Medical Memoranda

Monoamine Oxidase Inhibitors and L-Dopa

British Medical Journal, 1970, **3**, 388

The increasing use of L-dopa in the treatment of Parkinsonism has drawn attention to the way in which this catecholamine precursor may interact with other drugs commonly given to such patients. It was reported (Degkwitz *et al.*, 1960) that a monoamine oxidase (M.A.O.) inhibitor potentiated the pressor effect of intravenous L-dopa in psychiatric patients, and a similar effect has been shown in Parkinsonian patients given L-dopa by mouth (Barbeau *et al.*, 1962). In view of the large doses of L-dopa now being given to Parkinsonian patients, many of whom are depressed, we felt that it was important to assess the degree of risk from combination therapy with M.A.O. inhibitors and to study how the hypertension could be controlled. This study was performed under the auspices of the Medical Research Council Working Party on L-dopa, and the proposal was accepted by the University College Hospital and Medical School Committee on the Ethics of Clinical Investigations. The nature and purpose of the study was understood by the patient and his family.

Methods and Results

The patient was a 57-year-old man with an 11-year history of idiopathic Parkinsonism previously treated with benzhexol 5 mg. t.d.s. and imipramine 25 mg. t.d.s. There was no evidence of disease in the cardiovascular system. On his admission to hospital the imipramine was changed to phenelzine 15 mg. t.d.s. After 10 days the effect of oral L-dopa was observed by using techniques previouslv described (Elis *et al.*, 1967).

The effect of 50 mg. L-dopa on the patient's blood pressure and pulse rate is shown in the Chart. When the systolic pressure reached 180 mm. Hg an α-adrenoreceptor blocker, phentolamine, was given intravenously. Satisfactory control was achieved with a total dose of 9 mg. During this study no alteration was seen in the electrocardiogram, but 45 minutes after the administration of L-dopa the patient reported that his limbs felt "much looser," and clinical assessment confirmed a definite reduction in the degree of rigidity at the wrists. This effect lasted for five minutes. There was no alteration in the Parkinsonian tremor at this time.

Next day the experiment was repeated, using 25 mg. L-dopa, but no change in blood pressure, pulse rate, electrocardiogram, or rigidity was seen with this dose.

Three weeks after the M.A.O. inhibitor had been discontinued single doses up to 500 mg. of L-dopa produced no effect on the patient's blood pressure.

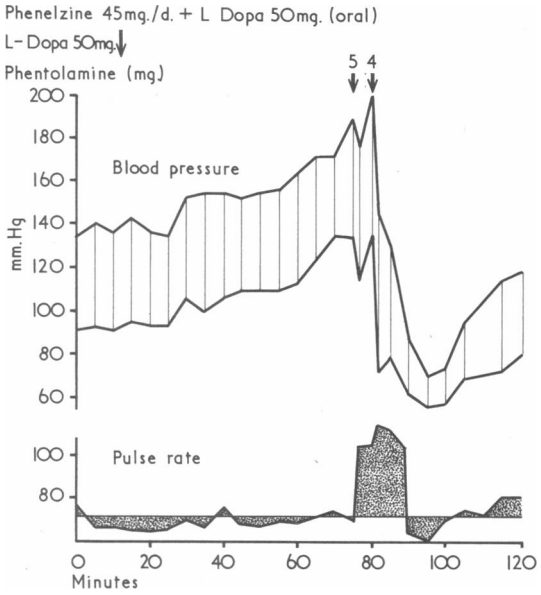
Comment

These results confirm that a dose of L-dopa which normally produces no effect on the blood pressure can cause a dramatic rise when given to a Parkinsonian patient taking phenelzine. The extent of this rise is related to the dose of L-dopa. Our results are similar to those obtained with tranylcypromine (Barbeau *et al.*, 1962) and isocarboxazid (Birkmayer and Hornykiewicz, 1962). Therefore we did not think it necessary to repeat this potentially dangerous experiment with other patients and different M.A.O. inhibitors.

Though the exact mechanism by which the combination raises the blood pressure is not clear, it has been shown that an α-adrenoreceptor blocker controls this hypertension in non-Parkinsonian patients (Hodge *et al.*, 1964). Catecholamine metabolism is abnormal in patients with idiopathic Parkinsonism (Goodall and Alton, 1969); nevertheless, our results suggest that intravenous phentolamine is effective treatment of hypertensive crises due to L-dopa in such patients. We recommend that management in such cases should follow the principles recently outlined by Simmons *et al.* (1970).

An interesting feature in our patient was the absence of any change in pulse rate when the blood pressure rose. This is compatible with the increased blood pressure being caused by dopamine rather than by noradrenaline or adrenaline (Horowitz *et al.*, 1962). It is unlikely that the benzhexol therapy had sufficient atropine-like effect at the vagal endings to modify the pulse rate.

The results of this study emphasize a previous warning that combination therapy with amine precursors and M.A.O. inhibitors is potentially dangerous (Sjöqvist, 1965). Therefore M.A.O. inhibitors should be withdrawn from all patients with Parkinsonism before L-dopa is given. We have seen two patients who became confused and paranoid when given L-dopa two weeks after M.A.O. inhibitor therapy had been discontinued. We therefore recommend that at least one month should elapse before L-dopa is given. If patients on L-dopa require antidepressives we use either imipramine or amitriptyline, which seem to be safe.



Effect of L-dopa 50 mg. on patient's blood pressure and pulse.

We wish to thank the patient for his willing co-operation, Mr. A. R. Williams for dispensing L-dopa and matching control capsules, Mr. B. R. Graham for technical assistance, Mr. V. K. Asta for preparing the Chart, and Dr. E. J. Ross for allowing us to study a patient under his care. K.R.H. is supported by a Medical Research Council grant, and A.J.B. is a Wellcome Trust Research Fellow in Clinical Pharmacology. The L-dopa used was donated by Roche Products Ltd.

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