Autoregulation of Cerebral Blood Flow in Orthostatic Hypotension

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Background and Purpose—We sought to evaluate cerebral autoregulation in patients with orthostatic hypotension (OH).

Methods—We studied 21 patients (aged 52 to 78 years) with neurogenic OH during 80° head-up tilt. Blood flow velocities (BFV) from the middle cerebral artery were continuously monitored with transcranial Doppler sonography, as were heart rate, blood pressure (BP), cardiac output, stroke volume, CO2, total peripheral resistance, and cerebrovascular resistance.

Results—All OH patients had lower BP (P<.0001), BFV_diastolic (P<.05), CVR (P<.007), and TPR (P<.02) during head-up tilt than control subjects. In control subjects, no correlations between BFV and BP were found during head-up tilt, suggesting normal autoregulation. OH patients could be separated into those with normal or expanded autoregulation (OH_NA; n=16) and those with autoregulatory failure (OH_AF; n=5). The OH_NA group showed either no correlation between BFV and BP (n=8) or had a positive BFV/BP correlation (R²>75) but with a flat slope. An expansion of the “autoregulated” range was seen in some patients. The OH_AF group was characterized by a profound fall in BFV in response to a small reduction in BP (mean ΔBP <40 mm Hg; R²>.75).

Conclusions—The most common patterns of cerebral response to OH are autoregulatory failure with a flat flow-pressure relationship or intact autoregulation with an expanded autoregulated range. The least common pattern is autoregulatory failure with a steep flow-pressure relationship. Patients with patterns 1 and 2 have an enhanced capacity to cope with OH, while those with pattern 3 have reduced capacity. (Stroke. 1998;29:104-111.)

Key Words: autoregulation • cerebral blood flow • hypotension, orthostatic • ultrasonics

Symptoms of OH such as dizziness, lightheadedness, weakness, blurred vision, impairment of concentration, and loss of consciousness occur when cerebral perfusion is sufficiently impaired. Cerebral hypoperfusion develops when cerebral autoregulation fails in the face of a severe reduction in BP. OH is typically seen in generalized autonomic failure, as occurs in multiple system atrophy and in the autonomic neuropathies such as diabetic neuropathy.1 Although there is a positive correlation between the fall in BP during HUT and symptoms of orthostatic intolerance,2 patient complaints can be vague or nonspecific. In addition, the obvious symptoms of OH, such as lightheadedness or visual blurring, are often absent or delayed in the elderly, where the main symptom is orthostatic cognitive impairment in approximately 50% of patients.2 Therefore, an objective indicator of impaired cerebral perfusion is needed.

Cerebral perfusion cannot be predicted from the BP alone, since the relationship between BP and cerebral perfusion is nonlinear because of autoregulation. The primary goal of cerebral autoregulation is to maintain constant blood flow during variations in BP.3 Within the autoregulated range (~80 to 160 mm Hg SBP), cerebral blood flow remains constant despite alterations in BP. In many patients with chronic OH, MBP remains within the autoregulated range. Some patients may also have an expansion of their autoregulated range so that cerebral perfusion remains stable even when SBP falls to 60 mm Hg4 in the upright position. The aim of our study was to evaluate the range of responses of cerebral perfusion to reduction in BP and to attempt a quantitative evaluation of autoregulation, based on the standardized stress of HUT.

Subjects and Methods

Control Subjects and Patients

We studied 21 patients with neurogenic OH (9 men and 12 women; mean age, 61.76±2.4 years [range, 52 to 78 years]). Eight patients had been diagnosed with multiple system atrophy, 3 with pure autonomic failure, 6 with diabetic neuropathy, and 4 with idiopathic autonomic failure. Neurogenic OH was considered to be present if HUT induced a fall in SBP of ≥30 mm Hg, DBP ≥10 mm Hg, or MBP ≥15 mm Hg, and an autonomic reflex screen (to evaluate the severity and distribution of adrenergic, sudomotor, and cardiovascular autonomic failure) confirmed generalized autonomic failure. Autonomic failure was quantitated with the use of a composite autonomic scoring scale1 (all patients scored 7 to 9 on the scale of 1 to 10, where 0=normal and 10=the most severe autonomic failure). All our patients with multiple system atrophy and pure autonomic failure fulfilled the criteria recommended by the consensus panel.6 All patients were off regular medications for at least 1 week before the studies, and insulin-dependent diabetic patients were studied when under stable glycemic control.

Fourteen healthy control subjects (6 men and 8 women; mean age, 61.6±2.3 years [range, 29 to 77 years]) were also studied. Age was not significantly different between the groups. Normal control subjects were selected as follows. Mayo Clinic histories were reviewed, and all subjects also completed a questionnaire directed at ruling out peripher-
The TCD system (Multigon Industries) was used to continuously monitor cerebral BFV during the tilt-table test and during hyperventilation. The left MCA was sonicated from the anterior temporal window by placing the probe on the temporal area, above the zygomatic arch. The polytetrafluoroethylene probe was positioned to record the maximal MCA velocity and fixed at the desired angle with the polytetrafluoroethylene probe holder, which allowed three-dimensional manipulation of the probe angle. Stable positioning of the probe is crucial for continuous data recording and for data evaluation. Doppler shift, a difference between the frequency of the emitted signal (2 MHz) and its echo (frequency of the reflected signal), was then used to calculate the velocity of blood flow by means of Fourier transform. Spectral analysis of blood flow velocities is then presented as a waveform, similar to the BP waveform. Analog flow velocity waveforms were continuously recorded and used for off-line detection of systolic (BFV_S) and diastolic blood flow velocities (BFV_D) on a beat-to-beat basis. Mean blood flow velocity (BFV_M) was computed according the formula described above (see derived and calculated variables in “Selected Abbreviations and Acronyms”). Several assumptions must be made to evaluate cerebral autoregulation with TCD monitoring. An assumption that the diameter of the MCA does not change must be made to relate MCA flow velocity to blood flow. Flow velocity can be increased because of an increased flow through the arterioles distal to the probe or by a constriction of the insonated vessel. The changes in BFV_M, pulsatility index, and resistance index therefore reliably reflect, under nonextreme circumstances, changes in the tone of arterioles and, perhaps, small arteries. Additionally, cerebral BFV correlates well with cerebral blood flow measured with xenon clearance or with laser Doppler flow. We expressed CVR as mm Hg/cm per second. It can alternatively be expressed in units of dyne.s/cm^2 by multiplying by 1333.

**Impedance Cardiography**

Changes in thoracic impedance during the cardiac cycle largely reflect changes in thoracic aortic volume and hence in left ventricular outflow. Impedance cardiography (NCOM3-R7 Cardiodynamic Monitor, BoMed Medical Manufacturing) used eight electrodes placed on the thoracic outlet and inlet. All subjects had normal cardiovascular function and were free of intraventricular conduction defects, intracardiac shunts, or valvular insufficiency that may confound SV and CO measurement. Values of SV and CO were calculated with the use of Kubicek’s equation. This equation uses adjustments for the body surface area that may account for interindividual variation of the impedance estimate.

**Respiration and CO₂**

Respiratory frequency was measured with a nasal thermistor and sampled at 4 Hz. CO₂ was measured with a Puritan Bennett 254 airway gas monitor calibrated with 5% CO₂. All data were simultaneously acquired; outlying values and extrasystoles were removed. Time series were then averaged over 30-second intervals for each parameter for each individual. These individual temporal profiles were subsequently averaged to provide mean temporal profiles for each parameter for OH and control groups.

**Evaluation of Autoregulation**

With autoregulation, cerebral blood flow remains stable when BP changes within the autoregulated range. In normal subjects, resting BP is well within the autoregulated range, and changes in BP of ≤30 mm Hg result in an insignificant change in BFV. In this situation no significant correlation should exist between ΔBP and BFV. To obtain an estimate of the range of autoregulation or severity of its impairment, we evaluated BPV responses to the larger changes in MBP induced by HUT. The indices evaluated were as follows.

**Pressure-Flow Relationship**

Regressions of BFV_M against MBP and BFV_S against SBP were undertaken. We plotted BFV against BP for the entire time series (during rest and 30-second averages during HUT) and fitted a linear regression line. When R^2>=0.75, the regression coefficient was also
obtained. The coefficient of determination ($R^2$) provides an index of autoregulatory failure, and the slope provides an index of the severity of such a failure. These linear regressions were obtained over a large range of BP changes from supine to standing in OH patients but over a more narrow range in control subjects.

**Autoregulatory Curve**

In addition to an evaluation of the slope of the flow–BP curve, we also obtained the BFV_M corresponding to the maximal fall of BP during HUT to provide insights into the range of autoregulatory responses to HUT. We constructed the autoregulatory curve for maximal change of MBP ($\Delta$MBP) in response to HUT and corresponding blood flow values ($\Delta$BFV_M), accepting BFV_M as long as it did not exceed the break point. Differences between rest and HUT were evaluated from time profiles averaged over 30 seconds. The following formulas were used:

$$\Delta$MBP = supine MBP – MBP minimum during HUT (30-second average)

$$\Delta$BFV_M = supine BFV_M – BFV_M at MBP minimum during HUT (30-second average)

**Statistical Analysis**

All parameters were compared before and after HUT in OH patients and control subjects with the use of unpaired two-tailed $t$ tests\(^1\) and two-way ANOVA. We used a $2\times2$ contingency table (Fisher’s exact test) to compare categorical outcomes between control and OH groups. $P<.05$ was considered significant. Data are presented as mean±SE.

**Results**

**Rest–Tilt Comparisons**

The effect of HUT on the cardiovascular and cerebrovascular hemodynamic indices is summarized in Table 1. Compared with the control group, OH patients had higher resting supine heart rate ($P=.007$), SBP ($P=.03$), DBP ($P=.003$), and MBP ($P=.008$) than the control group, while blood flow velocities (BFV_S, BFV_M, BFV_D), cardiovascular indices (SV, CO), and TPR and CVR were not different.

With HUT, the control group demonstrated a significant increase in HR ($P<.001$) and DBP ($P<.02$) and fall in SV ($P=.001$). In the OH group, HUT evoked a similar HR increment. However, other systemic and cerebrovascular indices responded quite differently. Compared with control subjects, there was a significantly greater fall in PP ($P<.001$). OH patients had a different pattern of systemic and cerebrovascular responses: BP (SBP, DBP, MBP; $P<.001$) and TPR consistently fell rather than rose ($P<.02$) during HUT; indices of cerebral flow (BFV_D, BFV_M) and PF also declined significantly during HUT. During HUT, CO was larger in OH patients, partially compensating for a diminished cerebral blood flow, while other cardiac indices did not change. CFR during HUT was significantly lower in OH patients than control subjects ($P<.001$). Both groups showed a mild reduction ($<10\%$) of CO$_2$ with HUT ($P=NS$ between groups). These data indicate that cerebral perfusion in the MCA territory was compromised in patients with OH during HUT.

**Hyperventilation**

Control subjects and OH patients underwent a similar reduction in CO$_2$ and HR in response to hyperventilation (Table 2). The control subjects, but not the OH group, underwent significant hyperventilation–induced changes in cerebral perfusion (BFV_S, BFV_M, BFV_D) and in CFR. Since the reduction in CO$_2$ was not different in OH patients compared with control subjects, these data suggest that the vasoconstrictor response to CO$_2$ is reduced in OH patients.

**Autoregulation**

Fig 1 shows the temporal profiles of MBP and BFV_M during rest and HUT in a normal control subject (A), an OH patient with “preserved” autoregulation (B), and an OH patient with
autoregulatory failure (C). In the normal control subject, BP increased and BFV_M remained stable during HUT (A). The flow-pressure relationship failed to regress (Fig 1A, right panel). A large fall of BP (>80 mm Hg) resulted in only a mild reduction of BFV_M in the OH patient (B). The fall in BFV_M was modest relative to the fall in BP, reflecting the flat flow-pressure curve (Fig 1C, right panel). In contrast, autoregulatory failure, manifested as a large fall in BFV_M for a relatively small BP reduction (<40 mm Hg), was seen in the OH patient with autoregulatory failure (Fig 1C), reflecting the steep flow-pressure curve (Fig 1C, right panel).

Flow-Pressure Relationship

We used regression analysis to test the hypothesis that positive flow-pressure correlation and a linear flow-pressure relationship can be predictive of autoregulation failure (see “Evaluation of Autoregulation” in “Subjects and Methods”). Control subjects either did not have a significant positive correlation of flow to pressure (13 of 14) or had a negative slope of regression (1 of 14). Negative slope indicates an increase in BP during HUT. In contrast, 13 of 21 OH patients showed a significant correlation between BFV_M and MBP (r= .0015, OH versus control, Fisher’s exact test). As shown in Fig 1, no significant correlation was found in control subjects (1A). In the OH patient with expanded autoregulatory range (B), flow-pressure correlation was significant (r=.99) with a relatively flat slope of regression (0.26). In contrast, high correlation (r=.99) and a steep slope of regression (1.22) were present in the OH patient with autoregulatory failure. The slopes of the linear regressions for those OH patients with significant coefficients of determination (R^2>.75) are plotted in Fig 2. When the coefficient of determination was not significant, a default of 0 was accepted. Values of 8 OH patients resembled control values, and 13 of 21 OH patients had a positive slope, mostly (10 of 21) with slopes <1 cm/s per millimeter of mercury.

Change in BFV With Maximal MBP Decrement During HUT

The relationship between ΔBFV_M and maximal ΔMBP in all patients is shown in Fig 3. ΔMBP in control subjects ranged from -20 to 18 mm Hg and was associated with an insignificant ΔBFV_M. The OH group was separated into two groups, the first with autoregulatory failure (OH_AF) and the second with relatively preserved and often expanded autoregulation (OH_NA) (Fig 3).

Orthostatic Hypotension With Autoregulatory Failure

A subgroup of five OH patients had autoregulatory failure (OH_AF), as seen in Fig 3. The relationship between ΔBFV_M and maximal ΔMBP of this group was characterized by mild OH, large ΔBFV_M, high correlation coefficients, and steep flow-pressure regression slopes. ΔMBP was modest, ranging from 20 to 33 mm Hg. In contrast, the fall in BFV_M was very large, ranging from 10 to 60 cm/s. The coefficients of determination consistently exceeded 0.86, and the slopes of individual BFV_M versus MBP linear regressions were positive, ranging from 0.53 to 1.80 cm/s per millimeter of mercury. The reduction of cerebral flow (ΔBFV_M) was larger in the OH_AF patients than would be predicted for a relatively small decline of BP. The BP reduction (ΔMBP) was lower in OH_AF than OH_NA patients (28.7±2.7 versus 46.9±5.6 mm Hg; P<.01). In contrast, cerebral flow velocity (ΔBFV_M) diminished more in the OH_AF (35.3±8.6 cm/s) than in the OH_NA group (11.6±2.1 cm/s; P=.055).

<table>
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<tr>
<th>Variable</th>
<th>Control Subjects</th>
<th>OH Patients</th>
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<tr>
<td>HR</td>
<td>Rest 62.5±1.8</td>
<td>OH 74.3±3.0</td>
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<tr>
<td>SBP</td>
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<td>148.2±7.1</td>
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Table 2. Mean Values of Cardiovascular and TCD Parameters in Control Subjects and OH During Hyperventilation

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*P<.05, comparisons between groups during hyperventilation.
†P<.05; ††P<.01; †††P<.001, comparisons between rest and HV within group.

Controls, n=13; OH patients, n=10.
Orthostatic Hypotension With Normal or Extended Autoregulation

In this group of 16 OH patients, autoregulation was relatively preserved, despite a large ΔMBP ranging from 10.8 to 91.95 mm Hg. In response to this large ΔMBP, ΔBFV_M changed only modestly, from −3 to 25 cm/s. Eight patients with mild OH (ΔMBP <40 mm Hg and modest ΔBFV_M <15 cm/s) showed no correlation between ΔMBP and ΔBFV_M, closely resembling control subjects. A positive correlation between ΔBFV_M and ΔMBP was found in the remaining 8 OH patients, who demonstrated severe OH (ΔMBP 40 to 92 mm Hg). However, the slope of regression was flatter (<0.5) than in the OH_AF group. The absolute minimum MBP was not different in OH_NA (MBP 56.9±4.3 mm Hg) compared with the OH_AF patients (MBP 56.9±8.7 mm Hg).

To address the possible concern that the differences in slopes could be related merely to the magnitude of ΔMBP in response to HUT, we separately assessed ΔBFV_M during the first 30 to 60 seconds of HUT, which was associated with a smaller reduction of BP (ΔMBP). At this time ΔMBP was <40 mm Hg in all OH patients. During this period, when ΔMBP was small, the OH-AF group was still easily separable from the OH_NA group on the basis of ΔBFV_M. For the OH_NA group, the mean ΔBFV_M in response to ΔMBP of 28.9±3.8 mm Hg was 7.57±1.2 cm/s, resulting in a slope of 0.26 cm/s per millimeter of mercury, not significantly different from control values. In contrast, the OH_AF group had a mean ΔBFV_M response of 24.9±10.3 cm/s in response to ΔMBP of 16.2±5.1 mm Hg, resulting in a slope of 1.54 cm/s per millimeter of mercury, significantly steeper (P<.001) than that of either control subjects or OH_NA. The standing time (before tilt-back) was not different among these subgroups of OH patients, despite large differences in ΔMBP.

Discussion

There are three main findings of the present study. First, it is possible to quantitate autoregulatory failure with the use of regression analysis. Second, we make the novel finding that patients with OH have three patterns of autoregulatory responses. One group (n=8) has impaired autoregulation but with a flat flow-BP curve. A second group (n=8) has intact autoregulation, with an expansion of their autoregulated range. Group 3 (n=5) has a failure of autoregulation, with a steep flow-BP curve. Patients with patterns 1 and 2 have an increased capacity to cope with OH, while those with pattern 3 are greatly disadvantaged.

The symptoms of orthostatic intolerance are manifestations of impaired cerebral perfusion resulting in cerebral hypoxia. It is therefore paradoxical that attention has been focused almost exclusively on cardiovascular indices of orthostatic intolerance.
Only limited information is available on cerebral perfusion in the autonomic disorders. Within the autoregulated range, a change in BP results in an insignificant change in cerebral perfusion. Previous studies\textsuperscript{14–16} in patients with OH have demonstrated an expansion of the autoregulated range at both the upper and lower limits, so that cerebral perfusion remained relatively constant with the patient in the supine position (when supine hypertension might be present) and in response to standing (when OH occurs). Some studies have additionally demonstrated that cerebrovascular reactivity is dynamic. Changes in MCA MFV\textsubscript{M} with HUT with or without isoproterenol can precede alterations in BP.\textsuperscript{17,18} The responses in orthostatically symptomatic subjects\textsuperscript{18} and those who develop postprandial hypotension\textsuperscript{19} appear to differ from those of nonsymptomatic subjects. They may have a paradoxical increase in CVR, as surmised from an increase in the pulsatility and resistance indices. Also of interest is the observation that MCA changes suggestive of ischemia can be induced with hyperventilation in susceptible subjects.\textsuperscript{20}

To establish the autoregulated range (within which a change in pressure results in insignificant changes in flow) and the break points above and below which flow changes with pressure, BP has been increased by the infusion of an \(\alpha\)-agonist such as angiotensin\textsuperscript{21} or norepinephrine\textsuperscript{22} and reduced with vasodilators\textsuperscript{23} or lower body negative pressure.\textsuperscript{22} Other investigators have attempted to devise approaches that do not require the infusion of vasoactive agents. These include the transient hyperemic response that develops after the release of ipsilateral carotid compression.\textsuperscript{24,25} The response is akin to the MCA flow velocity changes that occur during phase IV of the Valsalva maneuver. We chose a nonpharmacological method of changing BP, since \(\alpha\)-agonists or antagonists, by their direct action on arterioles, change the dependent (flow) as well as the independent variable (BP).\textsuperscript{26} Tissues that autoregulate have no, or only a weak, correlation of change in flow to corresponding change in pressure. In contrast, tissues that do not autoregulate have a linear or curvilinear relationship.\textsuperscript{26–28} The slope of the relationship provides a quantitative description of the magnitude of the failure. These observations are in agreement with the work of Nelson et al,\textsuperscript{29} who described a linear relationship between cerebral perfusion pressure and mean flow velocity below the autoregulated range (break point). Kiel and Shepherd\textsuperscript{30} also noted that the pressure-flow relationship became progressively more linear with failure of autoregulation.

As determined by regression analysis of response to HUT, three patterns of response are evident in our patients with OH. No correlation between flow and pressure was found in normal control subjects and 8 of 21 patients with OH, confirming the presence of intact autoregulation. These patients have an increased capacity to cope with OH, since they have an expanded autoregulated range. A similar group (\(n=8\)) exhibited failure of autoregulation but with a flat flow-BP relationship. Only modest changes in BFV\textsubscript{M} occurred in response to the wide range of BPs that extended from supine hypertension to mild OH at the beginning of HUT, to maximal fall in BP at the end of HUT in this group of OH patients (OH\textsubscript{NA}). The third pattern (OH\textsubscript{AF}) was characterized by a “passive profile” of flow velocities (BFV\textsubscript{M}), which diminished in parallel with BP. As expected, a strong positive flow-pressure correlation was found. These patients had a steep BFV\textsubscript{M}-MBP slope, so that even a mild reduction of MBP induced a profound fall in BFV\textsubscript{M} in these patients. All the OH patients ultimately became symptomatic on HUT. For convenience, we have combined the patients with completely preserved autoregulation with those with
autoregulatory failure but with a flat and expanded “autoregulatory” curve. We think this approach is reasonable since the patients with these two patterns have an increased capacity to cope with OH compared with normal subjects. Our data emphasize the utility of regression analysis. Specifically, we suggest that the emphasis on dividing patients into those who autoregulate and those who do not is less helpful than a quantitative description of the flow-BP relationship. Patients with pattern 2 have autoregulatory failure and hence no longer have break points, but because they have a flat curve, they have enhanced tolerance of OH. In contrast, patients with pattern 3 (OH_AF) were characterized by mild OH and a steep flow-BP relationship, indicating severe autoregulatory failure. These patients develop cerebral hypoperfusion in response to small drops in BP. The observation that the great majority of patients with OH have only mild autoregulatory failure and a flat slope provides an explanation of why modest improvements in BP result in dramatic improvements in symptoms. The standing time before onset of presyncope, manifested as tilt duration, was not different among patients within the three OH subgroups, indicating that the results of cerebrovascular compensation (as expanded autoregulation or autoregulatory failure with flat slopes) enabled these patients to remain upright as long as patients with only modest OH (and autoregulatory failure with steep slopes).

One limitation of the present analysis is that patients with OH underwent greater MBP alterations than control subjects. The study does not exclude the possibility that a modest regression might exist in control subjects if large changes in BP were induced, ie, simulating patients with mild autoregulatory failure with flat slopes. A large error is improbable, since regression coefficient and slope induced by small changes in BP in the OH group were similar to those induced by large changes in MBP (not shown). The requirement of $R^2 \geq .75$ was selected because of the large numbers of data points and the desire to accept only robust regressions, in view of differences in $\Delta$MBP among the groups.

Adrenergic failure results in impaired vascular sympathetic innervation and a fall in peripheral resistance during orthostasis. With preserved myogenic and neurogenic autoregulation, cerebral arterioles should respond to the elevated BP in the supine position by vasoconstriction, thereby keeping flow constant. However, since at least a part of cerebral autoregulation is neurogenic, central sympathetic denervation would result in cerebral vessels passively distending during the period of higher BP and assuming a smaller caliber during OH. The fall in central resistance during HUT, in parallel with the fall in peripheral resistance, suggests that cerebral arterioles remain passively dilated and poorly responsive to the BP changes. Thus, cerebrovascular vasomotor reserve seems to be reduced with only a limited capacity to compensate for changes in BP. Previous studies\textsuperscript{2,3,5} using the reactive hyperemia test have also demonstrated that cerebral circulation passively follows the rise and fall in BP in the supine position in patients with multiple system atrophy and autonomic failure.\textsuperscript{3,5} The possibility of a passive vasodilatation has also been raised based on comparisons between MCA flow velocity and $^{[13]}$Xe washout measurements of cerebral blood flow in patients with multiple system atrophy and autonomic failure during $45^\circ$ HUT.\textsuperscript{16} Cerebral flow did not change, while a mild reduction of MCA velocity (by 16%) was observed. Sensitivity to CO$_2$ and a capacity to vasodilate is usually preserved in these patients.\textsuperscript{15} In our study, vasoconstrictive response and CO$_2$ sensitivity were tested as a response to CO$_2$ reduction during hyperventilation in the supine position. Indeed, for a similar relative change of CO$_2$, the vasomotor response and MCA flow reduction were reduced in the OH patients, suggesting that some impairment in the metabolic component of autoregulation also existed.

In conclusion, the change in BP over a wide range from supine hypertension to OH presents a significant challenge for the regulation of cerebral perfusion. A range of autoregulatory responses to changes in BP exists in patients with OH. The majority of patients with OH have either normal or only mild autoregulatory failure, with expansion of the “autoregulated” range, and develop symptoms only with profound falls in BP. In approximately one in four patients, more severe autoregulatory failure occurs, and cerebral hypoperfusion occurs with relatively small change of BP. Cerebral hypoperfusion may place the patient at significant risk to health and may cause injury.

Acknowledgments

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