Abstract

Parkinsonism is an Idiopathic, Chronic, Progressive, Degenerative disorder of basal ganglia or nigrostriatal pathway. Parkinson disease is a brain disorder. Parkinsons disease occurs when certain nerve cells (neurons) in substantia nigra(a part of brain) die or become impaired. These cells produce a vital chemical known as dopamine which allows smooth, coordinated function of the body's muscles and movement. When approx. 80% of these nerve cells (dopamine producing cells) are damaged, the symptoms of parkinson disease appear. It develops gradually, often starting with a barely noticeable tremor in just one hand. But while tremor may be the most well-known sign of Parkinson's disease, the disorder also commonly causes a slowing or freezing of movement. Friends and family may notice that your face shows little or no expression and your arms don't swing when you walk. Speech often becomes soft and mumbling. Parkinson's symptoms tend to worsen as the disease progresses. While there is no cure for Parkinson's disease, many different types of medicines can treat its symptoms. In some cases, your doctor may suggest surgery.

Key Words: Parkinsonism, Degenerative diseases, tremors, dementia.

Introduction

Parkinson's disease (also known paralysis agitans) is a progressive degenerative disorder of the central nervous system. Movements are mainly affected early in the course of the disease. Generally cognitive and behavioural problems arise later with dementia commonly occurring in the advanced stages of the disease. Typically PD becomes apparent around the age of 60 years, and it is unusual before the age of 40 years. The most obvious
symptoms are shaking, rigidity, slowness of movement, and difficulty with walking and gait. Among other symptoms are sensory, sleep, and emotional problems.

The main symptoms are collectively called Parkinsonism or Parkinsonian syndrome and they can be due to many causes. By definition Parkinson's disease is idiopathic (has no known cause), although some atypical cases have a genetic origin. Many risk and protective factors have been investigated; there is an increased risk of PD in those exposed to pesticides and a reduced risk in smokers.\(^1,2\)

History

It is a relatively common neurodegenerative disease afflicting approximately 1% of all adults over the age of 65. The disease was not formally recognized and its symptoms were not documented until 1817, when British apothecary James Parkinson published an essay on the Shaking Palsy. It was first described by James Parkinson in 1817 as paralysis agitans or the “shaking palsy”. PD was then known as paralysis agitans (shaking palsy in English). The term "Parkinson's disease" was coined several decades later by French neurologist Jean-Martin Charcot.\(^3\)

Pathophysiology

The basal ganglia, a group of "brain structures" innervated by the dopaminergic system, are the most seriously affected brain areas in PD. The primary symptoms of Parkinson's disease result from greatly reduced activity of dopamine-secreting cells due to cell death in the pars compacta region of the substantia nigra. The most characteristic pathological finding in PD is a progressive accumulation of Lewy bodies in the substantia nigra and several other brain regions. The pathology of the disease is characterized by the accumulation of alpha-synuclein protein into inclusions called Lewy bodies in neurons, and from insufficient formation and activity of dopamine produced in certain neurons of parts of the midbrain. Diagnosis of typical cases is mainly based on symptoms with tests such as neuroimaging being used for confirmation.\(^4,5\) Difference in muscular activity in normal state and in Parkinsonism as shown in figure-1.
During movement, signals pass from the brain's cortex, via reticular formation and spinal cord (pathway A), to muscles, which contract. Other signals pass, by pathway B, to the basal ganglia; these damp the signals in pathway A, reducing muscle tone so that movement is not jerky. Dopamine, a nerve transmitter made in the basal ganglia, is needed for this damping effect. Another transmitter, acetylcholine, inhibits damping effect.

In Parkinson's disease, degeneration of parts of the basal ganglia causes a lack of dopamine within this part of the brain. The basal ganglia are thus prevented from modifying the nerve pathways that control muscle contraction. As a result, the muscles are overly tense, causing tremor, joint rigidity, and slow movement. Most drug treatments increase the level of dopamine in the brain or oppose the action of acetylcholine.
Symptoms

The symptoms of Parkinson's disease vary from person to person. Early signs may be subtle and can go unnoticed for months or years. Symptoms typically begin on one side of the body and usually remain worse on that side. Parkinson's signs and symptoms may include.

- **Tremor**: The characteristic shaking associated with Parkinson's disease often begins in a hand. A back-and-forth rubbing of your thumb and forefinger, known as pill-rolling, is common. However, many people with Parkinson's disease do not experience substantial tremor.

- **Slowed motion (Bradykinesia)**: Over time, Parkinson's disease may reduce your ability to initiate voluntary movement. This may make even the simplest tasks difficult and time-consuming. When you walk, your steps may become short and shuffling. Or your feet may freeze to the floor, making it hard to take the first step.

- **Rigid muscles**: Muscle stiffness often occurs in your limbs and neck. Sometimes the stiffness can be so severe that it limits the range of your movements and causes pain.

- **Impaired posture and balance**: Your posture may become stooped as a result of Parkinson's disease. Imbalance also is common, although this is usually mild until the later stages of the disease.

- **Loss of automatic movements**: Blinking, smiling and swinging your arms when you walk are all unconscious acts that are a normal part of being human. In Parkinson's disease, these acts tend to be diminished and even lost. Some people may develop a fixed staring expression and unblinking eyes. Others may no longer gesture or seem animated when they speak.

- **Speech changes**: Many people with Parkinson's disease have problems with speech. You may speak more softly, rapidly or in a monotone, sometimes slurring or repeating words, or hesitating before speaking.

- **Dementia**: In the later stages of Parkinson's disease, some people develop problems with memory and mental clarity. Alzheimer's drugs appear to alleviate some of these symptoms to a mild degree.6,7,8,9

Causes

Many symptoms of Parkinson's disease result from the lack of a chemical messenger, called dopamine, in the brain. This occurs when the specific brain cells that produce dopamine die or become impaired. But researchers
still aren't certain about what sets this chain of events in motion. Some theorize that genetic mutations or environmental toxins may play a role in Parkinson's disease. The basal ganglia (BG) and extra pyramidal pathways play an important role in modulating and smoothing voluntary muscle movement. An imbalance between excitatory and inhibitory influences in these structures can result in disorders of movement and tone, collectively termed extra pyramidal syndromes (EPS). Idiopathic Parkinsonism is the most common form; other similar conditions are often described as Parkinsonism.\textsuperscript{10,11} Many diseases or lesions can cause EPS as shown in table- 1.

Table-1: Many diseases or lesions can cause EPS.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Variety</th>
<th>Possible causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-</td>
<td>Idiopathic Parkinsonism disease (most common form)</td>
<td>Impaired dopamine metabolism reactive free radical damage neurotoxin (e.g., MPTP)</td>
</tr>
<tr>
<td>2-</td>
<td>Infective</td>
<td>Viral encephalitis, syphilis,</td>
</tr>
<tr>
<td>3-</td>
<td>Iatrogenic</td>
<td>Neuroleptics, metochlopramide</td>
</tr>
<tr>
<td>4-</td>
<td>Traumatic</td>
<td>Head injury, tumour</td>
</tr>
<tr>
<td>5-</td>
<td>Ischaemic</td>
<td>Arteriosclerosis, atherosclerosis</td>
</tr>
<tr>
<td>6-</td>
<td>Toxic</td>
<td>Heavy metals, carbon monoxide, pyridine</td>
</tr>
</tbody>
</table>

**Risk Factors**

Risk factors for Parkinson's disease include:

- **Age**: Young adults very rarely experience Parkinson's disease. It ordinarily begins in middle or late life, and the risk continues to increase with age.

- **Heredity**: Having one or more close relatives with Parkinson's increases the chances that you'll also develop the disease, although your risk is still less than 5 percent. Recent evidence suggests a crucial role for small contributions from many different genes that program brain architecture.

- **Sex**: Men are more likely to develop Parkinson's disease than women are.

- **Exposure to toxins**: Ongoing exposure to herbicides and pesticides puts you at slightly increased risk of Parkinson's.\textsuperscript{12,13,14}
Treatment and Drugs

Your initial response to Parkinson's treatment can be dramatic. Over time, however, the benefits of drugs frequently diminish or become less consistent, although symptoms can usually still be fairly well controlled. Your doctor may recommend lifestyle changes, such as physical therapy, a healthy diet and exercise, in addition to medications. In some cases, surgery may be helpful.

Medications

Medications can help manage problems with walking, movement and tremor by increasing the brain's supply of dopamine. Taking dopamine itself is not helpful, because it is unable to enter your brain.

- **Levodopa**: The most effective Parkinson's drug is levodopa, which is a natural substance that we all have in our body. When taken by mouth in pill form, it passes into the brain and is converted to dopamine. Levodopa is combined with carbidopa to create the combination drug Sinemet. The carbidopa protects levodopa from premature conversion to dopamine outside the brain; in doing that, it also prevents nausea. In Europe, levodopa is combined with a similar substance, benserazide, and is marketed as Madopar.

As the disease progresses, the benefit from levodopa may become less stable, with a tendency to wax and wane ("wearing off"). This then requires medication adjustments. Levodopa side effects include confusion, delusions and hallucinations, as well as involuntary movements called dyskinesia. These resolve with dose reduction, but sometimes at the expense of reduced Parkinsonism control.

**levodopa and carbidopa combination**

- For Parkinson's disease:
  - For oral tablet dosage form:
    - Adults—At first, 1 tablet three or four times a day. Your doctor may need to change your dose, depending on how you respond to this combination medicine.
    - Children and teenagers—Use and dose must be determined by your doctor.

- For oral extended-release tablet dosage form:
• Adults—at first, 1 tablet two times a day. However, you may need to take more than this.

  Your doctor will decide the right dose for you, depending on your condition and the other medicines you may be taking for Parkinson's disease.

• Children and teenagers—Use and dose must be determined by your doctor.

Dopamine agonists: Unlike levodopa, these drugs aren't changed into dopamine. Instead, they mimic the effects of dopamine in the brain and cause neurons to react as though dopamine is present. They are not nearly as effective in treating the symptoms of Parkinson's disease. However, they last longer and are often used to smooth the sometimes off-and-on effect of levodopa. Examples - Parlodel (bromocriptine), Celance (pergolide), Revanil (lysuride), Requip (ropinirole), Cabaser (cabergoline), Pramipexol (mirapex), Britaject (apomorphine) (injection).

This class includes pill forms of dopamine agonists, pramipexole (Mirapex) and ropinirole (Requip), as well as a patch form, rotigotine (Neupro). Pergolide (Permax) has been withdrawn from the market because of its association with heart valve problems. A short-acting injectable dopamine agonist, apomorphine (Apokyn), is used for quick relief.

The side effects of dopamine agonists include those of carbidopa-levodopa, although they're less likely to cause involuntary movements. However, they are substantially more likely to cause hallucinations, sleepiness or swelling. These medications may also increase your risk of compulsive behaviors such as hyper sexuality, compulsive gambling and compulsive overeating. If you are taking these medications and start behaving in a way that's out of character for you, talk to your doctor.

MAO B inhibitors: These types of drugs, including selegiline (Eldepryl) and rasagiline (Azilect), help prevent the breakdown of both naturally occurring dopamine and dopamine formed from levodopa. They do this by inhibiting the activity of the enzyme monoamine oxidase B (MAO B)-the enzyme that metabolizes dopamine in the brain. Side effects are rare but can include serious interactions with other medications, including drugs to treat depression and certain narcotics.15,16,17

Catechol O-methyltransferase (COMT) inhibitors: These drugs prolong the effect of carbidopa-levodopa therapy by blocking an enzyme that breaks down levodopa. Tolcapone (Tasmar) has been linked to liver damage and liver failure, so it's normally used only in people who aren't responding to other therapies.
Entacapone (Comtan) doesn't cause liver problems and is now combined with carbidopa and levodopa in a medication called Stalevo.

**Anticholinergics:** These drugs have been used for many years to help control the tremor associated with Parkinson's disease. A number of anticholinergic drugs, such as trihexyphenidyl and benztropine (Cogentin), are available. However, their modest benefits may be offset by side effects such as confusion and hallucinations, particularly in people over the age of 70. Other side effects include dry mouth, nausea, urine retention especially in men with an enlarged prostate and severe constipation. Example- Artane (benzhexol), Disipal (orphenadrine), Cogentin (benztropine), benzocaine.

**Antivirals:** Doctors may prescribe amantadine (Symmetrel) alone to provide short-term relief of mild, early-stage Parkinson's disease. It also may be added to carbidopa-levodopa therapy for people in the later stages of Parkinson's disease, especially if they have problems with involuntary movements (dyskinesia) induced by carbidopa-levodopa. Side effects include swollen ankles and a purple mottling of the skin.

**Physical therapy:** Exercise is important for general health, but especially for maintaining function in Parkinson's disease. Physical therapy may be advisable and can help improve mobility, range of motion and muscle tone. Although specific exercises can't stop the progress of the disease, improving muscle strength can help you feel more confident and capable. A physical therapist can also work with you to improve your gait and balance. A speech therapist or speech pathologist can improve problems with speaking and swallowing. 18,19,20

**Surgery:** Deep brain stimulation is the most common surgical procedure to treat Parkinson's disease. It involves implanting an electrode deep within the parts of your brain that control movement. The amount of stimulation delivered by the electrode is controlled by a pacemaker-like device placed under the skin in your upper chest. A wire that travels under your skin connects the device, called a pulse generator, to the electrode. Deep brain stimulation is most often used for people who have advanced Parkinson's disease who have unstable medication (levodopa) responses. It can stabilize medication fluctuations and reduce or eliminate involuntary movements (dyskinesias). Tremor is especially responsive to this therapy. Deep brain stimulation doesn't help dementia and may make that worse.
Like any other brain surgery, this procedure has risks—such as brain hemorrhage or stroke-like problems. Infection also may occur, requiring parts of the device to be replaced. In addition, the unit's battery beneath the skin of the chest wall must be surgically replaced every few years. Deep brain stimulation isn't beneficial for people who don't respond to carbidopa-levodopa.

**Deep brain stimulation:** It involves implanting an electrode deep within your brain. The amount of stimulation delivered by the electrode is controlled by a pacemaker-like device placed under the skin in your chest. A wire that travels under your skin connects the device to the electrode.

**Lifestyle and home remedies:** If you've received a diagnosis of Parkinson's disease, you'll need to work closely with your doctor to find a treatment plan that offers you the greatest relief from symptoms with the fewest side effects. Certain lifestyle changes also may help make living with Parkinson's disease easier.

**Healthy eating:** Eat a nutritionally balanced diet that contains plenty of fruits, vegetables and whole grains. These foods are high in fibre, which is important for helping prevent the constipation that is common in Parkinson's disease.

If you take a fibre supplement, such as psyllium powder, Metamucil or Citrucel, be sure to introduce it gradually and drink plenty of fluids daily. Otherwise, your constipation may become worse. If you find that fibre helps your symptoms, use it on a regular basis for the best results.²¹,²²

**Walking with care:** Parkinson's disease can disturb your sense of balance, making it difficult to walk with a normal gait. These suggestions may help:

- Try not to move too quickly.
- Aim for your heel to strike the floor first when you're walking.
- If you notice yourself shuffling, stop and check your posture. It's best to stand up straight with your head over your hips and your feet eight to 10 inches apart.

**Avoiding falls:** In the later stages of the disease, you may fall more easily. That's because Parkinson's disease affects the balance and coordination centers in the brain. In fact, you may be thrown off balance by just a small push or bump. The following suggestions may help:

- Don't pivot your body over your feet while turning. Instead, make a U-turn.
Don't lean or reach. Keep your center of gravity over your feet.

Don't carry things while walking.

Avoid walking backward.

**Dressing**: Dressing can be the most frustrating of all activities for someone with Parkinson's disease. The loss of fine-motor control makes it hard to button and zip clothes, and even to step into a pair of pants. An occupational therapist can point out techniques that make daily activities easier. These suggestions also may help:

- Allow plenty of time so that you don't feel rushed.
- Lay clothes nearby.
- Choose clothes that you can slip on easily, such as sweat pants, simple dresses or pants with elastic waistbands.
- Use fabric fasteners, such as Velcro, instead of buttons.

**Coping and support**: Living with any chronic illness can be difficult, and it's normal to feel angry, depressed or discouraged at times. Parkinson's disease presents special problems because it can cause chemical changes in your brain that make you feel anxious or depressed. And Parkinson's disease can be profoundly frustrating, as walking, talking and even eating become more difficult and time-consuming.

Although friends and family can be your best allies, the understanding of people who know what you're going through can be especially helpful. Support groups aren't for everyone, but for many people, they can be a good resource for practical information about Parkinson's disease.

To learn about support groups in your community, talk to your doctor, a Parkinson's disease social worker or a local public health nurse. Or contact the National Parkinson Foundation or the American Parkinson Disease Association.

**Alternative medicine**

**Coenzyme Q10**: People with Parkinson's disease tend to have low levels of coenzyme Q10, and some research has suggested it may be beneficial. However, subsequent studies have not confirmed this benefit. You can buy coenzyme Q10 without a prescription in drugstores and natural food stores. Talk with your doctor before taking this supplement.
**Massage**: Therapy can reduce muscle tension and promote relaxation, which can be especially helpful to people experiencing muscle rigidity associated with Parkinson's disease. These services, however, are rarely covered by health insurance.

**Tai chi**: An ancient form of Chinese exercise, tai chi employs slow, flowing motions that help improve flexibility and balance. Several forms of tai chi are tailored for people of any age or physical condition.

**Yoga**: Yoga is another type of exercise that increases flexibility and balance. Most poses can be modified, depending on your physical abilities.\(^ {23,24,25}\)

**Conclusions**

Parkinson disease is a progressive and debilitating disease characterized by fluctuations of symptoms, both motor and nonmotor, in response to disease progression and response to medication as the disease state progresses. Current treatments for PD are focused primarily on dopamine replacement, with L-dopa the cornerstone of effective therapy. However, increasingly, nonmotor and nondopamine responsive symptoms are the cause of major morbidity in advanced PD. Recognition and treatment of these symptoms is important in improved care of individuals with PD.

Neuropsychiatric aspects have also important implications for the quality of life of patients with Parkinson's disease as well as their caregivers. Recent clinical and imaging studies suggest that in addition to fronto-subcortical deficits, temporal and parietal changes occur even in early Parkinson's disease. The frequency and characteristics of depression, anxiety and hallucinations have been further explored, and have underlined the frequent co-occurrence of these syndromes in Parkinson's disease. After working with following article it has found that PD requires further extensive research and we can not overlook at this disease.

**References**


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