Parkinson's Disease: Diagnosis and Treatment

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Learning Objectives

1. Distinguish Parkinson’s Disease from other conditions in patients who exhibit similar signs and symptoms, recognizing when referral is appropriate.
2. Select appropriate treatment strategies for patients with Parkinson’s Disease, including an assessment of medication and non-pharmacologic therapy use.
3. When indicated, coordinate referral to a neurologist and follow-up care for patients with Parkinson’s disease.
4. Establish collaborative care plans with patients and care givers, emphasizing adherence to prescribed medication and therapies.

Audience Engagement System

Step 1: Step 2: Step 3

CME Activity: Acute Coronary Syndromes, Broken Hearts and Silent Pains
PD: A Progressive Movement Disorder

Dopamine Deficiency …
- Dopamine facilitates/promotes motor activity
- Low levels require greater exertions for movement
- Dopamine depletion results in hypokinesis, an overall reduction in motor output

Parkinsonism

- Primary PD is idiopathic
  - Genetic etiology?
  - Is depression a prodromal sign or causal factor?
- Secondary parkinsonism w/known cause
  - Drug induced
  - Pesticide exposures/Agent Orange
  - Head trauma

Epidemiology

1,000,000 cases in US
- Incidence 10-15/100,000
- 100K deaths/year
  - Men:women (3:2)
  - 70 yrs average age of diagnosis
    - 1% over age 60, 10% over age 80

Pre-motor features

Disorders of
- Smell
- Sleep
- Speech
- Autonomic

Changes in
- Memory
- Mood
- Sensory

“Shaky, Slow, Stiff and Stumbling…”

4 cardinal motor symptoms
- Resting Tremor
- Bradykinesia
- Rigidity
- Postural instability (late finding)
<table>
<thead>
<tr>
<th><strong>Shaky: Tremor 4-6 hertz</strong></th>
<th><strong>Slow: Bradykinesia</strong></th>
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<td>(cycles per second)</td>
<td></td>
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<td>Most well-known symptom</td>
<td>Commonly disabling in the early stages</td>
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<tr>
<td>• Pill-rolling</td>
<td>• Problems with fine motor tasks</td>
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<tr>
<td>• Resting tremor</td>
<td>(writing, sewing, dressing)</td>
</tr>
<tr>
<td>– Disappears with voluntary movement and sleep</td>
<td>• Decreased blink rate (staring effect)</td>
</tr>
<tr>
<td>• 30% no tremor at onset</td>
<td>Modified by activity or emotional state</td>
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<tr>
<td>– Most develop as disease progresses</td>
<td>• Some barely able to walk yet may run if frighten</td>
</tr>
<tr>
<td>• Single arm or leg at onset, becoming bilateral</td>
<td>• Generally less difficulty when an external cue provided</td>
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<tr>
<th><strong>Stiff/Rigidity</strong></th>
<th><strong>Stumbling/Postural Instability</strong></th>
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<tr>
<td>Stiff joints</td>
<td>Late stages with impaired balance/falls</td>
</tr>
<tr>
<td>– lead-pipe rigidity</td>
<td>• Diminished arm swing</td>
</tr>
<tr>
<td>– cogwheel rigidity</td>
<td>• Retropulsion, inability to stop</td>
</tr>
<tr>
<td>• Asymmetrical, neck and shoulder muscles prior to face and extremities</td>
<td>• Gait festination - rapid shuffling steps and a forward-flexed posture when walking</td>
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<td>• With progression, affects the whole body and reduces the ability to move</td>
<td></td>
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<td>• Joint pain is often an initial manifestation of PD</td>
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<tr>
<th><strong>Sir William Richard Gowers (1886)</strong></th>
<th><strong>Non-Motor Signs/Autonomic Dysfunction</strong></th>
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<td></td>
<td>Can occur years before diagnosis</td>
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<tr>
<td></td>
<td>• Orthostatic hypotension, excessive sweating</td>
</tr>
<tr>
<td></td>
<td>, urinary incontinence &amp; altered sexual function</td>
</tr>
<tr>
<td></td>
<td>• Constipation and gastric dysmotility</td>
</tr>
<tr>
<td></td>
<td>• Double vision</td>
</tr>
<tr>
<td></td>
<td>• Impaired smell, paresthesias</td>
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AES QUESTION:
Parkinson's Disease is diagnosed by:
1. Specific diagnostic findings on MRI
2. Characteristic EEG tracings
3. Spinal fluid analysis
4. Brain biopsy

So, how do we diagnose PD?
Listen to our patients!
• Recognize clinical features
  – Pre-motor, motor, non-motor
  – UK Brain Bank Criteria

UK PD Society Brain Bank Criteria
Bradykinesia plus either rigidity, resting tremor, or postural instability
  • With 3 or more of the following required
    – Unilateral onset/asymmetry of motor symptoms
    – Progression over time
    – Response to levodopa for at least five years
    – Clinical course of at least ten years
  • Other possible causes ruled out

What other DX tests are needed?
NONE!
  – MRI?
  – DaT-SPECT?
Definitive Dx requires brain biopsy…

Typical symptomatic progression…

Treatment Considerations
Pharmacologic Treatment

- Initiate when symptoms interfere with life
- Drug selection depends on:
  - predominant symptom
  - disease severity
  - side effect profile
  - socioeconomic situation

AES QUESTION:
The best treatment for PD is to use:
1. Dopamine replacement
2. Dopamine agonists
3. MAO-B inhibitors
4. COMT inhibitors
5. Glutamate antagonists

Dopamine Replacement

Carbidopa/Levodopa (Sinemet, Parcopa)
- Provides natural/regulated effect
- Minimal drug interactions/contraindications
- Side effects
  - nausea, orthostatic hypotension, hallucinations, disrupted sleep, dietary interactions

Using Carbidopa/Levodopa

- Give enough Carbidopa
  - Start with 25/100 tid with meals
- Start with immediate release
- Adequate time to assess response
  - Slowly titrate to clinical effect

Mechanism of Action….
Dopamine Agonist

- Ropinirole (Requip)
- Pramipexole (Mirapex)
- Rotigotine (Neupro patch)
- Apomorphine subq (Apokyn)

Dopamine agonists

- Improve motor function
  - Less potent than L-dopa
  - Delay motor fluctuations / dyskinesia
- Side effects
  - Nausea, dizziness, postural hypotension, edema
  - Drowsiness with sudden sleep attacks
  - Impulse control disorders

Impulse Control Disorders

- Pathologic Gambling, Sexual Behavior, Compulsive Shopping
- 4% - 8% in some series
- Rare with L-dopa Monotherapy
- Reversible

MonoAmine Oxidase B inhibitors

Monoamine oxidase B inhibitors (MAO-B inhibitors) are used to treat Parkinson's disease by increasing the levels of dopamine in the brain. They work by inhibiting the enzyme monoamine oxidase B, which breaks down dopamine.

Selegiline / Rasagiline / Zelapar

- Monotherapy for motor symptoms
- Delay need for levodopa
- But more adverse effects and less effective than levodopa

Catechol-O-MethylTransferase inhibitors

Catechol-O-MethylTransferase (COMT) inhibitors work by reducing the breakdown of dopamine in the brain, which can help to improve motor symptoms in Parkinson's disease.

In summary, dopamine agonists are used to improve motor function by increasing dopamine levels in the brain, while also reducing the side effects of levodopa. Impulse control disorders are rare with L-dopa monotherapy and reversible. Selegiline, rasagiline, and zelapar are used as monotherapy or to delay the need for levodopa, while COMT inhibitors work to increase dopamine levels by reducing its breakdown.
Tolcapone (Tasmar)
Entacapone (Comtan/Stalevo)
Add to L-dopa when it appears to be wearing off before next dose
– Tolcapone associated with liver damage
– Entacapone marketed alone or in combination with L-dopa

Other Agents….
NMDA Antagonist
– Amantadine
  • potentiates dopamine effect
  • helpful to treat dyskinesia
Anticholinergics
– Trihexyphenidyl
– Benztropine (Cogentin)

What to Do?
• Younger than 65 and healthy
  – Consider Agonist initial therapy
• Older and if cognitive impairment or co-morbid medical problems
  – Use L-Dopa
• Financial issues
  – L-Dopa

Motor Fluctuations/Dyskinesia…
Motor fluctuations
– “On” time (less tremor/improved gait/balance)
– “Off” time (freezing/anxiety/sweats)
  • Medication timing
Dyskinesia
– Develops with dopaminergic drugs over time
– Involuntary flowing movements

• L-Dopa & Agonists and are both reasonable choices for initial therapy
  – But large randomized mobility trial favors L-Dopa
• L-Dopa possesses advantages for symptomatic treatment
• The long-term benefits of dopamine agonists are hypothetical

The Bottom Line …
• L-Dopa & Agonists and are both reasonable choices for initial therapy
• L-Dopa possesses advantages for symptomatic treatment
• The long-term benefits of dopamine agonists are hypothetical
• Speech and Swallowing Problems
• Postural Instability, Gait Problems & Falls
• Autonomic Insufficiency
• Constipation
• Sleep Disorders
• Hallucinations
  – Harbinger of dementia (30-60%)
  – A bad prognostic predictor
Cholinesterase Inhibitors?

2014 meta-analysis
• Slow cognitive decline
• No benefit in falls prevention

Interdisciplinary Allied Health Team

• PT, OT, Speech, Neuropsych, Social Worker
  – Caregiver
• Role of team for treating
  – Motor complications
    • rigidity, deconditioning, tremor, speech
  – Non-motor complication
    • drooling (speech therapy)
    • depression, anxiety, psychosis
    • constipation
  – Caregiver needs – burden of disease

Progression……

1-2 YEARS 3-5 YEARS 4-6 YEARS 5-7 YEARS
ONSET DIAGNOSIS HONEYMOON COMPLICATIONS COGNITIVE DECLINE DEATH

Practice Recommendations…

• Recognize the early signs for PD
• Utilize local PT/OT resources
• Treat when symptoms interfere with life
• Identify local/regional movement specialist
• Appreciate the importance of counseling

Questions
THANK YOU!

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