Dopamine Agonists, MAO-B Inhibitors, and More

Parkinson Society British Columbia
Parkinson's Medication Webinar Series
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Quick Recap + Introduction

- Levodopa is the most effective medication for treating the motor symptoms of Parkinson's disease (PD)
- However, not all individuals with PD are started on levodopa
- Medications from other classes may be used initially instead to manage PD. Some of these same medications can also serve as add-on therapy to levodopa in later stages of PD

Treatment Initiation

- There is no designated medication for initial treatment of PD
- Factors that influence which medication is selected include:
  - Severity of symptoms
  - Which hand it affects (dominant?)
  - Impact on ability to work, exercise, engage in hobbies, and activities of daily living
  - Cost
- *Shared decision making*

Terminology…

Wearing off

On-off phenomenon

Dyskinesia

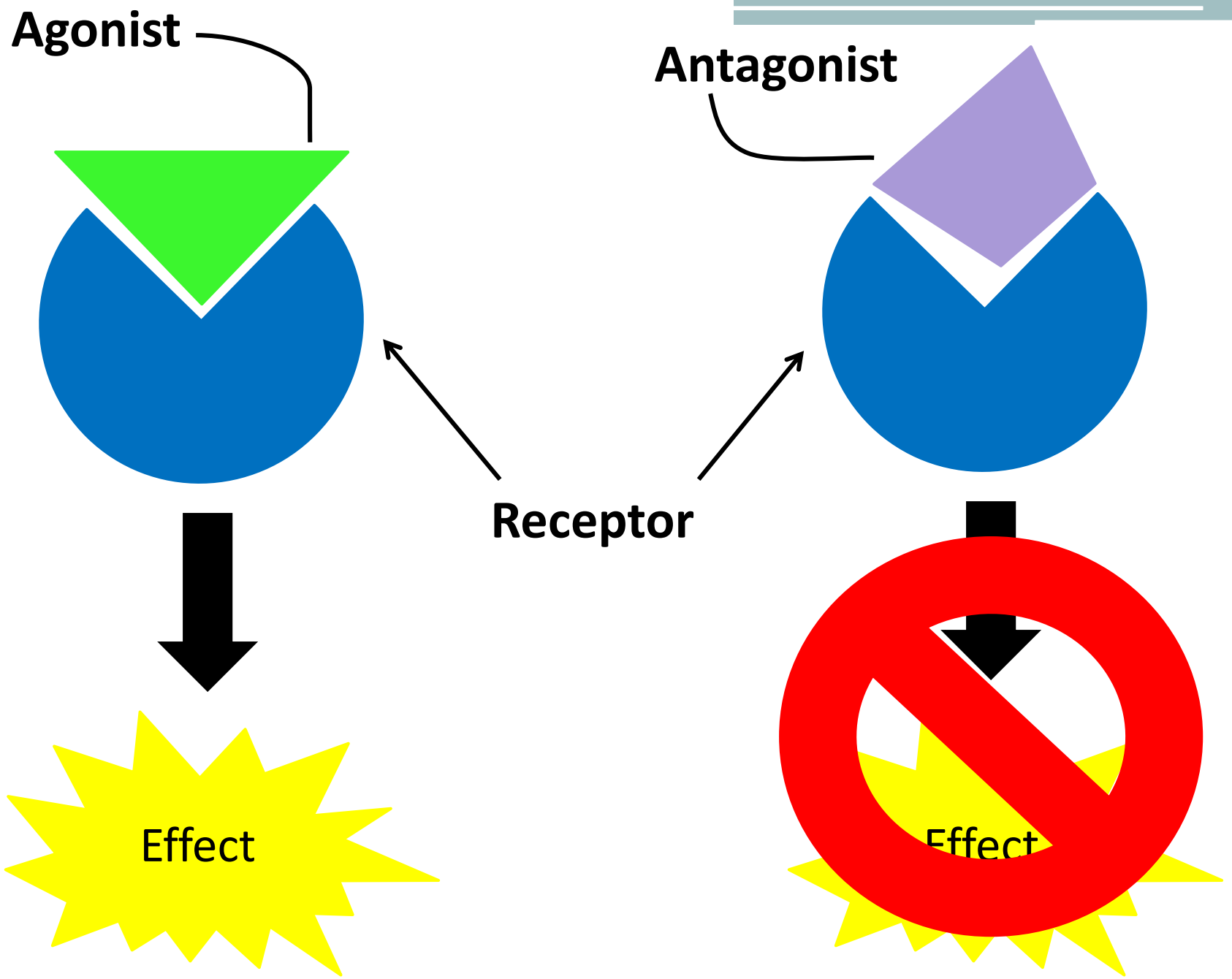
Receptor, Agonist, and Antagonist

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)

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
- It is **NOT** a symptom of PD, but side effect of some medications used to treat PD


Agonist
Antagonist
Receptor
Effect
Effect

Dopamine Agonists

- Mechanism of action: acts on dopamine receptors; mimics dopamine
- Examples:
  - Pramipexole (Mirapex®)
  - Ropinirole (ReQuip®)
  - Rotigotine (Neupro®)
  - Bromocriptine
  - Apomorphine (Movapo®)

Rotigotine

- Transdermal patch
- Applied once daily (every 24 hours)
  - May help improve adherence
- Application site reactions may occur
  - Switch application sites; the same site should be avoided for 14 days

Dopamine Agonists

- No good data that states one dopamine agonist is better than another at managing motor symptoms
- However, pramipexole, ropinirole, and rotigotine are preferred over bromocriptine
- Bromocriptine is associated with the risk of causing pleuropulmonary and cardiac valve fibrosis

Dopamine Agonists

- Second most effective class of medications used to treat motor symptoms of PD
- Can be used as monotherapy in early PD to control symptoms
- They can also be used as an adjunct to levodopa to help manage motor complications in later PD
  - Can reduce off-time
  - May lead to a decrease in levodopa dose
  - *Preferred: pramipexole, ropinirole, and rotigotine*

Dopamine Agonists

- Associated with less motor complications (e.g. wearing off, on-off phenomenon, and dyskinesia) than levodopa
- However, dopamine agonists are associated with more side effects

Side Effects of Dopamine Agonists

- Nausea
- Orthostatic hypotension
  - i.e. lightheadedness when standing up from sitting or lying down position
- Drowsiness
- Leg edema (swelling)
- **Sudden sleep attacks**
- **Hallucinations**
- **Impulse control disorders**
  - Gambling, excessive shopping, binge eating, hypersexuality

Counselling Points

- In regards to treatment initiation:
  - Start at a low dose, and gradually increase to clinically effective dose
    - Helps minimize side effects, and allows for tolerance to develop
- In regards to side effects:
  - Family members, care partners, and/or caregivers should also be made aware of the potential side effects
  - If impulse control disorders develop, the dopamine agonist will be either decreased or discontinued by the physician

Apomorphine

- Subcutaneous injection
- Used in individuals that are still experiencing “off” episodes even after the PD therapy has been optimized
  - Wearing off and unpredictable on-off fluctuations
- Used **during** an “off” episode
  - Used intermittently – rescue medication
- Onset of action: 10 minutes
  - Effects last for approximately 90 minutes

MAO-B Inhibitors

- Mechanism of action: helps prevent dopamine degradation in the brain, thus increasing its concentration
- Examples:
  - Rasagiline (Azilect®)
  - Safinamide (Onstryv®)
  - Selegiline

MAO-B Inhibitors

- May be used as monotherapy to treat mild symptoms in early PD
  - Rasagiline and selegiline
- Rasagiline may also be used as an adjunct to levodopa in later PD to decrease off-time
- Safinamide is indicated as add-on therapy only (i.e. not used as monotherapy) to levodopa to help decrease off-time

- → Rasagiline and safinamide helps with wearing off

Side Effects of MAO-B Inhibitors

- Insomnia
- Hallucinations
- Nausea
- Dyskinesia
- Orthostatic hypotension*
  - *High blood pressure more common with safinamide

Tyramine and MAO-B Inhibitors?

Question:

Can taking a medication such as rasagiline inhibit the breakdown of tyramine, leading to high levels of tyramine in the body, causing a severe increase in blood pressure?

(Tyramine is a compound that can be found in high amounts in certain foods such as sauerkraut, aged cheeses, and cured meats)

Tyramine and MAO-B Inhibitors?

Answer:

- Monoamine oxidase (MAO)
  - Two subtypes: MAO-A and MAO-B
- When MAO-B inhibitors are used at the recommended doses for PD, dietary tyramine restriction is not required
- Drug monograph for Azilect (rasagiline) states that foods with very high amounts (i.e. greater than 150 mg) of tyramine should be avoided due to the potential of causing a severe increase in blood pressure even when taken with recommended doses of Azilect

Be mindful and remember moderation

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
- There is a combination tablet of levodopa/carbidopa/entacapone (Stalevo®)

COMT Inhibitors

- Used to help manage wearing off
  - Entacapone may decrease off-time by 1 to 1.5 hours per day
- Levodopa dosage may need to be reduced when entacapone started if dyskinesia occurs
  - Discussion with physician

Side Effects of COMT Inhibitors

- Nausea
- Diarrhea
- Urine discolouration (orange/brown)
  - Harmless
- Dyskinesia

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 of Anticholinergics

- 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 of Amantadine

- Confusion
- Insomnia
- Dizziness
- Hallucinations
- Ankle edema
- Livedo reticularis

Take Home

- Dopamine agonists and MAO-B inhibitors can also be used to treat the motor symptoms of PD
- The different classes of medications each have a unique mechanism of action, and when used together can help effectively manage PD symptoms
- No two people are alike when it comes to Parkinson's, which highlights the importance of the medication regimen being tailored to each individual
  - Webinar #3: Medication Management
    - Friday, June 26th from 2:00 pm to 3:00 pm

Thank you!

Questions?

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