



MEDICAL AND SURGICAL TREATMENT FOR MOTOR FLUCTUATIONS AND DYSKINESIA IN PARKINSON DISEASE

Levodopa is converted to dopamine in the brain. It is effective in managing the initial symptoms of Parkinson disease, however over time the effectiveness is reduced and this results in *motor fluctuations*. Motor fluctuations are periods of the day with poor or no response to medication (off time). This alternates with periods of improved function (on time).

Over time people on levodopa or dopamine agonist therapy develop involuntary movements. These are called *dyskinesia*. Dyskinesia in Parkinson disease is caused by medications. This can affect quality of life and may cause disability.

Neurologists from the American Academy of Neurology are doctors who treat diseases of the brain and nervous system. They believe people with Parkinson disease should know which drugs and surgical treatments reduce their off time and dyskinesia.

Experts in Parkinson disease reviewed all of the available studies about medical treatments and deep brain stimulation (DBS) for dyskinesia and motor fluctuations. They made suggestions that will help doctors and people with Parkinson disease make choices in their care. In some cases, there were not enough published data for or against specific therapies.

Medical Treatments to Reduce Off Time

Neurologists looked at all of the studies for medications that reduce off time. While there is stronger evidence* for some drugs, there is not enough evidence* to recommend the value of one drug over another.

There is **strong** evidence* that the following two drugs can decrease off time.

- *Entacapone* is in a group of drugs called *catechol-O-methyltransferase (COMT) inhibitors*. COMT inhibitors increase the length of time that each separate dose of levodopa therapy is effective and reduces per day off time. Entacapone acts in the bowels to increase the amount of levodopa absorbed. Side effects may include dizziness, drowsiness, hallucinations, or change in urine color.
- *Rasagiline* is in a group of drugs called *monoamine oxidase (MAO) inhibitors*. They slow the breakdown of naturally occurring dopamine and dopamine produced from levodopa. Side effects may include headache, depression, or flu-like symptoms.

There is **good** evidence* that these medications may reduce off time:

- *Ropinirole*, *pramipexole*, and *pergolide* are *dopamine agonists*. They act directly on dopamine receptors. They act like dopamine; they stimulate the dopamine system.

Side effects may include confusion, mild nausea, or decreased appetite. Due to potential side effects such as heart and breathing difficulties, pergolide should be used with caution.

- *Tolcapone* is a COMT inhibitor. In rare cases, tolcapone has caused severe liver damage resulting in death. Notify your doctor immediately if you develop nausea, vomiting, abdominal pain, unusual fatigue, loss of appetite, yellow skin or eyes, itching, dark urine, or clay colored stools. These symptoms may be early signs of liver damage. Liver tests should be done often on people taking tolcapone.

There is **weak** evidence* that the following drugs may reduce off time:

- *Apomorphine* and *cabergoline* are dopamine agonists. They act directly on dopamine receptors. Apomorphine is injected like insulin and works rapidly. Apomorphine may cause depression, dizziness, or hallucinations. Cabergoline may cause dizziness, headache, and weakness. As of December 2005, cabergoline was not available in the United States.
- *Selegiline* and *orally-disintegrating selegiline* are MAO-B inhibitors. Side effects may include dizziness or drowsiness, abdominal pain, and anxiety.

Medical Treatments to Reduce Dyskinesia

The Parkinson disease experts also reviewed all of the available data for drugs that reduce dyskinesia.

- *Amantadine* reduces stiffness. There is **weak** evidence* that amantadine may be considered for reducing dyskinesia. Side effects may include confusion, leg swelling or rash, constipation, dizziness, lightheadedness, drowsiness, or headache.
- *Clozapine* is a drug used for schizophrenia. There is **not enough** evidence* for the use of clozapine in reducing dyskinesia. Side effects may include decrease in white blood cells, seizures, or inflammation of the heart muscle. Due to the potential harmful effects, frequent blood monitoring is required.

Surgical Treatment

A surgical procedure called *deep brain stimulation (DBS)* may help improve motor fluctuations and dyskinesia in people with Parkinson disease.

DBS is directed at three primary targets for Parkinson. All three of these structures are deep in the brain. In DBS, an electric probe (electrode) is placed in the brain. A wire from the electrode is routed beneath the skin to a pacemaker device implanted near your collarbone. The pacemaker and electrode stimulate a specific brain structure with pulses of electricity. This regulates the structure in the brain to improve off time and involuntary movement. Only special medical centers perform this procedure.

Side effects may include thought process and speech disorders, visual and sensory disturbances, abnormal gait, lack of coordination, headaches, and seizures.

Readers should be aware that it is not easy to study surgical therapies in the same way as other medical therapies. It is difficult to design a study where neither the physician nor the

patient know if the patient went through the real surgical procedure or a comparison (sham) procedure. Therefore, the evidence that DBS successfully treats Parkinson disease is weakened by the research methods involved.

There is **weak** evidence* that DBS using an electrode implanted in the core of the subthalamus may improve function and reduce motor fluctuations, dyskinesia, and drug usage. There is **not enough** information* to make suggestions about DBS in the other two areas of the brain—the thalamus and globus pallidus.

There is some evidence that response to levodopa, age, and duration of Parkinson disease may predict how successful DBS of the subthalamus will be.

Your doctor should discuss potential side effects of this treatment with you. The decision to use this procedure depends on your condition and the risk for complications compared to successful outcomes.

Ten to 20 percent of people with Parkinson disease may be eligible for surgical treatments. Surgery may help long-term by reducing symptoms and improving quality of life. Talk to your neurologist early in your disease to discuss the potential for future surgical treatments.

Talk to your neurologist

Not every treatment works for every patient. A treatment decision will depend on other medical conditions you have and potential side effects. All treatments have some side effects, the choice of which side effects can be tolerated depends on the individual. Your doctor should discuss serious side effects, if any.

This is an evidence-based educational service of the American Academy of Neurology. It is designed to provide members and patients with evidence-based guideline recommendations to assist with decision-making in patient care. It is based on an assessment of current scientific and clinical information, and is not intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on the circumstances involved.

*After the experts review all of the published research studies they describe the strength of the evidence supporting each recommendation:

Strong evidence = More than one high-quality scientific study

Good evidence = At least one high-quality scientific study or two or more studies of a lesser quality

Weak evidence = The studies while favorable are weak in design or strength of the evidence

Not enough evidence = Either different studies have come to conflicting results or there are no studies of reasonable quality