Br. J. clin. Pharmac. (1977), **4**, 185S-186S

NOMIFENSINE IN PARKINSONISM

D.M. PARK, L.J. FINDLEY & P.F. TEYCHENNE
The London Hospital, Turner St, London E1 2AD, UK

1 The effect of nomifensine was compared with that of placebo in a double-blind crossover study in patients with parkinsonism.

2 Of the 29 patients who entered the study, three were previously untreated and 26 continued their L-DOPA or other antiparkinsonian therapy, or both, during the trial.

3 Clinical assessments were made at fortnightly intervals throughout the study.

4 The most noticeable improvement during active treatment—namely, tremor, facial expression and finger flexion were moderate in extent.

5 When placebo was substituted for active drug a significant deterioration of physical signs and functional disability occurred ($P<0.001$).

6 Elderly patients fared less well than younger patients, and the most common adverse effect was involuntary movements.

Introduction

The effect of nomifensine on dopaminergic transmission in the CNS is already well documented. Extensive studies in rat suggested that it could possess useful antiparkinsonian properties, possibly mediated by a direct agonist action. This hypothesis has been tested in patients with Parkinson's disease and is reported briefly here. It has been reported in full elsewhere (Teychenne *et al.*, 1976).

Methods

Twenty-nine patients were admitted to the trial. Three were previously untreated. Of the remainder five were treated only with benzhexol, orphenadrine or amantadine, seven with one of these drugs and levodopa, and fourteen with levodopa alone or combined with carbidopa.

Every patient received nomifensine for 2 weeks, during which the dose was increased to a maximum of 200 mg daily. Active treatment was then continued for 6, 8, 10, 12 or more weeks, after which placebo was substituted for nomifensine for a standard period of 6 weeks.

The patients and the single clinical assessor were unaware when active treatment ended and placebo treatment began. The introductory period and the transfer to placebo were supervised, however, by two other observers.

At every visit each patient was weighed, his blood pressure was measured, and routine haematological monitoring and estimations of serum aspartate and alanine aminotransferases were made. In addition, electrocardiography was carried out.

The clinical assessments of physical signs and functional disability were made according to the method described by Calne *et al.* (1974).

For each patient the results of the last three evaluations while on active drug were compared with the three evaluations while on placebo.

Results

The mean age of the patients who entered the study was 69 yr. Twenty satisfactorily completed the period of treatment with active drug. During treatment, tremor and facial expression improved most out of the physical signs, but other features also improved. All aspects of functional disability improved. Of the timed tests, finger flexion improved significantly ($P = 0.01$). All improvements were, however, only moderate in degree.

When placebo was substituted for active drug, there was a significant deterioration in physical signs and functional disability ($P = 0.01$).

There was some evidence that the more elderly patients responded less favourably to nomifensine, but this could not be related to concomitant antiparkinsonian therapy.

Adverse Effects

Side-effects were fairly frequent, and the most common were involuntary movements similar to those associated with levodopa treatment. Indeed, most occurred in patients concomitantly treated with levodopa. Six patients complained of insomnia, five of nausea and five of headaches. All symptoms were controlled by reducing the dose of nomifensine and abolished by its withdrawal.

A woman aged 66 yr with mild to moderate parkinsonism, already treated with orphenadrine, experienced some dramatic motor phenomena when her dose of nomifensine reached 200 mg daily. The first episode consisted of a sudden involuntary turning of her whole body for a few minutes duration. During the second episode her legs "folded up" and she was brought slowly to the ground. In the third episode, she claimed to be unable to move while in bed at night, for about 6 hours.

A man of 69 yr with severe disabling parkinsonism was receiving nomifensine 200 mg daily. He suffered from agitation, restlessness, confusion and episodic deep rapid breathing most marked about 20 min after his divided dose of nomifensine.

A woman receiving levodopa reached a dose of nomifensine 100 mg daily but felt unwell, "fumbly" and unable to walk about 1 h after taking the treatment. Stopping the levodopa did not abolish the symptoms. A man of 58 yr experienced involuntary movements 30 min after taking nomifensine.

In these four cases, symptoms disappeared on withdrawal of nomifensine.

Conclusions

Nomifensine produced a significant but moderate therapeutic effect in parkinsonism. Adverse effects, particularly involuntary movements, resembled those of levodopa. Elderly patients seemed to tolerate nomifensine less well. Nomifensine may be particularly helpful for those patients whose parkinsonism is complicated by depression.

References

CALNE, D.B., TEYCHENNE, P.F., CLAVERIA, L.E., EASTMAN, R., GREENACRE, J.K. & PETRIE, A. (1974). Bromocryptine in parkinsonism. *Br. med. J.*, **4**, 442-444.

TEYCHENNE, P.F., PARK, D.M., FINDLEY, L.J., ROSE, F.C. & CALNE, D.B. (1976). Nomifensine in parkinsonism. *J. Neur., Neurosurg., Psychiat.*, **39**, 1219-1221.