information

MEDICAL OPTIONS FOR PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

It is primarily related to a lack of dopamine as a result of degeneration of dopamine producing neurons within the mid – brain. Dopamine is a neurotransmitter which conveys messages between neurons to ensure effective planning, initiation and maintenance of movement. Most pharmaceutical treatment options focus on restoring the balance of dopamine and other neurotransmitters by several means.

- Dopamine Replacement Therapy
- Dopamine Agonists

NB: The medications in this information sheet are listed in alphabetical order.

Dopamine Replacement Therapy (Levodopa)

The use of levodopa to replace dopamine remains the gold standard treatment for Parkinson's and a positive response to levodopa will assist in the process of diagnosis. Levodopa can have a positive effect on the symptoms of bradykinesia and muscle rigidity. Tremor is the least responsive symptom to levodopa.

Levodopa is a precursor to dopamine and crosses the blood brain barrier where it is converted to dopamine and corrects the imbalance of neurotransmitters. In order to ensure it passes the blood brain barrier and to prevent the breakdown of levodopa the addition of decarboxylase inhibitors (either Carbidopa or Benzedride) is necessary.

In Australia, levodopa is currently available as:

- Duodopa® is a gel form of levodopa which is delivered directly into the duodenum via a PEGJ tube.
- Kinson® is a generic form of levodopa and is available in one dose only (100/25)
- Levo - Carbidopa® is a generic form of levodopa and is available in one dose only (250/25)
- Madopar® is available in standard, controlled release (HBS) and a dispersible form when more rapid action is required. Several dosages are available.
- Sinemet® is available in standard and controlled release (CR) forms with several dosages available. It may also be prescribed as a liquid which must be prepared freshly every 24 hours and refrigerated.
- Stalevo® is levodopa with carbidopa and an additional ingredient (entacapone) and will be discussed under COMT inhibition.

Dopamine Agonists

These medications mimic dopamine and stimulate the dopamine receptors. They may be prescribed as initial therapy or in conjunction with levodopa.

There are two types of dopamine agonists (non ergoline derived and ergoline derived). Ergoline derived are used less commonly because of a small risk of fibrotic reactions (e.g. cardiac valve, pulmonary and pleural fibrosis) associated with long term use.

In Australia the more commonly used dopamine agonists are:

- Apomine® (apomorphine) given by subcutaneous injection or via a subcutaneous infusion using a pump.
- Movapo® (apomorphine) as above
- Neupro® (rotigotine) is a trans dermal patch which is applied to different skin areas each day. It is important to hold the patch firmly in place for 60 seconds to ensure fixation. Neupro® must not be worn during an MRI scan or cardioversion.
- Sifrol® (Pramipexole) is available in an extended release (ER) formulation which is taken once daily and normal release which is taken three times a day.

Less frequently used dopamine agonists are:

- Cabaser ® (cabergoline)
- Parlodel® (bromocriptine)

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Potential Adverse Effects of Dopaminergic Medications (Levodopa and Dopamine Agonists)

When medications are first introduced there are some common effects which are usually short lived and manageable as the body adjusts. These include:

- Nausea and occasionally vomiting. It is recommended that medication is taken with food initially. Motilium® (Domperidone) may be prescribed. Other anti nausea medications such as Maxolon® and Stemetil® should be avoided as they can worsen the Parkinson's symptoms.
- Dizziness due to a drop in blood pressure on standing may occur - avoid rising quickly.

Other possible side effects are:

- Ankle swelling may occur with dopamine agonists
- Constipation - this may occur as a side effect of medication in addition to being a symptom of Parkinson's. Additional fluids and a high fibre diet are recommended.
- Hallucinations are usually related to progression of the condition and long term dopaminergic medications. They may or may not be frightening.
- Increased dreams, which may be vivid, may occur due to Parkinson's but may be exacerbated due to medications.
- Motor fluctuations – these include 'wearing off' of the benefit of the medication before the next dose is due. Dyskinesias (involuntary movements) may develop with long term use of levodopa especially with higher doses.
- Sedation or excessive sleepiness may occur and is more common with dopamine agonists.

Treatment with dopaminergic medications (especially at higher doses) can sometimes lead to behavioural changes e.g. obsessive compulsive disorder. This may take the form of gambling, excessive shopping, eating, increased libido or an interest in pornography.

If you believe that you are experiencing side effects from medications this should be discussed with your treating specialist of General Practitioner. They may consider adjusting the choice or dose of medication.

Other forms of medications used in the management of Parkinson's are:

- COMT Inhibition
- MAO Type B Inhibition
- Amantadine
- Anticholinergic Therapy

COMT Inhibition

Catechol-O-methyltransferase (COMT) is a naturally occurring enzyme which metabolizes both levodopa and dopamine. By inhibiting the action of COMT more levodopa is available – in theory, providing a more prolonged response to each dose .

Currently, in Australia, the available COMT inhibitors are:

- Comtan® (entacapone) is taken with each dose of levodopa – taken by itself Comtan® has no therapeutic action. It is available in one dose only.
- Stalevo® is a combination of levodopa, carbidopa and entacapone and is available in several doses.

COMT inhibitors may exaggerate existing levodopa side effects. Discoloration of urine is a non harmful side effect. A small percentage of people taking these medications may experience diarrhoea. This may occur after being on the medication for an extended period of time.

MAO Type B Inhibition

Monoamine oxidase (MAO) is a naturally occurring enzyme which is responsible for the breakdown of dopamine. MAO Type B inhibitors are reputed to scavenge free radicals formed by the oxidative metabolism of dopamine hence the unproven theory that they may have a neuro protective effect.

Currently, in Australia, the available MAO Type B inhibitors are:

- Azilect® (rasagiline mesylate) – taken once a day
- Eldepryl® (selegiline hydrochloride) – taken twice a day with the second dose taken no later than noon otherwise sleep may be disturbed.
- Selgene® (selegiline hydrochloride) – as above

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Drug interactions may occur with these medications. Pethidine and some forms of antidepressants should be treated with caution. It is essential to discuss this with the treating specialist.

Amantadine

Amantadine is an antiviral agent and its mode of action in Parkinson's is not clear. It is reported to give some improvement to symptom control. More recently it has been used to reduce dyskinesia.

Currently, in Australia amantadine is available as:

- Symmetrel® (amantadine hydrochloride)

Possible side effects are insomnia, confusion, swollen ankles and a mottled rash on the lower limbs.

Anticholinergic Therapy

Prior to the development of dopaminergic replacement therapy, anticholinergic therapy was the only treatment option available. Anticholinergics correct the imbalance between dopamine and acetylcholine. They can be useful in addressing tremor.

Currently in Australia the available anticholinergics are:

- Akineton® (biperiden hydrochloride)
- Artane® (benzhexol hydrochloride)
- Benztrop® (benztropine mesylate)
- Cogentin ® (benztropine mesylate)

These are rarely used due to commonly occurring side effects such as dry mouth, urinary retention, blurred vision and confusion. The development of the newer forms of medications has also reduced the use of anticholinergic therapy.

MEDICATION WARNING

Some medications used in the treatment of other medical conditions have the potential to alter the dopamine system. It is important to consider the possibility that treatment for other conditions may cause or worsen Parkinson's symptoms.

The most commonly prescribed medications which are not recommended in Parkinson's are:

- Maxolon® Pramin® (metoclopramide)
- Stemetil® Stemzine® (prochlorperazine)
- Serenace® (haloperidol)

If treatment for nausea or vomiting is required Motilium® is a safe alternative.

SUMMARY

The medications described in this information sheet are used in the treatment of Parkinson's in Australia. The pharmaceutical management of Parkinson's is complex and medications should be prescribed by a specialist such as a neurologist or a geriatrician. Medications will need to be reviewed and changed as the condition progresses. It is important to have regular reviews.

As each person with Parkinson's presents differently, it is essential that the medical management be prescribed on an individual basis bearing in mind potential side effects.

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