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PARKINSON'S DISEASE - a patient's guide

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What is it?

Parkinson's disease is a fairly common movement disease affecting both men and women, more common in older persons. The cause is unknown. The prevalence is about 150 per 100 000 population. The substantia nigra, a critical area of the brain that controls movement and coordination, is affected, as well as other nearby brain structures such as the nigrostriatal pathways and the locus coeruleus. As a result, the amount of dopamine (a neurotransmitter - chemical messenger) is reduced in these areas. Under the microscope, characteristic Lewy bodies are seen.

What are the symptoms?

Due to the reduced dopamine activity, the clinical features appear. These are:

Tremor - frequency about 4-6 Hz, usually worse when the limb is at rest, and reduces with movement of the limb. It is often initially worse on one side.

Rigidity - increased tone and tension in the limbs, often described by doctors as "cogwheeling".

Bradykinesias - this means reduced movement and slowness of movement. The gait may thus become shuffling with many small steps, the speech may become soft, and swallowing difficulties may arise.

These three features are the cardinal ones originally described by Dr James Parkinson as "The Shaking Palsy". However, a number of other features occur:

Joint and muscle pain due to immobility.

Poor righting reflexes and therefore a risk of falling.

Dribbling.

Constipation.

Postural hypotension resulting in dizziness on standing.

Dementia - occurs in about one third of patients, usually in the later stages of the disease.

In addition to Parkinson's disease, a syndrome similar to Parkinson's disease (parkinsonism) can occur secondary to various causes:

Certain drugs, particularly anti-psychotic drugs and anti-nausea drugs (phenthiazine, haloperidol, prochlorperazine, metoclopramide).

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Past encephalitis.

Progressive supranuclear palsy - a rare disease characterised by parkinsonism, eye movement paralysis and other features.

Shy-Drager syndrome - a rare disease characterised by parkinsonism, severe postural hypotension and urinary difficulties.

These cases of parkinsonism can often be distinguished clinically from true Parkinson's disease. For example, tremor is not often present in parkinsonism.

What can be done to help?

Drug treatment is only required when the disease interferes with normal activity for that person. Therefore it may be delayed longer in an elderly frail patient, than in a younger active person. Drugs are introduced at the lowest possible dose and increased slowly, monitoring the response.

L-dopa

This is the mainstay of treatment. L-dopa is able to cross into the brain, and there is transformed to dopamine (decarboxylation), which is an active neurotransmitter. L-dopa is often combined with a decarboxylase inhibitor as in Sinemet or Madopar. This inhibitor (which cannot cross into the brain) causes higher levels of L-dopa to be available to cross into the brain, and also reduces some of the side effects outside the brain of dopamine.

L-dopa will improve about 80 % of Parkinson's disease patients. Patients with parkinsonism tend to respond less well.

L-dopa can cause side-effects of nausea, vomiting, postural hypotension, and in some cases, confusion. In patients who have been treated for some time (years), it can cause jerky involuntary movements (dyskinesias) which can be painful, and need to be distinguished from the tremor of Parkinson's disease.

Dopamine agonists

These agents, the best known being bromocriptine, act directly on the dopamine receptor. They have a longer duration of action than L-dopa, but tend to be less effective. Bromocriptine is a non-specific dopamine agonist and acts on several different subtype dopamine receptors. Newer dopamine agonists are being developed which act on only certain receptors, therefore reducing side effects.

Other nonspecific dopamine agonists include lisuride and pergolide.

Anticholinergic drugs

These drugs are not as effective as L-dopa. They are not commonly used in New Zealand, although they have been popular in the USA. They cause side effects of dry mouth, urinary

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hesitancy, constipation, glaucoma and confusion and hallucinations, particularly in the elderly. For this reason, they are often not used in older patients. Two examples of anticholinergic drugs are Benzhexol and Orphenadrine.

Amantadine

This drug was originally developed as an anti-viral agent, but was found to improve Parkinson's disease. However it is often poorly tolerated because of its propensity to cause confusion and psychosis, and is not often used.

Selegiline

This is a monoamine-oxidase B inhibitor that acts in the brain. It thus reduces the breakdown of dopamine in the brain. In certain patients it smooths out the response to L-Dopa. Some studies suggest that it delays the need for L-dopa in untreated patients, but whether this makes any difference to the final state of the patients long term is unknown.

Apomorphine

Apomorphine is a dopamine agonist that is short acting and can help patients when they are "frozen". Unfortunately it needs to be given by subcutaneous injection, and is not freely available.

COMT inhibitors

These drugs inhibit the enzyme Catechol - O - methyl-transferase, another enzyme that breaks down dopamine. Two of these drugs have recently been developed for the treatment of Parkinson's Disease. They are tolcapone, now available in New Zealand, and entacapone. They can, in a proportion of patients, improve control of the Parkinson's Disease. Liver failure (which can be fatal) has occurred rarely with Talcopone, and therefore its use is restricted to specialists in New Zealand and blood monitoring is mandatory.

Surgery

Surgery is not commonly performed. However, in cases of very severe tremor, thaladotomy can help. A similar procedure, pallidotomy, can also improve Parkinson's Disease, particularly dyskinesias. Auckland Hospital Neurosurgery Unit has some experience of these procedures.

Future trends

Dopamine agonists that act on specific receptor subtypes, therefore reducing side effects are being trialed. These include ropinerole and pramipexole. Carbergoline, a dopamine agonist with a very long duration of action, may prove useful as it may produce a sustained smooth response.

Deep brain stimulation is an interesting therapy where fine electrodes are placed deep in the brain. These electrodes can be activated via generators as required by the patient.

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Stimulation inhibits overactive neurones and improves Parkinson's symptoms. Further experience with this therapy is awaited.

Transplantation to replace the dying substantia nigra neurones has been attempted. There are reports of success using foetal tissue, and study into the use of nerve growth factors, which stimulate nerve regeneration, continues.