Antiparkinson drugs

Drugs used in parkinsonism

The use of pharmacotherapy will depend upon the degree of incapacity of the patient and is generally not justified until symptoms compromise working ability and social relationships; although levodopa is used in the early stages in some patients. Close supervision is then needed to ensure that treatment regimens are tolerated and that appropriate changes are made to the regimen as the disease progresses. The most effective form of therapy is a combination of **levodopa** and a peripheral dopa-decarboxylase inhibitor, such as carbidopa. The response to levodopa with carbidopa is a compromise between increased mobility and adverse effects. Dyskinesias may be dose limiting and increasingly frequent with increased duration of treatment. Many factors including tolerance and progression of the disease may result in complications after 2–5 years of treatment. 'End-of-dose' deterioration occurs when there is a reduced duration of benefit from a dose, resulting in disability and dystonias. The 'on-off' phenomenon is characterized by sudden swings from mobility to episodes of akinesia, tremor and rigidity lasting from a few minutes to several hours. Amelioration of these effects can sometimes be achieved by administering levodopa in a sustained-release preparation or in a greater number of fractionated doses throughout the day. Psychiatric symptoms inducing disruption of sleep, vivid dreams and hallucinations are characteristic adverse effects that may occur at any time, especially in the elderly, and may require dose reduction or withdrawal of levodopa.

Treatment for idiopathic parkinsonism is often initiated with a dopamine receptor agonist such as bromocriptine [not on WHO Model List]. Supplementary use of amantadine [not on WHO Model List], bromocriptine or the monoamine-oxidase-B inhibitor, selegiline [not on WHO Model List] can be of value either to enhance the effect of levodopa or to reduce 'end-of-dose' fluctuations and 'on-off' effects. Anticholinergic (more correctly termed antimuscarinic) drugs such as **biperiden** are usually sufficient in drug-induced parkinsonism.

Levodopa with carbidopa

Carbidopa is a representative peripheral dopa decarboxylase inhibitor. Various drugs can serve as alternatives

Tablets, levodopa 100 mg with carbidopa 10 mg, levodopa 250 mg with carbidopa 25 mg

Uses

all forms of parkinsonism other than drug-induced **Contraindications:**

concurrent use of monoamine oxidase inhibitors; angleclosure glaucoma; confirmed or suspected malignant melanoma

Precautions:

pulmonary disease, peptic ulceration, cardiovascular disease (including previous myocardial infarction); diabetes mellitus, osteomalacia, open-angle glaucoma, history of melanoma (risk of activation), psychiatric

illness (avoid if severe); close monitoring of hepatic, haematological, psychiatric, cardiovascular, and renal function required in long-term therapy; elderly: avoid rapid dose increases; warn patients to resume normal activities gradually; avoid abrupt withdrawal; pregnancy (toxicity in animals) (Appendix 2), breastfeeding (Appendix 3); **interactions:** Appendix 1

Parkinsonism, by mouth, **ADULT** expressed in terms of levodopa, initially 100 mg (with carbidopa 10 mg) twice daily, increased by 100 mg (with carbidopa 10 mg) every few days as necessary, to a maximum of

levodopa 1.5 g

ADMINISTRATION. Optimum daily dose must be determined for each patient by careful monitoring and be taken after meals

Adverse effects:

nausea, anorexia and vomiting, particularly at the start of treatment; postural hypotension at the start of treatment, particularly in elderly and those receiving antihypertensives; excessive drowsiness and sudden onset of sleep (warn patient of these effects); confusion, vivid dreams, dizziness, tachycardia, arrhythmias; reddish discoloration of body fluids; insomnia, headache, flushing, gastrointestinal bleeding, peripheral neuropathy; taste disturbances, pruritis, rash, liver enzyme changes; psychiatric symptoms including psychosis, depression, hallucinations, delusions and neurological disturbances including dyskinesias may be dose-limiting; painful dystonic spasms ('end-of-dose' effects) and ('on-off' effects) after prolonged treatment (see notes above); neuroleptic malignant syndrome, on sudden withdrawal; rarely hypersensitivity

Biperiden

Biperiden is a representative anticholinergic drug. Various drugs can serve as alternatives Tablets, biperiden hydrochloride 2 mg *Injection* (Solution for injection), biperiden lactate 5 mg/ml, 1-ml ampoule

Uses:

drug-induced extrapyramidal symptoms (but not tardive dyskinesias) and adjunctive treatment of parkinsonism

Contraindications:

angle-closure glaucoma; untreated urinary retention; prostatic hypertrophy; myasthenia gravis; gastrointestinal obstruction

Precautions:

elderly; cardiovascular disease, hepatic or renal impairment; avoid abrupt withdrawal; pregnancy and breastfeeding; **interactions:** Appendix 1

SKILLED TASKS.

May impair ability to perform skilled tasks, for example operating machinery, driving

Dosage:

Drug-induced extrapyramidal symptoms, parkinsonism, by mouth, **ADULT**, as biperiden hydrochloride, initially 1 mg twice daily, increased gradually to 2 mg 3 times daily; usual maintenance dose 3–12 mg daily in divided doses

Drug-induced extrapyramidal symptoms, parkinsonism, by intramuscular injection or slow intravenous injection

, **Adult** , as biperiden lactate, 2.5–5 mg repeated as necessary to maximum 20 mg in 24 hours **Adverse effects:**

drowsiness, dry mouth, constipation, blurred vision; hesitancy of micturition, dizziness, tachycardia, arrhythmias; confusion, excitement, agitation, hallucinations, and psychiatric disturbances with high dosage, especially in the elderly and other susceptible patients, may require withdrawal of treatment; impaired memory

Drugs used in essential tremor and related disorders ESSENTIAL TREMOR

It can be treated with beta-blockers such as **propranolol** (120 mg daily) (section 7.2) which may be of value if the tremor results in physical or social disability.

DYSTONIAS

If no identifiable cause is found and the patient does not go into spontaneous remission, a trial of **levodopa** should be given to determine whether the patient has dopamine-responsive dystonia. If there is no response within three months, the drug should be withdrawn and small doses of an anticholinergic drug such as **biperiden** should be given. The dosage may be increased gradually and up to 16 mg daily may be tolerated. In patients who fail to respond to either levodopa or an anticholinergic, other drugs including diazepam, baclofen, carbamazepine or phenothiazines may be of value. Psychological treatments have also been used successfully in the management of dyskinesias.

CHOREA

Choreiform movements can be induced by certain drugs including levodopa, phenytoin and antipsychotic drugs. Huntington disease is the most common of the hereditary choreas. Drug treatment is symptomatic and does not alter the progression of the disease. The aim of

therapy is to reduce dopaminergic transmission which results from excessive or enhanced cholinergic activity. Antipsychotic drugs antagonize dopamine and usually lessen the chorea temporarily. Tetrabenazine [not included on WHO Model List], the dopamine-depleting drug, is used to control movement disorders in Huntington chorea and related disorders.

TICS

Tics which resemble choreiform movements are commonly associated with anxiety. However, in the more complex multiple tic disorder, Tourette syndrome, treatment with antipsychotic drugs may be required.

TARDIVE DYSKINESIA

It is associated with chronic administration of antipsychotic drugs. It is characterized by involuntary, repetitive, choreiform movement of the cheek, mouth and fingers. The first step of treatment should always be discontinuation of the antipsychotic drug or dosage reduction if the underlying psychotic disorder permits.