Assessment of Autonomic Nervous Function in Elderly Subjects with or without Postprandial Hypotension

Shinji Teramoto, Masahiro Akishita, Yoshinosuke Fukuchi*, Kenji Toba, and Yasuyoshi Ouchi

To examine the role of autonomic nervous dysfunction in postprandial hypotension (PPH) in elderly persons, we non-invasively assessed autonomic nervous function in 50 elderly subjects with or without PPH, defined as a reduction of more than 20 mmHg in systolic blood pressure (SBP) after a meal. The heart rate response to the reduction of SBP during head-up tilt was less and the coefficient of variation of R-R intervals was smaller in subjects with PPH than in those without PPH. The responses to cold pressor test, hyperventilation test, and mental arithmetic test were normal in all subjects. The magnitude of \( \Delta \text{SBP} \) after meal ingestion closely correlated with \( \Delta \text{SBP} \) during tilt-table examination, but did not correlate with the results of the cold pressor test, hyperventilation test, or mental arithmetic test. Stepwise multiple regression analysis revealed that the magnitude of the BP reduction and heart rate increase during the tilt-table test were independent predictors of the magnitude of \( \Delta \text{SBP} \) after meal ingestion. The results indicate that impaired afferent pathways of baroreflexes, including baroreceptors, may play an important role in the pathogenesis of postprandial hypotension in the elderly and that the magnitude of the fall in SBP during tilt-table testing may be related to the degree of the postprandial reduction in BP in elderly persons. (Hypertens Res 1997; 20: 257-261)

Key Words: postprandial hypotension, autonomic nervous function, elderly, tilt-table test

Methods

Subjects

Fifty patients 65 years or older who were consecutively admitted to the geriatric ward of the University of Tokyo Hospital were recruited into this study. Subjects with a history of neurologic disease, cardio-pulmonary disease, or antihypertensive medical treatment and current smokers were excluded. Because diabetes mellitus is known to affect autonomic nervous function, subjects with a fasting plasma glucose concentration of more than 110 mg/dl were also excluded. Although no subject had overt heart disease, three subjects had hypertension. Most of the subjects had osteoporosis. The subjects were divided into two groups according to the decrement in postprandial systolic blood pressure (SBP): a PPH group, consisting of subjects with a reduction in SBP of more than 20 mmHg after a meal; and a non-PPH group, consisting of those with a reduction in SBP of less than 20 mmHg after a meal. All tests were done in the morning after an overnight fast. The subjects were not allowed to take any medication in the morning. The examinations started between 8:00 and 9:00 AM. Before enrollment, informed consent was obtained orally.
Meal Study Protocol

The subjects were first placed in the sitting position, and SBP and heart rate (HR) were measured with an automated oscillometric tonometer (Nihon Korin BP-203i, Tokyo, Japan). Before breakfast, SBP, diastolic BP (DBP), and mean BP and HR were measured every 5 min for 15 min. Each subject then ingested a standardized 700-kcal meal, consisting of 70% carbohydrates, 15% fat, 15% protein, and no caffeine, in the sitting position. We requested that the meal was easy to digest and not too hard. The meal was prepared by cooks at Tokyo University Hospital. The subjects were encouraged to finish the meal within 15 min. Monitoring of SBP, DBP, and HR was reinitiated 15 min after the start of meal ingestion and performed in the sitting position every 5 min up to 60 min after meal ingestion.

Tilt-table test

On the day of examining the postprandial blood pressure, all subjects underwent a tilt-table test approximately 2 h after the morning meal. After the patients had remained recumbent on a tilt table for 15 min, the response of arterial pressure and heart rate to a 70-degree passive head-up tilt was recorded every minute for 15 min with an automated oscillometric tonometer (14, 15).

Coefficients of variation of R-R interval (CVRR)

The subjects were instructed to lie on a bed and rest for at least 30 min. The coefficients of variation of the R-R interval (CVRR) were calculated from 100 electrocardiographically recorded R-R intervals with the use of an autonomic analyzer (R-110F, Fukuda Denshi Co., Tokyo, Japan). Data were rejected when atrial or ventricular premature beats were noted on recording 100 consecutive beats.

Hyperventilation test

To test the responsiveness of the vasomotor center to hyperventilation, arterial blood pressure after hyperventilation for 1 min was continuously recorded with an automated oscillometric tonometer. Hyperventilation was induced by having the subjects breathe as deeply and as quickly as possible for 60 s (15).

Cold pressor test (CPT)

After the subjects rested quietly on a bed for 30 min, the arterial pressure response to a cold stimulus was measured in a room maintained at a temperature between 20°C and 22°C. The subject’s right hand was completely immersed in iced cold water (4°C) for 1 min (16). BP and pulse rate at the left arm were recorded automatically with an oscillometric tonometer every minute before and during the CPT.

Mental arithmetic test

To examine the effect of mental stress on blood pressure, the subjects were instructed to serially subtract 7 from 100 (15). The change in blood pressure at the left arm was continuously recorded with an oscillometric tonometer.

Statistical Analysis

The statistical significance of differences between the PPH group and non-PPH group were analyzed with Student’s unpaired t-test. P values of <0.05 were considered to indicate statistical significance. All data in the text, tables, and figures are expressed as means ± SE.

The univariate and bivariate relationships of anthropometric measurements and the results of autonomic function testing with the magnitude of postprandial hypotension were determined with Stat View 4.0 (Abacus Concepts, Inc., CA, USA). Seventeen variables, including age, anthropometric measurements, and data from autonomic function testing, were then entered stepwise into multiple linear regression models, with the magnitude of the postprandial reduction in SBP as the dependent variable. The first variable considered for entry into each model was the one with the strongest correlation with the dependent variable. The probabilities of the F statistics were 0.05 to enter and 0.10 to remove a variable from the model. The stepwise procedure was then repeated, allowing only the variables that were significant in the first model to be included, and using F statistics of 0.001 to enter and 0.0025 to exit the model.

Results

Of the 50 subjects, 16 showed a significant fall in SBP (more than 20 mmHg from the baseline value), and these subjects comprised the PPH group. The remaining subjects comprised the non-PPH group. The mean age of the PPH group and non-PPH group was 73.9 ± 1.7 and 74.3 ± 0.8 yr, respectively.

Table 1. Anthropometric Data and Blood Pressure and Heart Rate during Meal Ingestion in Elderly Subjects with or without Postprandial Hypotension

<table>
<thead>
<tr>
<th>Group</th>
<th>non-PPH</th>
<th>PPH</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>16</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>74.3 ± 0.8</td>
<td>73.9 ± 1.7</td>
</tr>
<tr>
<td>(range)</td>
<td>68 - 85</td>
<td>66 - 83</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.2 ± 0.7</td>
<td>157.3 ± 1.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50.7 ± 0.8</td>
<td>48.1 ± 2.1</td>
</tr>
<tr>
<td>BMI</td>
<td>20.8 ± 1.3</td>
<td>19.3 ± 0.17</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>132 ± 3</td>
<td>142 ± 5*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77 ± 2</td>
<td>82 ± 3</td>
</tr>
<tr>
<td>ΔSBP</td>
<td>−7 ± 1</td>
<td>−23 ± 1**</td>
</tr>
<tr>
<td>ΔPR</td>
<td>68 ± 2</td>
<td>67 ± 1</td>
</tr>
<tr>
<td>ΔPR</td>
<td>8 ± 1</td>
<td>6 ± 1</td>
</tr>
</tbody>
</table>

Presented as means ± SE. n, number of subjects; PPH, postprandial hypotension, defined as a fall in SBP more than 20 mmHg; BMI, body mass index; SBP, systolic blood pressure before meal; DBP, diastolic blood pressure before meal; ΔSBP, (SBP after meal) − (SBP before meal); ΔDBP, (DBP after meal) − (DBP before meal); ΔPR, pulse rate before meal; ΔPR, (PR after meal) − (PR before meal); *p < 0.05, **p < 0.01 as compared with the corresponding value in the non-PPH group.
Anthropometric data and postprandial BP data are summarized in Table 1.

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In the PPH group, the mean fall in SBP was more than 20 mmHg. The reduction in SBP in the PPH group was significantly greater than that in the non-PPH group (Fig. 1-A). There was no difference in changes in HR after head-up tilt between the PPH and non-PPH groups (Fig. 1-B).

The value of CVRR in the elderly subjects ranged from 0.5% to 4.1%. The mean value of CVRR in the PPH group was significantly smaller than that in the non-PPH group (Fig. 1-C).

The mean reduction in SBP after hyperventilation was approximately 18 mmHg in all subjects. There was no difference in the drop in SBP after hyperventilation between the PPH and non-PPH groups (Fig. 1-D).

The mean increase in SBP after cold pressor stress was 24 ± 6 mmHg in the PPH group and 20 ± 7 mmHg in the non-PPH group (Fig. 1-E). The mean increase in pulse rate after cold pressor stress was 7 ± 5 beats/min in the PPH group and 4 ± 5 beats/min in the non-PPH group. There was no difference in cold pressor responses between the PPH group and non-PPH group.

The increase in BP after mental arithmetic stress in the PPH group was similar to that in the non-PPH group (Fig. 1-F).

Relationship of Anthropometric Variables and Results of Autonomic Function Testing with the Magnitude of Postprandial Hypotension

Anthropometric variables did not correlate with the magnitude of BP reduction. The magnitude of \( \Delta BP \) in the passive tilt-table test significantly correlated with the fall in BP after a meal (Fig. 2). There was a positive but fairly weak relationship between CVRR and the magnitude of postprandial hypotension (Table 2). However, there was no re-
The relationship between the change in BP after hyperventilation and the drop in BP after a meal (Table 2). Variables derived from the cold pressor test and mental arithmetic test did not correlate with the magnitude of postprandial hypotension (Table 2).

In the multiple regression model, BP response and HR response in the tilt-table test were significant independent correlates of the magnitude of BP reduction after meal ingestion (coefficient of BP response, 0.638 ± 0.05; coefficient of HR response, 0.331 ± 0.149). Body mass index, age, CVRR, and other variables were not predictors of the magnitude of postprandial hypotension.

Discussion

A postprandial reduction in BP is more commonly encountered in elderly than in young subjects (1-4). Although inadequate compensation by the sympathetic nervous system for meal-induced splanchnic blood pooling (1, 5, 10, 11), impaired baroreflex function (12, 13), an inadequate postprandial increase in cardiac output (17), impaired peripheral vasoconstriction (18, 19), and hormonal mechanisms (5, 8, 9, 20) have been implicated in the pathophysiology of PPH, the mechanism underlying the reduction in BP after meals in elderly individuals has yet to be delineated (21).

In the present study, we compared autonomic nervous function between elderly subjects with PPH and those without PPH. The value of CVRR in the subjects with PPH was significantly smaller than that in the subjects without PPH and was positively associated with the magnitude of the change in BP after a meal. Furthermore, the responses of heart rate to various stress tests, including tilt-table test and CPT, were poor in the subjects with PPH. The greater ΔSBP and the smaller ΔHR and ΔSBP during tilt-table test in the subjects with PPH than in those without PPH suggest that elderly subjects with PPH have impaired baroreflex function. This may be consistent with an impaired cardioacceleration response to BP reduction after meals in older subjects with PPH. However, there was no difference in the arterial-pressure response to hyperventilation between the PPH and non-PPH groups. The subjects in both groups showed a normal reduction in BP after hyperventilation. Because decreased arterial pressure after hyperventilation is thought to indicate intact vasomotor center responsiveness, the results imply that the vasomotor center does not have a major role in the pathogenesis of postprandial alterations in BP. In addition, no significant difference was found in mean ΔSBP and ΔHR during cold pressor test between the two groups. A normal response of arterial pressure to the painful cold stimulus was observed in both the PPH and non-PPH groups, indicating that the sympathetic control of peripheral circulation in PPH subjects is not substantially impaired. The magnitude of the increase in BP in response to mental stress was similar in both the PPH and non-PPH groups. A normal response in the mental arithmetic test may be in agreement with the results of the hyperventilation test and cold pressor test. These results suggest that central function and vasomotor function of the baroreflex arc are intact in older subjects with PPH. Therefore, an age-related decline in baroreflex function, affecting in particular afferent pathways including baroreceptors, may be an important factor in the development of postprandial hypotension in older persons.

In the tilt-table test, ΔSBP during the head-up tilt strongly correlated with the magnitude of ΔSBP after a meal in the subjects. The results suggest that the response of SBP during tilting may predict the risk of a postprandial reduction in BP in elderly persons. In fact, multiple regression analysis revealed that the magnitude of BP reduction during tilting was an independent predictor of the postprandial BP reduction. Although the prevalence of orthostatic hypotension and PPH are known to increase with aging, the pathophysiological mechanisms of those conditions may not be the same (2-4). However, it is possible that both alterations in BP may, at least in part, reflect common functional and pathological disorders in elderly persons, such as impaired vasoconstriction, increased vascular wall rigidity, decreased baroreflex function, and the presence of potential dehydration (22, 23). At present, the causal relationship between PPH and syncope is still controversial. However, PPH may reduce cerebral blood flow, resulting in syncope, falls, or both after meal ingestion. Because some episodes of unexpected syncope may be caused by PPH in the elderly, the prediction and assessment of postprandial reduction in SBP may help to decrease the risk of falls and unexpected syncope in elderly patients (24).

This study has several limitations. First, hormonal variables were not measured. Several gastrointestinal peptides, including insulin, somatostatin, and vasoactive peptides, may play a pathogenic role in postprandial hypotension (5, 8, 13, 15). Because the effects of carbohydrates on blood pressure are primarily caused by glucose, which stimulates insulin release, insulin has been implicated in the

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<thead>
<tr>
<th>Table 2. Relationships between ΔBP after Meal and Variables of Autonomic Nervous Function Testing</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Tilt ΔSBP</td>
</tr>
<tr>
<td>Tilt ΔHR</td>
</tr>
<tr>
<td>CV</td>
</tr>
<tr>
<td>HVT ΔSBP</td>
</tr>
<tr>
<td>CPT ΔSBP</td>
</tr>
<tr>
<td>CPT ΔHR</td>
</tr>
<tr>
<td>MAT ΔSBP</td>
</tr>
</tbody>
</table>

Tilt ΔBP, ΔBP during tilt-table test; Tilt ΔHR, ΔHR during tilt-table test; CV, coefficient of variation of R-R intervals; HVT ΔSBP, ΔSBP during hyperventilation test; CPT ΔSBP, ΔBP during cold pressor test; CPT ΔHR, ΔHR during cold pressor test; MAT ΔSBP, ΔBP during mental arithmetic test.
pathogenesis of postprandial hypotension. Thus, further studies are needed to define the role of gastrointestinal peptides on postprandial hypotension in the elderly. Second, hypertensive subjects were included in this study. Previous studies have suggested that significant reductions in BP after meals frequently occur in elderly subjects who are hypertensive, but not in those who are normotensive (25, 26). In fact, the mean SBP in the PPH group was significantly greater than that in the non-PPH group in the present study. Therefore, our results may be influenced by the subjects' history of hypertension. Because the age-related decline in baroreflex function can be affected by the history of hypertension, elderly hypertensive subjects may be liable to meal-associated hypotension. In conclusion, an age-related decline in baroreflex function may have an important role in the pathogenesis of postprandial hypotension in the elderly. The magnitude of the fall in SBP during the tilt-table test may be related to the degree of the postprandial reduction in SBP in elderly persons.

References
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