Effect of a Low Fat Diet on Carbohydrate Metabolism in Patients with Hypertension

MARIO PARILLO, ANN COULSTON, CLARIE HOLLENBECK, AND GERALD REAVEN

SUMMARY Plasma glucose and insulin responses to both a 75-g oral glucose challenge and to conventional meals were determined in eight patients with hypertension and compared with values of a control population. The results indicated that patients with hypertension had significantly higher than normal plasma glucose and insulin concentrations in both situations. Furthermore, when dietary carbohydrate was increased by 16% of total calories (with a reciprocal reduction in dietary fat), the hyperglycemia and hyperinsulinemia present in patients with hypertension were accentuated. Since low fat–high carbohydrate diets are usually recommended for patients with hypertension, these data suggest that abnormalities of glucose and insulin metabolism associated with hypertension would be increased if patients with high blood pressure followed conventional dietary advice. Since hyperglycemia and hyperinsulinemia have been shown to be associated with an increased risk of developing coronary artery disease, it may be appropriate to reevaluate the clinical utility of low fat–high carbohydrate diets in the treatment of hypertension. (Hypertension 11: 244–248, 1988)

KEY WORDS • hypertension • coronary artery disease

A GROWING body of evidence suggests that patients with hypertension have associated abnormalities of carbohydrate metabolism. For example, a relationship between hypertension and obesity has been noted,1–4 and there are data suggesting that the link between the two may involve changes in carbohydrate metabolism. Obesity is associated with insulin resistance and hyperinsulinemia.5–7 and lowering of blood pressure in obese persons with physical training correlates with the associated reductions in plasma insulin concentrations, not with weight loss.8 In addition, the fall in blood pressure following physical training is limited to persons who were hyperinsulinemic at the outset.9 Thus, it appears that the metabolic derangements associated with obesity, not obesity per se, are important in the etiology of hypertension, and hyperinsulinemia may represent the crucial link. Further evidence of the possible relationship between hypertension and hyperinsulinemia is documentation of a significant correlation between degree of blood pressure elevation and plasma insulin concentration independent of body weight.9–12

The importance of hyperinsulinemia in the syndrome of hypertension may not be limited to its possible etiological role. Three studies13–15 in the past few years have indicated that hyperinsulinemia may be a risk factor for coronary artery disease (CAD). Given evidence that antihypertensive treatment does not reduce morbidity and mortality caused by CAD,16–18 it seems appropriate to wonder if this is because treatment did not improve and might even have accentuated hyperinsulinemia associated with hypertension. In this regard, the low fat–high carbohydrate diet recommended by a recent National Institutes of Health Conference19 to reduce the risk of CAD has been shown to elevate plasma insulin concentrations.20–22 Since patients with hypertension are likely to be encouraged to consume such diets, we felt it reasonable to see what would happen to their ambient insulin levels when this was done under controlled conditions.

Subjects and Methods

Eight subjects, three women and five men, who were receiving antihypertensive medication were recruited for these studies. These subjects volunteered in response to a newspaper story describing our interest in assessing the effect of diet on carbohydrate metabolism in patients with hypertension and were recruited without prior knowledge of their plasma glucose or
insulin levels. In addition, eight persons with normal blood pressure volunteered to serve as a control group.

The clinical characteristics of the subjects with hypertension are presented in Table 1. It can be seen that the blood pressure was well controlled in most, and all but one were taking a diuretic. The control population consisted of five men and three women, with a mean age of 47 ± 4 years, body mass index of 23.6 ± 0.9 kg/m², and blood pressure of 130 ± 3/81 ± 3 mm Hg. Thus, the two groups were comparable in terms of age and degree of obesity, as estimated by calculation of body mass index. With the exception of hypertension, all subjects were in good general health and taking no other medication known to alter glucose or insulin metabolism.

Experimental Design

A standard oral glucose tolerance test was performed in all 16 subjects, and plasma glucose and insulin concentrations were measured. In addition, plasma glucose and insulin concentrations were determined at hourly intervals from 0800 to 1600 in response to a control mixed-meal diet containing (as percentage of total calories) 19% protein, 41% fat, and 40% carbohydrate. This diet will be described in greater detail subsequently. Breakfast was consumed at 0800 and lunch at 1200 during the day of hourly sampling.

In addition, the effect of varying dietary carbohydrate intake on ambient plasma glucose and insulin concentration was studied in the eight subjects with hypertension. This comparison was conducted in a crossover design, with two 15-day periods randomly assigned. Four hypertensive subjects began with the control diet, and four began with the high carbohydrate diet. Subjects reported daily for their meals and were encouraged to continue their usual level of physical activity. Body weight was maintained within 0.5 kg of admission weight throughout the study. All hypertensive subjects completed both dietary periods sequentially.

Diet

All food consumed by the subjects during the 30-day period of diet comparison was provided by the Stanford University General Research Center kitchen. The study diets were designed at two carbohydrate levels, 40 and 56% of calories. The dietary fiber content of the diet was 14 g/1000 kcal in the 40% carbohydrate diet and 18 g/1000 kcal in the 56% carbohydrate diet. The protein content of the diet was held constant at 19% of calories, and total fat intake varied with the carbohydrate content from 41% to 25% of calories. The ratio of polyunsaturated fat to saturated fat was held constant at 0.4 in both diets, and daily cholesterol intake averaged 150 mg/1000 kcal. Thus, each person consumed between 300 and 400 mg of cholesterol per day. In addition, dietary content of sodium (44 mEq/1000 kcal) and potassium (35 mEq/1000 kcal) were similar in the two diets. Total daily caloric intake was divided into three meals and an evening snack. Twenty percent of the daily caloric requirement was consumed at 0800, and 40% at 1200 and 1800. A portion of the caloric requirement from the evening meal was provided in the evening snack. Fasting and postprandial plasma samples were obtained on Days 14 and 15 of each diet period at hourly intervals from 0800 to 1600 for measurement of glucose and insulin concentration, and the results of these 2 days on each diet were averaged.

Statistics

The results are expressed as means ± SEM. Analysis of variance (ANOVA) was used to estimate the statistical significance of differences between the two groups, as well as the effect of the two diets.

Results

Mean plasma glucose and insulin concentrations in response to a 75-g oral glucose challenge are shown in Figure 1. It is apparent that both plasma glucose and insulin concentrations during the glucose tolerance test were higher in subjects with hypertension, and this difference was significant by two-way ANOVA (p < 0.001).

Figure 2 displays mean hourly values for plasma glucose and insulin from 0800 to 1600 in the two experimental groups. When the two groups were compared by two-way ANOVA, the day-long responses were significantly higher (p < 0.01-0.001) in the subjects with hypertension.

This effect of variation in dietary carbohydrate intake on day-long plasma glucose and insulin concentrations is depicted in Figure 3. It can be seen from

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>BMI (kg/m²)</th>
<th>Blood pressure (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>M</td>
<td>25.8</td>
<td>130/90</td>
<td>Hydrochlorothiazide + triamterene</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>F</td>
<td>19.7</td>
<td>140/96</td>
<td>Atenolol + clonidine</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>25.5</td>
<td>135/90</td>
<td>Hydrochlorothiazide</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>F</td>
<td>23.9</td>
<td>138/84</td>
<td>Chlorthalidone</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>M</td>
<td>23.7</td>
<td>120/82</td>
<td>Chlorthalidon + metoprolol</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>F</td>
<td>20.4</td>
<td>140/87</td>
<td>Hydrochlorothiazide + triamterene</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>M</td>
<td>24.6</td>
<td>128/85</td>
<td>Hydrochlorothiazide</td>
</tr>
<tr>
<td>8</td>
<td>63</td>
<td>M</td>
<td>27.6</td>
<td>139/86</td>
<td>Hydrochlorothiazide + triamterene</td>
</tr>
</tbody>
</table>

BMI = body mass index.
these data that mean plasma glucose and insulin responses were higher when dietary carbohydrate was increased, and these differences were statistically significant (by two-way ANOVA; \( p < 0.001 \)). On the other hand, it should be emphasized that the differences in plasma glucose concentrations were modest.

**Discussion**

Several previous reports have demonstrated that subjects with hypertension are hyperglycemic or hypoinsulinemic, or both, when compared with a control population, and this was also true of the two experimental groups we studied. Furthermore, the current results document the fact that the ability to demonstrate these differences does not depend on the use of an artificial oral glucose challenge; they can be shown to exist throughout the day when subjects are consuming conventional meals. Thus, it seems reasonable to conclude that there is an increased incidence of glucose intolerance in subjects with hypertension, and this increase appears to be associated with an increase in circulating insulin levels. These metabolic changes are consistent with the view that insulin resistance exists in patients with high blood pressure, and there is now preliminary evidence that this is the case.

The low fat–high carbohydrate diet used in this study is essentially identical in composition to the diet recently recommended by a consensus conference sponsored by the National Institutes of Health to be followed by "all Americans" in an attempt to reduce the risk of CAD. We have previously shown that consumption of low fat–high carbohydrate diets will increase ambient plasma glucose or insulin concentrations, or both, in normal subjects, subjects with endogenous hypertriglyceridemia, and patients with non-insulin-dependent diabetes mellitus. Thus, the finding that similar changes were seen in hypertensive subjects was not surprising. A great deal of uncertainty exists as to why it has been so difficult to demonstrate a reduction in morbidity and mortality caused by CAD in patients undergoing treatment for hypertension. In this regard, it has become increasingly apparent that abnormalities of lipoprotein metabolism exist in persons with untreated hypertension, and that these defects can be accentuated once antihypertensive medication is initiated. Since all of the described changes in lipoprotein metabolism would increase the risk of CAD, recent inquiry has focused on the possibility that these findings might help explain why risk of CAD does not seem to be reduced with antihypertensive treatment. The current data emphasize the fact that defects in carbohydrate metabolism also exist in patients with hypertension. Moreover, both hyperglycemia and hyperinsulinemia have been shown in prospective epidemiological studies to increase the risk of CAD. More pragmatically, the data presented in this article indicate that the defects in carbohydrate metabolism are accentuated when patients with hypertension follow current dietary recommendations.
Although this report has emphasized the possible harmful effects of low-fat–high carbohydrate diets on glucose and insulin metabolism in patients with hypertension, control of dietary fat intake is also important in this patient population. Specifically, there is evidence that hypercholesterolemia increases the risk of CAD at any given level of blood pressure,\textsuperscript{41,42} and it would seem prudent to prescribe diets for patients with high blood pressure that are likely to result in the lowest possible plasma low density lipoprotein–cholesterol concentration. Indeed, this is precisely why low fat–high carbohydrate diets have been recommended for general use.\textsuperscript{19} However, plasma low density lipoprotein–cholesterol concentration is also quite sensitive to the ratio of polyunsaturated to saturated fat in the diet,\textsuperscript{43,44} and increasing the dietary intake of polyunsaturated and monounsaturated fat may be as effective as reducing total fat intake in regulation of plasma low density lipoprotein–cholesterol concentration. Thus, the best overall diet for patients with hypertension may be one in which the relative amounts of fat and carbohydrate in the diet are not substantially changed, but the intake of monounsaturated and polyunsaturated fat is increased and that of saturated fat decreased. In this manner it should be possible to prevent the changes in glucose and insulin metabolism associated with a low fat–high carbohydrate diet without compromising the goal of lowering plasma low density lipoprotein–cholesterol concentration. Indeed, we have shown that this approach is quite effective in patients with non-insulin-dependent diabetes mellitus.\textsuperscript{22}

In conclusion, we have shown that patients with hypertension, as a group, are hyperglycemic and hyperinsulinemic. Furthermore, we have demonstrated that these metabolic abnormalities are accentuated when hypertensive patients consume diets that are likely to be recommended to them. All but one of the hypertensive subjects studied were receiving hypertensive medication, and we cannot be sure if the changes noted were due to the high blood pressure or the anti-hypertensive medication. Indeed, since seven of the eight subjects with hypertension were taking a diuretic, it could be argued that the changes seen were all secondary to the metabolic effects of this particular class of antihypertensive drugs. On the other hand, hyperglycemia and hyperinsulinemia have been documented in patients with untreated hypertension,\textsuperscript{10–12, 28–30} and low fat–high carbohydrate diets have been shown to produce similar changes in a variety of patient populations.\textsuperscript{20–22} Thus, we believe it reasonable to suggest that changes quantitatively similar to those we noted would occur in any group of hypertensive persons—treated or untreated. On the other hand, it is certainly possible that drugs used to treat hypertension are capable of ameliorating or accentuating the defined changes in carbohydrate metabolism. Unfortunately, the number of subjects in the current study were too few, and the drug treatment program too varied, to provide any useful insights into this issue of obvious importance. However, the need to understand the impact of various antihypertensive drugs on glucose and insulin metabolism should not obscure the importance of the current results, which demonstrate that the diet conventionally recommended for patients with hypertension may increase the risk of CAD. This is a matter of potentially great clinical importance, and one that requires further study.

References

13. Pyorlal K. Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: results from two population studies in Finland. Diabetes Care 1979;2:131-141
22. Coulston AM, Hollenbeck CB, Swislocki ALM, Chen Y-DI,


35. Goldman AL, Steele BW, Schnaper HW, Fitz AE, Frohlich ED, Perry HM. Serum lipoprotein levels during antihypertensive therapy. JAMA 1980;224:1691–1695


Effect of a low fat diet on carbohydrate metabolism in patients with hypertension.
M Parillo, A Coulston, C Hollenbeck and G Reaven

Hypertension. 1988;11:244-248
doi: 10.1161/01.HYP.11.3.244

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://hyper.ahajournals.org/content/11/3/244

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally
published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center,
not the Editorial Office. Once the online version of the published article for which permission is being
requested is located, click Request Permissions in the middle column of the Web page under Services.
Further information about this process is available in the Permissions and Rights Question and Answer
document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/