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, tolcapone)
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 carbiopa/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
- Drawbacks
  - 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