
INTRO TO THE TREATMENT & MANAGEMENT OF PARKINSON'S DISEASE

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Please consult your doctor or pharmacist

DEFINITION of Parkinson's Disease (PD)

- A slowly progressive, degenerative Central Nervous System (CNS) disorder.
- Characterized by:
 - 1) slow and decreased movement
 - 2) muscular rigidity
 - 3) resting tremor, and
 - 4) postural instability.

Please consult your doctor or pharmacist



ETIOLOGY

- One of the most common neurodegenerative disorders in patients over 65yrs; prevalence of approximately 1 to 2 /100 people.
- Manifests after approx. 80% of striatal dopamine or 50% of nigral cells have been lost in the brain.
- With the exception of a small portion of patients with PD inherited genetically, etiology is unknown

SIGNS & SYMPTOMS

- Tremor (at rest); Muscle pain/stiffness
- Movement problems: bradykinesia (slowed), hypokinesia (decreased), and akinesia (unable to initiate movement).
- Posture and gait problems (walking-shuffling)
- Reduced ability in speech, difficulty swallowing, very small handwriting, drooling.
- Other related conditions: dementia (memory or cognitive issues), depression, pain syndromes (neuropathies), insomnia and fatigue.

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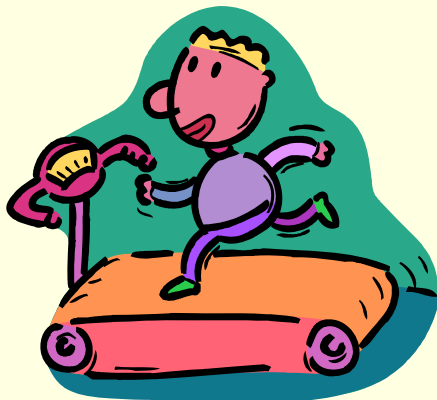
GOALS OF THERAPY

- To start treatment only when symptoms interfere with one's social or economic life.
- To reduce symptoms to a level that allows the patient to perform usual activities.
- To balance benefit against risk (side effects) as disease advances.
- To manage side effects appropriately

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NON-PHARMACOLOGICAL CHOICES

- It is important to maintain independence and deal with emotional stress as it arises.
- Rehab services – advice on safety, posture, energy conservation, speech, swallowing, and adaptive devices (aids).
- Moderate exercise is recommended (physio)
- Joining local support groups for Parkinson's.



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PHARMACOLOGICAL CHOICES



- Currently, drugs available for treatment of PD offer only *temporary* relief from symptoms; they do not arrest or reverse the neuronal degeneration caused by the disease.
- Essentially, we want to replenish the dopamine (DA) in the CNS/brain in order to send the proper messages to the muscles.
- DRUGS = Various mechanisms of action.

Please consult your doctor or pharmacist

IMPORTANT CONCEPTS IN MEDICATION MANAGEMENT

- As needs of an individual change, so do the medication needs. Re-evaluation is key.
- ‘Start low’ and ‘go slow’ – must be patient, as effects of the treatment may not be immediate.
- Deciding ‘when’ or ‘how’ to treat depends on each individual – do not compare to another person.
- Certain meds may not be tolerated, while others may have a more favorable response.



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1) LEVODOPA

LEVODOPA -----> **DOPAMINE**
(metabolic precursor)

- With a peripheral decarboxylase inhibitor*:

Levodopa/Carbidopa* ... **Sinemet® (Reg/CR)**

Levodopa/Benserazide* **Prolopa®**

- Many strength variations available
- Has been considered the 'gold-standard' for many years

Please consult your doctor or pharmacist

LEVODOPA (CONT'D)

Ideal to start this agent only when absolutely necessary (i.e. >70 years, severe disease) – however, can be done sooner (patient dependent)

Effective in improving motor function and Activities of Daily Living (ADL).

Good for improving *most* symptoms; *except* for resting tremor and balance problems.

Relief provided only *symptomatic* and lasts only while drug is *present* in the body.

Usually start with immediate/regular release; however, there may be less side effects with CR formulation

Overall dose of levodopa can be decreased by 60-80% with use of decarboxylase inhibitors (e.g. Sinemet)

LEVODOPA (CONT'D)

- Gradual increases when treatment is 1st initiated
- Most patients require 400-1000mg/day of levodopa in divided doses (every 2-5hrs) w/ at least 100mg of carbidopa.
- **Ideal** is to 'Take on an Empty Stomach' 1 hour before or 2 hours after a meal.
- **However, due to nausea side effect, can be taken with a snack** (containing little/no protein) waiting a **MINIMUM of 30 min before or after mealtime.**
- The protein interaction can cause a 'delayed response' of the Levodopa (caution).
- Side effects: nausea/vomiting, motor complications (dyskinesias/'on-off'effect), postural hypotension, hallucinations, confusion, somnolence/SIAS etc.

Please consult your doctor or pharmacist

Managing ‘on-off’ or ‘freezing’ effects:

- Shorten intervals between doses; crushing ½ to 1 tab CR formulation or using immediate release tablet to overcome delay btw doses.
- Can help to provide relief within 20-30 min
- Switching from immediate release only tablets to CR formulation.
- Some patients may require both formulations
- May need to add a low dose dopamine agonist, or other suitable alternative if the above does not work.

2) DOPAMINE AGONISTS

- **Ropinirole** (Requip®), **Pramipexole** (Mirapex®) – (D2/D3) – newer agents (generics now available)
- **Bromocriptine** (D2) and **Pergolide** (D1/D2) – older ergot derivatives – (generally less used due to side effects)

-Mechanism of action: These agents directly activate or stimulate dopamine receptors in the basal ganglia (brain).

-No dietary restrictions as with levodopa

-NB in improving motor and ADL function (however, somewhat less effective than levodopa)

Side effects: similar to levodopa; plus -ankle edema, *pleural/pericardial fibrosis (rare); dyskinesias, but no 'on-off' effects (etc).

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DOPAMINE AGONISTS (CONT'D)

■ WHEN TO USE THESE AGENTS:

- Particularly important in the later stages of disease when response to levodopa diminishes, or the 'on-off' effects are prominent (longer half lives).
- Therapy may be initiated w/ these agents in patients w/ earlier disease onset (younger patients) because they tend to have a longer disease course (higher risk of motor complications) and levodopa can be reserved for later if possible.
- Not typically used as initial therapy in pts > 65 yrs*
- Patient does not already have compulsive habits with gambling, shopping or other (caution as this may be a side effect).

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3) MONOAMINE OXIDASE INHIBITORS (TYPE B)

- **Selegiline** (Deprenyl®) – MAO-B inhibitor
- Used as an initial treatment in some pts as it is thought to slow the neurodegenerative process and delay the need to use levodopa by about 1 year (not proven)
- Can be used as an add-on agent as well in some cases
- Provides modest benefits in motor function.
- Mechanism of action: prevents oxidative metabolism (breakdown) of dopamine (therefore prolongs effect of DA).
- Dose: 5-10mg/day
- Side effects: dyskinesias, confusion, insomnia, dizziness, dry mouth & nausea (re: prolonged levodopa) etc.

MONOAMINE OXIDASE

INHIBITORS (TYPE B) – cont'd

- **Rasagiline** (Azilect®): New MAO-B inhibitor (similar to selegiline)
- May also have neuroprotective effects and can be used in early disease onset.
- Drug/Drug and Drug/Food Interactions:
- Watch with cough and cold remedies – best to avoid DM and D products; Pseudafed PE and anything with pseudoephedrine
- Avoid other antidepressant agents
- Avoid meperidine (Demerol) for pain
- Watch with 'tyramine' consumption – beer, red wines, aged cheeses and meats (etc)

Please consult your doctor or pharmacist

4) ANTI-CHOLINERGIC AGENTS

- **Benztropine** (0.5 – 2mg 3x/day)/ **trihexyphenidyl** (2 – 5mg 3x/day)/ **procyclidine** (2.5-5mg 3x/day)
- Helpful with *tremor*, sometimes improves *rigidity*.
- Decreases Acetylcholine (Ach); relative increase in Dopamine (DA) by achieving correct balance in brain
- A legitimate 1st choice for younger patients (<60 ideal); when tremor is affecting work performance; good cognitive function
- Also considered as ‘add on’ therapy; not usually a good choice for older patients due to side effects unless absolutely necessary.
- **Side effects**: dry mouth*, constipation, urinary retention, confusion, hallucinations, blurred vision
- Consider – drug/drug interactions

Please consult your doctor or pharmacist

5) AMANTADINE (Symmetrel®)

- Useful in treating early, mild Parkinson's for 50% of patients; doses of 100-300mg/day
- **Amantadine** may reduce drug-induced dyskinesia by up to 60% (re: levodopa) and improve 'wearing-off'.
- Can provide modest benefits in motor function and *may* be considered 1st line in some cases (e.g. early disease onset).
- Minimum 2 week trial to determine efficacy
- Little effect on tremor; good for rigidity, bradykinesia and akinesia.
- Side effects: confusion, insomnia, hallucinations, ankle edema

6) COMT INHIBITORS –

- **Entacapone** (Comtan®) is the agent of choice in select patients
- Catechol-O-methyl transferase = COMT
- Inhibit the breakdown (metabolism) of levodopa; therefore acts as useful 'add on' to levodopa (to prolong levodopa effect).
- Good addition to consider when effects of levodopa/carbidopa alone are diminishing.
- 200mg with each levo/carbidopa tablet**
- SE's – diarrhea, dyskinesias, urine changes etc.

Please consult your doctor or pharmacist

New agents or formulations on the horizon:

- Approved by Health Canada in 2007:
Duodopa® – levodopa/carbidopa (new formulation for advanced PD)
- Approved by FDA in 2007/recall – late 2008?
Neupro® – rotigotine – transdermal dopamine agonist

More information to come.....

In the US - STALEVO®

- STALEVO® is a levodopa therapy that also contains entacapone in one product formulation (same thing as adding entacapone to levo/carbidopa).
- Entacapone helps levodopa last longer by blocking a substance in the body called a COMT enzyme. This enzyme breaks down levodopa before it reaches the brain.
- When less levodopa is broken down, more is available to the brain. Increased availability of levodopa may lead to smoother and steadier levels of dopamine in the brain. which may

Please consult your doctor or pharmacist.

INDIVIDUALIZING THERAPY

- Symptoms treated
- Age of onset
- Response to treatment
- Progression of disease state
- Impact of side effects

*Therapy can differ greatly between patients!

MANAGEMENT OF SYMPTOMS & OTHER ADVERSE EFFECTS

- **NAUSEA** – take meds with snack; or *domperidone* 30 min prior
- **ORTHOSTATIC HYPOTENSION** – rise slowly from seated or lying position; *diet* (increase salt & water) or add *fludricortisone*
- **HALLUCINATIONS/DELUSIONS** – safe ‘antipsychotic’ agents (*quetiapine/clozapine*)
- **FLUCTUATIONS IN RESPONSE** – *controlled release formulations/add-on therapy*
- **PAIN** – start with heat/ice; Over-the-Counter meds; *Gabapentin* in some cases may help

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MANAGEMENT OF SYMPTOMS & OTHER ADVERSE EFFECTS (cont'd)

- **DEPRESSION** – support groups; medication use requires *monitoring*
- **CONSTIPATION** – increase water & fibre intake; stool softeners
- **INSOMNIA** – could be due to drugs or disease (*zopiclone* may be helpful; try non-drug things first)
- **FATIGUE** – Modafinil may be useful in some cases
- **DRY MOUTH** – saliva replacement products e.g. Moi-Stir®

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VITAMINS AND MINERALS

- Patients with Parkinson's may be more prone to osteoporosis.
- Recommended to take 1000-1500mg/day of calcium and 800IUs/day of vitamin D.
- These supplementary guidelines are for people who have poor overall intake of dairy products (or those who avoid them).
- A one-a-day vitamin/mineral supplement may also be helpful
- Exercise regularly (e.g. physiotherapy)

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HERBAL THERAPIES

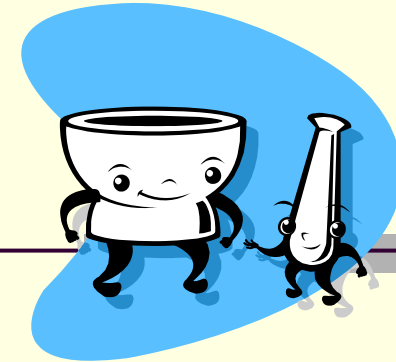
- COENZYME Q10 ??
- VITAMIN B12 ??

****MUST** be used with caution and under physician supervision.

The high amounts needed to show benefit are often very difficult to consume on a daily basis and will come with a cost!

****BUT REMEMBER:** little is known about the possible interactions between herbal products and your PD symptoms or medications!

SUMMARY



- NUTRITION
- EDUCATION (MEDICATIONS, DISEASE)
- VITAMINS & MINERALS/ HERBAL REMEDIES
- PHYSICAL ACTIVITY (PHYSIO)
- LEARNING COPING STRATEGIES (support groups)
- MASSAGE THERAPY – good for the MUSCLES and the MIND!
- TRIAL & ERROR* - WATCH FOR CHANGES IN Side Effects and/or decreased RESPONSE TO TREATMENT and communicate this to your DR ASAP!!

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CONCLUSION



- DO NOT GIVE UP HOPE!!
- LEARN TO GAIN CONTROL OF YOUR SITUATION & LEARN NEW WAYS OF DOING THINGS.
- MAINTAIN POSITIVE ATTITUDE/OUTLOOK
- TAKE ONE DAY AT A TIME!
- KNOWLEDGE IS THE BEST MEDICINE!

Please consult your doctor or pharmacist

REFERENCES

- “A manual for people living with PD” – Parkinson Society of Canada (July 2003)
- An Update on PD – Currents in Practice / Parkhurst Exchange (January 2005)
- Lippincott Pharmacology Text
- Compendium of Pharmaceuticals and Specialties 2004/2005/2006
- Therapeutic Choices - 4th edition

Please consult your doctor or pharmacist