Medication Management of Parkinson Disease

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Motor Features of PD and Treatment

The Parkinson’s Complex

- Parkinsonism
- Substantia Nigra
- Pons
- Basal Forebrain
- Medulla
- Amygdala
- Hypothalamus
- Olfactory Bulb
- Spinal Cord (intermediolateral column)
- Peripheral Autonomic Nervous System (heart, intestinal track, bladder)
- Neocortex
- Olfactory Cortex
- Temporal Cortex
Treatment Principles

- Independent function as long as possible
- Individualize therapy
- Prioritize protective therapy
- Promote activity
- Best Rx: combination of meds - lowest dose of each
Treatment Options

• Neuroprotective Rx
  – No definitive evidence
  – Exercise

• Symptomatic Rx
  – Motor & non-motor sx
  – Pharmacological & Surgical

• Restorative - experimental only
  – Remove α-synuclein
Neuroprotective Rx

- Yes? Selegiline, rasagiline, exercise
- Current studies: inosine, isradipine, others
- No: Co Q, creatine
- ?? DBS
Exercise in PD

• The value of exercise in PD cannot be overstated as a first & foremost therapy
  – cardiovascular benefits, improved activity, better mood & sleep
  – Stabilized function compared “non-exercisers”
  – Focus on flexibility

Brain Power!
Drug Classes in PD

- **Dopaminergic agents**
  - **Levodopa** (SINEMET, STALEVO, RYTARY, DUOPA)
  - **Dopamine agonists** (MIRAPEX, REQUIP, NEUPRO, APOKYN)

- **COMT inhibitors** (COMTAN)

- **MAO-B inhibitors** (selegiline, AZILECT)

- **Anticholinergics** (ARTANE)

- **Amantadine** (SYMMETREL)
Sites of Action of PD Drugs

- Levodopa
- Amantadine
- Selegiline
- Rasagiline
- Dopamine agonists: pramipexole, ropinirole, rotigotine, apomorphine
- Trihexyphenidyl

- BBB: carbidopa, benserazide, entacapone
Levodopa - Cornerstone of Treatment

- Most effective med
- Prolongs survival
- Combined with carbidopa
- Protein in diet interferes with delivery to brain
- Forms: regular, long-acting & dissolvable
Levodopa – induced motor complications

- More likely in young person
- Want to avoid pulsatile stimulation
- Fluctuations
  - End of dose ‘wearing off’
    - ‘off’ vs. ‘on’
  - Unpredictable ‘offs’
  - Sudden ‘offs’
- Freezing of gait
- Dyskinesias
Treatment Strategy

• Initial therapy
  – Based on physiological age, ~ 70 yo
  – DA agonist in young person
  – Levodopa in older person

• Use DA agonist & other meds
  – to Rx residual symptoms
  – Smooths out response

• ≤ 400 mg levodopa

• Use long acting levodopa preparations
Entacapone

- Potentiates levodopa
- Extends benefit of each LD dose
- Only prescribe with levodopa
- Max: 8 tabs per day (200 mg each)
Stalevo: carbidopa / entacapone / levodopa

- **Dosage:**
  - Stalevo 50: 12.5/200/50
  - Stalevo 100: 25/200/100
  - Stalevo 150: 50/200/150

- *Do not take more than one tablet at a time*
- Cost is similar to taking them separately
Rytary

- Approved in January 2015
- Capsule contains
  - immediate & variety of extended release beads
- Standard switching regimens
- Still take 3 – 4 x daily
- Can be sprinkled
Duopa

- Approved January 2015
- Carbidopa/levodopa gel
- Tube is placed in stomach to deliver medication
- More stable blood levels of levodopa
- Improves motor symptoms, QoL, dyskinesia
- Safe & feasible for up to 16 years
- Alternative to DBS
Duopa
Dopamine Agonists

- Pramipexole (MIRAPEX)
- Ropinirole (REQUIP)
- Rotigotine (NEUPRO)
- Apomorphine (APOKYN)
Apomorphine Injection (APOKYN)

- Rapid “off” period rescue
  - 0.1 to 0.6 ml; pen injection system
- Treatment of unpredictable, frequent severe ‘offs’
- Works in 10 min, lasts 45 min
- Pretreat & perhaps continue anti-nausea med
- Initiate with nurse home visit; use specialty pharmacy
Apomorphine infusion

- Subcutaneous – since 1987
- Daily infusion 16 hrs/dy
- Reduces off time by 58%
- Less dyskinesias

Manson et al. Mov DO 2002;6:1235-1241
**Dopamine Agonists**

- Directly stimulate dopamine receptors
- Bypasses dopamine (sick) neurons
- No problem with protein intake
- Longer half-life than levodopa
- Do not cause dyskinesia
Dopamine Agonists: Common Adverse Effects

- Nausea, vomiting
- Dizziness, postural hypotension
- Headache
- Confusion, hallucinations, paranoia
- Compulsive & impulsive behavior*
- Excessive daytime sleepiness*
"Punding" is a stereotypical motor behavior in which there is an intense fascination with repetitive handling and examining of mechanical objects, such as taking apart watches and radios or sorting and arranging of common objects, such as lining up pebbles, rocks, or other small objects.
Excessive Daytime Sleepiness

- Sudden, irresistible onset of sleep
- With (or without) warning signs
- DA agonists >>> levodopa
- Driving caution
- Dose adjustment, switching, adjunct medication
• Inhibits dopamine metabolism
• May be neuroprotective
• Dosage:
  – Selegiline (ELDEPRYL) 5 mg at breakfast and lunch
  – Rasagilnine (AZILECT) 1 mg in AM
  – ZELAPAR - dissolves
• Side effects: insomnia, hallucinations, agitation
• Potential interactions with antidepressants & narcotics
• Demerol interaction: fatal?
Anticholinergics

- Avoid in elderly
- Balances with dopamine level in brain
- Effective mainly for tremor and rigidity
- Common agents (Start low, go slow)
  - Trihexyphenidyl: 2-15 mg/day
  - Benztropine: 1-4 mg/day
- Side effects:
  - ↓ ST memory, dry mouth, constipation, urinary retention, delirium, confusion, hallucinations
Amantadine

- Antiviral agent; Activating
- Also ↓ dyskinesias
- Multiple mechanisms
- Side effects – swelling, skin change
- 100 - 400 mg/day
- Renally excreted – watch for toxicity
Physical Therapy: Goals

- Maximize independence, safety, function
- Maintain or increase activity level
- Prevent falls:
  - optimize balance & gait
- Prevent frozen shoulder:
  - ROM exercises
Besides motor symptoms, there is effective treatment for:

- Depression
- Anxiety
- Drooling
- Sleep disorders
- Constipation
- Urinary sx
- Light-headedness
- Excessive sleepiness
- Soft speech
- Thinking problems
- Sweating
- Restless legs syndrome
- Impotence
- Hallucinations, delusions
- Seborrhea
- Difficulty with daily tasks
In The Pipeline

- Apomorphine subcutaneous pump
- Accordion pill levodopa preparation
- Inhaled levodopa
- Levodopa pump patch
- Long acting amantadine for dyskinesia
- Potentially neuroprotective
  - Phenylbutyrate
  - Isradipine
  - Inosine

And A LOT More!
Lastly!

• Always bring a list of your meds & your actual meds to clinic
• NPF has a “when you are hospitalized” checklist (awareincare.org)
• Keep a log of medications you have tried for PD, depression, sleep, etc. & your reactions
The Surgical Treatment of Parkinson’s Disease