TREATMENT OPTIONS FOR PARKINSON’S DISEASE

Karin M. Durant, Pharm.D.
Florida Hospital East Orlando
Goals of Therapy

- Symptom management
  - Tremor, rigidity, bradykinesia, gait disturbances (freezing)

- Halting or slowing the disease progression
  - Neuroprotection
Current Therapies Available

- Levodopa/Carbidopa
  - Sinemet®, Atamet®
- COMT Inhibitors
  - Entacapone (Comtan®), Tolcapone (Tasmar®)
- Combination products:
  - Levodopa/Carbidopa/Entacapone (Stalevo®)
Current Therapies Available

- **Anticholinergics**
  - Benztropine (Cogentin®), Trihexyphenidyl (Artane®), Biperiden (Akineton®), Amantadine (Symmetrel®)

- **Dopamine Agonists**
  - Bromocriptine (Parlodel®), Pramiprexole (Mirapex®), Ropinirole (Requip®), Apomorphine (Apokyn®)

- **MAO-Inhibitors**
  - Selegiline (Eldepryl®), Rasagiline (Azilect®)
Why is Levodopa always given in combination with Carbidopa (Sinemet®)?

Levodopa is broken down by enzymes before it reaches the brain. Carbidopa inhibits this enzyme activity allowing levodopa to reach the brain where it is metabolized to dopamine. This allows a lower dose of levodopa to be used which helps limit side effects such as nausea and vomiting.
Levodopa/CARBIDOPA

- Levodopa is converted to dopamine
- Reduces extrapyramidal movements, rigidity, tremor and gait disturbances
- Available as immediate release, extended release and dissolvable oral formulations
- Doses and frequencies vary widely among patients and may vary over time
- Do not take within 2 weeks of Selegiline or if history of narrow angle glaucoma
Levodopa/Carbidopa

- Avoid sudden withdrawal
- Side effects: nausea, vomiting, loss of appetite, dyskinesia, confusion, orthostatic hypotension (feeling faint upon standing)
- Proteins can interfere with levodopa absorption
  - Take 30-60 minutes before a meal
  - For nausea, take with crackers or other low protein foods
COMT Inhibitors

- Entacapone (Comtan®), Tolcapone (Tasmar®)
- Selective inhibitor of COMT, which is the major metabolizing enzyme of levodopa
- No effect on Parkinson’s symptoms without levodopa – used in combination with levodopa
- Multiple drug interactions
- Side effects: nausea, diarrhea, hallucinations, confusion, dyskinesia, orthostatic hypotension
- Tasmar® has been associated with a risk of acute fulminant (sudden and severe) liver failure
- Avoid sudden withdrawal
Stalevo®

- Combination product containing levodopa, carbidopa, and entacapone
- March 2010 FDA Safety Announcement
  - Patients taking Stalevo may be at increased risk of developing prostrate cancer
- August 2010 FDA Safety Announcement
  - Patients taking Stalevo may be at increased risk of cardiovascular events such as heart attack and stroke
Anticholinergics

- Benztropine (Cogentin®), Trihexyphenidyl (Artane®), Biperiden (Akineton®), Amantadine (Symmetrel®)
- Cogentin® is available as an injection
- Reduces extrapyramidal movements, rigidity, tremor and gait disturbances
- Side effects: dry mouth, urinary retention, sedation, constipation, blurred vision, confusion, increased intraocular pressure, impaired heat regulation, peripheral edema (amantadine)
- Avoid sudden withdrawal
Dopamine Agonists

- Bromocriptine (Parlodel®), Pramiprexole (Mirapex®), Ropinirole (Requip®), Apomorphine (Apokyn®)
- Exact mechanism in Parkinson’s disease is unknown
- Reduces extrapyramidal movements, rigidity, tremor and gait disturbances
- Apomorphine is given by subcutaneous injection
  - Rotate injection sites
Dopamine Agonists

- Watch for drug interactions
- Side effects: Nausea, constipation, drowsiness, confusion, dizziness, insomnia, dyskinesias, orthostatic hypotension, hallucinations
- Take oral products with food to minimize stomach upset
- Use Apomorphine with caution in patients with cardiovascular disease
- Avoid sudden withdrawal
MAO Inhibitors

- Selegiline (Eldepryl®), Rasagilnine (Azilect®)
- Selective inhibitor of monoamine oxidase, type B
  - Blocks the breakdown of dopamine
- May also increase dopamine activity
- Effective when used by itself or in combination with Levodopa
- Reduces extrapyramidal movements, rigidity, tremor and gait disturbances
- Improves mood
MAO Inhibitors

- Major drug interactions, including antidepressants, Ma Huang, Kava, St John’s Wort and Ginseng
- Side effects: nausea, vomiting, indigestion, constipation, dry mouth, weight loss, headache, orthostatic hypotension, hallucinations
- Use caution with tyramine containing foods such as wine, aged cheese, and liver
Vitamins/Herbs/Supplements

- Coenzyme Q10
- Vitamins C and E (antioxidants)
- Ginkgo biloba
- Ginger

The FDA does not regulate herbs and supplements
Protective Treatments

- Recent research is now focusing on neuroprotective effects of the medications.
- Goal is to halt or slow the disease progression.
- Initiating treatment in early disease (before symptoms require treatment) has been studied.
- Levodopa, Rasagiline, Coenzyme Q10, Simvastatin.
Role of Rasagiline

- Has demonstrated some neuroprotective properties

- Results of recent studies:
  - Improved Unified Parkinson’s Disease Rating Scale (UPRDS) scores over a 6.5 year period in patients who started therapy early vs. late
  - Early treatment with rasagiline 1mg daily showed benefits that may be consistent with a disease modifying effect. This same effect was not seen with a dose of 2mg daily.
Role of Coenzyme Q10

- Nutraceutical product that has been used in angina, congestive heart failure, and cardiac surgery
- Potent antioxidant
- Improves mitochondrial function (increases cell energy)
- Side effects: nausea, lack of appetite, diarrhea
Role of Coenzyme Q10

- Results of recent studies:
  - Adding Coenzyme Q10 in midstage Parkinson’s disease does not improve symptoms or UPDRS scores
  - Combination of Coenzyme Q10 and Creatine may produce additive protective effects against dopamine depletion, reduce lesions, and improve motor performance in a mouse model
Role of Coenzyme Q10

- **QE3 Study**
  - National Institute for Neurological Disease and Stroke (NINDS)
  - Designed to examine high dose Coenzyme Q10 in slowing the progression of Parkinson’s or providing neuroprotection
  - Study halted in early June 2011
  - Investigators determined that there was no neuroprotective or symptomatic benefit
The Role of Simvastatin

- Simvastatin (Zocor®) is an antihyperlipidemic
  - Other medications in this class include: Pravastatin (Pravachol®), Atorvastatin (Lipitor®), Lovastatin (Mevacor®), Rosuvastatin (Crestor®)

- Reviewed for reduction in the incidence of dementia as well as prevention of disease progression
The Role of Simvastatin

- Results of recent studies:
  - May reduce dementia
    - Also shown with atorvastatin to a lesser extent
    - Lovastatin does not appear to reduce
  - Prevents some neurotoxic damage in rat models
  - May provide cell protection and improve motor function in mice models
    - Pravastatin also protected cells but to a lesser extent
Important Points About Medications

- Each person is unique!
  - Different symptoms are present
  - Different medications, doses, and frequency may be needed
- Always take your medication on time
  - Do not double doses
- Store your medications in a cool, dry place
- Do not crush or chew extended release products
- Always check with your physician and pharmacist
- Check the $4 drug lists (currently only benztropine and trihexyphenidyl)
Karin M. Durant, Pharm.D.
Director of Pharmacy
Florida Hospital East Orlando
Phone: 407-303-6707
karin.durant@flhosp.org
Questions?