

NEW APPROACH OF PARKINSON'S DISEASE AND ITS CLINICAL MANAGMENT

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Summary

Parkinson is a neurodegenerative disorder of central nervous system which, is characterised by several manifestations like tremor, bradykinesia, rigidity etc. The main cause of this happening is the depletion of dopaminergic neurons in brain. There are several medication meant to control this disease but none are meant to truly cure this. Medication mainly includes levodopa along with its several combination, COMT inhibitor, dopamine agonist, amantadine etc.

Key words: Parkinson disease, neurodegenerative disorder, dopaminergic neurons, levodopa.

Introduction

Parkinson's disease (PD) is a common progressive neurodegenerative disorder. The major pathological hallmarks of PD are the selective loss of nigrostriatal dopaminergic neurons and the presence of intraneuronal aggregates termed Lewy bodies (LBs)¹. Parkinson's disease is an illness of the central nervous system that leads to severe impairment of motor skills and difficulty in controlling body movements².

CAUSES OF PARKINSON'S DISEASE

Parkinson's disease (PD) is one of the most common chronic neurodegenerative disorders. The pathologic hallmark of the disease is the loss of dopaminergic neurons in the Substantia Nigra pars compacta (SNpc) and the presence of intracytoplasmic inclusions named Lewy bodies, formed mainly by α -synuclein and ubiquitin³. The loss of substantia nigra neurons results in depletion of the neurotransmitter dopamine in these areas. There is evidence that genetic factors play a key role in development of PD. The development of PD involves an interaction between genes and environmental factors⁴.

SIGNS AND SYMPTOM OF PARKINSON'S DISEASE

A) PRIMARY SYMPTOM

Tremor

Rhythmic oscillations of some body part, usually at a joint. In Parkinson disease tremor is present when there is minimal voluntary activity (tremor at rest).

Dyskinesia

Repetitive involuntary choreiform movements of the tongue, limbs, hands, and trunk.

Akinesia

Decreased voluntary movement.

On-off effect

Sudden onset of Parkinsonian symptoms with a usual therapeutic dose of L-dopa that may be the result of progression of the disease with loss of dopamine nerve terminals in the striatum.

Bradykinesia

Characterised by slowness in voluntary action of the body like, slow in movement.

B) SECONDARY SYMPTOMS

In addition to the motor disturbances experienced by the patients suffering from Parkinson's disease (PD), several non-motor symptoms also affect the PD patients: neurobehavioral symptoms (dementia, depression, anxiety, psychosis), autonomic (postural hypotension, urinary symptoms, gastro intestinal symptoms, diaphoresis), sleep disorders (insomnia, somnolence, REM sleep behaviour disorder, apnoea), sensitive-motor (fatigue, diplopia, restless legs syndrome), and sensory symptoms. Hyposmia is a common symptom in PD and could be a predictor of future PD. Visual dysfunction and hearing dysfunction among others must be considered in patients with PD⁵. Urinary disorders are the most frequent non-motor symptom in Parkinson's disease. They usually present as nocturia, urgency and increased mictorial frequency (pollakiuria).

MEDICATION GUIDELINES FOR PARKINSON'S DISEASE⁶

Below are general guidelines to taking your medication. Be sure to ask your doctor or pharmacist for guidelines specific to your treatment.

- Do not split pills, or pull capsules apart unless directed by your doctor.
- Drink six to 10 glasses of water a day.
- Warm baths or physical activity may help with digestion and absorption of your medication.
- Know the names of your medications and how they work. Know the generic and brand names, dosages, and potential side effects. Always keep a list of your medications and their dosages with you, and exactly how you are taking them. Keep the list with you in your wallet or purse.
- Take your medications exactly as prescribed by your doctor.
- Do not stop taking or change your medications unless you talk to your doctor first. Even if you feel good, continue to take your medications. Stopping your medications suddenly can make your condition worse.
- Do not double the dose of your medication.
- Have a routine for taking your medications. Take them at the same time each day. Get a pillbox that is marked with the days of the week, and fill it at the beginning of the week to make it easier to remember.
- Keep a drug calendar and note every time you take a dose.
- If you miss a dose of your medication at the scheduled time, don't panic. Take it as soon as you remember. However, if it is almost time for your next dose, skip the missed dose and return to your regular medication schedule. Set an alarm clock if necessary.
- Do not keep outdated drugs. Throw old medicines away.
- Store drugs in a dry area away from moisture (unless your doctor or pharmacist tells you the medicine needs to be refrigerated).
- Always keep medications out of the reach of children.

- Know what side effects to expect from your medications. Contact your doctor immediately if you experience any unusual or unexpected side effects after taking your medication.
- Do not share your medications with others.
- Keep your medications in your carry-on luggage when you travel. Do not pack your medications in a suitcase that is checked, in case the suitcase is lost.
- Take extra medication with you when you travel in case your flight is delayed and you need to stay away longer than planned.
- Do not wait until you are completely out of medication before filling your prescriptions; call the pharmacy at least 48-hours before running out. If you have trouble getting to the pharmacy, have financial concerns or have other problems that make it difficult for you to get your medications, let your doctor know. A social worker may be available to help you.

TREATMENT OF PARKINSON'S DISEASE

A) COMMONLY USED MEDICATIONS FOR PARKINSON'S DISEASE⁷

LEVODOPA / CARBIDOPA

Levodopa is one of the main drugs used to treat Parkinson's symptoms. It can be used at all stages of the condition. Levodopa is a chemical building-block that your body converts into dopamine. It replaces the dopamine that is lost in Parkinson's disease. Levodopa is given with benserazide or carbidopa, to make sure it can enter the brain more efficiently. Benserazide plus levodopa is known as **co-beneldopa**. Carbidopa plus levodopa is known as **co-careldopa**.

DOPAMINE AGONISTS

Dopamine agonist drugs are one of the main ways to treat Parkinson's symptoms. Parkinson's symptoms are caused by a decrease in the levels of the chemical messenger dopamine, due to the death of the nerve cells in the brain that make it. Dopamine agonist drugs act like dopamine to stimulate your nerve cells. Dopamine agonists are used at all stages of Parkinson's. You might take them alone when treatment is being started, or alongside levodopa to help it work better. Treatment with dopamine agonists has to be started carefully, with the dose gradually increased until you and your specialist or Parkinson's nurse are happy that your symptoms are under control.

COMT INHIBITORS

COMT inhibitors are used to treat the symptoms of Parkinson's. COMT inhibitors do not help Parkinson's on their own – they have to be used with levodopa. COMT inhibitors reduce Parkinson's symptoms by blocking an enzyme that breaks down levodopa, prolonging its effect.

Advantages of COMT inhibitors: When used with levodopa, COMT inhibitors can reduce the daily 'off' time and increase the 'on' time. In many cases, the dose and frequency that levodopa is taken can also be reduced. The terms 'on/off' or 'motor fluctuations' refer to the period when people can no longer rely on the smooth and even symptom control that their drugs once gave them.

Some disadvantages of COMT inhibitors: These drugs can increase the side effects caused by levodopa, notably dyskinesias (unwanted involuntary movements), nausea and vomiting. If these side effects increase after starting the drug, people should raise the issue with their healthcare professional, as reducing the levodopa dose can often help. Be aware that other drugs (for Parkinson's or other conditions) can affect the action of COMT inhibitors. The combination of apomorphine and entacapone needs careful supervision. Other reported side effects of COMT inhibitors include abdominal pain, diarrhoea and discoloured urine.

MAO-B INHIBITORS

They prevent the breakdown of the chemical messenger dopamine in the brain, by blocking an enzyme that breaks it down, called monoamine oxidase type B (MAO-B). They are used to make levodopa last longer or reduce the amount required.

Advantages of MAO-B inhibitors: A MAO-B inhibitor can be used on its own in early Parkinson's, or in combination with other drugs at all stages of Parkinson's. These drugs are mainly available as tablets. There is also a form that dissolves on the tongue. This may help if you have trouble swallowing. MAO-B inhibitors may reduce fluctuations in effectiveness of drugs that some people with Parkinson's experience after the first few years. By itself, selegiline has very few side effects. Because Zelapar is absorbed better, a smaller dose is needed.

Some disadvantages of MAO-B inhibitors: When selegiline is taken together with levodopa, side effects such as dyskinesias (uncontrolled voluntary movements), hallucinations or vivid dreaming may sometimes occur or worsen. When people have taken rasagiline on its own (without levodopa), the most commonly reported side effects have been: headache, aching joints, indigestion, flu-like symptoms, depression.

ANTICHOLINERGICS PARKINSON'S DRUGS

Anticholinergics are a type of drug, less commonly prescribed now, used to treat the symptoms of Parkinson's. They block the action of acetylcholine, a chemical messenger that helps to send messages from your nerves to your muscles. Anticholinergics may be useful in the early stages of Parkinson's when symptoms are mild. They tend to improve tremor more than slowness and stiffness. They can be prescribed alone in the early stages, before levodopa is necessary, although they can be used in conjunction with levodopa or a glutamate antagonist too. Anticholinergics can be used to reduce excess saliva. They can also reduce bladder contractions that can cause a strong, frequent urge to urinate.

Side effects and problems of anticholinergics: Another reason these drugs are not a first choice for treating Parkinson's are their side effects. Some people may experience confusion, a dry mouth, constipation and blurred vision when taking anticholinergics. Anticholinergics may interfere with levodopa absorption in the small bowel, which reduces the effectiveness of Madopar or Sinemet. Anticholinergics are not usually prescribed to older people with Parkinson's because there is an increased risk of memory loss and, in men, problems urinating.

GLUTAMATE ANTAGONIST

There is one glutamate antagonist, amantadine, that can be prescribed to treat Parkinson's symptoms. The generic name is amantadine, but it is prescribed under the name Symmetrel®.

Exactly how this drug works for Parkinson's is not known yet. It may modify levels of certain chemicals in the brain. It is not used very often and is most likely to be given along with other drug treatments for Parkinson's. It is available in capsules and as syrup. The drug has only a mild effect, helps only a minority of people and its effectiveness may be short-lived. It may have a stimulatory effect and can help some people with tiredness. It can be used to treat tremor and stiff muscles and it can reduce unwanted involuntary movements without making other symptoms worse.

Side effects of glutamate antagonist: It is not a first-choice treatment for Parkinson's and has a limited effect. Side effects include: blurred vision, fainting, confusion or dizziness, swelling of the ankles or a mottled appearance on the skin of the lower leg.

APOMORPHINE

Apomorphine is one of the main drugs used to treat Parkinson's symptoms. It is available in a generic form or under the brand name APO-go®. Apomorphine is given by injection or infusion. It's a subcutaneous dopamine agonist – subcutaneous means under the skin. Apomorphine is the strongest known dopamine agonist. It is usually prescribed to give additional or alternative benefit for people who have had Parkinson's for some time. This could include those who are finding that their drugs are less effective, and who are experiencing 'wearing off' or sudden and unpredictable 'on/off' fluctuations.

B) SURGICAL TREATMENT OF PARKINSON'S DISEASE

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) and antiparkinsonian medication (Meds) have proved to be effective therapies for treating bradykinesia in Parkinson's disease. Medication and DBS had similar effects in that both treatments increased movement speed, increased the amplitude of the first agonist burst, increased burst duration, reduced the number of agonist bursts, reduced contraction, increased the size of the antagonist EMG, and reduced the centroid time of the antagonist EMG. There was a positive association between the level of bradykinesia OFF treatment and the level of bradykinesia following DBS and medication. The movement speed of neurologically normal control subjects' was over 40% higher during both flexion and extension movements when compared with the patients during Meds plus STN DBS. The changes in the muscle activation patterns provide a mechanism of action for the pharmacological and surgical interventions used to treat bradykinesia in Parkinson's disease⁸.

PREVENTION OF PARKINSON'S DISEASE

Prevention and treatment strategies that involve appropriate patient education, inquiry about possible compulsive eating behaviour, careful DRT dosing and weight monitoring before and throughout dopamine agonist therapy. There are not typical methods to control Parkinson's symptoms in advance. People take extra fruits plus vegetables, large amount of fibre eatables, fish, and omega 3 rich oils while those which take smaller amount of red meat and dairy might has a few defence in opposition to Parkinson's symptoms. However, the cause for this reason is not cleared yet.

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