Community Clinics in Clinical Pharmacology

Parkinson's disease

M MACE, M D RAWLINS

British Medical Journal, 1979, 1, 1266

Problem

This 65-year-old man has been under the care of this practice for only five months. About three years ago he noticed increasing tremor of both his hands, and Parkinson's disease was diagnosed. He was given levodopa, 500 mg thrice daily, but this made him vomit so much that it was stopped. He was treated with benzhexol, 2 mg thrice daily, which improved his mobility but made little difference to his tremor. He has continued on this drug ever since, but he has become incapacitated by his illness: he needs help with dressing and eating, and rarely leaves the house. Is there any other treatment we should consider?

Advice

I saw the patient this morning. He has the classical features of Parkinsonism with the typical facies, a tremor of both hands, akinesia of his trunk and limbs, and a shuffling gait. He has a persistent glabella reflex and "cogwheel" rigidity of his limbs, but no signs suggestive of more widespread degenerative changes or of hypertension. I agree that he has Parkinson's disease.

I do not feel that he has had an adequate trial of levodopa. Firstly, levodopa should be given in combination with a dopa-decarboxylase inhibitor (carbidopa or benserazide) that doesn't cross the blood-brain barrier: by this means, levodopa is converted to dopamine quite normally within the brain, but less so elsewhere. The likelihood of nausea, vomiting, and cardiac arrhythmias is thereby reduced. Decarboxylase inhibitors are available only as combined preparations with

levodopa (Madopar or Sinemet), which is reasonable. Secondly, levodopa should *always* be started off at a low dose—increasing every fourth or fifth day either until a complete therapeutic response has been obtained or until adverse reactions appear. When "titrated" in this way, levodopa-induced nausea and vomiting rarely limit the dose, and can be controlled with metoclopramide (although this may itself cause dystonias). The most frequent dose-limiting effects are involuntary movements, which may include chorea, athetosis, dystonias, and facial dyskinesias. Delusions, hallucinations, and behavioural changes may sometimes develop, and these are also usually dose-limiting.

For the present, therefore, I suggest you continue treatment with benzhexol but also start him on a low dose of levodopa. Both Madopar 125 and Sinemet 110 contain 100 mg levodopa, and I would recommend one tablet twice daily to begin with. If you increase the dose cautiously every fourth or fifth day—and try to reduce the interval between doses—you should achieve a worthwhile and sustained benefit.

Anticholinergic drugs produce a limited—albeit useful—therapeutic effect that may be additive with the benefit from levodopa, but dosages must again be on an individual basis in the light of the clinical response. Dose-limiting side effects are those of cholinergic "blockade" (atropine-like), including dryness of the mouth, constipation, urinary retraction, blurring of vision, and mental confusion. This patient has none of these, and so I suspect that he would benefit from an increase in the dose of benzhexol. I would wait, however, until you had set his levodopa treatment to the optimal amount before changing the dose of his anticholinergic treatment.

If the combined response to levodopa and anticholinergic drugs is inadequate then it may be worth trying the effect of amantadine. It improves rigidity and akinesia but is less potent than levodopa. Tolerance, however, develops quickly and after six weeks its therapeutic effects will have worn off completely in half of those patients who have been treated.

Postscript

Taking a dose of levodopa of 250 mg (Sinemet 275) thrice daily and benzhexol, 4 mg thrice daily, he can dress and feed himself, as well as leave the house on his own.

Whickham Health Centre, Whickham, Newcastle upon Tyne

M MACE, MB, MRCP, general practitioner

Department of Pharmacological Sciences (Clinical Pharmacology),
Newcastle upon Tyne NE1 7RU

M D RAWLINS, MD, FRCP, professor of clinical pharmacology