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Largest-ever trial in Parkinson's disease shows that for long-term treatment levodopa is better than newer drugs

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For long-term treatment of newly diagnosed Parkinson's disease (PD), the old drug levodopa provides better mobility and a higher quality of life than the two main alternatives, dopamine agonists (DA) and monoamine oxidase type B inhibitors (MAOBI), according to the largest-ever trial of PD treatment (PD MED), published in *The Lancet*.

PD is the second most common neurodegenerative disorder (after Alzheimer's) in the UK, with 8000 new cases each year and over 100 000 people living with the disease. The most widely used treatment is the drug levodopa, although after prolonged use patients can develop involuntary muscle spasms (dyskinesias) and motor fluctuations (movement problems). There is less risk of developing these complications with DAs or with MAOBIs than with levodopa, but other side effects including nausea, hallucinations, oedema, and sleep disturbance are increased with these newer drugs.

"Previous studies included too few patients, had short follow-up, and focused on the clinicians' assessments of motor symptoms rather than asking patients how the drugs affected their overall quality of life. So, for many years there has been uncertainty about the risks and benefits of starting treatment with these different classes of PD drugs"*, explains study leader Professor Richard Gray from the University of Oxford in the UK.

The PD MED trial randomly assigned 1620 people with early PD to levodopa-sparing therapy (DA or MAOBI) or levodopa. With up to 7 years of follow-up, self-reported scores on scales measuring mobility and quality of life showed small but persistent benefits of starting treatment with levodopa rather than the other drugs. Patients in the levodopa group also reported significantly better scores on the activities of daily living, stigma, cognition, communication, and bodily discomfort scales than those taking levodopa-sparing therapy despite more involuntary muscle spasms.

According to Professor Gray, "Although the differences in favour of levodopa are small, when you consider the short- and long-term benefits, side-effects, quality of life for patients, and costs, the old drug levodopa is still the best initial treatment strategy for most patients."

He adds, "In current clinical practice, most patients younger than 70 years are treated initially with a DA to avoid levodopa-related motor complications. However, we found levodopa better than the more expensive DAs at all ages."*

Professor Carl Clarke, the clinical coordinator of the study from the University of Birmingham, UK, added, "The PD MED trial is the largest drug trial ever performed in Parkinson's disease. It is likely to change clinical practice worldwide, with the majority of patients from now on starting therapy with levodopa."

Writing in a linked Comment, Professor Anthony Lang and Dr Connie Marras from Toronto Western Hospital, Ontario, Canada say, "PD MED provides reassuring data showing that in most patients with Parkinson's disease, who have an older age of onset, how treatment is initiated generally does not matter because outcomes are very similar…Finally, and perhaps most importantly, the results of this study will help to persuade physicians and reassure patients that the fears that have served

as the groundwork in establishing levodopa phobia—that often results in patients experiencing unnecessary and easily managed disability and reduction in quality of life in the early years of their disease—are unfounded".

More information: Paper: www.thelancet.com/journals/lan … (14)60683-8/abstract

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