Mechanisms Mediating Postprandial Blood Pressure Reduction in Young and Elderly Subjects

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The objective of this study was to clarify potential differences in hormonal, neurogenic and hemodynamic mechanisms mediating postprandial blood pressure (BP) reduction. In 12 age- and body mass index-matched young normotensive (NT) subjects, 21 elderly NT, 17 young hypertensive (EH) patients, and 32 elderly EH, we measured BP, blood glucose, plasma insulin (IRI), and norepinephrine (NE) levels before and every 30 min for 3 h after a 75 g oral glucose solution ingestion. Cardiac output (CO) and total systemic resistance (TSR) were also measured before and 1 h after oral glucose ingestion. Postprandial BP reduction, defined as 10% or more decline in mean BP was recognized in 3/12 (25%) young NT, 9/21 (43%) elderly NT, 5/17 (29%) young EH, and 20/32 (63%) elderly EH. The most consistent finding was that the IRI response to glucose was high in all subjects with postprandial BP reduction regardless of age or level of BP, although changes in blood glucose levels showed no major differences. The NE level was low in young and elderly NT with postprandial BP reduction, but in EH the level was not different. Increases in CO in elderly subjects with postprandial BP reduction was significantly less than that in subjects without postprandial BP reduction. In addition, the decrease in TSR in young subjects with postprandial BP reduction was significantly greater than that in subjects without postprandial BP reduction, while the decrease in elderly subjects was not different between the subjects with and without postprandial BP reduction. In conclusion, postprandial BP reduction in elderly EH appears to be associated with hyperinsulinemia independent of age and BP status. The vasodilator effects of insulin may contribute to postprandial BP reduction. A second conclusion is that impairment of sympathetic nervous system responses to insulin may also contribute to altered postprandial hemodynamic responses especially in EH, suggesting multiple mechanisms in origin of postprandial BP reduction.

KEY WORDS: Postprandial hypotension, insulin, hemodynamics, essential hypertension, norepinephrine.

Received April 29, 1994. Accepted August 21, 1995.

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Research Projects on Aging and Health by the Ministry of Health and Welfare of Japan (94A2101).

Postprandial blood pressure (BP) reduction has been found in elderly subjects, but not in relatively healthy elderly subjects and elderly hypertensive patients. Some of these studies did not find a postprandial decline in BP in young subjects; however, Fagan et al reported postprandial alterations in hemodynamic responses in young normotensive subjects. Our laboratory has
also reported postprandial BP reduction after oral glucose ingestion not only in elderly but also in young subjects.

In this study, the prevalence of postprandial BP reduction was evaluated by using two definitions in the young and elderly population and in the normotensive and hypertensive population. The hormonal (insulin, neurogenic (norepinephrine), and hemodynamic (cardiac output [CO], total systemic resistance [TSR]) aspects were also examined in response to glucose ingestion in order to delineate potential differences in the four study groups. The results suggest that postprandial BP reduction occurs in young normotensive subjects at low frequency and in elderly subjects at high frequency. Postprandial BP reduction is consistently associated with exaggerated insulin responses in both the young and elderly, and at all levels of baseline BP. However, the failure of insulin to activate the sympathetic nervous system responses may lead to greater impairment of postprandial hemodynamic responses, especially in elderly hypertensive subjects.

METHODS

Twelve normotensive subjects under the age of 60 years (mean age 47.8 ± 2.6 years, mean weight and body mass index [BMI], 58 ± 3 kg, 22.0 ± 0.2 kg/m²), 21 elderly normotensive subjects from age 60 to 90 years (77.9 ± 1.5 years, 56 ± 2 kg, 21.8 ± 0.3 kg/m²), 17 younger hypertensive patients (49.0 ± 1.9 years, 59 ± 4 kg, 21.9 ± 0.2 kg/m²) and 32 elderly hypertensive patients (76.0 ± 1.4 years, 57 ± 3 kg, 21.7 ± 0.2 kg/m²) were studied. None of the subjects had diabetes mellitus, obesity, congestive heart failure, renal dysfunction, autonomic failure, or other serious illness. Hypertension was defined as a supine BP reading of 140/90 mm Hg or higher on three or more separate visits. The hypertensive patients were stage I to II of the World Health Organization classification. Normotension was defined as supine BP reading of 140/90 mm Hg or lower on three or more separate visits. The average BP readings of the normotensive and hypertensive groups were 116.1 ± 18.4/65.8 ± 9.3 mm Hg and 166.3 ± 4.6/97.8 ± 7.7 mm Hg in young and 119.0 ± 10.3/72.2 ± 8.3 mm Hg and 168.2 ± 8.1/97.6 ± 10.1 mm Hg in elderly subjects, respectively. This study was approved by the Ethics Committee of Osaka University Medical School and informed consent was obtained.

All hypertensive patients were untreated or antihypertensive medications were stopped at least 4 weeks preceding this study. Subjects were admitted for 14 days and placed on a controlled moderately sodium-restricted diet (7 g NaCl, 1800 cal/day) and asked to abstain from alcohol and not to drink coffee or to smoke for at least 48 h before the study. On day 15 of the diet after overnight fasting and recumbency, each subject was kept in the supine position and samples for measurement of blood glucose (BG), plasma insulin (immunoreactive insulin, IRI), and norepinephrine (NE) levels were collected through a cannula placed into a left arm vein. Blood pressure, pulse rate, BG, plasma IRI, and plasma NE concentration were measured before and every 30 min for 3 h after ingestion of 75 g/225 mL glucose solution. Cardiac output and blood flow in the abdominal aorta were measured before and 1 h after oral glucose ingestion. Total systemic resistance was calculated by dividing blood pressure by cardiac output (mm Hg·L⁻¹·min⁻¹).

Blood pressure and pulse rate were measured with an automated sphygmomanometer (A&D, TM-2713, Tokyo, Japan). Postprandial BP reduction was defined as a decline of 10% or more in mean BP. Plasma IRI was measured by radioimmunoassay and plasma NE by high performance liquid chromatography with detection using the fluorometric method. Cardiac output was measured by echocardiography (Aloka, SECT SCAN SSD-650CL, Tokyo, Japan) and blood flow in the abdominal aorta was measured below the origin of hepatic and mesenteric arteries by a Doppler method. (Hayashi, HADECO ES-1000SP, Tokyo, Japan).

Statistical Analyses Values are shown as mean ± SD. Comparisons of frequency of postprandial BP reduction among the groups were examined by Logistic Analysis. Changes in variables within each group and differences among groups were examined by two-way analysis of variance (ANOVA). When differences were significant, Dunnett’s test was performed to assess the significance of differences of means from the basal values. A P < 5% was considered significant.

RESULTS

The hypertensive and normotensive groups did not differ significantly in age, male:female ratio (50% in each group), or relative body weight (±10% of ideal body weight). Postprandial BP reduction, defined as 10% or more decline in mean BP was recognized in 3/12 (25%) young normotensives (NT), 9/21 (43%) elderly NT, 5/17 (29%) young hypertensives (EH), and 20/32 (63%) elderly EH. Defined as a 20/10 mm Hg or more decline in systolic/diastolic BP, postprandial BP reduction was recognized in 1/12 (8%), 4/21 (19%), 1/17 (6%), and 18/32 (56%), respectively. Logistic analyses of the frequency of postprandial BP reduction showed significant differences between young and elderly subjects (χ² = 8.21, P = .0042), and between normotensive and hypertensive subjects (χ² = 5.19, P = .0227). The frequency of postprandial BP reduction was significantly greater in elderly hypertensives compared to elderly normotensives and was greater in young hypertensives compared to...
young normotensives. In this study, none of the subjects with postprandial BP reduction were symptomatic (fainting, dizziness, or syncope).

The top row of Figure 1 shows the changes in mean systolic and diastolic BP after oral glucose ingestion in the four study groups classified as with and without postprandial BP reduction. Postprandial BP reduction was recognized both in young and elderly normotensive subjects, with the fall predominantly in systolic BP. However, in the four study groups there was no significant differences in the time patterns of postprandial BP change. Pulse rates in young normotensive and young hypertensive subjects increased with postprandial BP reduction, and increased slightly, but not significantly, in elderly subjects (the second row of Figure 1).

The third row of Figure 1 shows mean blood glucose levels before and after glucose ingestion in the four study groups classified as with or without postprandial BP reduction. The mean changes in blood glucose levels were compared statistically by analysis of area under the curve. Glucose responses in subjects with postprandial BP reduction did not differ significantly from those in subjects without postprandial BP reduction (F = 2.89, P = .094 in young NT; F = 2.91, P = .090 in elderly NT; F = 0.09, P = .76 in young EH, and F = 0.54, P = .46 in elderly EH). On the other hand, in elderly subjects, glucose responses were greater than in young subjects (F -
11.97, P = .0007 in NT; F = 0.43, P = .512 in EH). Hypertensive patients also had greater increments in glucose compared to normotensive subjects (F = 9.97, P = .002 in young EH; F = 54.89, P = .0001 in elderly EH).

In the fourth row of Figure 1, the changes in mean plasma insulin levels in response to glucose are shown in the four study groups classified as with or without postprandial BP reduction. Subjects with postprandial BP reduction had significantly greater insulin responses (F = 22.51, P = .0001 in young NT; F = 2.09, P = .017 in elderly NT; F = 2.36, P = .13 in young EH; F = 4.61, P = .03 in elderly EH) than those subjects without postprandial BP reduction. In addition, insulin responses in elderly hypertensive patients were greater than in normotensive subjects (F = 0.09, P = .76 in young; F = 7.24, P = .008 in elderly patients).

The bottom row of Figure 1 shows mean plasma NE levels before and after glucose ingestion in the four study groups classified as with or without postprandial BP reduction. The plasma NE level response to glucose was significantly lower in young and elderly normotensive subjects with postprandial BP reduction than in those without it (F = 19.93, P = .0001 in young NT; F = 24.65, P = .0001 in elderly NT), whereas NE responses did not differ in hypertensive patients with and without postprandial BP reduction (F = 0.07, P = .79 in young EH; F = 1.52, P = .22, in elderly EH). Basal plasma NE levels were significantly greater in elderly normotensive (P = .002) and hypertensive subjects (P = .27) compared to young subjects. In the third row of Figure 1, changes in plasma NE from baseline to 60 min after glucose ingestion were greater in young NT subjects with postprandial BP reduction. On the other hand, these changes were significantly less in young HT patients with postprandial BP reduction than in subjects without it. In elderly subjects, these changes were very similar to each other regardless of BP status.

Cardiac output responses to glucose were significantly less in young and elderly normotensive and elderly hypertensive subjects with postprandial BP reduction than without it (the top row of Figure 2 and the fourth row of Figure 3). Abdominal blood flow responses to glucose were significantly greater in elderly subjects (normotensive, hypertensive) than in young subjects, and were most pronounced in elderly subjects with postprandial BP reduction (the fifth row of Figure 3). Changes in total systemic resistance in response to glucose ingestion were significantly greater in young subjects with postprandial BP reduction irrespective of blood pressure status. On the other hand, these responses in elderly subjects with postprandial BP reduction were very similar to those in elderly subjects without BP reduction (the bottom row of Figure 3). Furthermore, the changes in total systemic resistance in elderly hypertensive patients were greater than those in normotensive subjects.

**DISCUSSION**

In the present study, the frequency of postprandial BP reduction was examined in normotensive and hypertensive young and elderly subjects. Postprandial BP reduction was seen in all study groups including young, normotensive subjects. Furthermore, the study establishes that hypertensive patients show a high incidence of postprandial hypotension (> 50%), but even elderly normotensive subjects show a significant 43% rate of postprandial BP decline. It is important to note that all groups were without symptoms related to hypotension. The criteria for postprandial BP reduction using percent change in mean BP differs from other studies where absolute decline in BP was used. This endpoint was selected because absolute values may show significant differences in baseline BP levels between young and elderly normotensive and hypertensive subjects. In addition, because certain food components may have different effects on blood pressure, an oral glucose solution was selected instead of a meal to standardize comparisons among study groups. In these studies, where sodium intake was controlled, postprandial BP reduction was recognized in all groups with the fall predominantly in systolic BP. This is in good accordance with the report of Lipshitz et al in healthy elderly subjects, and it appears that this is also one of the reasons why postprandial BP reduction was less frequently noted when defined as the absolute decline of 20/10 mm Hg in systolic/diastolic BP. The reason for the fall predominantly in systolic pressure is also not clear, but could relate to our hemodynamic data where increased blood flow postprandially was a feature especially in the elderly.

Potential mechanisms of postprandial BP reduction were evaluated with particular attention to glucose, insulin, sympathetic nervous system activity, and hemodynamic responses to glucose. Recently, hyperinsulinemia and insulin resistance, characterized by diminished cellular glucose uptake in response to insulin, has been recognized as a component of essential hypertension that can occur in both lean and obese hypertensives. Insulin resistance is accompanied by hyperinsulinemia, which may influence BP control by stimulating sympathetic nervous system activity, renal sodium retention, or by direct effects on the vascular bed. In relation to the present study, it has been noted that elderly subjects may have a diminished insulin-induced activation of sympathetic nerve activity. In our study, insulin responses to glucose were increased in hypertensive patients and in elderly subjects when compared to normotensive and young subjects. Importantly, in all groups with postprandial BP reduction, the insulin response to glucose was also increased when
compared to subjects without postprandial BP reduction. This consistent hyperinsulinemia may be etiologic in postprandial BP reduction as insulin has proven vasodilator responses.\(^2\) The fact that the exaggerated insulin response was seen in all groups indicates that age and basal BP are not determinants of this abnormal response. What other factors explain abnormal insulinemia in postprandial BP reduction need to be explored.

The present study also confirms that mean plasma NE levels, as an index of sympathetic nerve activity, are higher in hypertensive subjects in general and in both elderly normotensives and hypertensives, when compared to young study groups. In addition, in young and elderly normotensives with postprandial BP reduction, the mean peak of NE was less, whereas this was not the case in young and elderly hypertensive subjects with postprandial BP reduction. In addition, the changes in plasma NE after glucose ingestion are more exaggerated in normotensives than hypertensives with postprandial BP reduction. In the normal response to food ingestion, increases in plasma NE may occur in response to glucose ingestion and insulin release as proposed in the studies of Landsberg and colleagues\(^2\) and Mark and colleagues.\(^2\) These changes may occur to offset the proposed vasodilatory effect of insulin and serve as a compensatory cardiovascular response to minimize postprandial blood pooling in the splanchnic
arterial bed. The present study suggests that in elderly normotensive subjects and hypertensive subjects of both age groups with postprandial BP reduction, there is an impaired relationship between insulin-mediated stimulation of sympathetic nerve activity to maintain blood pressure responses to oral glucose ingestion. The age-associated increase in plasma NE levels in normotensive and hypertensive elderly hypertensive individuals may help to offset this failure of insulin to activate norepinephrine re-

FIGURE 3. Changes in mean BP, plasma insulin, and norepinephrine levels, cardiac output, blood flow in the abdominal aorta, and total systemic resistance, from baseline to 60 min after 75 g glucose ingestion in young and elderly normotensive and hypertensive subjects. Open bars = subjects without postprandial BP reduction; shaded bars = subjects with postprandial BP reduction. +P < .05, ++P < .01, +++P < .001 compared with the values in young subjects. §P < .05, §§P < .01 compared with the values in normotensive subjects.
haps, for example, insulin, is involved in the mediation of postprandial BP reduction in elderly hypertensives. However, the role of insulin in this process remains to be determined. In any case, the response of the sympathetic nervous system to meal-induced hypotension is not a simple function of insulin release, but rather a complex interaction between various stimuli and regulatory mechanisms.

The mechanisms responsible for postprandial BP reduction have been the subject of much research. One such mechanism is the conversion of glucose to insulin, which can lead to a decrease in peripheral resistance. In elderly hypertensives, the decrease in central blood volume that occurs with meal ingestion is accompanied by an increase in cardiac output. This increase in cardiac output helps to compensate for the decrease in peripheral resistance, thereby maintaining BP.

Another mechanism that may be involved in postprandial BP reduction is the activation of the sympathetic nervous system. In elderly hypertensives, the increase in cardiac output that occurs with meal ingestion is accompanied by an increase in sympathetic nervous system activity. This increase in sympathetic activity helps to maintain BP, even in elderly hypertensives who may be at risk for postprandial hypotension.

In conclusion, the mechanisms responsible for postprandial BP reduction are complex and involve interactions between the cardiovascular and neuroendocrine systems. The role of insulin in this process remains to be determined, but the activation of the sympathetic nervous system appears to be a key factor in maintaining BP in elderly hypertensives who are at risk for postprandial hypotension.
In conclusion, the mechanisms of postprandial BP reduction, which is frequently seen in elderly subjects with hypertension and which also can be seen in young normotensive subjects, appears to be caused in part by impairment of meal-stimulated insulin and sympathetic nervous system activity responses, leading to the previously described blunted hemodynamic responses to oral glucose ingestion. However, the differences in aortic blood flow response and in total systemic resistance in the young and old may indicate age-associated differences in hemodynamic adaptations to a meal. This study cannot rule out the possible role of other gastrointestinal factors that may have vasoactive properties.

ACKNOWLEDGMENTS

The authors would like to thank Professor Murray D. Esler for his thorough review of and constructive comments on this manuscript.

REFERENCES


