Parkinson's Patients More Likely to Stick With Certain 'Add-on' Drugs

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Of the three main types of oral drugs commonly added to levodopa therapy for patients with advanced Parkinson's disease, one might be the most effective, according to a new review.

People with Parkinson's disease often initially experience tremors, stiffness, slowed movement or difficulty with balance and coordination. These symptoms result from the destruction of brain cells that produce dopamine - an important chemical that transmits nerve impulses.

Many people with Parkinson's start treatment by taking levodopa, which the body converts to dopamine. After a time, however, levodopa alone is not always enough.

The three classes of drugs for add-on treatment are dopamine agonists, which stimulate dopamine receptors in the brain, drugs known as COMT inhibitors and MAOB inhibitors, which slow the breakdown of dopamine in the body.

Of these, dopamine agonists might be most effective, according to a new review.

The irony for patients and doctors alike is that while all of the add-on drugs help improve functional motor skills, they simultaneously might increase numerous other side effects such as dyskinesia, dizziness, sleep disturbances, nausea, constipation and even hallucinations.

Although the risk of side effects increased with all three types of add-on drugs, patients were most likely to continue treatment when they were taking dopamine agonists. This class includes medications such as pramipexole (Mirapex), ropinirole (Requip), cabergoline (Dostinex) and bromocriptine (Parlodel).

“There’s a tendency to think that stronger drugs give more adverse effects, but we didn’t find that with dopamine agonists,” says review co-author Carl E. Clarke, M.D., a neurologist at the University of Birmingham in England. “They seem to be as well tolerated as the other classes, so the results are quite positive in terms of using the agonists ahead of the other two.”

Parkinson’s disease is a chronic, progressive disorder affecting more than 6 million people worldwide, making it the most common degenerative condition of the brain after Alzheimer’s disease. Both illnesses are most common in the elderly, so with an aging U.S. population, their prevalence is likely to increase.

“No treatments have been proven to slow progression of the disease,” said William J. Weiner, M.D., director of the Maryland Parkinson’s Disease and Movement Disorders Center at the University of Maryland Medical Center. “Yet with treatment to alleviate motor symptoms, most patients can function extremely well for six to 10 years.”

Levodopa typically controls symptoms very well for up to five years, but eventually a patient’s symptoms start to reappear each day before the next dose is due - or symptoms might reappear and disappear unpredictably. Patients might also develop dyskinesia, which results in uncontrollable jerking and writhing movements.

Doctors can then add another medication to the levodopa therapy.

“The greater efficacy and reduced likelihood of patient withdrawal with dopamine agonist therapy possibly outweighs the disadvantage of increased side effects,” concludes the review.
This finding matches Weiner’s clinical experience gained from decades of treating people with the disease.

“Most [Parkinson’s] patients prefer to have these dyskinesias and other moderate side effects than to have more disabling motor complications like being unable to walk,” he says. “Hallucinations may be troublesome and frightening initially, but they are typically benign — a patient might think he sees a dog — and people can get used to them.”

The review appears in the current issue of The Cochrane Library, a publication of The Cochrane Collaboration, an international organization that evaluates research in all aspects of health care. Systematic reviews draw evidence-based conclusions about medical practice after considering both the content and quality of existing trials on a topic.

This review assessed data from 44 randomized trials involving 8,436 participants. The authors caution, however, that the studies compared each class of drugs against placebo, rather than conducting “head-to-head” comparisons of each class against the others.

This leaves open the possibility that the findings arose not from actual differences in the treatments, but rather from other factors such as differences in the types of people included in the various trials. A large trial featuring direct comparisons of the three drug classes currently is underway in the United Kingdom, Clarke said.

Of the drugs in the COMT inhibitor class, the review suggests that tolcapone (Tasmar) is as effective as the dopamine agonists. However, tolcapone has been linked to a few cases of fatal liver toxicity and can now only be prescribed in the United States with intense monitoring.

“Tolcapone is worth using in patients where [the alternative] is not working well, and we mustn’t discount it,” Clarke said. “This evidence clearly states that.”

The review disclosed that Clarke has received payments for consulting, lectures and travel from Boehringer-Ingelheim, GlaxoSmithKline, Lundbeck, Orion, Teva, UCB, and Valeant.

More information: Stowe R, et al. Evaluation of the efficacy and safety of adjuvant treatment to levodopa therapy in Parkinson´ s disease patients with motor complications (Review). Cochrane Database of Systematic Reviews 2010, Issue 7.

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