Best Medical Treatments for Parkinson's disease

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What is Parkinson's Disease (PD) ?

- Progressive neurologic disorder that results from the loss of specific cells in your brain that produce a chemical called dopamine

- Loss of dopamine leaves patients less able to control their movement
  - Slow
  - Stiff
  - Shaky

How is PD Treated?

- Since most symptoms of PD are caused by the lack of dopamine, many PD drugs are aimed at either temporarily replenishing or mimicking the effects of dopamine

- Debate over how and when to start
  - Depends on age of the patient, severity of PD and the presence of other co-morbidities
  - Most important factor:
    - » The need to maintain quality of life/ability to carry out activities of daily living

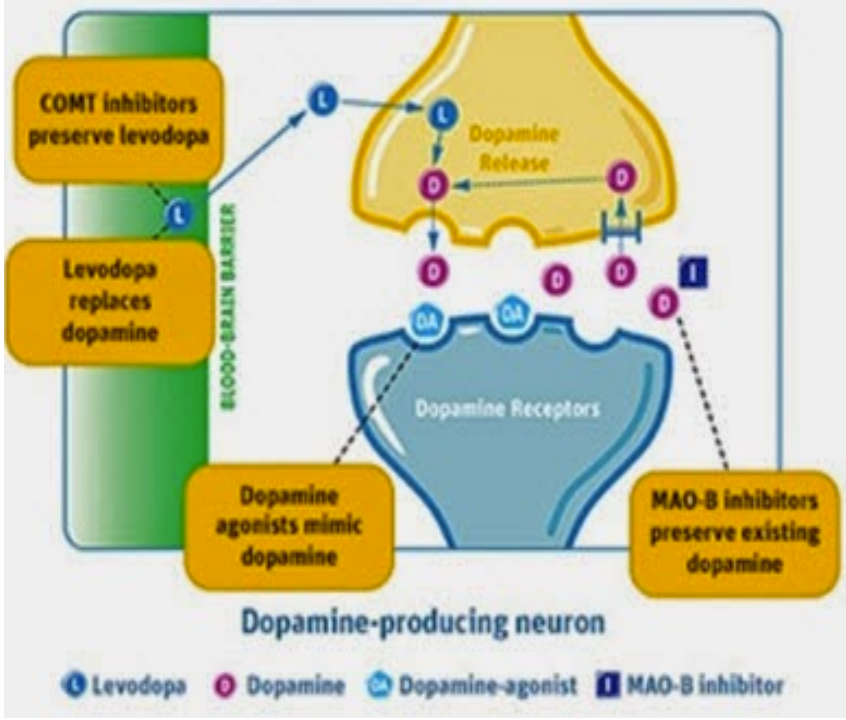
Treatment does not = Medication

- Supportive therapies
  - Exercise
  - Physical therapy
  - Occupational Therapy
  - Speech Therapy

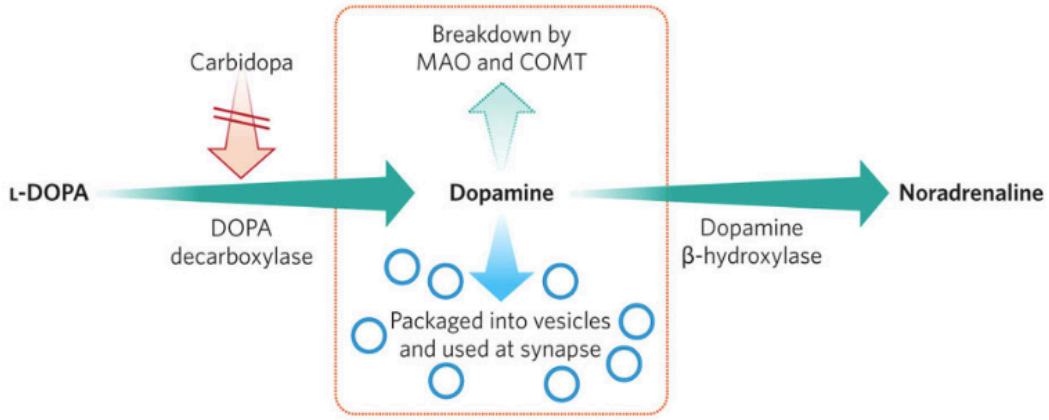
- Pharmacotherapy (medications)

How Do PD Medications Work ?

- Dopaminergics
  - Levodopa
  - Dopamine Agonists
  - MAOB Inhibitors
  - COMT Inhibitors
- Others
  - Amantadine
  - Trihexiphenidyl



Levodopa

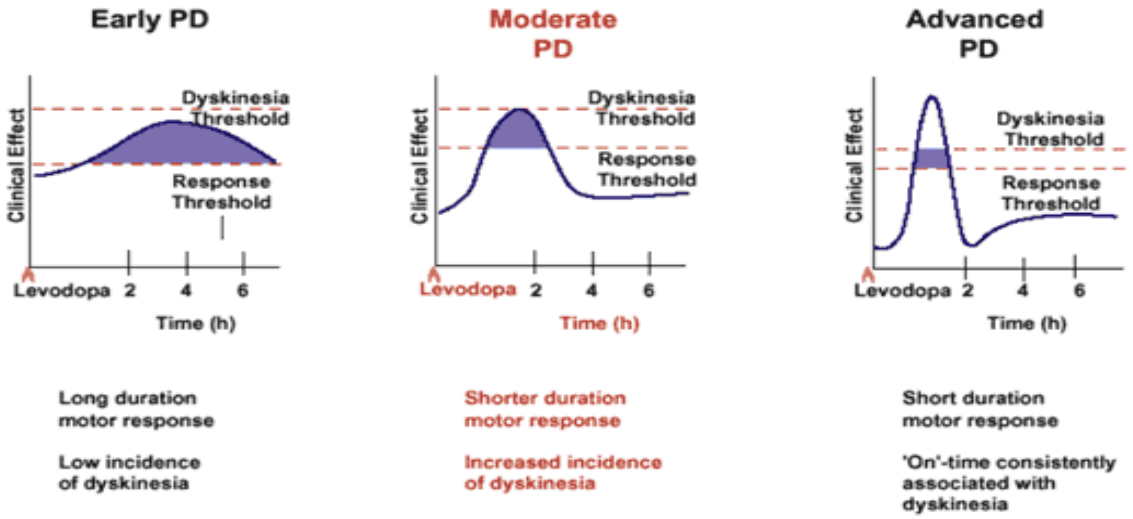


- The most efficacious drug therapy at all stages of PD
- Combined with carbidopa to slow its breakdown before it reaches the brain, therefore reducing side effects and increasing its availability
- In the US, known as “sinemet”
- Exists in immediate release and controlled release preparations

Side effects of L-dopa

- Short term: nausea, sleepiness, lightheadedness, confusion, hallucinations

- Long term: motor fluctuations and dyskinesia



Treatment of Motor Fluctuations

- Fluctuations can be reduced by maximizing "On" time
  - Increase frequency of levodopa administration
  - Dopamine agonists
  - Extend the half life of levodopa by slowing the breakdown of dopamine
    - » MAOB inhibitors
    - » COMT inhibitors (entacapone, tolcopone)

Dopamine Agonists

- Pramipexole (Mirapex), Ropinirole (Requip), Rotigotine (Neupro), Apomorphine
  - Mimic the effect of dopamine in the brain
  - Available in immediate and controlled release formulations
  - Can be used alone or in combination with levodopa
  - Less effective than levodopa

Dopamine Agonists

- Side effects:
  - Nausea, lightheadedness, leg swelling, hallucinations
  - Daytime sleepiness & sleep attacks (~ 5%)
  - Impulse control disorders (~10-15%)
    - » Compulsive gambling, shopping, eating or hypersexuality

L-dopa vs DA

DA Pros

- Less motor fluctuation and dyskinesia
- No dietary restrictions

Levodopa Pros

- More effective
- Cheaper
- Fewer side effects
  - ICD
  - Leg swelling
  - Sleep attacks

Long term disability and quality of life are similar whether started on initial levodopa or dopamine agonist

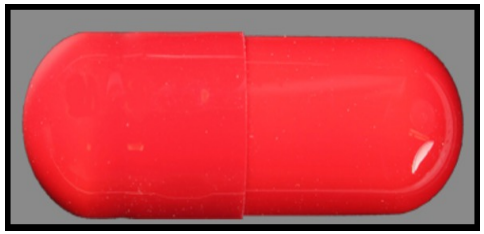
MAOB-Inhibitors

- Selegiline (Eldepryl, Zelapar), Rasagiline (Azilect)
  - Inhibit an enzyme that breaks down Levodopa, thus extending its action
  - Used alone or in combination with Levodopa
  - Mild symptomatic motor improvement

MAOB-Inhibitors

- Side effects:
  - Restlessness, agitation, insomnia
  - Drug and food interactions
    - » Serotonin Syndrome
      - – Antidepressants
      - – Cold Medication
      - – Foods high in tyramine
        - » Cheeses, smoked meats, fermented sausages, wine

Amantadine



- Most useful in early stages
  - Tremor, fatigue, bradykinesia
- In later stages
  - Reduction of dyskinesia
- Side effects:
  - Decrease concentration, agitation, hallucinations, dry mouth, blurred vision
  - Chronic use: livedo reticularis, leg swelling

Anticholinergics

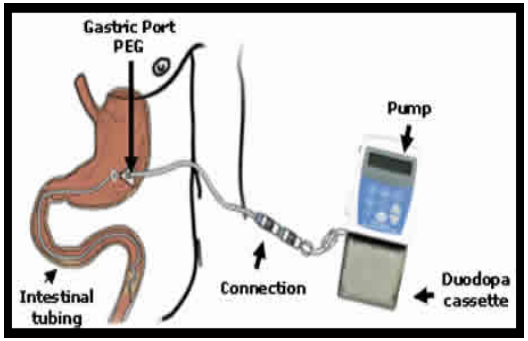
- Trihexyphenidyl (Artane)
  - Most useful for
    - » Tremor in early stages
    - » Dystonic (cramping) symptoms
    - » Younger onset
- Side effects:
  - Dry mouth, blurred vision, drowsiness, confusion, agitation

New Treatments for PD
Rytary

- Carbidopa/levodopa ER
- FDA approved in January 2015
- Contains IR & ER beads
- Designed to provide longer lasting benefit for patients
- When compared to standard c/l
  - Less frequent medication dosing (3.6 vs 5 doses per day); however more total pills/day
  - The daily total “off time” improved over an hour each day
  - Caution with long term effects (dyskinesia)

Duopa

- Continuous intestinal carbdiopa/levodopa infusion
- Available in Europe since 2004
- FDA approved in January 2015 for patients with advanced stage PD
- When compared to standard medical therapy
  - Total daily “off” time improved by 2 hours
- Draw backs
  - Need for small feeding
  - Complications related to the tube or the pump are common
  - Pump requires changing dopamine cassette once or twice per day
  - Not been compared against DBS



Common Misperceptions

- "I heard/read that levodopa stops working after 5 years"
  - » No
- "I heard that levodopa is bad for you or speeds up progression"
  - » Levodopa therapy is not toxic & does not accelerate Parkinson's disease progression
  - » In some patients, it may be the preferred drug
  - » All therapies should be considered

Conclusion

- Each patient experiences a different range of symptoms
  - Not all treatments are of equal value to all patients
- Work closely with your treatment team to find a regimen that is right for you