The Effect of Age and Sodium Depletion on Cardiovascular Response to Orthostasis

RICHARD P. SHANNON, JEANNE Y. WEI, ROBERT M. ROSA, FRANKLIN H. EPSTEIN, AND JOHN W. ROWE

SUMMARY To test the hypothesis that normal age-related limitations in cardiovascular homeostasis may become clinically significant under stress, the cardiovascular response to postural change was assessed in six young and six old healthy subjects before and after modest diuretic-induced sodium depletion. Before diuresis, systolic blood pressure was maintained (from 110 ± 4 to 113 ± 6 mm Hg) while heart rate increased 22% (from 67 ± 2 to 82 ± 5 beats/min) at 3 minutes after 60-degree upright tilt in young subjects. After a significant diuretic-induced weight reduction and natriuresis, the young again maintained systolic blood pressure (from 110 ± 4 to 110 ± 6 mm Hg) and increased heart rate 49% (from 68 ± 2 to 101 ± 5 beats/min; p < 0.05, compared with prediuresis values) in response to the same postural stimulus. During the prediuresis tilt, the older subjects showed no change in systolic blood pressure (from 132 ± 4 to 134 ± 6 mm Hg) and a 9% increase in heart rate (from 68 ± 3 to 74 ± 2 beats/min). After a similar significant weight reduction and sodium loss, the older subjects showed a significant reduction in systolic blood pressure (from 132 ± 6 to 108 ± 6 mm Hg; p < 0.05) and a 17% increase in heart rate (from 69 ± 4 to 81 ± 3 beats/min; p < 0.05) during tilt compared with values in young subjects. Three of six elderly subjects noted postural symptoms. These results suggest that, although the healthy old may appear well compensated under optimal conditions, decreased cardiovascular reserve renders them susceptible to postural change following mild sodium depletion. (Hypertension 8: 438-443, 1986)

KEY WORDS • blood pressure • orthostasis • sodium depletion • cardioacceleration • postural stress • hypotension • baroreflex function • age

ALTHOUGH aging diminishes baroreceptor reflex response in humans,1-7 the clinical significance of the blunted baroreflex response in the healthy elderly remains uncertain. Some studies suggest that this diminished baroreceptor reflex activity renders the elderly susceptible to falls and orthostatic hypotension, generally defined as a reduction in blood pressure of at least 20 mm Hg of systolic and 10 mm Hg of diastolic pressure on assumption of upright posture.5,8 However, these studies have been confounded by inclusion of subjects with varying degrees of illness in addition to advanced age.

To test the hypothesis that the normal age-related limitation in cardiovascular homeostasis may become clinically significant under stress, we characterized the time course and magnitude of blood pressure and heart rate response to upright tilt in carefully screened, healthy, community-dwelling young and old volunteers before and after mild diuretic-induced sodium depletion.

Subjects and Methods

Six young (age, 23-35 years) and six old (age, 65-80 years) healthy, community-dwelling subjects participated in this study. Nine subjects were men and three were elderly women. Eleven subjects were white and one young subject was black. The protocol was approved by the Human Experimentation Committee of the Beth Israel Hospital, and all participants gave informed consent before the study. All were thoroughly screened by history, physical examination, labora-
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Table 1. Body Weight and Serum Sodium and Potassium Concentrations Before and After 2 Days of Diuretic Therapy in Old and Young Subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Time</th>
<th>Body weight (kg)</th>
<th>Albumin (g/dl)</th>
<th>Na⁺ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>31 ± 2</td>
<td>Prediuresis</td>
<td>74 ± 3</td>
<td>4.3 ± 0.2</td>
<td>142 ± 1.0</td>
<td>4.2 ± 0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postdiuresis</td>
<td>72 ± 3*</td>
<td>4.6 ± 0.2*</td>
<td>137 ± 0.7</td>
<td>3.6 ± 0.1*</td>
</tr>
<tr>
<td>Old</td>
<td>74 ± 4</td>
<td>Prediuresis</td>
<td>64 ± 5</td>
<td>3.9 ± 0.1</td>
<td>142 ± 0.7</td>
<td>4.4 ± 0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postdiuresis</td>
<td>62 ± 5*</td>
<td>4.1 ± 0.1*</td>
<td>138 ± 0.6*</td>
<td>3.7 ± 0.1*</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
*p < 0.001, †p < 0.01, compared with prediuresis values.
resulted in insignificant weight loss in both groups (young, 0.7 ± 0.4; old, 0.5 ± 0.3 kg), and there was no difference in the response of either group to 60-degree postural tilt under these conditions. Thus, diet restriction alone did not influence the cardiovascular response to orthostasis.

In the young subjects, systolic blood pressure did not change significantly during the postural stimulus before or after diuresis (Figure 1). There was a significant increase in resting diastolic pressure after diuresis (mean, 6 mm Hg) and further significant increases in diastolic pressure during the postdiuresis tilt (mean, 5–7 mm Hg), which were greater than those observed before diuresis (mean, 1–4 mm Hg; Table 2).

Resting heart rate in the young subjects was similar before and after diuresis (Table 3). Before diuresis, the young subjects showed a 22% increase in heart rate in the 3 minutes after tilt. This response was enhanced to a 49% posttilt increase after the diuretic-induced sodium loss.

The rate at which cardioacceleration (ΔRR/Δt) occurred in the young subjects was also examined (Table 4). Cardioacceleration during the first 18 seconds after tilt was greater after diuresis than before (Figure 2). The rate of cardioacceleration in the latter portion of the first minute was also greater after diuresis, but the difference did not reach statistical significance. Thus, the young subjects not only increased the magnitude of heart rate response to a postural stimulus, but did so quite abruptly after modest sodium losses. None of the young subjects showed symptoms during the tilt before or after diuresis.

Although resting systolic blood pressure was maintained during postural stimulus under basal (prediuresis) conditions in older subjects, there was a significant postural drop in systolic pressure after diuresis (mean, -22 mm Hg). Before diuresis, the old subjects demonstrated a significant increase in diastolic pressure (mean, +15 mm Hg) in response to tilt (see Table 2). After modest diuresis, although the old subjects still manifested an increase in supine resting diastolic pressure (mean, +6 mm Hg), they failed to mount a significant increase in diastolic pressure in response to tilt (see Figure 1).

Heart rate in the old subjects increased significantly in response to tilt under basal conditions and was further augmented after diuretic-induced sodium depletion.

Following equivalent sodium depletion, significant age differences became apparent in the cardiovascular response to tilt. In response to upright posture, the old subjects showed a marked decline in systolic pressure and failed to augment heart rate or cardioacceleratory response to the same degree as the young subjects. Figure 3 illustrates the age difference in the pattern and magnitude of RR interval changes. Under prediuresis conditions, the young subjects displayed substantial short-term variability in the rate of change of RR inter-

<table>
<thead>
<tr>
<th>Table 2. Blood Pressure Response to 60-Degree Upright Tilt Before and After Diuretic-Induced Volume Depletion in Six Old and Six Young Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Young</td>
</tr>
<tr>
<td>Pre-Diuresis</td>
</tr>
<tr>
<td>Post-Diuresis</td>
</tr>
<tr>
<td>Old</td>
</tr>
<tr>
<td>Pre-Diuresis</td>
</tr>
<tr>
<td>Post-Diuresis</td>
</tr>
</tbody>
</table>

Values are means ± SEM.  
*P < 0.05, compared with pre-diuresis values in young subjects; †P < 0.02, compared with values at −1 minute. ‡P < 0.02, compared with pre-diuresis values in old subjects.
TABLE 3. Heart Rate Response to 60-Degree Upright Tilt Before and After Diuretic-Induced Volume Depletion in Six Old and Six Young Subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Minutes after tilt</th>
<th>% change over</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-18</td>
<td>18-60</td>
<td>Pre-diuresis</td>
</tr>
<tr>
<td>Young</td>
<td></td>
<td></td>
<td>67±2</td>
</tr>
<tr>
<td></td>
<td>0-18</td>
<td>18-60</td>
<td>77±3</td>
</tr>
<tr>
<td>Old</td>
<td></td>
<td></td>
<td>68±4</td>
</tr>
<tr>
<td></td>
<td>0-18</td>
<td>18-60</td>
<td>90±2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>97±5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>101±6</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
*p < 0.02, compared with postdiuresis values in old subjects; †p < 0.05, compared with pre-diuresis values in young subjects.

Discussion

In the present study, healthy, community-dwelling elderly subjects demonstrated sufficient cardiovascular reserve to maintain blood pressure during a 60-degree upright tilt under basal conditions. After 2 days of modest sodium depletion, however, the elderly subjects uniformly showed significant declines in systolic pressure following postural provocation. The younger subjects were able to maintain blood pressure despite similar provocation. Thus, a limitation in blood pressure homeostasis was unmasked in healthy elderly subjects after a modest physiological stress.

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Other studies have employed pharmacological manipulations of arterial pressure to assess cardiovascular response in the elderly.\(^1\) We chose to use the 60-degree upright tilt as a postural stimulus because it simulates more closely the physiological changes associated with orthostasis yet allows for a controlled, reproducible experimental condition. This sudden postural stimulus is an acute test of baroreflex function designed to defend against the moment-to-moment alterations in blood pressure imposed by forces such as gravity. Failure of this system to respond rapidly and adequately may predispose to syncope. We imposed a modest physiological stress, diuretic-induced sodium loss, to further test the functional reserve of the cardiovascular system. Although we did not measure fluid volume directly, the diuretic-induced negative sodium balance, coupled with the observed weight reduction and significant increase in serum albumin concentration, suggests a reduction in extracellular volume.

One possible explanation for the age-related differences in cardiovascular response is related to differences in the magnitude of the diuretic-induced sodium losses. Although the magnitude of weight reduction was equivalent between groups, it represented a slightly higher percent reduction in the elderly (3.2% vs 2.7%). However, net negative sodium balance was slightly less in the elderly subjects in response to diuresis. Thus, differences in stress were unlikely to account for the observed cardiovascular differences. The young subjects showed a trend toward increased diastolic pressure, whereas the elderly showed an increase in diastolic pressure during tilting. It has been suggested that the initial phase of cardioacceleration depend on parasympathetic withdrawal, while subsequent increases involve sympathetic stimulation.\(^3\)\(^-\)\(^6\)

Our data suggest that the elderly subjects showed a diminished response during both the initial and later stages. Diminished \(\beta\)-adrenergic responsiveness in the elderly is well described,\(^13\)\(^-\)\(^15\) but limitations in the withdrawal of parasympathetic tone are less well recognized, although this phenomenon has been observed in disease states such as diabetes mellitus and Chagas' disease.\(^20\)\(^-\)\(^22\)

The substantial variability in heart rate response in the young subjects (\(\Delta RR/\Delta t\)), which disappeared after diuresis and was absent altogether in the old subjects, may relate to differences in intrinsic parasympathetic tone. Such age-related differences in heart rate variability have been noted with respiration.\(^21\) The parasympathetic system may be more prominent in the young under basal conditions but may be withdrawn rapidly in response to tilting after sodium depletion. The relative lack of variability in the elderly subjects suggests that the prompt withdrawal of parasympathetic tone is a less prominent feature of the cardiovascular response to postural stimulus in advanced age, even in the face of sodium depletion. The predominating influence of even weak, vagal activity over strong, sympathetic stimulation to cardioacceleration has been well described.\(^16\)

The clinical implications of these observations are important. First, the healthy elderly appear to be able to maintain their blood pressure against gravity under usual circumstances. This is accomplished by less reliance on heart rate and perhaps greater dependence on peripheral vasoconstriction, as manifested by the increase in diastolic pressure during tilting. It has been shown that the elderly are similarly less reliant on heart rate in their cardiovascular response to exercise but maintain cardiac output by augmenting end-diastolic volume.\(^24\) If extracellular sodium is diminished, dependence on Starling's mechanism may be compromised and cardiac output reduced. Thus, sodium depletion may be a particularly serious insult to the adaptive cardiovascular response to posture in the elderly. Second, the elderly are at greater risk of sodium and volume depletion due to age-related decreases in thirst, renin response, and urinary concentrating ability.\(^25\) The diuretic-induced sodium and volume changes in these subjects were mild and similar to those seen with diarrhea, vomiting, or short-term renal losses. Thus, the morbidity of such intercurrent illness may be compounded by unrecognized cardiovascular limitations unmasked by sodium depletion. This point underscores the importance of attention to weight and fluid balance in the sick elderly. Third, limitations in the cardiovascular response to posture may serve as a non-osmotic stimulus to vasopressin release predisposing to hyponatremia, which is seen with increasing frequency in the elderly under the stress of illness or drugs such as diuretics.

Although further studies are needed to explore the possible mechanisms, our results provide support for...
the view that age-related changes in adaptive cardiovascular capacity occur in the absence of disease and contribute to the vulnerability of the elderly to orthostatic symptoms.

Acknowledgment

We are grateful to the nursing and nutrition services of the Clinical Research Center for excellent assistance in the studies. We are grateful to Gigi Shaidani, Thomas Lincoln, Julia Longstreet, and Joyce Y. Quindipan for assistance in manuscript preparation.

References

The effect of age and sodium depletion on cardiovascular response to orthostasis.
R P Shannon, J Y Wei, R M Rosa, F H Epstein and J W Rowe

Hypertension. 1986;8:438-443
doi: 10.1161/01.HYP.8.5.438

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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