

Medication Management



Parkinson Society British Columbia
Parkinson's Medication Webinar Series
Friday, June 26th, 2020

Amy Tran, B.Sc.(Pharm.), RPh

Take one tablet three times daily

Take one tablet four times daily

Take one tablet five times daily (7 am, 11 am, 3 pm, 7 pm, 11 pm)

Take one tablet six times daily

Take 10 tablets daily in divided doses as directed



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

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 Parkinson's disease (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

Dyskinesia

- Irregular, uncontrollable, involuntary movement
- Can affect different parts of the body and it can also spread
- Chorea
 - Can present as wriggling, head bobbing, fidgeting, twisting, squirming movements
- Dystonia
 - Involuntary muscle contractions, resulting in abnormal and sustained postures
- Side effect of some medications used to treat PD and **NOT** PD itself
 - Most commonly seen with levodopa

Dopamine Agonists

- Mechanism of action: acts on dopamine receptors; mimics dopamine
- Examples: pramipexole (Mirapex[®]), ropinirole (ReQuip[®]), rotigotine (Neupro[®]), apomorphine (Movapo[®]), bromocriptine
- Side effects: nausea, orthostatic hypotension, drowsiness, leg edema (swelling), **sudden sleep attacks, hallucinations, impulse control disorders**

MAO-B Inhibitors

- Mechanism of action: helps prevent dopamine degradation in the brain, thus increasing its concentration
- Examples: rasagiline (Azilect[®]), selegiline, safinamide (Onstryv[®])
- Side effects: insomnia, hallucinations, nausea, dyskinesia, orthostatic hypotension*
 - *high blood pressure more common with safinamide

COMT Inhibitors

- Mechanism of action: helps reduce levodopa clearance before it gets into the brain
- Example: entacapone (Comtan[®])
- Taken together with levodopa
 - Extends duration of action of levodopa
- Side effects: dyskinesia, nausea, diarrhea, urine discolouration (orange/brown)

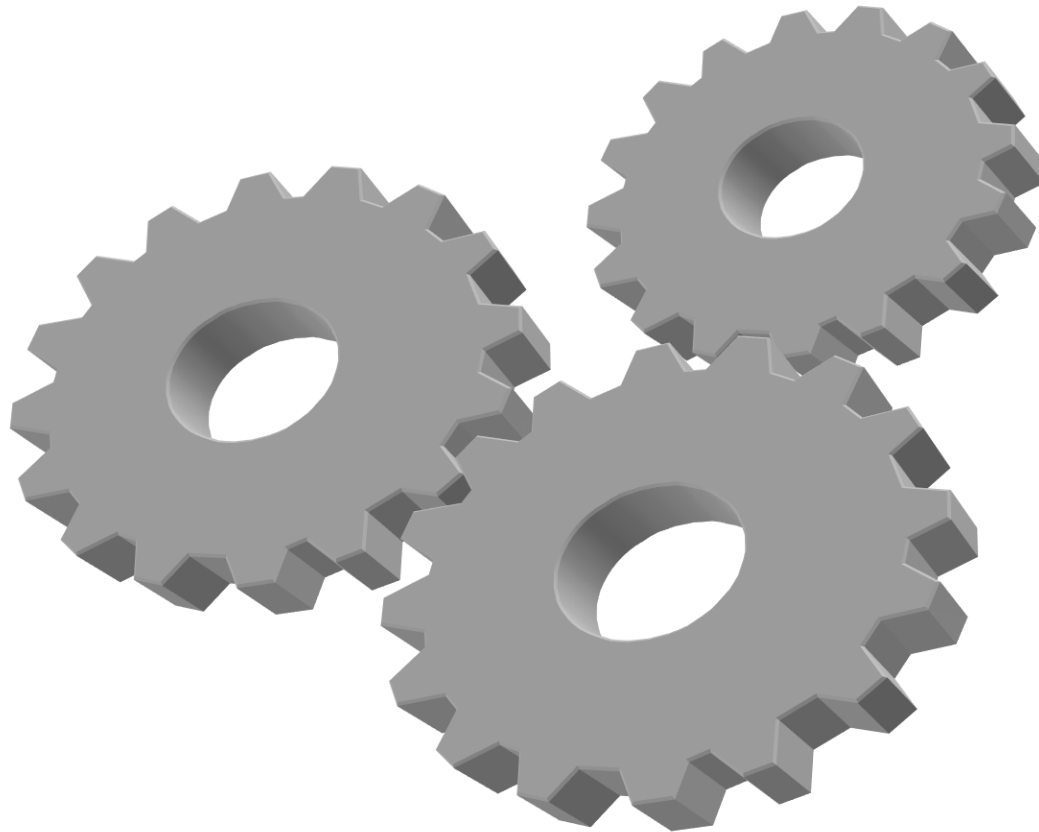
Anticholinergics

- Mechanism of action: postulated to balance cholinergic and dopaminergic activity
- Examples: trihexyphenidyl (Artane[®]), benztropine (Cogentin[®])
- May be used to treat tremor in younger individuals
- Side effects: dry mouth, blurred vision, urinary retention, constipation, drowsiness, **confusion**, **memory impairment**

NMDA Receptor Antagonists

- Mechanism of action: unclear; believed to increase dopamine release and inhibit dopamine reuptake
- Example: amantadine
- Helps reduce dyskinesia
- Side effects: confusion, insomnia, dizziness, hallucinations, ankle edema, livedo reticularis

Putting It All Together



Terminology

- **Wearing off (end-of-dose effect)**
 - Medication effects are beginning to fade
 - PD symptoms are returning before the next scheduled levodopa dose
- **“On” state**
 - Medication has “kicked in” and you have improved mobility and function
- **“Off” state**
 - Medication effects have worn off and PD symptoms have returned

Motor Fluctuations

- Wearing off (end-of-dose effect)
- Why?
 - As PD progresses, the number of neurons that are able to store and re-use dopamine decreases, thus affecting the length of symptom control
- Time between doses decreases (i.e. increased dosing frequency)

Wearing Off

- Possible methods used to treat wearing off:
 - Increase dosing frequency of levodopa
 - Add medication(s) from a different class
 - Entacapone
 - Dopamine agonist
 - MAO-B inhibitor
 - Switch from levodopa IR to CR

Levodopa and Dyskinesia

- Changing your levodopa dosage and/or how often it's taken so you get enough in each dose to control your symptoms, but not too much that it causes dyskinesia

Dyskinesia

- Possible methods used to treat dyskinesia:
 - Smaller doses of levodopa more frequently
 - Add amantadine
 - Add dopamine agonist
 - Stop entacapone
 - Stop MAO-B inhibitor
 - Switch from levodopa CR to IR

*What are my current PD
medications?*

What can I do?

Optimize
current medication
regimen

Keep Track!

- 1) Write down what time you take your medication(s)
 - Also include approximate meal times
- 2) Am I experiencing any side effects? Is it due to my PD medication(s) or is it due to other medications?
 - Ask your pharmacist
- 3) When does my medication kick in? When am I experiencing wearing off?
 - How long am I “on” for? When do I start slowing down?
- 4) Do I experience dyskinesia?

**Writing it down helps you keep track of what works
for YOU and what does not**

Case #1 - Alice

Medication(s)	Instructions
Levodopa/carbidopa IR 100/25 mg	Take one tablet three times daily

Alice's regimen:

- She takes one tablet at 8:00 am, 2:00 pm, and 8:00 pm
- She has breakfast at 8:30 am, lunch at 12:00 pm, and dinner at 5:30 pm

Case #2 - Brian

Medication(s)	Instructions
Levodopa/carbidopa IR 100/25 mg	Take one and one-half tablets four times daily
Pramipexole 0.5 mg	Take one tablet three times daily
Amantadine 100 mg	Take one capsule twice daily

Brian's regimen:

- He takes his levodopa/carbidopa IR tablets at 7:30 am, 11:30 am, 3:30 pm, and 7:30 pm
- He takes a pramipexole tablet at 7:30 am, 3:30 pm, and 10:30 pm
- He takes his amantadine at 7:30 am and 12:30 pm
- He has breakfast at 8:00 am, lunch at 12:30 pm, and dinner at 5:30 pm

Counselling point(s):

- Take all amantadine doses by mid-afternoon (side effect: insomnia)

Case #3 - Cathy

Medication(s)	Instructions
Levodopa/carbidopa IR 100/25 mg	Take two tablets five times daily
Levodopa/carbidopa CR 200/50 mg	Take one tablet daily at bedtime
Entacapone 200 mg	Take one tablet five times daily
Rasagiline 1 mg	Take one tablet once daily

Cathy's regimen:

- She takes her levodopa/carbidopa IR tablets at 7:30 am, 10:30 am, 1:30 pm, 4:30 pm, and 7:30 pm
- She takes her levodopa/carbidopa CR tablet at 10:30 pm
- She takes an entacapone tablet at 7:30 am, 10:30 am, 1:30 pm, 4:30 pm, and 7:30 pm
- She takes her rasagiline at 10:30 am
- She has breakfast at 8:00 am, lunch at 12:00 pm, and dinner at 5:30 pm

Counselling point(s):

- Entacapone only useful when taken together with levodopa
- Take rasagiline in the morning (side effect: insomnia)

Counselling Points

- Miss a dose of levodopa?
 - Take that dose as soon as you remember (as appropriate), and move the subsequent doses accordingly
- Exercise may cause one to “use up” or “burn through” their levodopa dose faster
 - May require a slightly shorter dosing interval or an extra dose of levodopa on the days where engaging in strenuous physical activity









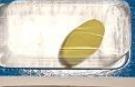














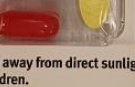


Do not stop taking a medication unless directed to do so by your physician

But, I Have a Life!

- “Last minute plans to go out for dinner”
 - “Going to a friend’s place this evening”
 - “Family visiting from out of town, so we are going to be walking around”
- Be open to being flexible with your dosing when needed, and having a dose (or two) in pocket





	MORNING 7am-9am 	MIDDAY 11am-1pm 	EARLY EVENING 4pm-6pm 	BEDTIME 8pm-10pm 
MON				
TUES				
WED				
THURS				
FRI				
SAT				
SUN				

Store in a cool dry place away from direct sunlight.
 Keep out of reach of children.
 Take the contents of one 'blister' at the correct time as directed.

Take one tablet three times daily

Take one tablet four times daily

Take one tablet five times daily (7 am, 11 am, 3 pm, 7 pm, 11 pm)

These times can change

Take one tablet six times daily

Take 10 tablets daily in divided doses as directed



Take Home

- Treatment is tailored to you and your symptoms
- Choose the dose that works best for you
 - i.e. good symptom management with minimal dyskinesia
- Timing the doses to match the response duration
 - May involve increasing the number of doses per day
- Communicate with your healthcare team
 - Keep us updated



Thank you!

Questions?

amytalksmeds@gmail.com

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