Effects of Acute Carbohydrate Administration on Central and Peripheral Hemodynamic Responses to Mental Stress

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Essential hypertension is closely related to conditions with impaired glucose tolerance and hyperinsulinemia. To evaluate a possible interaction between the sympathetic nervous system and carbohydrate ingestion on the circulatory responses to psychosocial stress, we compared the hemodynamic effects of an oral glucose challenge with those observed after placebo in 10 glucose-tolerant, normotensive young men at rest and during standardized mental stress. After glucose, resting cardiac output increased by 20% (p<0.05), which was mainly due to an increased heart rate (+14%; p<0.001). Since total peripheral resistance decreased by 13% (p<0.02), mean arterial pressure was unaffected by glucose. In spite of this, glucose loading was associated with a slight increase in systolic blood pressure and a gradual decrease of diastolic blood pressure. Resting forearm blood flow was unaffected by glucose. The stress response after placebo was characterized by the expected increase in cardiac output and mean arterial pressure, and an unchanged total peripheral resistance. By contrast, in the postprandial state the pressor response to stress was solely dependent on an increased systemic vascular resistance, and cardiac output was unaffected by stress. After glucose, the stress-induced muscular vasodilation in the forearm was reduced to 40% of that observed after placebo (p<0.01). Thus, acute carbohydrate administration has significant hemodynamic effects in humans. Furthermore, during the postprandial period there is a marked alteration of the pattern of the circulatory responses to psychosocial stress, characterized by attenuated muscular vasodilation and a rise in systemic vascular resistance. (Hypertension 1991;18:790–797)

Several recent studies have suggested a relation between essential hypertension and glucose intolerance.1–5 More specifically, patients with hypertension are hyperinsulimemic when compared with normotensive control subjects, indicating that essential hypertension is associated with a defect in insulin-stimulated glucose uptake.3–5 Furthermore, a direct relation between plasma insulin and height of blood pressure has recently been demonstrated.2,6

Experimental studies have provided evidence that insulin is a vasoactive agent and may exert excitatory influences on the adrenergic nervous system.7,8 In view of the fact that early developmental phases of hypertension often are associated with hemodynamic and neurohormonal signs of increased adrenergic activity, the putative link to metabolic factors and insulin deserves pathophysiological interest. In humans, insulin infusion into supraphysiological levels increases circulating norepinephrine concentrations, muscle sympathetic outflow, and heart rate.9–12 The precise hemodynamic mechanisms influenced by insulin have not been clarified in humans, but in dogs a high rate of infusion of insulin has been shown to significantly increase cardiac output, heart rate, and blood pressure.13 It has therefore been suggested that hyperinsulinemia may be involved in the pathogenesis of essential hypertension and contribute to the hemodynamic changes underlying some forms of blood pressure elevation.14–16 However, in two recent studies insulin infusion for 7 days in conscious dogs did not increase mean arterial pressure or plasma catecholamines.17,18

Despite the fact that the potential relevance of hyperinsulinemia for the hemodynamic alterations in essential hypertension is an issue of considerable clinical interest, little is still known about the relation between high physiological levels of insulin and sym-
pathoadrenal activity. In particular, the possibility of an interaction between metabolic factors and other stimuli that increase sympathetic activity, such as behaviorally induced arousal, has not been explored.

The aim of the present study was to investigate the hemodynamic effects of acute carbohydrate administration and to explore its possible influences on sympathoadrenal activation and hemodynamic responses to highly standardized mental stress. To determine the clinical significance of these mechanisms, it was considered important to raise insulin to true physiological levels and also to study the hyperinsulinemia in a physiological context (i.e., in the presence of elevated plasma glucose concentrations). For this reason, oral glucose administration was used to induce hyperinsulinemia, although this choice ruled out the possibility of distinguishing the effects of hyperglycemia from those of hyperinsulinemia per se.

Methods

Subjects

Ten glucose-tolerant, normotensive, nonobese subjects participated in the study. They were all apparently healthy, nonsmoking men who were not being treated with medication nor did they have a history of cardiovascular disease, including diabetes mellitus and essential hypertension. All subjects had normal fasting blood glucose values and negative family histories for diabetes mellitus. Two of the subjects had one parent with hypertension; none of the others had a family history of essential hypertension. The mean age, weight, and height of the participants were 27.7 years (range, 24-36 years), 73.8 kg (range, 67-80 kg), and 186 cm (range, 180-195 cm), respectively. Mean body mass index was 21.5 (range, 19.6-22.8). The nature, purpose, and potential risks of the study were carefully explained to each subject before informed consent to participate was obtained. The protocol was approved by the Ethics Committee of the University of Göteborg, and the study was conducted according to the declaration of Helsinki.

Experimental Protocol

The experiments were performed in the morning in the postabsorptive state after an overnight fast (8-12 hours) and followed a highly standardized procedure. Each participant was instructed to refrain from heavy exercise and avoid emotional excitement before the experiment. To avoid interference with the catecholamine analyses, the subjects were not allowed to ingest methylxantine-containing products 24 hours before each experiment.

The general design of the study is outlined in Figure 1. Each subject underwent two experiments on separate days with at least 1 week in between. They ingested either 1 g glucose per kg body wt dissolved in 250 ml warm water or placebo (1.5 g sodium cyclamate) given in the same volume. A small amount of lemon juice was added to improve palatability. The glucose and placebo solutions were administered in a double-blind manner in random order.

Procedure

On arrival in the laboratory, an 18-gauge polyethylene arterial catheter (Viggo Products, British Viggo, Swindon, UK) was inserted percutaneously into the brachial artery of the nondominant arm by means of the Seldinger technique. The catheter was advanced approximately 15 cm in a proximal direction. An indwelling venous catheter (Venflon, Viggo, Helsingborg, Sweden) was inserted percutaneously into an antecubital vein of the same arm. A strain-gauge plethysmographic device was applied on the forearm of the dominant arm, and electrodes for vectorcardiography with modified Frank leads (i.e., leg electrodes moved to the anterior iliac spine) were fixed.

The subject was then left alone in the recumbent position in a quiet, dimly lit, and air-conditioned room for 60 minutes. The subject was asked to try to relax and to avoid unnecessary communication with the examiner throughout the resting periods of the experiment. The initial resting period was followed by a prestimulation baseline period from -20 to 0 minutes. The test solutions were then ingested during a 5-minute period. Seventy minutes after the ingestion, the subject was asked to perform rapid mental arithmetic for approximately 15 minutes (serial subtraction of 7 from 700) trying to keep pace with a metronome (Reference 19; see also Reference 20 for reproducibility data on this method). After a reassuring comment, the subject was asked to resume a relaxed attitude for a 20-minute after-stress baseline period.

Arterial blood samples for determination of plasma glucose, serum insulin, and plasma catecholamines were obtained at rest before stimulation, at 30 and 60 minutes after stimulation, after 10 minutes of stress, and at 10 minutes after cessation of stress (Figure 1).
Hemodynamic Measurements

Intra-arterial blood pressure was recorded continuously throughout the experiment with an electrical transducer (EMT 35, Siemens-Elema, Stockholm, Sweden) on a Mingograph 81 (Siemens-Elema) with a paper speed of 5 mm/sec. Average systolic and diastolic blood pressures were determined for each 5-minute period of the experiment by planimetry of the blood pressure recording. Mean arterial pressure was obtained by electrical damping of the blood pressure signal.

Cardiac output was determined with the dye-dilution technique using indocyanine green (Cardio-green, Hynson, Westcott & Dunning Products, Beckton Dickinson and Co., Cockeysville, Md.) and a cuvette densitometer (Brechtelsbauer, Munich, FRG). Each dye-dilution curve was computer-integrated, and the mean of one to four injections on each point of measurement was used for further analysis. Stroke volume was obtained by dividing cardiac output by heart rate. To obtain total peripheral resistance, mean intra-arterial blood pressure was divided by cardiac output.

Forearm blood flow was studied by venous occlusion plethysmography with a mercury-in-rubber strain-gauge. On each point of measurement, mean resting forearm blood flow (ml/min x 10^-3 x dr x 10^-3) was calculated from five to eight separate recordings. Resting forearm vascular resistance (mm Hg x min^-1 x 10^-3 x ml^-1) was calculated as the ratio of mean arterial blood pressure to forearm blood flow.

Heart rate was monitored beat-to-beat by a computerized vectorcardiograph (MIDA 1000, Ortivus Medical AB, Täby, Sweden). Since all hemodynamic recordings could not, for technical reasons, be performed simultaneously, the recordings were done in the following way. Intra-arterial blood pressure and heart rate were monitored continuously and were averaged over 5-minute periods. At the end of each phase of the experiment, serial cardiac output determinations and forearm blood flow recordings were performed. During the latter recordings, which took approximately 5 minutes, the pressure signal was electrically damped to get mean arterial pressure; systolic and diastolic blood pressures were not recorded.

Biochemical Assays

The first 5 ml of blood was always discarded. Eleven millilitres of blood for assay of catecholamines was drawn into ice-chilled tubes containing 220 μM glutathione-EDTA (60 mg/ml and 90 mg/ml, respectively) and immediately was placed on ice. Within 2 minutes of collection the samples were centrifuged at +4°C and 2,000g for 5 minutes. Plasma aliquots were stored at −70°C until assay. Plasma catecholamines (epinephrine and norepinephrine) were analyzed in duplicate by high-performance liquid chromatography with electrochemical detection (Electro-chemical Detector 641, Waters, Millipore Ltd., Griesenheim, FRG). All samples from each subject were analyzed in the same assay run. Dihydroxybenzylamine was used as internal standard to compensate for incomplete recovery. In our laboratory, the intra-assay variation coefficients for basal and stress levels are 2.5% and 3.3% for norepinephrine and 8.6% and 8.1% for epinephrine, respectively. The detection limit is estimated as 50–100 fmol/l plasma, when defined as the concentration equivalent to five times the baseline noise.

Serum insulin was determined in duplicate by radioimmunoassay (Diagnostic Products Corp., Los Angeles, Calif.). Plasma glucose was determined in duplicate with the glucose oxidase technique using an automatic analyzer (Greiner G-400, Schweiz).

Statistical Analysis

Standard statistical methods were used. Unless otherwise stated, values are presented as mean±SEM. Effects of placebo and glucose during the two experiments were evaluated by two-way analysis of variance (ANOVA) for repeated measurements with the subject as the random factor. The analyses were performed separately for the resting period after placebo but fell 13% after glucose, with a
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Significant treatment x period interaction \( F(2,18) = 10.4, p = 0.001 \). Mental stress induced significant increases in the plasma levels of both catecholamines \( F(2,18) > 11.4, p < 0.004 \). However, the stress-induced increases of the plasma norepinephrine and epinephrine concentrations were similar after placebo and glucose \( F(2,18) < 1.3, p > 0.05 \).

Changes of intra-arterial blood pressure and heart rate throughout the two experiments are shown in Figure 3. During the first 60 minutes after ingestion of glucose, there was a slight but gradual decrease in diastolic blood pressure in comparison with the placebo condition \( F(11,99) = 5.1, p = 0.009 \). By contrast, systolic blood pressure increased gradually on both days \( F(11,99) = 13.4, p < 0.0001 \). This increase was slightly more pronounced after the glucose load than after placebo \( F(1,99) = 2.7, p = 0.06 \). Also, the increase in pulse pressure was significantly greater after glucose \( F(11,99) = 4.2, p = 0.02 \). Heart rate increased significantly after glucose as compared with placebo, as indicated by a significant treatment x period interaction \( F(11,99) = 4.3, p = 0.008 \).

In response to mental stress, there were highly significant increases of both systolic and diastolic blood pressure, and heart rate \( F(5,45) > 37.0, p < 0.0001 \). There were no significant differences in the levels or patterns of activation of any of the three variables during stress. However, heart rate was maintained on a slightly higher level both before, during, and after the stress experiment \( F(1,9) = 4.4, p = 0.07 \), whereas the differences between the two conditions regarding systolic and diastolic blood pressure tended to decrease after stress.

Levels and changes of central hemodynamics are shown in Table 1 and Figure 4 (upper panel), respectively. After carbohydrate administration, cardiac output increased by approximately 20% \( t \) test, \( p < 0.05 \) but was unchanged after placebo. The difference between the two conditions was significant \( F(1,9) = 8.3, p = 0.02 \). The elevation of cardiac output after glucose was mainly due to an increased heart rate \( t \) test, \( p < 0.001 \), whereas there was only a small and insignificant increase in stroke volume. ANOVA indicated a significant interaction between the two treatments \( F(1,9) = 13.5, p = 0.005 \). Furthermore, there was a significant interaction between glucose and placebo on systemic vascular resistance \( F(1,9) = 13.5, p = 0.005 \). Since carbohydrate administration was associated with a fall in total peripheral resistance of approximately 13% \( t \) test, \( p < 0.02 \), mean arterial pressure was practically unchanged after the glucose load. After placebo, there were no significant variations in any of the central hemodynamic parameters, save a slight but significant increase in mean arterial pressure (+3%; \( t \) test, \( p < 0.01 \)). Resting forearm blood flow and forearm vascular resistance were unchanged, both after glucose and placebo (Figures 4 [upper panel] and 5).
TABLE 1. Hemodynamic Effects of Placebo and Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Rest</th>
<th>60 Minutes after stimulation</th>
<th>Stress</th>
<th>After-stress baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>P</td>
<td>76.7±1.5</td>
<td>79.3±1.5</td>
<td>91.7±2.7</td>
<td>81.8±1.7</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>77.8±2.6</td>
<td>78.8±2.4</td>
<td>90.4±3.0</td>
<td>80.2±2.2</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CO (l/min⁻¹)</td>
<td>P</td>
<td>6.28±0.41</td>
<td>6.24±0.49</td>
<td>7.49±0.54</td>
<td>6.84±0.44</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>6.79±0.54</td>
<td>8.06±0.64</td>
<td>7.84±0.49</td>
<td>7.75±0.51</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>p&lt;0.005</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>P</td>
<td>52.3±2.3</td>
<td>54.0±2.6</td>
<td>66.9±3.3</td>
<td>55.4±1.9</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>51.5±3.1</td>
<td>58.4±3.1</td>
<td>73.0±4.0</td>
<td>58.3±3.0</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>p&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>P</td>
<td>121±7</td>
<td>117±9</td>
<td>114±9</td>
<td>125±9</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>134±11</td>
<td>139±11</td>
<td>109±7</td>
<td>134±11</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>p&lt;0.005</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TPR (mm Hg×l⁻¹×min⁻¹)</td>
<td>P</td>
<td>12.7±0.9</td>
<td>13.4±1.0</td>
<td>12.7±0.7</td>
<td>12.3±0.7</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>12.0±0.8</td>
<td>10.4±0.8</td>
<td>11.9±0.7</td>
<td>10.8±0.7</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>p=0.0004</td>
<td>p=0.09</td>
<td>p&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>FBF (ml×min⁻¹×dl⁻¹)</td>
<td>P</td>
<td>2.60±0.29</td>
<td>2.75±0.39</td>
<td>4.68±0.67</td>
<td>3.01±0.45</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>2.74±0.37</td>
<td>2.93±0.51</td>
<td>3.59±0.47</td>
<td>3.28±0.52</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>NS</td>
<td>p=0.06</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>FVR (resistance units)</td>
<td>P</td>
<td>34.2±4.9</td>
<td>34.0±4.4</td>
<td>23.8±3.6</td>
<td>33.5±5.2</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>34.4±5.7</td>
<td>34.0±5.3</td>
<td>29.5±4.8</td>
<td>29.6±4.2</td>
</tr>
<tr>
<td>P vs. G</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SEM. P, placebo; G, glucose; MAP, mean arterial pressure; CO, cardiac output; HR, heart rate; SV, stroke volume; TPR, total peripheral resistance; FBF, forearm blood flow; FVR, forearm vascular resistance.

In response to mental stress, the changes of central hemodynamics were markedly different after the glucose load as compared with placebo. Whereas cardiac output was maintained on higher level throughout the stress experiment after glucose administration \(F(1,9)=11.9, \ p=0.007\), there was no further increase during the mental arithmetic task in contrast to the 23% increase in cardiac output observed after placebo [placebo versus glucose; \(F(2,18)=7.3, \ p=0.01\)]. However, the reverse pattern was observed in total peripheral resistance; systemic vascular resistance increased by approximately 18% after glucose (\(t\) test, \(p=0.02\)) but fell slightly, as expected, after placebo [placebo versus glucose; \(F(2,18)=11.9, \ p=0.002\)]. Thus, although the

![Figure 4](http://hyper.ahajournals.org/)  
*Bar graphs show changes of central and peripheral hemodynamics from prestimulation to prestress periods (upper panel), from prestress to stress periods (middle panel), and from prestimulation to stress periods (lower panel) after glucose (filled bars) and placebo (open bars). MAP, mean arterial pressure; CO, cardiac output; HR, heart rate; SV, stroke volume; TPR, total peripheral resistance; FBF, forearm blood flow; FVR, forearm vascular resistance.*
mean arterial pressure increased significantly in response to the stress task on both occasions \(F(2,18)=51.1, p<0.0001\), the underlying hemodynamic mechanisms were entirely different after glucose administration and placebo.

During the placebo condition, the increase in cardiac output was solely dependent on an increased heart rate (±24%; \(t\) test, \(p<0.001\)), since the stroke volume was unaffected by stress. However, in spite of the fact that cardiac output was not affected at all by the mental stress stimulus after glucose administration, the heart rate response to stress was preserved (glucose +26% versus placebo +24%). No significant differences regarding the stress-induced heart rate changes were observed between the two treatments \(F(2,18)=2.0, p>0.05\). Thus, after glucose the lack of an increase in cardiac output during stress was due to a rather marked drop in stroke volume, which fell by approximately 20% \(t\) test, \(p<0.0001\); placebo versus glucose; \(F(2,18)=8.0, p=0.009\).

In the forearm, stress led to the expected marked increase in forearm blood flow during the placebo condition \(t\) test, \(p<0.001\) and a drop in forearm vascular resistance (−29% ; \(t\) test, \(p<0.01\)). However, after glucose this muscular vasodilatory response was markedly attenuated (placebo versus glucose; \(F(2,18)=6.6, p=0.008\). The stress-induced increase in forearm blood flow was only 30% after the glucose load as compared with 74% after placebo.

Figure 4 (lower panel) shows the combined effects of glucose and stress (i.e., the hemodynamic pattern present during mild mental arousal and physiological hyperinsulinemia in comparison with the resting, unstimulated condition. There was no significant difference between the two conditions regarding the major hemodynamic variables mean arterial pressure, cardiac output, and total peripheral resistance. However, the increase in heart rate was considerably greater after glucose than after placebo (glucose +43% versus placebo +29%; glucose versus placebo, \(t\) test, \(p<0.005\)), which, however, was compensated for by a more marked decrease of stroke volume after glucose.

In spite of the unchanged systemic vascular resistance, the stress response after glucose was associated with a forearm vasodilation that was only some 40% of the dilatory response observed after placebo.

**Discussion**

**Hemodynamic Changes During the Postprandial Period**

This study demonstrates that acute oral carbohydrate administration has significant systemic hemodynamic effects in humans: increased cardiac output and heart rate and reduced total peripheral resistance. These alterations are associated with increases in systolic blood pressure and pulse pressure. However, in this group of glucose-tolerant, normotensive men no significant increase of mean arterial pressure was observed. Except for the unchanged mean arterial pressure, our findings are very similar to the hemodynamic changes observed by Liang and co-workers\(^\text{13}\) during euglycemic hyperinsulinemia in dogs. In their study, insulin infusion was associated with significant increases in cardiac output, heart rate, and left ventricular contractility but a reduction in total peripheral resistance. It has been convincingly demonstrated with the euglycemic hyperinsulinemic clamp technique that these effects are present also when hypoglycemia is prevented. Therefore, it is conceivable that hyperinsulinemia as such may be responsible for the hemodynamic effects of a glucose load.

However, the reciprocal changes of cardiac output and total peripheral resistance during glucose loading suggest that complex hemodynamic mechanisms are involved. Increased contractility has been shown to be an effect of insulin both in vitro models and in the intact heart.\(^\text{23–26}\) However, neither increased contractility nor fluid retention could be the sole factors underlying the hyperkinetic circulation since the major alteration behind the increased cardiac output in the postprandial state was an elevated heart rate. Because a direct chronotropic effect of insulin is unlikely,\(^\text{13}\) it is reasonable to assume that the major mechanism behind the elevated cardiac output is increased sympathetic activity.

Accordingly, a measurable rise in circulating plasma norepinephrine concentrations has been shown in several previous studies, although this effect is mainly seen with large, supraphysiological doses of insulin.\(^\text{7,9}\) More specifically, it was recently demonstrated with the microelectrode nerve recording technique that oral glucose loading is associated with an increased muscle sympathetic outflow.\(^\text{11,12}\) In the present study, no consistent effect on the levels of circulating arterial norepinephrine was observed after glucose, but it may well be
that the variability of plasma catecholamine levels masks minor changes in their neural release rate during physiological hyperinsulinemia.

However, although it has been assumed that the effect on sympathetic activity is due to a direct stimulatory action of insulin on the hypothalamus, it cannot be ruled out that the increased sympathetic drive is a secondary, reflex phenomenon to compensate for a postprandial fall in systemic vascular resistance due to increased splanchnic blood flow. Direct, vasodilating properties of insulin have been demonstrated in vitro, and similar effects have been observed both in laboratory animals and humans. Alternatively, it has been speculated that vasoactive gut peptides may contribute to the splanchnic vasodilation, although attempts to identify any such hormone have been disappointing. The changes are due to osmotic effects of the glucose load is unlikely, since packed red blood cell volume has been shown to decrease rather than increase after glucose administration.

Whether this vasodilatory effect is present also in muscular vascular beds is a matter of controversy. Increased forearm blood flow has been observed both in response to supraphysiological and physiological levels of insulin. However, in a recent study no effect on forearm blood flow could be demonstrated in either normotensive or hypertensive subjects when physiological doses of insulin were infused locally into the brachial artery. Also, in the present study we observed no increase in forearm blood flow by glucose administration per se. It is likely that differences in insulin levels, duration of hyperinsulinemia, and method of administration may account for some of the differences in effects on peripheral hemodynamics between these studies.

Effects of Stress

After carbohydrate administration, the normal stress response pattern (i.e., increase in cardiac output and mean arterial pressure, and a slight decrease in systemic vascular resistance) was reversed into a vasoconstrictor response. The findings of an unaltered amplitude of the pressor response to stress, despite this markedly different pattern of activation, may be an illustration of what Julius recently has called "the blood pressure seeking properties of the central nervous system." It appears that when the cardiac output is already set on a higher level as in the postprandial situation, the pressor response is instead expressed through peripheral vasoconstriction. Interestingly, however, the tachycardia associated with the stress response was preserved after glucose, and the effects of this chronotropic response were thus completely offset by a decrease in stroke volume.

The mechanisms behind the stress-induced decrease in stroke volume in the postprandial state are unknown. Normally, inotropic influences and centralization of blood volume to the cardiopulmonary area help maintain stroke volume during stress in spite of the higher rate of emptying of the heart. Since considerably lower stress levels of circulating epinephrine were reached after glucose than after placebo, one may speculate that the contribution of epinephrine to the a-mediated centralization of blood volume would be smaller in the postprandial state. Another interesting possibility has to do with the fact that insulin has been shown to interact with catecholamines at the receptor level, antagonizing the effect of norepinephrine on cardiac cells. If so, the inotropic effect of adrenergic stimulation during stress may be partly blocked by insulin, which could possibly contribute to a decrease in contractility and stroke volume.

Under physiological conditions, the regional hemodynamic pattern during acute stress is characterized by peripheral muscular vasodilation, which is typically counterbalanced by vasoconstriction in some other vascular beds (e.g., kidney and portal circulation). However, after glucose loading the muscular vasodilatory response of stress was apparently reduced to some 40% of that observed after placebo. Despite its vasodilatory effects during rest, conditions, insulin has been suggested to increase vascular reactivity to pressor stimuli such as norepinephrine and angiotensin II, possibly by its interaction with intracellular cation homeostasis. If so, one may speculate that increased reactivity to neurogenic stimulation or humoral vasoconstrictor agents released during stress may counteract the vasodilation normally associated with the stress response as such. Such a mechanism may explain the reduced muscular vasodilation during stress. Also, the contribution of circulating epinephrine to b-mediated vasodilation would be less after glucose, since lower stress levels of epinephrine were reached on the day of the carbohydrate administration.

Implications for Hypertension

In the present study, glucose loading was associated with small but consistent increases in systolic blood pressure and pulse pressure. However, since diastolic blood pressure tended to decrease after glucose, mean arterial pressure was unaffected. By contrast, significant effects on mean blood pressure have been observed both in laboratory animals and humans when high rate infusions of insulin were used. In the human studies, circulating insulin concentrations threefold to 12-fold above the peak level observed in the present study were reached, and it is therefore possible that the effect is dose-dependent. This interpretation is supported by the fact that in the study by Rowe and coworkers, an increase in mean arterial pressure was only observed during high rate infusion of insulin with 5 milliunits/kg/min (resulting in a mean plasma insulin level of approximately 600 microunits/ml) but not after the lower 2 milliunit infusion (mean plasma insulin, 154 microunits/ml).

It has also been shown that insulin infusion during normoglycemia induces a dose-dependent increase in
circulating plasma norepinephrine.7 Furthermore, it appears that this relation is preserved in subjects with peripheral insulin resistance.36 If this is true also for the hemodynamic effects, these findings suggest that the cardiovascular activation after glucose ingestion may be augmented in subjects with more pronounced hyperinsulinemia due to insulin resistance.

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References


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