Good Start Program 2021
Medication Management

Katelyn C. K. Bird, MD
Assistant Professor of Neurology
Boston University School of Medicine
OVERVIEW

- Brief Parkinson’s Disease Review
- Goals of Medication Treatment
- Current Medications used to Treat *early* Parkinson’s Disease
- When to Start Medications
- Clinical Trials

Any medical information provided is solely for the purpose of providing information and is not intended as medical advice. Our healthcare professionals cannot recommend specific treatments or make a diagnosis. We encourage you to direct any specific questions to your personal healthcare providers.
PARKINSON’S DISEASE REVIEW

• Neurodegenerative disease affecting dopamine containing brain cells, or neurons.

• Motor Symptoms: Tremor, bradykinesia (slowness), rigidity (stiffness), and postural instability (balance difficulties)

• Non-Motor Symptoms: blood pressure changes, constipation, urinary changes, mood, difficulties with sleep, etc., can also occur
A FRESH VIEW OF PARKINSON’S DISEASE

Parkinson’s disease results from the loss of neurons in part of the brain called the substantia nigra. Researchers now suggest that its symptoms are a late sign of a more extensive disease that begins in the brain stem and spreads throughout the brain in six stages.

http://www.nature.com/nature/journal/v437/n7063/images/4371220a-i3.0.jpg
GOALS OF THERAPY

• Parkinson’s Disease symptoms are TREATABLE!

• No medication to slow down or cure but many medications to control motor (and non-motor!) symptoms by targeting dopamine.

• Patients treated with medication have lower morbidity and mortality compared to those not on medication
TIMELINE OF US DRUG APPROVAL

Levodopa-carbidopa approved May 1975

Benztropine approved 1996 (used since 1970 trials)

1st Dopamine agonists approved 1997

Tolcapone approved 1998- Removed from market Dec 2018

Deep Brain Stimulation Approved 2002

Rotigotine patch approved 2012

Tolcapone reformulated and approved 2008

Entacapone approved 1999

Apomorphine approved 1999, then again 2004

1st MAO-B approved 1998

Bromocriptine approved 1975, used in PD in 1976

Amantadine approved 1990

Trihexyphenidyl approved 2003 (used in trials since 1945)

Deep Brain Stimulation Approved 2002

Tolcapone reformulated and approved 2008

Duopa (L-dopa intestinal gel) Approved 2015

Rytary approved 2015

GoCovri approved 2015

Osmolex approved 2018

Inbrija approved 2018

Safinamide approved 2017

Istradefylline approved 2019

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Rytary approved 2015

GoCovri approved 2015

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Inbrija approved 2018

Safinamide approved 2017

Istradefylline approved 2019
CURRENT TREATMENTS

Levodopa (L-dopa)
- Carbidopa-Levodopa/Sinemet®, Parkacina®
- Rytary®
- Duopa®
- Inbrija®

Dopamine Agonists
- Pramipexole/Mirapex®
- Ropinirole/Requip®
- Rotigotine/Neupro®
- Apomorphine/Apokyn®/Kynmobi®

Anti-Cholinergics
- Trihexyphenidyl/Artane®
- Benztropine/Cogentin®

Other
- Istradefylline/Nourianz®
• First introduced for Parkinson’s Disease in 1969.
• Carbidopa is added to levodopa to decrease nausea (the most common early side effect).
• Carbidopa/levodopa = Sinemet
INTERACTION WITH PROTEIN

- Levodopa is absorbed into the brain in 30 min.
- Protein interferes with levodopa absorption.
- Levodopa should be taken one half hour prior to meals or one hour after meals for maximum absorption.
LEVODOPA

• All must be taken multiple times daily to be effective in PD although there are long-acting formulations (Rytary®, Sinemet CR®)

• Benefits: reduced tremor, reduced rigidity, improved speed of movement >> improved energy, improved thinking, improved balance.
LEVODOPA FACTS AND FICTION

• Myth: Levodopa will only work for 5 years.
• Myth: Levodopa speeds up Parkinson’s disease.
• Myth: You should postpone taking the next dose of levodopa.
• Fact/Myth: Delaying start of levodopa delays risk of development of dyskinesia.
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[Diagram showing the process of neurotransmitter release and uptake]
DOPAMINE AGONISTS

- Act on dopamine receptors directly
- Do not compete with protein in food (take at any time!)
- Lasts longer in system than levodopa
- Effective as first-line medication in early Parkinson’s Disease or as an add-on treatment in intermediate and advanced cases
- Need to be started at low doses and increased gradually
WHEN TO START DOPAMINE AGONISTS

• PROS
  • Can be dosed once daily (XL, patch)
  • Less risk of dyskinesias than levodopa
  • Less risk of nausea than levodopa

• CONS
  • More risk of impulse control disorders (ICD)
    • Gambling, sexual behaviors, eating, compulsions
  • More risk of drowsiness and sleep attacks
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**Other**
- Istradefylline/Nourianz®

**COMT Inhibitors**
- Tolcapone/Tasmar®
- Entacapone/Comtan®
- Entacopone-Carbidopa-Levodopa/Stalevo®
- Opicapone/Ongentys®

**MAO-B Inhibitor**
- Selegiline/Zelapar® (disintegrating tablet)/Eldepryl®
- Rasagiline/Azilect®
- Safinamide/Xadago®

**Anti-Viral**
- Amantadine/Symmetrel®
- Amantadine ER/Gocovri®
- Amantadine ER/Osmolex®
COMT INHIBITORS

• COMT inhibitors decrease breakdown of levodopa.
• COMT inhibitors should be used in combination with levodopa to be effective - an “extender” medication.
• Some dosed with each dose of levodopa, others once daily.
• Side effects: diarrhea, abdominal pain, discoloration of urine / body fluids
• Stalevo® is a combination pill of Carbidopa-Levodopa with entacapone (COMT inhibitor).
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MAO-B INHIBITORS

- Decrease breakdown of dopamine
- Dosed once or twice per day
- Side effects: headache, arthralgia, nausea, concerns about drug-drug interactions; Selegiline may contribute to insomnia (metabolized to an amphetamine metabolite).
- Effective as first-line medication in early Parkinson’s Disease or as an add-on treatment in intermediate and advanced cases.
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AMANTADINE

- Introduced as an antiviral agent and reported useful in Parkinson’s Disease in the 1960s.
- Improves tremor, slowness, and rigidity, and levodopa-induced dyskinesias
- Long-acting formulation available (Gocovri®, Osmolex®)
- Side effects: Confusion, swelling, constipation, dry mouth
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ANTI-CHOLINERGICS

• Several medication options available, usually dosed 2 or 3 times per day
• Effective as first-line medication in early tremor-predominant Parkinson’s Disease or as an add-on treatment
• Side Effects: dry mouth, blurred vision, constipation, nausea, difficulty emptying the bladder
WHEN TO START MEDICATIONS

• No medication to slow down or cure but many medications to treat symptoms.
• Start medications when quality of life is affected.

Dr. Bird’s Rules of Thumb for Medication Initiation:
• Tremor Predominant -> start with anticholinergic or antiviral
• Younger Patients -> start with dopamine agonists
• Older Patients -> start with levodopa or MAO-B

• As the disease progresses the medication doses need to be increased to maintain motor functioning.
ORGANIZATION OF MEDICATIONS

- Polypharmacy is the **RULE** not the **EXCEPTION**.
- It is important to keep medications organized.
- Ideally patients should wake up and go to sleep around the same time everyday. This helps to keep the medication times stable.
MEDICATION ADJUSTMENT

Keep track of your PD symptoms and let your doctor know!
NON-MOTOR SYMPTOMS
NON-MOTOR SYMPTOMS OF PD

- REM Behavior Disorder
- Sleep problems (90%)
  - Fatigue (58%)
  - Insomnia
  - Poor sleep maintenance/consolidation
- RLS
- Autonomic dysfunction
  - Constipation (20-79%)
  - Urinary frequency (25-50%)
  - Orthostatic Hypotension (60%)
- Mood disorder
  - Anxiety
  - Depression (22%)
  - Apathy (40%)
  - Pseudobulbar Affect
CLINICAL TRIALS
WHAT ARE CLINICAL TRIALS?

• Studies on human participants that are designed to answer specific questions.

• Observational vs Interventional

• Importance of Trials:
  • The projected number of people with Parkinson’s disease in the most populous nations will double by 2030 to 9.5 million people worldwide.
  • 30% of trials don’t recruit anyone and 85% finish late
  • 1% of those with PD participate in clinical trials
  • 71% of PD pts are unaware of trials
CURRENTLY AVAILABLE INTERVENTIONAL CLINICAL TRIALS

Neuraly Prism Study
• Evaluate NLY01 (diabetes medication - SQ GLP-1 Agonist) to slow the progression of Parkinson’s
• Eligibility:
  • PD Diagnosed within last 3 years
  • Age must be 30 - 80
  • Not taking any PD medications (or not greater than 30 days)
• Study duration is 1 year
• For more information call Ray James, BS, RN 617-638-7745
MORE CLINICAL TRIALS (NOT MEDICINES)

- SPARX3 - test exercise for disease modification
- WHIP PD - walking and mHealth to increase participation
CURRENTLY AVAILABLE OBSERVATIONAL TRIALS

- PPMI – Michael J Fox and AV-133
- FoxInsight.org
- SearchPD
- MicroPD
- Biofind
- The Cure Parkinson Trust in UK
RESOURCES FOR TRIALS AND THERAPIES

- Healthcare Team
- Local PD Support Group
- American Parkinson Disease Association (APDA) www.apdama.org
- Michael J Fox Foundation www.foxtrialfinder.com
- Parkinson Foundation http://parkinson.org/
- NIH www.clinicaltrials.gov
- Center Watch www.centerwatch.com
- PSG www.parkinson-study-group.org
- PD Pipeline www.pdpipeline.org
OUR TEAM

Parkinson’s Disease and Movement Disorders Center at Boston University Medical Campus

Telephone: 617-638-8456

Website: bumc.bu.edu/parkinsonsdisease
THANK YOU!

Questions?