

OVERVIEW OF PARKINSON'S DISEASE TREATMENT OPTIONS



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OVERVIEW

- Common classes of medications
- Common side effects
- What new therapies to expect in the coming years
- What therapies beside medication?

WHAT ARE THE TREATMENT OPTIONS?

Medications



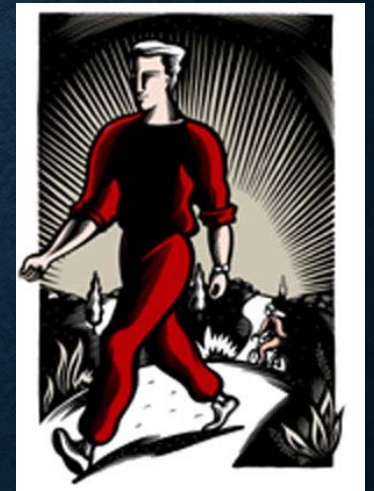
Surgical



Exercise



Healthy diet
Mindfulness



MEDICINE

- Carbidopa/levodopa (Sinemet, Rytary)
- Dopamine Agonists (pramipexole, ropinirole)
- COMT-inhibitors (entacapone)
- MAO-I's (selegiline, rasagiline)

LEVODOPA – “OLDIE BUT GOODIE”

- Also known as..
 - Carbidopa-Levodopa
 - Sinemet
 - L-dopa
- FDA Approved over 35 years ago
- Still the strongest medicine
- Still the safest, best tolerated



LEVODOPA

- How does it work?
 - Brain converts it into Dopamine
- So, restores some of the supply of dopamine to the brain
- Restores some of the dopamine signal to get moving again

SIDE EFFECTS

- Nausea
- Fatigue
- Visual hallucination, illusions
- Dyskinesias (extra movements)
- Orthostatic hypotension (low blood pressure when standing)
- Cognitive changes

RYTARY: (NOT A NEW DRUG! BUT A NEW WAY TO DELIVER AN OLD DRUG!)

RYTARY formulation

An extended-release carbidopa and levodopa treatment

RYTARY is formulated in a 1:4 carbidopa to levodopa ratio.



Each capsule contains both:

- Immediate-release beads.
- Extended-release beads.²

RYTARY:

Indications:

- Significant on- off times or dyskinesia
- Frequent dosing of Sinemet (carbidopa-levodopa)
- Morning off symptoms

Important to know that Rytary is the same as C/L but stays in blood for a longer time (4-5 hrs)

SIDE EFFECTS:

- Nausea
- Orthostatic hypotension
- Hallucinations and delusions

DOPAMINE AGONISTS

- Pramipexole (Mirapex)
- Ropinirole (ReQuip)
- Apomorphine (Apokyn), “rescue”
- Rotigotine (Neupro), “the patch”

AGONISTS

- How do they work?
 - Is not converted to dopamine
 - Instead, it **acts like** dopamine
- Directly activates the part of the brain that starts that signal to get moving.

AGONISTS ADVANTAGES (+)

- Longer acting, smoother response
- Less ups and downs (Fluctuations)
- Less extra movements (dyskinesias)
- Helpful in early PD, in younger patients
- Helpful as adjunct (boost) to Levodopa

AGONIST DISADVANTAGES (-)

- Not as strong as levodopa
- More side effects
 - Sleepiness, hallucinations, lightheadedness, nausea, ankle swelling
 - Impulse control problems (gambling, shopping, eating, internet).
- Less helpful in more advanced PD, older patients

AGONISTS



- Apomorphine (Apokyn)
- Injected under the skin
- Rapid-onset (about 10 minutes) so can help “rescue” from sudden off’s, severe freezing
- Side effects: nausea/vomiting, low blood pressure



AGONISTS

- Rotigotine (Neupro Patch)
 - (+) Easy patch system
 - (+) Once a day
- Works same as pramipexole, ropinirole
- If pramipexole and ropinirole work well but you have symptoms in between... patch is a good choice!



LEVODOPA VS. THE AGONISTS

THE BIG QUESTIONS

- Do the agonists prevent dyskinesias?
- Does levodopa cause dyskinesias and fluctuations?
- Do the agonists protect brain cells?
- Is Levodopa toxic?
- Is there tolerance to levodopa? (Will it only work for so long?)

LEVODOPA VS. THE AGONISTS

ANSWERS

- The focus of lots of research
- Levodopa has more dyskinesias, but does not quicken onset
- Levodopa not thought to be toxic
- Actually better survival with treatment
- Best answer is to treat each person individually

COMT-INHIBITORS

- Entacapone (Comtan) :
 - Works by blocking breakdown of levodopa
 - Levodopa stays around longer
- Stalevo (Entacapone + Levodopa):
 - Just helps by taking less pills



MAO-INHIBITORS

- Selegiline (Eldepryl) - older
- Rasagiline (Azilect) – 2006
- Also works by blocking breakdown of dopamine
- ??? Neuroprotective
- Mild effect on symptoms

OTHER MEDS

- Amantadine, helps reduce dyskinesias, and mildly helps PD symptoms, 2-3 times a day
- Amantadine ER (Gocovri), once at night formulation, FDA approved for dyskinesia , reduces off time symptoms
- Amantadine ER (Osmolex), for off time symptoms, not approved for dyskinesia, once a day
- Artane and Cogentin, both decrease tremor, but have lots of side effects (mainly sleepiness)

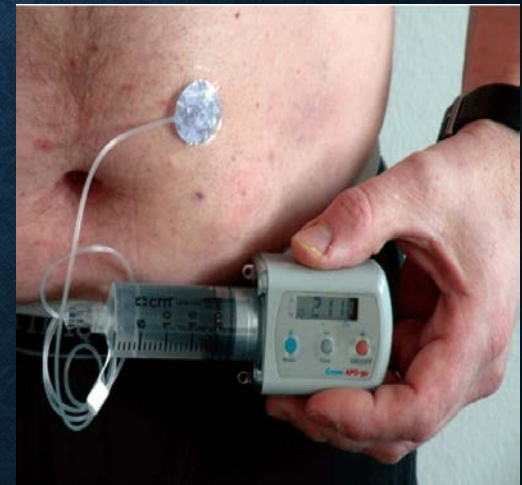
XADAGO (SAFINAMIDE)

- Approved in 2017 as an add on treatment.
(should be taken together with sinemet)
- Improves on time without worsening dyskinesia.
- Blocks MAOB enzyme that breaks down dopamine, therefore increases dopamine availability in the brain
- Possible side effects: dyskinesia, falls, nausea, insomnia

**WHAT IS COMING DOWN THE
PIPE LINE?!**

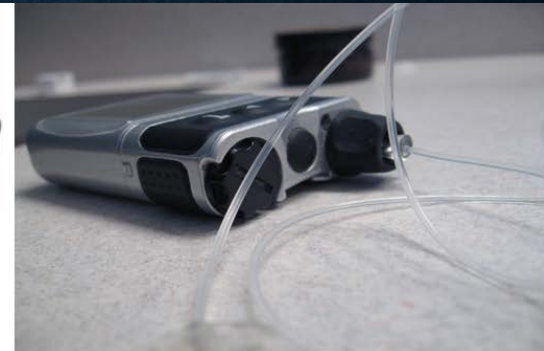
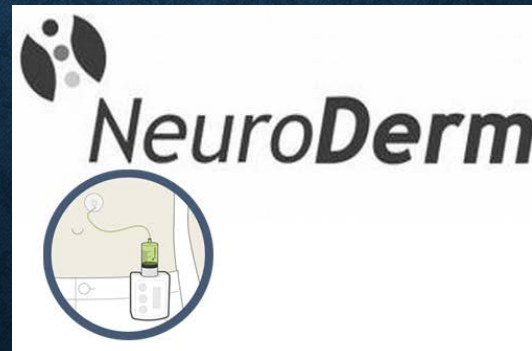
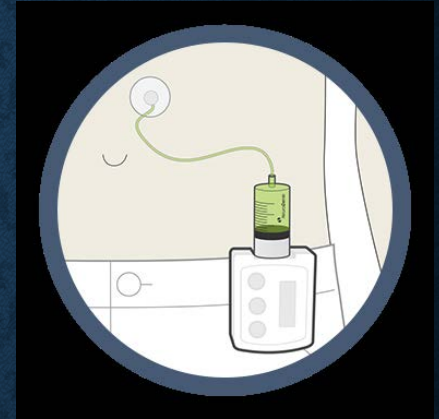
CONTINUOUS APOMORPHINE

- Subcutaneous infusion of apomorphine
- Normally used as a 16-h daytime treatment, but can be given over 24 h in the case the patient needs night-time effect.
- Pros: reduces “off” time, No need for surgery
- Con’s: needle should be changed daily, can cause skin breakdown and accesses, requires co treatment with anti nausea medication.



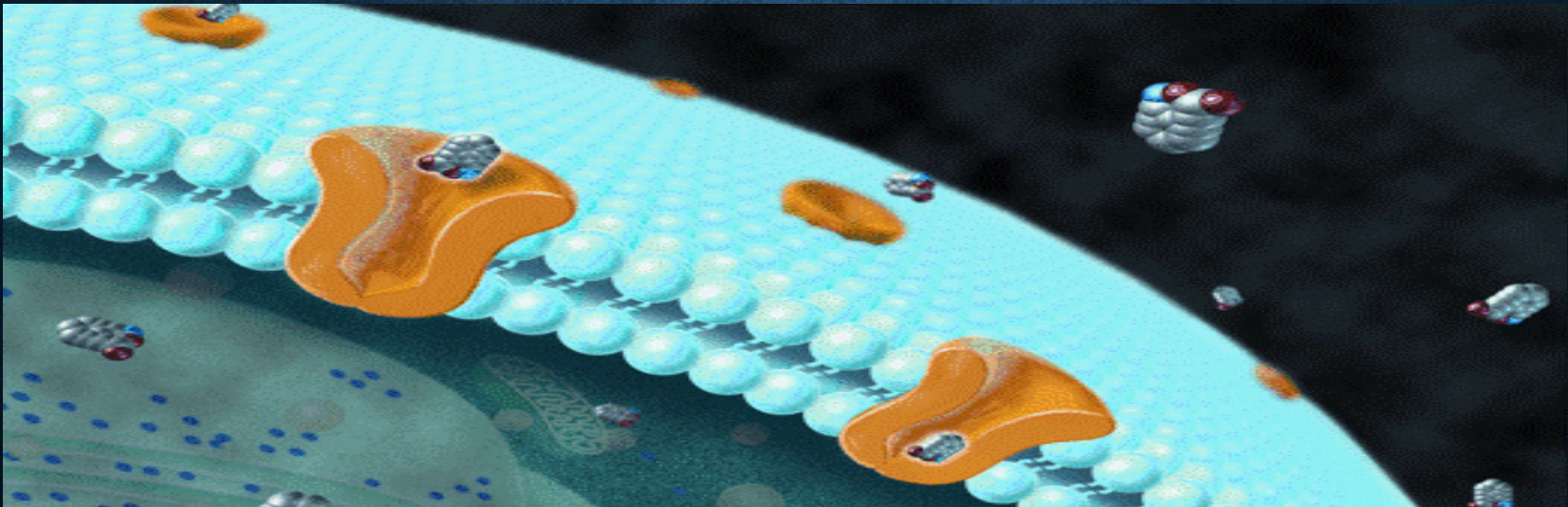
LEVODOPA PATCH

- **ND0612:** continuous subcutaneous delivery through a custom patch pump
- Pump patch: size of a credit card
- Belt pump: reservoir in small pump
- Drug stored in reservoir and pumped through skin through micro-needles into the blood stream
- 24 hour infusion



XP 21279

- L-dopa prodrug (changes to Levodopa after absorption)
- What is good about this?
 - Absorbed everywhere in the GI tract



XP 21279

- Decrease OFF time without increasing dyskinesias
- Decrease dosing frequency
- The long length of colon provides extra absorption that helps with a more steady dose of medication in blood

MELEVODOPA

- Liquid formulation
- What is good about this?
 - Absorbed more rapidly than usual CD/LD formulation

INHALED FORMULATION

- **CVT-301:**

inhaled formulation of L-dopa
to treat OFF episodes

- **Results:**

- Improvement in
movements scores
Reduced daily OFF time



COMT INHIBITORS

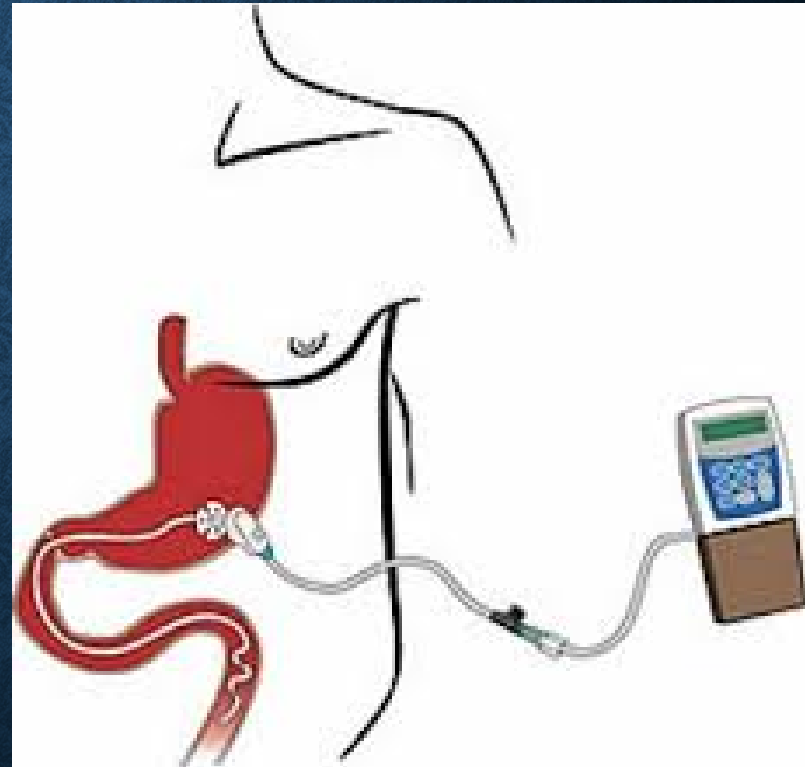
- **Opicapone:** Entacapone family
- What is good about this?
- Once daily dosing
- Decreases OFF time and increased ON time w/o troublesome dyskinesia
- Just as good as entacapone!

CAFFEINE

- May reduce dyskinesia
 - Self reported caffeine consumption higher than 12oz/day was associated with less frequent dyskinesia as compared with consumers of less than 4oz/day

DUODOPA

- Continuous infusion of carbidopa/levodopa through PEG tube



DUODOPA

- What is good about this?
 1. No more pills
 2. Continuous infusion throughout the day will provide a more steady state
 3. If for any reason you are not a candidate for DBS or do not want to go through brain surgery...



DUODOPA

- What is NOT so good about this?
 1. The cassette is not very light/small
 2. You should keep the PEG site clean to avoid infections



COMMON QUESTIONS:

- What are the possible side effects of Duopa?

Complications of device insertion

Abdominal pain

Procedure pain

Nausea

Excessive granulation tissue

Most of these side effects are rare, especially with good care before and after the surgery and an expert surgical team

NON-PHARMACOLOGIC TREATMENTS

- **Nutrition**- balanced diet, protein intake, weight loss
- **Exercise**- Physical therapy for gait impairment, balance
- **Speech therapy and swallowing therapy**
- **Cognitive therapy through speech or OT**
- **Support**- home health aides, day cares, support groups
- **Psychiatric care** – can be the most difficult part, but has many effective treatments

SUMMERY POINTS

- There are several different classes of medications
- Its common to use combination of different classes
- Therapy is tailored to manage individual patient's symptoms
- We can just treat the symptoms, can't cure the disease
- It is best to use benefit of non medical approaches as well.

•Thank you 😊