



Patient Webinar Series presented by WE MOVE

Novel Approaches to the Management of Parkinson's Disease A Syllabus for People Living with Parkinson's disease

Introduction to PD

PD is the second most common disease of the nervous system that worsens over time. As many as one million Americans have PD, most of whom are older than 60 years of age.

- ▣ The symptoms of PD—the slowness of movements, tremor, stooped posture, and problems with balance—are caused by a loss of brain cells (neurons) in the part of the brain that controls movement. It is now clear that the loss of neurons begins years before the first symptoms of PD appear. This finding raises the issue of whether it would be possible to spot the disease process early on, before the person with PD actually has significant symptoms.
- ▣ At the same time, new types of drugs and new ways of getting the drugs into the body have improved the treatment for PD in both the early and late stages of the disease.
- ▣ It has also become clear that PD causes many other symptoms that do not affect movement (nonmotor symptoms). These nonmotor symptoms may lead to significant impairment and problems with daily activities.

Brain Imaging: An Aid to Diagnosis?

The diagnosis of PD is made based on the results of a doctor's examination. Many researchers wonder whether taking pictures of the living brain (brain imaging) could help to make the diagnosis or even spot the disease process before a person with PD develops symptoms.

Telling the difference between PD and several other diseases can be challenging for doctors when the disease is in its earliest stages. This is difficult even for doctors who specialize in movement disorders. The disorders that are most likely to be confused with PD are progressive supranuclear palsy (PSP), multiple system atrophy (MSA), essential tremor (ET), and vascular parkinsonism. One goal of using brain imaging in the clinic would be to aid in distinguishing these disorders.

As of now, no brain imaging technique can reliably tell the difference between PD and these other conditions. Future improvements may change that. Two types of imaging are used experimentally: positron emission tomography (PET) and single photon emission computed tomography (SPECT). In each, a harmless radioactive substance is injected into the person's blood vessel and travels to the brain. The person lies inside a large machine that detects the radioactivity and uses it to create a picture of the brain. People with PD have specific changes in their brains that can be detected with these methods.

Brain Imaging: Preclinical Detection?

A major goal of research into PD is to develop a treatment that can slow or even stop the process that destroys neurons. This is called a neuroprotective treatment. If a neuroprotective treatment existed, it might be given to people at the very beginning of their disease, or even before a person who is known to be at risk for developing PD has symptoms. The purpose would be to delay or even prevent the development of symptoms. So far, no such therapy exists.

Brain imaging might be used to identify people who are at risk of developing PD. Small research studies have been done to look at the use of brain imaging for this purpose. Some researchers hope to combine brain imaging with other tests to better identify people who are at risk. One such test is a smell test, since people who develop PD tend to also lose their sense of smell.

Despite these intriguing developments, experts agree that the routine use of brain imaging, either for diagnosis or detecting people at risk of developing PD, must await further progress.

New Therapies

Selegiline ODT (Zelapar[®]) and rasagiline (Azilect[®]) are both in a category of drugs called monoamine oxidase-B inhibitors. They are used for symptom relief in PD. Both help reduce “off” time. Off time is time when a person’s symptoms are not adequately controlled by medications.

A new formulation of selegiline, called Zelapar, received Food and Drug Administration (FDA) approval in 2006. This new formulation is based on a technology called Zydis[®], which incorporates the selegiline into a tablet that dissolves in the mouth in several seconds and does not need to be taken with water. Absorption through the mucous membranes of the mouth avoids “first pass” metabolism in the liver; this new method of delivery (ODT) leads to relatively higher blood levels of selegiline and relatively lower levels of by-products when compared with the oral swallowed selegiline tablet. This may be particularly helpful for people who have trouble swallowing or who prefer not to take their medicine with water. Data from a clinical study showed that Zelapar[®] significantly reduced off time, with improvements observed in some patients after one week of treatment.

When taking Zelapar at therapeutic dose (i.e., 2.5 mg once daily), there are no required dietary restrictions with tyramine-containing foods. At this dose, people treated with Zelapar are able to take medications containing amines and consume tyramine-containing foods without risk of uncontrolled hypertension. Safe use of Zelapar at doses above 2.5 mg daily without dietary tyramine restrictions has not been established.

A new drug, Azilect[®] (rasagiline tablet) also received FDA approval for the treatment of PD in 2006. The recommended dose is 1.0 mg once daily if used alone early in the disease. When used along with levodopa, the recommended dose is 0.5 mg once daily, with the option of increasing to 1.0 mg daily if needed to help control symptoms. Pills are available in both 0.5-mg and 1.0-mg doses.

People who take Azilect should avoid certain foods, beverages, dietary supplements, and over-the-counter cough/cold medications that contain a substance called tyramine due to the risk of uncontrolled hypertension. Foods and beverages containing tyramine:

- air-dried or fermented meats
- pickled hering
- fava beans
- soy beans and soy products (including soy sauce)
- aged cheeses
- red wine
- non-pasteurized beer
- sauerkraut
- yeast extracts

Drugs containing tyramine include any drugs containing

- Pseudoephedrine
- Phenylephrine
- Phenylpropanolamine
- Ephedrine

Symptoms of uncontrolled hypertension include severe headache, blurred vision/visual disturbances, difficulty thinking, stupor/coma, seizures, chest pain, unexplained nausea or vomiting, or signs or symptoms of a stroke. Should you experience any of these symptoms, seek immediate medical attention.

CONTRAINDICATION: DO NOT TAKE ANY OF THE FOLLOWING MEDICATIONS WITH ZELAPAR OR AZILECT:

- Meperidine (Demerol[®], Mepergan[®], Isonipecaine[®], Pethidine[®])
 - Tramadol (Ultram[®])
 - Methadone (Dolophine[®], Methadose[®])
 - Propoxyphene Darvocet-N[®], Genagesic[®], Wygesic[®], E-Lor[®]
 - Dextromethorphan (Benylin[®], Delsym[®], Hold[®] DM, Pertussin[®], Robitussin[®], Simply Cough[®], Sucrets[®], Triaminic[®], Vicks[®] 44 Cough Relief, Alka-Seltzer Plus[®], and other combinations)
 - St. John's wort
 - Tricyclic antidepressants, including amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine, and others
 - SSRI (selective serotonin reuptake inhibitor) or SNRI (serotonin-norepinephrine reuptake inhibitor) antidepressants, including Paxil[®], Zoloft[®], Prozac[®], Luvox[®], and Celexa[®], as well as others
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Entacapone and Tolcapone: A New Pill, and a Less Restrictive Warning

Two drugs that help prolong the effect of levodopa and reduce “off” time are entacapone and tolcapone. They are in a category of drugs called COMT inhibitors.

Entacapone is available in a separate tablet (Comtan[®]) or in combination with levodopa in a single tablet (Stalevo[®]). Comtan[®] is taken with each levodopa dose. Stalevo[®] may be more convenient for some patients because it reduces the number of pills that must be taken.

Tolcapone (Tasmar[®]) has a somewhat more potent effect and longer duration of action than entacapone. It is taken three times a day. Reports of three deaths from liver damage in people who had taken tolcapone prompted the FDA to place a strict warning on the package of Tasmar[®] shortly after it became available. The FDA has recently relaxed that warning after reviewing the records of thousands of people who have taken the drug. Liver tests are now required before starting the drug, then every two to four weeks for the first six months, and then periodically thereafter, as the physician recommends. Tests are also required when increasing the dose of tolcapone. The test is done with a simple blood sample to look for levels of liver proteins, which, when high, may indicate liver damage. If these levels rise too high, the patient should stop taking tolcapone, under the supervision of the doctor.

The doctor may decide to lower the levodopa dose when starting a COMT inhibitor. Both tolcapone and entacapone may cause diarrhea, which is sometimes severe enough to prevent continued treatment. These medicines may cause urine to be orange colored, but this is harmless and is not a cause for alarm.

Dopamine Agonists

Dopamine agonists have become one of the main medications used to treat PD. Agonists are often used alone in early PD and in combination with levodopa in those people with more advanced disease. Three new developments in dopamine agonist therapy merit attention.

Ergot-Derived Agonists

Pergolide (Permax[®]) is a dopamine agonist which has been widely used in the management of people with Parkinson’s disease. Many movement disorder doctors now recommend that people who are taking pergolide consider switching to one of the dopamine agonists not made from ergot. Pramipexole (Mirapex[®]) and ropinirole (Requip[®]) are two dopamine agonists that are not made from ergot and have FDA approval for the treatment of PD. Switching from an ergot-based dopamine agonist to a nonergot-based dopamine agonist has led to improvement in the fibrosis in most cases; however, these drugs may have other side effects. For more information on dopamine agonists, please go to www.wemove.org.

Apomorphine: A New Treatment Option

Apomorphine injectable (Apokyn®) is a new dopamine agonist that is injected under the skin rather than taken as a pill. It is most often used in advanced PD as a “rescue” therapy for patients who have unexpected “off” episodes, or when a dose of levodopa hasn’t yet begun to take effect. Injected apomorphine acts quickly, usually in about 10 minutes, and a single dose can last up to 90 minutes.

People who are going to take Apokyn® must first be treated with a drug called trimethobenzamide (Tigan® or Tebamide®) for three days to avoid nausea. Once the Apokyn® is started, the person should keep taking trimethobenzamide for at least 6 weeks and then slowly stop taking the trimethobenzamide if the Apokyn® is not causing nausea. The first injection of Apokyn® should take place in the doctor’s office, and the person should be watched for side effects, such as low blood pressure.

Apokyn® comes in a cartridge that is inserted into a pen injector. A dial is turned to select the desired dose, and the injection is given by either the person with PD or a caregiver as needed for rescue from off periods. People often use Apokyn® first thing in the morning to increase their ability to move while waiting for their first dose of levodopa to take effect. Apokyn® is also used to counteract off periods during the day, especially in those people who have rapid or unpredictable wearing off.

New Treatment Strategies

PD is classified as a movement disorder, but there is a growing recognition that nonmotor symptoms are an important part of the disease and, in many people, are more disabling than the motor symptoms (Table).

Possible Nonmotor Symptoms in PD

Neuropsychological	Autonomic	Other
Depression	Sexual dysfunction	Insomnia
Anxiety/restlessness	Urinary dysfunction	Excess daytime sleepine
Psychosis	Constipation	Pain
Slowed thinking	Drooling	Tingling, aching limbs
Memory impairment	Drenching sweats	Seborrhea dermatitis
Dementia		Abdominal bloating
Vivid dreams		Flatulence
Orthostatic hypotension		

Mild to moderate depression affects up to half of all people with PD, but it is often not recognized by doctors, including neurologists. Psychosocial counseling and the use of antidepressant medications may be beneficial. Anxiety and restlessness are even more common. When anxiety and restlessness are associated with off periods, a change in the dose of medications used to treat PD may help. Antidepressant medications may also improve anxiety, and some people may need to take anti-anxiety medications. Seeing things that are not really present (called visual hallucinations) are a common side effect of levodopa and other medications used to treat PD. People who are older, have some dementia, or are taking several different drugs have a higher chance of having visual hallucinations. Stopping amantadine (a drug that may be used to treat PD) or

dopamine agonists may help. Taking antipsychotic drugs such as quetiapine (Seroquel®) or clozapine (Clozaril®) may also be useful. Older antipsychotic drugs are usually not used because they can worsen PD-related symptoms.

Problems with sexual function, such as erectile dysfunction, loss of interest in sex, and inability to achieve orgasm, are common nonmotor features of PD. A drug called sildenafil has been reported to be effective in some men with PD who have erectile dysfunction, and this drug may also improve depression. Hypersexuality, as well as compulsive gambling or compulsive shopping, has been associated with use of dopamine agonists in a small percentage of men and women who take these drugs.

Difficulty controlling urine (called urinary incontinence) in people with PD is usually related to bladder spasms. Incontinence can be treated with oxybutynin (Ditropan®). Reddened and flaking skin, called seborrheic dermatitis, can be treated with coal tar shampoo and ketoconazole cream (Nizoral®).

People with PD often report having pain in their joints and muscles. People can keep a chart of their pain cycle to assess if the pain responds to levodopa. The pain is not usually caused by problems in the joints or muscles themselves. Instead, it is often a localized cramp or rigid muscle that responds to an increase in levodopa medication.

For more detailed information about PD, please visit the WE MOVE Web site at www.wemove.org. You are invited to join our online community of people affected by a movement disorder. Post your questions on the PD Discussion Board at www.wemove.org/cgi-bin/ultimatebb.cgi.

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