2018 Symposium: Overcoming Parkinson Disease

Medical Management of Motor Symptoms

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Disclosures - None
The primary pathologic event in Parkinson disease is loss of the dopamine neurons in the substantia nigra (SNc), which send projections to the medium spiny neurons in the striatum.
Dopamine Replacement Therapy:

**carbidopa levodopa**

- 25/100 mg 25/250 mg
- 10/100 mg
  - Standard oral formulation (aka Sinemet®)
  - Oral dissolving tablets (aka Parcopa®)
- Usually taken a minimum of three times daily

- Possible side effects:
  - Nausea, abdominal discomfort, dyskinesias, dystonia, worsening of orthostatic hypotension, drowsiness, confusion, hallucinations, paranoia, rash
Carbidopa levodopa: What about the protein effect?

- Some patients with PD find that their levodopa works less effectively when they take it with food (especially protein) or on a full stomach.
- However, only ~1/3 of PD patients have this!
- Don’t arrange your life/meal schedule around dose times until you do some trial and error and find out if you are one of these patients.

- Some patients become nauseated when taking their carbidopa levodopa on an empty stomach, but most do not have this problem.

Remember, every person is different!
Dopamine Replacement Therapy:  dopamine agonists

- **Pramipexole** (aka Mirapex®)
  - 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg
  - ER: 0.375 mg, 0.75 mg, 1.5 mg, 2.25 mg, 3 mg, 3.75 mg, 4.5 mg

- **Ropinirole** (aka Requip®)
  - 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg
  - ER: 2 mg, 4 mg, 6 mg, 8 mg, 12 mg

- **Rotigotine** (aka Neupro®) patch
  - 1 mg, 2 mg, 3 mg, 4 mg, 6 mg, 8 mg patches

Possible side effects:

- Worsening of orthostatic hypotension, drowsiness, confusion, hallucinations, impulse control disorders, ankle swelling, paranoia, nausea, abdominal discomfort, dyskinesias, dystonia, rash, withdrawal syndrome
Why do PD patients develop “wearing off?”
Dopamine neurons:

3-6 Hz tonic firing as well as phasic firing in response to stimuli
Early PD

- Remaining dopamine neurons are able to take up excess levodopa from the blood and store it as dopamine in the presynaptic terminals.
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Early PD

- Dopamine concentration maintained at constant levels in part due to presynaptic storage of dopamine
Later PD

- As more dopamine neurons are lost, the presynaptic stores of dopamine become depleted
Later PD

- Postsynaptic concentration of dopamine in the striatum becomes closely linked to blood levels of levodopa
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Adjunctive Medications for Motor Fluctuations

- Carbidopa levodopa ER 25/100 mg, 50/200 mg

- Pramipexole, Ropinirole, Rotigotine

- MAO-B inhibitors:
  - Rasagiline 1 mg (aka Azilect®)
  - Selegiline 5 mg twice daily
  - Safinamide (aka Xadago®) 50-100 mg daily
Adjunctive Medications for Motor Fluctuations

COMT inhibitors

- Entacapone (aka Comtan®)
  - 200 mg usually taken with each levodopa dose
  - Side effects: orange urine, diarrhea, rash, dyskinesias, other side effects of boosted levodopa dose

- Carbidopa-levodopa-entacapone (aka Stalevo®)
  - Combination tablet that comes in six different strengths

- Tolcapone (aka Tasmar®) 100 mg
Rytary®

- Capsule contains beads of both immediate release and extended-release carbidopa levodopa
- 23.75/95 mg, 36.25/145mg, 48.75/195 mg, 61.25/245 mg
Others Medications

- **Amantadine** 100 mg one to three times daily
  - Suppresses dyskinesias, has modest effect on tremor, slowness, stiffness

- Anticholinergic drugs: trihexyphenidyl, benztropine
  - May help tremor and other motor symptoms of PD (particularly dystonia), but are almost always limited by side effects:

*Side effects:* dry mouth, worsened constipation, urine retention, dry eyes, confusion, forgetfulness, hallucinations, paranoia, drowsiness
Dystonia in PD

Botulinum toxin injections
Thank You!