MANAGING PARKINSON DISEASE: UPDATES IN THERAPEUTICS

Parkinson disease (PD) is a debilitating disease for over one million people in the United States characterized by slow movement, resting tremor, and rigidity all resulting from inadequate dopamine levels. Mental disorders such as depression and psychosis are also very prevalent in these patients. This issue of CLIPs briefly summarizes an article that provides an overview of signs and symptoms of PD and offers an in-depth look at treatment options that are available. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Symptoms

- **Motor**
  - Tremor at rest- can be hard to notice; may only be in a few fingers. Does not present in 20% of patients at diagnosis.
  - Rigidity- more likely felt by an examiner than observed from other people.
  - Bradykinesia- slow movements found in all PD patients.
  - Gait and balance problems- usually occur after a few years than at initial presentation and is characterized by walking with small steps and freezing in place.

- **Non-motor**
  - Craniofacial features- masked facies, drooling, anosmia, hypophonia, dysarthria, dysphagia
  - Sensory features- paresthesia, pain
  - Autonomic features- urinary disturbance, constipation, sexual dysfunction
  - Neuropsychiatric features- depression, anxiety, apathy, dementia, psychosis
  - Others- fatigue, sleep disturbance, seborrheic dermatitis, eye abnormalities

Diagnosis

- Most often diagnosed around between age 60-70 years but can present as young as the teenage years
  - Age 10-20 years: juvenile onset PD
  - Age 21-40 years: young onset PD
- The classic way to diagnose is a clinical test given to those experiencing motor symptoms already. Patients are given dopamine and if they respond well they are given the diagnosis of PD.
- DaTscan is approved to diagnose PD as well. It is a dopamine transporter ligand that tags presynaptic dopaminergic neurons in the basal ganglia. Parkinson patients have decreased signal at these neurons.
- For those less than 50 years of age, Wilson disease needs to be ruled out as a cause. Brain tumors need to also be considered in those who are young at presentation or do not satisfy classic diagnostic criteria.
- Secondary causes for PD symptoms include: drugs (e.g., metoclopramide, prochlorperazine, risperidone, olanzapine), strokes in the basal ganglia, and normal pressure hydrocephalus
- Parkinson-plus syndromes include classic PD features plus other symptoms not normally associated with PD including: poor response to levodopa, early rather than late postural instability, axial rigidity, early dementia, and supranuclear palsy. If a patient fits this criteria they may have one of these alternative diagnoses:
  - Progressive supranuclear palsy
  - Multiple system atrophy
  - Corticobasal degeneration
  - Lewy body dementia

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### Motor Management

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<th>Treatment</th>
<th>Examples</th>
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<td>Nonpharmacologic treatment</td>
<td>Education, support services, exercise, nutrition</td>
<td>Start these at the point of diagnosis to help slow disease progression.</td>
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<tr>
<td>Dopamine precursor</td>
<td>Levodopa/carbidopa</td>
<td>Many patients develop motor fluctuations and dyskinesias after a few years use. Most effective and cheapest treatment available.</td>
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<td>Dopamine agonists</td>
<td>Pramiapexole, ropinirole, bromocriptine</td>
<td>Good in younger patients with milder symptoms. Long acting for once daily dosing but more side effects than levodopa.</td>
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<td>Anticholinergics</td>
<td>Trihexyphenidyl, benztropine</td>
<td>Good for tremor and drooling but not for rigidity, bradykinesia, and balance. Many side effects, especially in elders.</td>
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<td>MAO-B inhibitors</td>
<td>Selegiline, rasagiline</td>
<td>Not as effective as levodopa or dopamine agonists but better side effect profile. Many drug and food interactions.</td>
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<td>Neuroprotective agents</td>
<td>Coenzyme Q10, creatine, inosine calcium channel blockers (CCBs)</td>
<td>Creatine, inosine, and CCBs all show some promise to being protective in studies. CoQ10 has not had success.</td>
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<td>COMT inhibitors</td>
<td>Tolcapone, entacapone</td>
<td>Slows the breakdown of dopamine and extends the half-life of levodopa. Reduces side effects due to levodopa wearing off in advanced patients. Very expensive.</td>
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<td>NMDA receptor antagonist</td>
<td>Amantadine</td>
<td>Dopamine releasing agent that is used to treat flu. Good for treating dyskinesias. Many side effects.</td>
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<td>Deep brain stimulation</td>
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<td>Best therapy to improve quality of life but expensive and risky.</td>
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### Nonmotor Management

- **Dementia**: patients with PD are at an 80% risk of developing dementia. In dementia many of the Parkinson agents cannot be used as they enhance side effects. Levodopa is the only treatment in this case. For dementia, rivastigmine is the only FDA-approved option however, its effects aren’t great and it may transiently increase PD symptoms.

- **Psychosis**: nearly half of patients will have episodes of psychosis with PD. Patients who develop this should have lab tests done to rule out infection or electrolyte imbalance as the cause. Parkinson drugs should be discontinued slowly until levodopa/carbidopa is left and its dosage should be reduced to lowest possible to help manage the psychosis. For patients still needing more therapy for psychosis clozapine can be added but weekly monitoring is required for risk of agranulocytosis. Quetiapine is first line for psychosis in PD for better adverse effect profile but it is not as effective as clozapine. Other antipsychotics should not be used to treat Parkinsonian psychosis.

- **Mood disturbances**: depression and anxiety cause a lot of problems and decreased quality of life in many Parkinson patients. Most antidepressants work well. Tricyclic antidepressants may be better than SSRIs for those who can tolerate side effects.

### In the Future

- Trials are being conducted now in newly diagnosed patients to find a biomarker for PD. This will help to obtain more definitive diagnoses. Patients can be diagnosed quicker and get needed treatment to minimize PD progression.

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