

# Levodopa for Parkinson's



Parkinson Society British Columbia  
Parkinson's Medication Webinar Series  
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Amy Tran, B.Sc.(Pharm.), RPh

# Why a Whole Presentation on Levodopa?

- The most effective medication for treating the motor symptoms of Parkinson's disease (PD)
- Eventually all individuals with Parkinson's will add levodopa to their medication regimen
- Response to levodopa changes as PD progresses
- To help ensure that you get the most out of your levodopa

# Levodopa: The Gold Standard

- Motor symptoms of PD
  - Bradykinesia (slow movement)
  - Rigidity
  - Tremor
    - Some may find that levodopa does not help treat their tremor
  - Postural instability (balance problems)
    - Levodopa does not improve balance

# Levodopa

- Mechanism of action: converted from levodopa to dopamine and stored in neurons; replenishes depleted dopamine
- Combined with carbidopa or benserazide
  - To prevent the conversion of levodopa to dopamine in the periphery → decreasing side effects (e.g. nausea and vomiting)
  - Helps levodopa get into the brain
- Examples:
  - Levodopa/carbidopa (Sinemet®)
    - Immediate-release (IR)
    - Controlled-release (CR)
  - Levodopa/benserazide (Prolopa®)
  - Levodopa/carbidopa/entacapone (Stalevo®)
  - Levodopa/carbidopa intestinal gel (Duodopa®)

# Onset of Action of Levodopa

- How long it takes to start working
- Immediate-release: Approximately 30 minutes
- Controlled-release: Approximately 1 to 2 hours
  - Absorption can be erratic
  - Delayed; depends on the individual

# Counselling Points

- Immediate-release
  - Try making it the first thing you take in the morning
  - \*Use as needed\*
    - Waking up in the middle of the night? Chew tablet and take with carbonated beverage to help speed up onset of action
- Controlled-release
  - May be used at bedtime to help with managing symptoms during the middle of the night

# How to Take Levodopa

- Take on an empty stomach (helps increase absorption)
  - 30 to 60 minutes before meals
  - 1 to 2 hours after meals
- Space from iron
- Protein rich foods may block levodopa absorption
  - Decreasing its effectiveness

# Side Effects of Levodopa

- Nausea
  - Take with crackers, toast, or fruit
- Vomiting
- Orthostatic hypotension
  - i.e. lightheadedness when standing up from sitting or lying down position
- Confusion
- Hallucinations
- Motor complications
  - **Motor fluctuations** and **dyskinesia**



# Motor Fluctuations

- As PD progresses, response to levodopa changes
  - Long lasting and stable → progressively shorter and/or more erratic
- Examples:
  - Wearing off (end-of-dose effect)
  - On-off phenomenon
  - Dose failure
  - Delayed on
  - Unpredictable off

# Motor Fluctuations

- Wearing off (end-of-dose effect)
  - Medication effects are beginning to fade
  - PD symptoms are returning before the next scheduled levodopa dose
- On-off phenomenon
  - Unpredictable fluctuations between PD symptoms being well-controlled (“on” state) to poorly controlled (“off” state)

# Motor Fluctuations

- Dose failure
  - Dose of levodopa does not provide therapeutic benefit
- Delayed on
  - Delay in onset of effect from dose of levodopa
- Unpredictable off
  - PD symptoms return unexpectedly

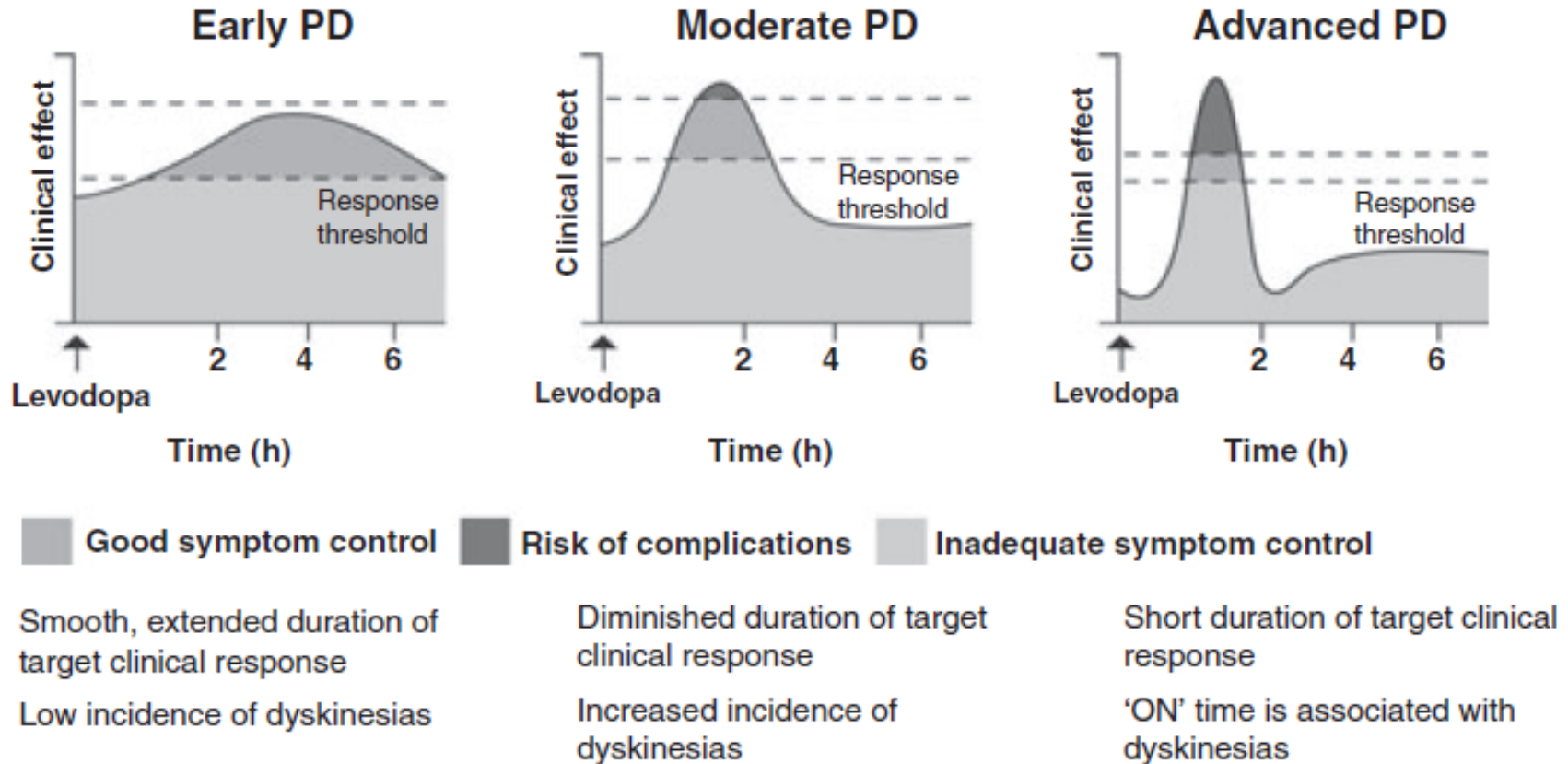
# Dyskinesia

- Irregular, uncontrollable, involuntary movement
- Can affect different parts of the body and it can also spread
- Can look like twisting, squirming movements, or contortions of the body
- Wriggling, head bobbing, fidgeting
- Side effect of some medications used to treat PD and **NOT** PD itself
  - Most commonly seen with levodopa

# Dyskinesias

- Peak-dose dyskinesia
  - Levodopa levels are at their highest in the blood
- Diphasic (or biphasic) dyskinesia
  - Occurs when levodopa levels are rising or falling, but not when at peak levels
  - Dyskinesia-Improvement-Dyskinesia
- Off-period dystonia
  - Dystonia: Involuntary muscle contractions, resulting in abnormal and sustained postures
  - Occurs due to a dose of levodopa wearing off

## Change in levodopa response over time



# Motor Complications

- Risk factors for motor complications:
  - Younger age at disease onset
  - Higher doses of levodopa
  - Higher disease severity
  - Longer disease duration
- Counselling point:
  - Take the lowest effective dose of levodopa that provides good management of PD symptoms

# Two-Pronged Approach

- Adjusting levodopa dosing may help manage less troublesome motor complications
- For more prominent motor complications, adjusting levodopa in combination with using medication(s) from other classes is necessary



# Duodopa

- For patients with advanced PD who experience motor fluctuations and dyskinesias that cannot be managed by oral/transdermal therapy
- Continuous infusion of a levodopa/carbidopa gel that is delivered to the small intestine via a tube inserted through a surgical opening into the stomach
- Helps provide more stable levodopa levels throughout the day
  - Reducing off time

# Before Your Next Appointment

- See if current levodopa regimen can be optimized to help manage PD symptoms
- Delayed on:
  - Taking levodopa on an empty stomach?
    - 30-60 minutes before food
  - Protein intake?
  - Constipation?

# Mucuna Pruriens

- Mucuna pruriens (MP) is a legume that contains levodopa
- Shown to improve motor symptoms of PD in small studies that were also short in duration
  - Given single doses
- In a small study (14 patients), MP was given for eight weeks and levodopa/carbidopa was given for eight weeks. Seven patients discontinued MP due to gastrointestinal side effects or worsening of motor symptoms.

# Mucuna Pruriens

- Hard to confirm and/or control the amount of levodopa you receive when you use natural sources
  - Variability in levodopa content = variability in symptom management
  - Impurities? Other active compounds?
- The manufacturing of prescription and non-prescription medications is **standardized**. Rigorous testing is done to confirm safety and efficacy.
- Contains no carbidopa or benserazide
  - Need to take more levodopa to provide an effect and manage PD symptoms, which increases chance of more side effects (e.g. nausea, vomiting)

In regards to any natural health product, think about possible interactions with your current medications

\* Talk to Your Pharmacist \*

# Take Home

- Levodopa is the most effective medication to treat motor symptoms in PD
- Adjusting your levodopa dose and how it is taken may provide better management of PD symptoms
- Motor complications that arise in later stages of PD will require adjusting levodopa, and use of medications from other classes
  - Webinar #2: Dopamine Agonists, MAO-B Inhibitors, and More
    - Friday, June 12<sup>th</sup> from 2:00 pm to 3:00 pm

**Thank you!**

**Questions?**

<https://www.amytalksmeds.com>