CARDIOVASCULAR REFLEXES IN PARKINSONISM

J. L. REID, D. B. CALNE, C. F. GEORGE, C. PALLIS AND S. D. VAKIL

Departments of Medicine and Clinical Pharmacology,
Royal Postgraduate Medical School,
and Medical Research Council Clinical Pharmacology Research Group

(Received 25 January 1971)

SUMMARY

1. Cardiovascular reflex activity has been studied in thirty Parkinsonian patients, none of who had received levodopa or sympatholytic drugs.
2. Changes in blood pressure and pulse rate in response to Valsalva's manoeuvre and head-up tilt were investigated by intra-arterial recording.
3. Cardiovascular reflex function deteriorated with advancing age, but there was no correlation with either the duration or the severity of the Parkinsonism.
4. These results are discussed in relation to previous reports of hypotension in Parkinsonism.

Numerous therapeutic successes and several important adverse reactions have followed the adoption of levodopa (l-dopa) as treatment for Parkinsonism. The frequent occurrence of orthostatic hypotension as a reversible, dose-dependent effect of levodopa therapy has led to a resurgence of interest in the mechanisms of blood-pressure control in these patients. It has been reported that the blood pressure is lower than normal in Parkinsonism irrespective of drug administration and there have been suggestions of a generalized defect of catecholamine metabolism (Barbeau, 1970). More recently it has been found that plasma renin activity is decreased (Barbeau, Gillo-Joffroy, Boucher, Nowaczynski & Genest, 1969; Michelakis & Robertson, 1970). Shy & Drager (1960) have described six patients who presented with autonomic dysfunction including orthostatic hypotension and subsequently developed some of the clinical features of Parkinsonism.

To obtain further information on the control of blood pressure in Parkinsonian patients before administration of levodopa, we have studied the cardiovascular response to Valsalva's manoeuvre and to head-up tilt.

MATERIALS

Patients. Thirty patients were investigated, of these twenty-eight had idiopathic and two postencephalitic Parkinsonism. There were fifteen men and fifteen women, their ages ranging

Correspondence: Dr D. B. Calne, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London, W.12.
from 35 to 82 years. The duration of neurological illness was 1–40 years; six patients could not walk without support, twenty walked unaided but with difficulty, and in the remaining four the gait was normal. Twenty-eight of the patients had been on routine anti-Parkinsonian drugs for many years and this treatment was not altered; two were not receiving any drugs. None of the patients was receiving sympatholytic agents and none was in cardiac failure. All patients consented to intra-arterial cannulation, the purpose of the investigation having been fully explained.

Methods. In each case the right femoral artery was cannulated under local anaesthesia with a Seldinger needle. The intra-arterial pressure was measured with a Devices strain-gauge transducer and recorded on a Devices M4 polygraph. No morbidity was encountered.

For Valsalva’s manoeuvre patients were trained to blow up a column of mercury to 40 mm and to maintain this expiratory effort for 10–12 s. To study the effect of postural change an electrically driven tilt-table brought the patient from a horizontal position to a head-up angle of 35° over a period of 8 s. The blood pressure was recorded for 2 min in this position.

Determination of indices. Intra-arterial recording of the response to Valsalva’s manoeuvre allows sensitive measurement of the cardiovascular reflex adjustments to changes in blood pressure. Consistent results are attainable by deriving an index (Sharpey-Schafer, 1955; Gross, 1970) which takes into account how efficiently the patient had carried out the manoeuvre, this being measured by the percentage fall in pulse pressure during the expiratory strain. The fall in pulse pressure also represents the stimulus applied to the baroreceptors and activates the afferent side of the reflex arc. Two efferent arcs can be studied by recording: (i) the vasoconstrictor response (the maximum rise in diastolic pressure after strain, this representing alpha adrenergic activation of the vascular bed); (ii) the cardiac accelerator response (the maximum increase in pulse rate during strain, this representing beta adrenergic activation of the sinoatrial node and inhibition of vagal tone). These expressions of autonomic function will be referred to as the constrictor and accelerator indices respectively. The following ratios take into account the variation in stimulus which depends on the competence of the patient in maintaining expiratory strain.

\[
\text{Constrictor index} = \frac{\text{Maximum } \% \text{ rise in diastolic pressure}}{\text{Maximum } \% \text{ fall in pulse pressure}}
\]

\[
\text{Accelerator index} = \frac{\text{Maximum } \% \text{ rise in heart rate}}{\text{Maximum } \% \text{ fall in pulse pressure}}
\]

RESULTS

Constrictor index. The constrictor index ranged from 0 to 0·86. There was no correlation between this index and either the duration or the severity of Parkinsonism. However, there was a definite inverse linear relationship between the constrictor index and age (\(P<0.05\)). A comparison of regression analyses by the F test failed to reveal any significant difference between these results and observations made by Gross (1970) on normal subjects and patients with cerebrovascular disease. Fig. 1 shows the findings in thirty Parkinsonian patients together with the results obtained by Gross in fifteen normal subjects.

Accelerator index. Analysis of the accelerator index revealed relationships essentially similar to those found for the constrictor index. There was no correlation with the duration of
Cardiovascular reflexes in Parkinsonism

Parkinsonism or the extent of neurological disability. However, an inverse linear relationship with age was evident ($P < 0.05$). Again there was no significant difference (detected by an F test on the regression lines) between these results and the observations reported by Gross for normal subjects and patients with cerebrovascular disease. Fig. 2 shows a comparison between the observations on Parkinsonian patients and Gross's normal volunteers.

![Fig. 1](image1.png)

**Fig. 1.** Relation of age to constrictor index derived from Valsalva's manoeuvre in thirty Parkinsonian patients and eighteen normal subjects (Gross, 1970). ●, Controls; ○, idiopathic Parkinsonism; △, post-encephalitic Parkinsonism.

![Fig. 2](image2.png)

**Fig. 2.** Relation of age to accelerator index derived from Valsalva's manoeuvre in thirty Parkinsonian patients and eighteen normal subjects (Gross, 1970). ●, Controls; ○, idiopathic Parkinsonism; △, post-encephalitic Parkinsonism.

**Head-up tilt.** A direct linear relationship was evident between the changes in blood pressure after 1 min of head-up tilt to 35° from horizontal and the constrictor index of Valsalva's manoeuvre. Regression analysis revealed a significant correlation ($P < 0.05$, see Fig. 3). In all patients displaying a substantial fall in systolic pressure on tilting, the cardiovascular responses to Valsalva's manoeuvre were impaired. However, in several patients who exhibited negligible
change in blood pressure on tilting a decreased response to Valsalva's manoeuvre was observed, so the latter is probably a more sensitive test of baroreceptor reflex function.

\[ \begin{align*}
&0.8 \\
&0.7 \\
&0.6 \\
&0.5 \\
&0.4 \\
&0.3 \\
&0.2 \\
&0.1 \\
\end{align*} \]

\[ \begin{align*}
&-25 -20 -15 -10 -5 0 +5 +10 +15 +20 +25 \\
\end{align*} \]

Fig. 3. Regression analysis of the relation between constrictor index derived from Valsalva's manoeuvre and change in systolic blood pressure on 35° head-up tilt.

**DISCUSSION**

These observations indicate that with advancing age there is a steady decline in the cardiovascular reflex responses of patients with idiopathic Parkinsonism. A similar inverse relationship between age and cardiovascular responses has been reported in normal subjects (Gross, 1970; Appenzeller & Descarries, 1964) and in patients with cerebrovascular disease (Gross, 1970). Taking age into account, reflex function in the Parkinsonian group was compared with normal subjects and patients with cerebrovascular disease; no significant difference could be found. On the basis of these findings it seems probable that the decreased cardiovascular reflex responses of Parkinsonian patients when compared with healthy young adults is due to the steep rise in the prevalence of Parkinsonism with increasing age. The failure of cardiovascular reflex performance in Parkinsonian patients to correlate with either the duration of neurological disease or the severity of neurological deficit adds further support to this view.

The pathological basis for the deterioration of cardiovascular reflexes with increasing age is not understood. It has been suggested that cerebrovascular disease may be responsible (Johnson, Smith, Spalding & Wollner, 1965). The general decline in the number of functioning neurones in the central nervous system and the loss of peripheral nerve axons, which appear to be a non-specific result of ageing, may contribute. Degeneration of sensory end-organs has been demonstrated in the somatic nervous system of elderly subjects (Bolton, Winklemann & Dyck, 1966) and it is probable that the same changes take place in the autonomic nervous system. Other possibilities include changes in baroreceptor sensitivity or in smooth-muscle contractility due to replacement of muscle by fibrous tissue in the walls of blood vessels with advancing age.
ACKNOWLEDGMENTS

We wish to thank Professor C. T. Dollery for his advice, Miss E. Allbutt for administrative assistance, and Miss A. Petrie for help with the statistical analyses. This work was supported by The Wellcome Trust, the Medical Research Council, and Ward Blenkinsop and Co. Ltd.

REFERENCES


