

Treatment Options

At this time no treatment has been shown to slow or stop the progression of this disease. Instead, therapy is directed at treating the symptoms that are most bothersome to an individual with Parkinson disease. For this reason, there is no standard or “best” treatment for Parkinson disease. Treatment approaches include medication and surgical therapy.

Medications for Parkinson disease

Because individuals with PD have a range of symptoms, the choice of medication (and the decision whether to treat with medication) varies considerably between individuals. Moreover, over time, the dose of medications may need to be increased or new medications added.

Commonly Prescribed Medications

Levodopa is modified by brain enzymes to produce dopamine. The introduction of levodopa (or L-dopa) treatment more than 30 years ago revolutionized treatment of Parkinson disease. For most individuals, it reduces the symptoms of slowness, stiffness and tremor and to date remains the most effective treatment for many of the symptoms of Parkinson disease. Since blood enzymes would break down most of the levodopa before it reached the brain, it is always combined with an enzyme inhibitor called carbidopa. After being absorbed in the gastrointestinal tract, levodopa is transported to the brain, where it is converted into dopamine. It is subsequently released by brain cells and activates dopamine receptors allowing for normal function of the movement control centers of the brain.

Levodopa is available as a standard (or immediate) release formulation or a long-acting or “controlled-release” formulation. Controlled release may provide a longer duration of action by increasing the time it takes for the gastrointestinal tract to absorb levodopa. Over the years, a number of substitutes for levodopa have been developed. Unlike levodopa, these medications do not have to be modified by brain enzymes in order to activate dopamine receptors. As a class, these medications are called dopamine agonists and may be used in place of levodopa or in combination with it. Although dopamine agonists appear to cause motor fluctuations less frequently than levodopa, dopamine agonists are more likely to cause other side effects than levodopa, so physicians must consider a number of factors in deciding which medication to recommend. The various dopamine agonists differ in several respects, including chemical structure, duration of action, and side effects. The response to a particular dopamine agonist varies considerably between individuals, so that if one dopamine agonist does not offer benefit or causes bothersome side effects, another agonist may be tried.

A number of other medications can be used alone or in combination with levodopa or a dopamine agonist to improve movement for people with PD. These medications do not stimulate dopamine receptors but alter the movement control center by other means. The most commonly used medications are amantadine, anticholinergic medications, and selegiline.

Amantadine was initially developed as an antiviral medication. By coincidence it was found to help the symptoms of Parkinson disease. It may be used alone or in combination with levodopa or dopamine agonists. Amantadine reduces symptoms of fatigue, tremor

and bradykinesia in some people with early Parkinson disease. For people with more advanced PD, amantadine may reduce motor fluctuations, in particular, dyskinesias. Anticholinergic medications are the oldest class of medications available for Parkinson disease. Anticholinergic medications may reduce tremor or rigidity. They can be taken alone or in combination with levodopa. These drugs are rarely used in elderly patients or those with cognitive problems, because increased confusion can be one of their side effects.

Selegiline is an inhibitor of the enzyme MAO-B (monoamine oxidase B). Since this enzyme breaks down dopamine, inhibiting it prolongs the action of dopamine in the brain, and may improve the symptoms of Parkinson disease. It also has a mild antidepressant effect. Although early studies of selegiline initially led physicians to believe that it may delay the progression of Parkinson disease, currently there is no firm evidence that this is so.

List of Commonly Prescribed Medications

(Generic Name and Product Name)

In this section, we provide the names of commercially available preparations and a brief account of some of the more common side effects. The list of side effects is not complete, and patients should consult their physician if these or other ill-effects develop while they are taking any of these medications.

Levodopa preparations:

Standard release preparations:

levodopa/carbidopa (Sinemet® or Atamet®)

Extended release preparations:

levodopa/carbiopa (Sinemet CR®)

levodopa/benserazide (Madopar HBS®)

Side effects include nausea, vomiting, dry mouth, ankle swelling, constipation, feeling tired, confusion, hallucinations and dizziness. Dyskinesias (abnormal movements) may occur as the dose is increased. Response fluctuations may occur after 2-3 years of use.

COMT inhibitors:

entacapone (Comtan®)--available in the United States and many other countries.

tolcapone* (Tasmar®)--available in the United States, but not Canada or Europe.

*Because of concerns for liver toxicity, tolcapone is only indicated for patients whose symptoms are not adequately controlled by other medications. People taking tolcapone must have blood drawn periodically to monitor the liver function.

Side effects include diarrhea and dyskinesias.

Dopamine agonists:

bromocriptine (Parlodel®)

pramipexole (Mirapex®)

ropinirole (Requip®)

apomorphine (Apokyn®)

rotigotine (Neupro®) a patch-- currently off the market in the US.

Side effects include drowsiness, nausea, vomiting, dry mouth, confusion, hallucinations, dizziness, and feeling faint upon standing. While these symptoms are common when starting a dopamine agonist, they typically resolve over several days. Sleepiness, drowsiness, or sedation may be a significant side effect of some dopamine agonists in some people, and may interfere with driving or other activities.

Amantadine

Amantadine (Symmetrel®)

Side effects may include difficulty in concentrating, confusion, blurry vision, light headedness, ankle swelling, insomnia, nightmares, agitation, and hallucinations.

Anticholinergic medications:

Benzotropine mesylate (Cogentin®)

Trihexyphenidyl (Artane®)

Side effects may include dry mouth, blurred vision, sedation, delirium, hallucination, constipation, and urinary retention. Confusion and hallucinations may also occur.

Monoamine oxidase inhibitors type B preparations. They inhibit MAO-type B which raises the levels of dopamine in the brain.

selegiline Eldepryl®

rasagiline Azilect®

Side effects may include heartburn, nausea, dry mouth, and dizziness. Confusion, nightmares, hallucinations, and headache occur less frequently and should be reported to your physician.

Protective treatments

Current symptomatic treatments (PD medications) can significantly impact on the management of the disease. They do not, however, prevent disease progression. There is great interest in the development of neuroprotective therapies to halt the disease or delay its onset. Cell loss in the substantia nigra is the cause of symptoms of PD. The reason that it occurs is unclear. The occurrence of certain chemical reactions involving oxidation results in the production of substances (such as so-called free radicals or reactive oxygen species) that may be harmful to cells and lead to their deaths. Such oxidative stress may thus be important with regard to the development of PD.

Neuroprotective treatments may be most helpful at an early stage of PD, and this stresses the need for finding a simple biological marker. This would enable treatment to be initiated at the preclinical or early clinical phase of the disease.

Selegiline is an inhibitor of the enzyme MAO-B (monoamine oxidase B). Since this enzyme breaks down dopamine, inhibiting it prolongs the action of dopamine in the brain, and may improve the symptoms of Parkinson disease. It also has a mild antidepressant effect. While one early study of selegiline initially led physicians to believe that it may delay the progression of Parkinson disease, currently there is no firm

evidence that this is so. That initial study has never been duplicated. There are only theoretical grounds to believe it may slow the disease.

Levodopa: there is controversy as to whether this medication is toxic to neuronal cells or protective. There is no evidence that it worsens or slows the progression of Parkinson disease.

Coenzyme Q-10: Cells need energy to survive and function. They contain mitochondria, which are "batteries" that produce energy. In Parkinson disease, there seems to be a disturbance in the function of these batteries. Coenzyme Q10 affects the energy-generating mechanisms in cells. A recent study suggested that treatment with 1200 mg/day of coenzyme Q10 resulted in less disability over the fixed period of the study than lower doses of the same compound or a placebo. A larger trial did not confirm these findings. Patients are not advised to start taking large doses of coenzyme Q-10 at this time without discussing it first with their physician.

Dopamine agonists have been shown experimentally to protect dopamine cells. They may have antioxidant effects, inhibiting free radical formation and scavenging free radicals. They may also slow programmed cell death (apoptosis) which may be accelerated in Parkinson disease.

Experimental Treatments

Many patients inquire about "restorative" therapies, a category of procedures that includes transplantation of fetal cells or stem cells, growth factors, or gene therapy. The goal of these procedures is to correct the basic chemical defect of Parkinson disease by increasing the production of dopamine in the brain. Although theoretically very attractive, much more laboratory work must be done in order to make cell transplantation or growth factor therapies practical and effective. At this time, the restorative therapies are experimental and are not available as treatment.

WEBSITES

National Institute of Neurological Disorders and Stroke (NINDS)

BRAIN

P.O. Box 5801

Bethesda, MD 20824

Tel: (800) 352-9424

TTY (for people using adaptive equipment) (301) 468-5981

www.ninds.nih.gov

American Parkinson Disease Association

135 Parkinson Avenue

Staten Island, NY 10305

Tel: (800) 223-2732

email adpa@adparkinson.org

www.apdaparkinson.org

Pharmaceutical Research and Manufacturers of America

www.pfizer.com