Cerebral vasomotor reactivity in Parkinson’s disease, multiple system atrophy and pure autonomic failure

Tanya Gurevich*, Alexander Y. Gur, Natan M. Bornstein, Nir Giladi, Amos D. Korczyn

Neurology Department, Tel-Aviv Medical Center, Israel
Sieratzki Chair of Neurology, Tel-Aviv University, Israel

Received 3 February 2005; received in revised form 31 August 2005; accepted 16 November 2005
Available online 24 January 2005

Abstract

Parkinson’s disease (PD), multiple system atrophy (MSA) and pure autonomic failure (PAF) are neurodegenerative disorders frequently associated with orthostatic hypotension and syncope, though with different underlying mechanisms. Cerebral hemodynamic responses in these three neurodegenerative diseases are still incompletely studied and it is possible that they would be differentially affected. We measured blood flow velocity (BFV) in the middle cerebral artery (MCA) and vertebral artery (VA) in patients with these disorders and investigated whether cerebral vasomotor reactivity (VMR) differs in these three disorders.

Twenty-four patients (9 with PD, 10 with MSA and 5 with PAF) were studied. VMR was assessed in the MCA and VA, using transcranial Doppler (TCD) and Diamox test (injection of 1 g acetazolamide i.v.) with the patients in a recumbent position. The percent difference between BFV before and after acetazolamide injection was defined as VMR% and the results were compared by ANOVA.

The mean MCA and VA blood flow velocities were similar in the three disorders and within normal limits for our laboratory. The mean MCA VMR values were 37.5 ± 24.0%, 27.9 ± 28.0% and 38.0 ± 33.9% in PD, MSA and PAF, respectively. The VA VMR values were 22.9 ± 23.6%, 32.4 ± 38.0% and 18.9 ± 18.3%, respectively, with no significant differences between the groups.

We conclude that BFV is normal in PD, MSA and PAF and that the VMR, as investigated by TCD and the Diamox test, did not disclose differences in cerebral vasomotor responses between these conditions.

© 2005 Published by Elsevier B.V.

Keywords: Cerebral vasomotor reactivity; Parkinson’s disease; Multiple system atrophy; Pure autonomic failure; Autonomic function; Orthostatic hypotension; Diamox test

1. Introduction

Parkinson’s disease (PD), multiple system atrophy (MSA) and pure autonomic failure (PAF) are degenerative diseases of the nervous system with different clinical, anatomic and pathological features. Nevertheless, orthostatic hypotension (OH) frequently occurs in all, and syncope may be a prominent feature [1].

Autonomic disturbances are particularly prominent in MSA, resulting from loss of preganglionic neurons within the intermediolateral column of the spinal cord, accompanied by cell loss in the dorsal vagal nuclei [2,3]. In PD, autonomic insufficiency plays a much less prominent role and appears later in the course of the disease [4,5]. PD primarily affects the brain but the dorsal vagal nuclei are also affected very early [6]. However, autonomic symptoms may be ascribed not only to faulty central regulation, as presumed in the past, but also to autonomic nervous system changes in the periphery [7–9], since Lewy bodies were found in autonomic ganglia in PD [5,10,11] and cardiac scintigraphy shows cardiac sympathetic denervation [12,13]. Thus, dysautonomia in PD can be related to both central and peripheral components. PAF is the result of selective involvement of the peripheral autonomic nervous system, consisting of degeneration of
postganglionic sympathetic and parasympathetic neurons [14]. Normally, blood pressure falls are compensated for by increased sympathetic tone and cerebral vasodilation. The sympathetic recruitment is impaired in all three diseases, but it is unclear whether and to what extent cerebrovascular regulation is affected. Cerebral autoregulation has been studied by different methods in patients with MSA, but the results were not consistent, suggesting either impaired or intact cerebral autoregulation [15–19]. Preserved cerebral autoregulation was reported in PD [20,21].

We have resorted to measurement of CBF changes and assessment of cerebral vasomotor reactivity (VMR) by means of TCD before and after a vasodilatory stimulus, intravenous injection of acetazolamide (Diamox), which provides information regarding cerebral autoregulation and collateral circulation [22]. Our aim was to look for a simple tool of distinguishing of these disorders. The Diamox test is a safe, reproducible, validated and easy to perform method to assess cerebrovascular hemodynamics [22,23]. We used this method to compare VMR in patients with PD, MSA and PAF.

2. Patients and methods

Patients of our Movement Disorders Unit were recruited to the study. Ten patients had probable MSA (parkinsonian type in six and cerebellar type in four), nine had PD and five had PAF. Patients’ characteristics are given in Table 1. The clinical diagnosis was made by at least two movement disorders specialists based on a detailed history and neurological examination using accepted criteria: The United Kingdom Brain Bank clinical criteria as modified by Douglas et al. [24] were used to diagnose PD. MSA was diagnosed using the criteria of Gilman et al. [25]: most MSA patients had OH, confirmed by tilt table test and/or urination disturbances. MSA-P patients were poorly responsive to L-dopa. In addition, all PD and MSA patients underwent brain MRI or CT examinations and those with focal lesions were excluded. Patients with significant (more than 70%) stenotic changes of the extracranial carotid arteries, based on carotid Doppler assessment, were also excluded from the study.

All patients underwent prolonged (40 min) tilt test and cerebral VMR assessment with the Diamox test. Cerebral blood flow velocity (BFV) was measured at baseline in both middle cerebral arteries (MCA) and both vertebral arteries (VA), using TCD machine (Rimed, Trans-link 9900 TCD, Herzliya, Israel), and the measurement repeated 20 min after injection of 1 g acetazolamide i.v. The TCD examination was carried out with the patients in a supine position, and included transtemporal insonation of the MCA at a depth of 50–55 mm and transoccipital insonation of the VA at a depth of 60–90 mm, using a 2-MHz hand held probe [26]. The most powerful signal during a 10-s period was used for BFV measurement. Assessment of TCD and the Diamox test were performed by AG blindly to the clinical diagnoses of the patients. Blood pressure and heart rate were monitored before and after acetazolamide injection to ensure that the blood pressure remained within physiological limits.

Patients did not take their regular medications for at least 3 h before VMR assessment. The VMR was evaluated by calculating the percentage difference in peak systolic flow velocity in each artery at baseline and after acetazolamide injection [23]. The ANOVA test was used to compare VMR in the three groups. P-values < 0.05 were considered significant.

3. Results

All patients had orthostatic complaints and most had OH (Table 1), defined as a difference between systolic blood pressure in supine and recumbent position after 3 min of standing exceeding 20 mm Hg [27].

The results of the blood pressure changes, cerebral blood flow velocities (BFV) and VMR measurements are presented in Table 1. BFV were normal both in MCA and VA. VMR% of patients had PD MSA PAF

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>PD</th>
<th>MSA</th>
<th>PAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females/males</td>
<td>3/6</td>
<td>5/5</td>
<td>0/5</td>
</tr>
<tr>
<td>Age (years, mean±S.D.)</td>
<td>79.8±4.3</td>
<td>74.7±5.8</td>
<td>61.4±11.6</td>
</tr>
<tr>
<td>Disease duration (years, mean±S.D.)</td>
<td>7.3±4.9</td>
<td>4.1±3.2</td>
<td>2.4±1.7</td>
</tr>
<tr>
<td>Presence of orthostatic hypotension (number of patients)</td>
<td>8/9</td>
<td>8/10</td>
<td>5/5</td>
</tr>
<tr>
<td>Drop of systolic blood pressure from supine position after 3 min of standing</td>
<td>27.4±9.9</td>
<td>28.1±13.05</td>
<td>45.6±17.7</td>
</tr>
</tbody>
</table>

BFV—blood flow velocity, MCA—middle cerebral artery, Mixed VMR—normal on one side and pathological on the other, MSA—multiple system atrophy, PAF—pure autonomic failure, PD—Parkinson’s disease, S.D.—standard deviation, VA—vertebral artery, VMR—vasomotor reactivity.
4. Discussion

Syncope is a prominent symptom in the three disorders studied by us, resulting from orthostatic fall of blood pressure and cerebral perfusion, although the underlying pathophysiological mechanisms are of course different. Normally, cerebral autoregulation should compensate for the blood pressure fall by vasodilatation. We speculated that because MSA is a central autonomic disorder with brainstem involvement, and since the brainstem is critical for the control of cardiovascular function [28,29], VMR impairment in MSA could be more pronounced than in other neurodegenerative diseases with autonomic failure, but this has not been confirmed in the present study.

Previously, cerebral autoregulation has been studied by different methods in patients with MSA, but the results were not consistent. There are reports of both impaired and intact cerebral autoregulation [15–19,30]. In a few cases, cerebral autoregulation in MSA patients was evaluated by TCD with Valsalva maneuver or during tilting to upright position and was found to be impaired [29]. In a recently published study of cerebral hemodynamic responses to orthostasis in PD patients without symptoms of orthostatic dysregulation, impaired autonomic circulatory control was found, while cerebral hemodynamic regulation during orthostasis was unaffected [20]. In the present study, we attempted to measure the cerebral autoregulation capacity, i.e. whether the cerebral vessels can respond to acetazolamide. Presumably, if this response is reduced, there would also be an impaired response to orthostasis.

Our results show that baseline BFV were within normal limits in all three diagnostic categories. All our patients had orthostatic complaints, but in three of them OH was not recorded. Interestingly, in all these three patients the VMR was impaired in both MCA and VA arteries.

The three diagnostic groups were not strictly comparable in terms of age and disease duration (Table 1), but there was no correlation between age or disease duration and VMR. Furthermore, Valikovics et al. have found only slight and nonsignificant differences between normal subjects in their sixths and sevenths decades of life [31]. Thus, although PAF patients in our study were younger, these differences were small and unlikely to affect the VMR to a significant degree.

Our results failed to show differences between VMR in the three diseases. Of course, a small difference could still exist which was missed because of small number of cases in each subgroup. However, such differences, if they exist, would be small and lacking clinical relevance.

Acknowledgment

We are grateful to Ms. Margot Feinstein for her expert secretarial help.

References


