Orthostatic Tolerance, Cerebral Oxygenation, and Blood Velocity in Humans With Sympathetic Failure

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Background and Purpose—Patients with orthostatic hypotension due to sympathetic failure become symptomatic when standing, although their capability to maintain cerebral blood flow is reported to be preserved. We tested the hypothesis that in patients with sympathetic failure, orthostatic symptoms reflect reduced cerebral perfusion with insufficient oxygen supply.

Methods—This study addressed the relationship between orthostatic tolerance, mean cerebral artery blood velocity (Vmean), determined by transcranial Doppler ultrasonography, oxygenation (oxyhemoglobin [O2Hb], determined by near-infrared spectroscopy), and mean arterial pressure at brain level (MAPMCA, determined by finger arterial pressure monitoring [Finapres]) in 9 patients (aged 37 to 70 years; 4 women) and their age- and sex-matched controls during 5 minutes of standing.

Results—Supine MAPMCA (108±14 versus 86±14 mm Hg) and Vmean (84±21 versus 62±13 cm·s⁻¹) were higher in the patients. After 5 minutes of standing, MAPMCA was lower in the patients (31±14 versus 72±14 mm Hg), as was Vmean (51±8 versus 59±9 cm·s⁻¹), with a larger reduction in O2Hb (−11.6±4 versus −6.7±4.5 μmol·L⁻¹). Four patients terminated standing after 1 to 3.5 minutes. In these symptomatic patients, the orthostatic fall in Vmean was greater (45±6 versus 64±10 cm·s⁻¹), and the orthostatic decrease in O2Hb (−12.0±3.3 versus −7.6±3.9 μmol·L⁻¹) tended to be larger. The reduction in MAPMCA was larger after 10 seconds of standing, and MAPMCA was lower after 1 minute (25±8 versus 40±6 mm Hg).

Conclusions—In patients with sympathetic failure, the orthostatic reduction in cerebral blood velocity and oxygenation is larger. Patients who become symptomatic within 5 minutes of standing are characterized by a pronounced orthostatic fall in blood pressure, cerebral blood velocity, and oxygenation manifest within the first 10 seconds of standing. (Stroke. 2000;31:1608-1614.)

Key Words: cardiac output • hypotension, orthostatic • posture • ultrasonography, Doppler, transcranial

When standing, humans adjust the cardiovascular system to the gravitational displacement of blood to the lower part of the body by increasing systemic vascular resistance through autonomic reflex activity, but patients with sympathetic failure lack this ability to modulate vascular tone in the upright body position.1–3 Although their capability to maintain cerebral blood flow in response to a reduction in arterial pressure is reported to be preserved,4–7 patients with sympathetic failure often develop symptoms such as lightheadedness and blurred vision when upright.

We hypothesized that in patients with sympathetic failure, orthostatic symptoms reflect a reduced cerebral perfusion with an insufficiency of cerebral oxygen supply. Changes in cerebral tissue oxygenation can be assessed continuously and noninvasively by near-infrared spectroscopy (NIRS).8–10 This study addressed the relationship between orthostatic tolerance and estimates of cerebral perfusion in patients with sympathetic failure and healthy controls during orthostatic stress. The effect of standing on cerebral perfusion was evaluated by transcranial Doppler ultrasound (TCD)–determined middle cerebral artery (MCA) mean blood velocity (Vmean) and by NIRS-determined cerebral oxygenation. Arterial pressure, central blood volume, and beat-to-beat cardiac output (CO) were measured to follow systemic circulatory responses.

Subjects and Methods

Subjects

In 9 patients (age range, 37 to 70 years; 4 women), orthostatic hypotension was manifest as a fall >20 mm Hg in systolic arterial pressure and >5 mm Hg in diastolic pressure after 1 minute of standing.11 Orthostatic hypotension was related to pure autonomic failure in 8 patients, while in 1 patient orthostatic intolerance was
subsequent to multiple system atrophy. No patient had symptoms or signs of organic heart disease (Table 1). Nine sex-matched (5 men) and age-matched (32 to 71 years) subjects with no orthostatic intolerance formed a control group. The protocol was approved by the ethics committee of the Academic Medical Center, and informed consent was obtained.

**Protocol**

At least 2 hours after a light breakfast without caffeine-containing beverages, the subjects were instrumented at 9 AM in a room with an ambient temperature of 22°C. A test run was performed to familiarize the subjects with the protocol. After 10 minutes of supine rest, the subjects were asked to stand in a relaxed position for 5 minutes. Standing was terminated if the subject developed symptoms of orthostatic intolerance such as blurred vision, dizziness, or nonresponsiveness.

**Measurements**

Cerebral oxygenation was monitored with NIRS. NIRS is based on the transparency of tissue to light in the near-infrared region and the O2-dependent changes in absorption in cerebral tissue caused by chromophores, ie, mainly oxyhemoglobin and deoxyhemoglobin ($O_2Hb$ and $HHb$, respectively). The use of a modified Lambert-Beer law, changes in light absorption at different wavelengths are measured, and tissue oxygenation is monitored. To estimate the concentration changes in $O_2Hb$ and $HHb$, a differential path length factor of 6.0 was applied to account for the scattering of light in the tissue. A continuous-wave NIRS instrument (Oxymon) with 3 wavelengths (901, 848, and 770 nm) and 10-Hz sampling time was used. The NIRS optodes were attached on the right side of the forehead, with the transmitting and receiving optodes placed 5.5 cm apart. Since there is no standard for cerebral oximetry, calibration is not possible. However, NIRS determined tissue oxygenation changes in parallel with cerebral blood flow as determined by jugular bulb venous $O_2$ saturation. As an index of the central blood volume, thoracic electric impedance (TI) was measured by an impedance cardiograph (Kardio-Dynagraph, Diefenbach GmbH). An event marker identified changes in posture.

**Data Acquisition and Analysis**

The signals of arterial pressure, the spectral envelope of MCA velocity, $\text{PETCO}_2$, and marker were analog/digital converted at 100 Hz and stored on hard disk for off-line analysis. NIRS data were sampled at 10 Hz. Signals were routed through an interface providing electric isolation with offset and sensitivity adjustments when appropriate. Variables were also recorded on a polygraph on a thermo-writer (Graphite WR7700, Western Graphite Inc) for online inspection. The $V_{\text{mean}}$ was computed as the integral of the maximal frequency shifts over 1 beat divided by the corresponding beat interval. Mean arterial pressure (MAP) was the true integral of the arterial pressure waveform over 1 beat divided by the beat interval. MAP at the MCA level (MAPMCA) was calculated from MAP measured at heart level and the vertical finger-to-TCD probe distance. Heart rate (HR) was computed as the inverse of the interbeat pressure interval and expressed in beats per minute. CO was the product of SV and HR, and total peripheral resistance (TPR) was calculated as the ratio of the aortic input impedance. Peripheral arterial pressure appears too low to be applied in the model and to allow for reliable estimations of stroke volume (SV) from an arterial pressure signal. Thus, SV is tracked from peripheral arterial pressure in patients with cardiovascular disease, with septic shock, and under conditions of orthostatic stress with a limited offset of 3±9 mL in comparison to a thermodilution-based estimate.

As an index of the central blood volume, thoracic electric impedance (TI) was measured by an impedance cardiograph (Kardio-Dynagraph, Diefenbach GmbH). An event marker identified changes in posture.
Differences between patients and controls and between symptomatic and asymptomatic patients were analyzed by parametric or nonparametric tests where appropriate. A *P* value, *P* < 0.05 was considered to indicate a statistically significant difference.

## Results

### Patients Versus Controls

The control subjects tolerated standing without complaints. Orthostatic tolerance varied considerably between patients: 5 patients tolerated 5 minutes of standing without symptoms (asymptomatic), but 4 patients developed orthostatic complaints after 1 to 3.5 minutes of standing (symptomatic). In the supine position, blood pressure was higher in the patients but dropped during standing. The orthostatic fall in CO and MAP.MCA was larger in the patients because of absence of an increase in TPR. Resting HR did not differ between the 2 groups, and on standing HR increased to a comparable magnitude. Additionally, the resting TI and its orthostatic changes were similar in the 2 groups of subjects. Resting PETCO₂ was comparable for patients and control subjects but became lower in the patients during standing. Supine MCA Vmean was higher in the patients and decreased on standing but not in the controls. At the end of standing, the fall in O₂Hb was larger in the patients. HHb increased in both groups, with the larger increase in the patients (Figures 1 and 2, Table 2).

In the patients the correlation coefficient for MAP.MCA and MCA Vmean was 0.68 and for CO and MCA Vmean was 0.48 (*P* < 0.05). The correlation coefficient for MAP.MCA and O₂Hb was 0.41 and for CO and O₂Hb was 0.36 (*P* < 0.05). In the control subjects these values for MAP.MCA and MCA Vmean were 0.18, for CO and MCA Vmean 0.25, for MAP.MCA and O₂Hb 0.06, and for CO and HHb 0.39.

### Asymptomatic Versus Symptomatic Patients

In symptomatic patients supine blood pressure was higher, but Vmean did not differ. In symptomatic patients the reduction in MAP.MCA was greater after 10 and 30 seconds of standing. After 1 minute of standing the reduction in MAP.MCA was 94 ± 14 versus 59 ± 15 mm Hg in asymptomatic patients, and it was accompanied by a slightly lower CO. In the symptomatic patients the orthostatic fall in Vmean was larger, with a tendency for a larger postural reduction in O₂Hb and a lower PETCO₂. There was a tendency toward a larger TI in symptomatic patients (Figure 3, Tables 3 and 4). Figure 4 shows representative examples of the reduction in Vmean and O₂Hb during standing in a control subject and in an asymptomatic versus a symptomatic patient.

### Discussion

This study demonstrates that during orthostatic stress, the reduction in cerebral blood velocity and oxygenation in patients with sympathetic failure is larger than in healthy subjects. Patients who develop serious orthostatic complaints within 5 minutes of standing are characterized by a more pronounced orthostatic fall in blood pressure, cerebral blood velocity, and oxygenation manifest within 10 seconds of standing.

This report quantifies the postural changes in cerebral artery blood velocity and oxygenation, as measured by TCD and NIRS, in patients with sympathetic failure. TCD is used to evaluate cerebrovascular dynamics, including its autoregulation,34,35 in patients with sympathetic failure as well.34,35 The diameter of the MCA remains constant over an...
patients at a reduced arterial pressure and CO. We may speculate that under those circumstances the excessive fall in blood pressure might reduce the diameter of the MCA cerebral velocity and overestimate cerebral blood flow, but the data regard changes in blood velocity, not flow, and cannot be said to reflect a decrease in flow, however suggestive.

Given a constant arterial O₂ content, the cerebral tissue O₂ supply is predominantly a function of cerebral arterial blood flow. NIRS follows changes in cerebral oxygenation in parallel with cerebral blood flow as determined by ¹³⁵Xe clearance, and estimated cerebral O₂ saturation in humans during carotid clamping and declamping compares satisfactorily with jugular bulb venous O₂ saturation. The determination of cerebral tissue oxygenation by NIRS reflects the locally monitored cerebral cortex. Within the sampled volume, hemoglobin is contained in arterioles, capillaries, and venules, and the relative position of pigments determined by NIRS is unknown. From anatomic studies of brains, the ratio of venule to total vessel volume ranges from 2/3 to 4/5. Only ~5% of the blood is situated in the capillaries and ~20% in the arterioles, and it may be argued that NIRS determinations of local SvO₂ rather than tissue O₂ content. Yet, resting values of O₂Hb are higher than internal jugular SvO₂. Thus, the O₂Hb of the cerebral tissue measured by NIRS is not necessarily equal to the region perfused by the MCA, and it may be questioned whether the fall in the NIRS O₂Hb signal can be taken to reflect a fall in MCA territory perfusion. In this study the reduction in MCA blood velocity was accompanied by a fall in cerebral oxygenation under circumstances of considerable orthostatic hypotension. We consider that during head-up tilt in healthy subjects, even when the reduction in MAP is limited, cerebrovascular oxygenation is related to cerebral perfusion, as determined by TCD, and that NIRS properly reflects the reduction in O₂Hb associated with fainting. Comparable results have

\[ \Delta V_{\text{mean, cm/s}} \]

\[ \Delta P_{\text{MAP, mm Hg}} \]

\[ \Delta O_2 \text{Hb, mmol/L} \]

\[ \Delta \text{Hb, mmol/L} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]

\[ \Delta \text{O_2Hb (mmol/L)} \]

\[ \Delta \text{Hb (mmol/L)} \]

\[ \Delta SV, \% \]

\[ \Delta HR, \text{bpm} \]

\[ \Delta \text{CO, \%} \]

\[ \Delta \text{TPR, \%} \]

\[ \Delta \text{Tl, } \Omega \]

\[ \Delta O_2 \text{Hb (mmol/L)} \]

\[ \Delta \text{MAP (mm Hg)} \]

\[ \Delta \text{V_{\text{mean}} (cm/s)} \]
been obtained during lower body negative pressure and centrifuge studies. At rest, blood pressure was elevated in the patients but fell considerably on standing because of a large reduction in SV and CO unopposed by an increase in TPR (Table 2 and Figure 1). The large reduction in $V_{\text{mean}}$ and $O_2Hb$ indicates that with a fall in arterial pressure of this magnitude, autoregulatory mechanisms are not capable of preventing a symptomatic decrease in cerebral perfusion, as reflected by TCD and NIRS. Apart from the considerable fall in blood pressure and CO (Figure 2), the reduction in PetCO$_2$ may also have contributed to the reduction in MCA $V_{\text{mean}}$. On standing, in healthy subjects a slight decrease in PetCO$_2$ is common and can be explained by an increase in breathing rate in the upright position and changes of the ventilation-perfusion relationship.

### TABLE 3. Cardiovascular and Cerebral Perfusion and Oxygenation Responses in Sympathetic Failure

<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Stand 60 s</th>
<th>End of Standing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAP$_{\text{MCA}}$, mm Hg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>119±11* (110 to 134)</td>
<td>25±8* (14 to 33)</td>
<td>19±4* (14 to 23)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>99±9 (85 to 108)</td>
<td>40±6 (34 to 47)</td>
<td>38±12 (27 to 56)</td>
</tr>
<tr>
<td>$V_{\text{mean}}, \text{cm} \cdot \text{s}^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>83±27 (64 to 123)</td>
<td>45±6* (39 to 53)</td>
<td>44±2* (42 to 47)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>85±18 (68 to 114)</td>
<td>64±10 (53 to 77)</td>
<td>56±7 (49 to 62)</td>
</tr>
<tr>
<td>$\Delta O_2Hb, \mu\text{mol} \cdot \text{L}^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>0</td>
<td>−12.0±3.3 (−15.6 to −7.8)</td>
<td>−13.2±3.2 (−16.9 to −9.1)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0</td>
<td>−7.6±3.9 (−12.1 to −4.4)</td>
<td>−10.4±4.5 (−14.7 to −4.2)</td>
</tr>
<tr>
<td>$\Delta HHb, \mu\text{mol} \cdot \text{L}^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>0</td>
<td>6.5±1.9 (4.7 to 8.2)</td>
<td>8.1±2.9 (5.1 to 10.9)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0</td>
<td>3.9±2.3 (1.1 to 6.9)</td>
<td>6.9±2.8 (3.7 to 9.9)</td>
</tr>
<tr>
<td><strong>PETCO$_2$, mm Hg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>36±2 (32 to 38)</td>
<td>31±4 (25 to 35)</td>
<td>31±5 (25 to 35)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>38±8 (26 to 46)</td>
<td>36±8 (22 to 44)</td>
<td>35±6 (27 to 42)</td>
</tr>
<tr>
<td><strong>HR, bpm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>70±5 (62 to 74)</td>
<td>76±6 (73 to 83)</td>
<td>76±6 (71 to 83)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>63±12 (49 to 79)</td>
<td>81±16 (63 to 105)</td>
<td>84±14 (69 to 103)</td>
</tr>
<tr>
<td><strong>CO, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>100</td>
<td>68±13 (57 to 82)</td>
<td>60±12 (46 to 67)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>100</td>
<td>77±11 (65 to 89)</td>
<td>68±11 (57 to 84)</td>
</tr>
<tr>
<td><strong>Tl, Tt</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>65±16 (56 to 89)</td>
<td>67±15 (58 to 89)</td>
<td>68±14 (60 to 89)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>55±7 (47 to 66)</td>
<td>61±4 (57 to 67)</td>
<td>62±5 (55 to 67)</td>
</tr>
</tbody>
</table>

Values are mean±SD (range). *$P<0.05$, symptomatic vs asymptomatic patients.

### TABLE 4. Cerebral Perfusion and Oxygenation Responses to Orthostatic Stress (First 30 Seconds) in Sympathetic Failure

<table>
<thead>
<tr>
<th>Duration of Standing</th>
<th>10 s</th>
<th>20 s</th>
<th>30 s</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>$\Delta\text{MAP}_{\text{MCA}}, \text{mm Hg}$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>−60±13* (−69 to −40)</td>
<td>−78±12 (−88 to −61)</td>
<td>−86±10* (−97 to −73)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>−33±13 (−45 to −12)</td>
<td>−58±12 (−73 to −42)</td>
<td>−63±10 (−80 to −42)</td>
</tr>
<tr>
<td><strong>$\Delta V_{\text{mean}}, \text{cm} \cdot \text{s}^{-1}$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>−17±13 (−34 to −5)</td>
<td>−22±23 (−56 to −4)</td>
<td>−31±26 (−70 to −13)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>−10±10 (−22 to 3.9)</td>
<td>−16±16 (−34 to 9)</td>
<td>−21±14 (−42 to −4)</td>
</tr>
<tr>
<td><strong>$\Delta O_2Hb, \mu\text{mol} \cdot \text{L}^{-1}$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>−4.2±2.5 (−7.0 to −1.7)</td>
<td>−6.5±4.2 (−12.5 to −2.7)</td>
<td>−8.2±2.8 (−10.5 to −4.7)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>−1.8±2.2 (−4.0 to −1.4)</td>
<td>−5.1±5.0 (−12.8 to −2.0)</td>
<td>−5.9±4.9 (−12.4 to −1.1)</td>
</tr>
</tbody>
</table>

Values are mean±SD (range). Changes are in comparison to supine baseline values. *$P<0.05$, symptomatic vs asymptomatic patients.
In subjects with orthostatic hypotension due to sympathetic failure, orthostatic tolerance varies considerably, but the underlying mechanism is not well understood. In symptomatic recumbent patients, blood pressure but not MCA \( V_{\text{mean}} \) was higher, suggesting a shift in the relationship between cerebral perfusion pressure and blood velocity comparable to that in chronic hypertensive patients. The differences in MCA \( V_{\text{mean}} \) between symptomatic and asymptomatic patients were relatively small (Table 3), but the effects on orthostatic tolerance were dramatic. We believe that when these patients are upright, cerebral blood flow is close to the critical lower level of cerebral perfusion, and an additional small reduction elicits symptoms of cerebral hypoperfusion. This is supported by a recognizably larger fall to lower values in blood pressure and MCA \( V_{\text{mean}} \) in symptomatic patients, with cerebral oxygenation following this pattern. In patients with sympathetic failure, the postural fall in arterial pressure is amplified by the larger orthostatic fall in CO (Figure 1 and Table 2) because of enhanced venous pooling of blood, with an excessive reduction of venous return. This is compatible with the tendency for higher values for thoracic electric impedance in symptomatic patients, suggesting a smaller central blood volume. In addition, the decrease in \( P_{\text{ETCO}_2} \) on standing may have contributed to the cerebral hypoperfusion in the symptomatic patients. The fall in blood pressure, cerebral blood velocity, and oxygenation in the symptomatic patients was larger in the first 10 seconds of standing (Table 4 and Figures 3 and 4), suggesting that the rapidity of the reduction also contributes to trigger orthostatic symptoms.

The anomaly in dynamic plasma volume regulation in patients with autonomic failure is as yet not well understood. The level of upright arterial pressure is closely related to the magnitude of the blood volume, presumably because in this group of patients CO has become strictly dependent on venous return and the effective blood volume. There is no specific treatment for sympathetic vasomotor failure, and therapy should be focused on alleviating the patient’s orthostatic tolerance and reducing the orthostatic fall in CO by increasing the circulating volume.

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References


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