levodopa in treating symptoms is a delicate issue that must be tailored to each patient. This is a prime example of the complications that may arise when applying the gold standard treatment to every case. Healthcare providers need to take into consideration the age of the patient and the stage of the disease and must consistently weigh the benefits and risks of other medications that are available.

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Conflicts of interest
There are no conflicts of interest.

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