Does a High-Carbohydrate Diet Have Different Effects in NIDDM Patients Treated With Diet Alone or Hypoglycemic Drugs?

M. PARILLO, MD, PHD
R. GIACCO, MD
A.V. CIARDULLO, MD
A.A. RIVELLESE, MD
G. RICCARDI, MD

OBJECTIVE — To compare the effects of a high-carbohydrate diet on blood glucose and plasma lipids in NIDDM patients with either mild or severe glucose intolerance.

RESEARCH DESIGN AND METHODS — A crossover design with a 15-day intervention diet was used. Eighteen patients were separated into two groups on the basis of hypoglycemic treatment (diet, $n = 9$, or diet plus glibenclamide, $n = 9$) and were assigned to a 15-day treatment with a high-carbohydrate/low-fiber diet containing 60% energy from carbohydrate and 20% from fat or a low-carbohydrate/low-fiber diet with 40% energy from carbohydrate and 40% from fat and then crossed over to the other diet for 15 more days.

RESULTS — The high-carbohydrate diet produced a significant increase in postprandial blood glucose in patients on glibenclamide (13.6 ± 1.4 vs. 11.0 ± 1.8 mmol/l, $P < 0.02$), while no difference was recorded in the group on diet alone (9.7 ± 0.9 vs. 8.9 ± 0.6 mmol/l). Postprandial insulin levels were significantly higher after the high-carbohydrate diet in the group on diet alone (248 ± 32 vs. 192 ± 28 pmol/l, $P < 0.01$), while no significant differences were observed in the other group (226 ± 19 vs. 202 ± 24 pmol/l). The high-carbohydrate diet also induced a significant increase in fasting plasma triglyceride concentrations in both groups (1.36 ± 0.2 vs. 1.12 ± 0.2 mmol/l, $P < 0.05$, and 1.4 ± 0.3 vs. 1.1 ± 0.1 mmol/l, $P < 0.05$). No differences were observed in fasting plasma cholesterol and HDL.

CONCLUSIONS — The effects of the high-carbohydrate diet on blood glucose control in NIDDM patients differ according to severity of glucose intolerance.

In the recent past, diabetic patients were given low-fat/high-carbohydrate diets with the aim of reducing the risk of coronary heart disease (a major killer of NIDDM patients) and improving blood glucose control. However, the latest American Diabetes Association recommendations have abandoned the preference for a low-fat/high-carbohydrate diet; the current advice, instead, is that the percentage of calories from carbohydrate will vary and is individualized based on the patient's habits and glucose and lipid goals (1). This latter statement is based on recent evidence showing that, contrary to previous beliefs, high-carbohydrate diets might have detrimental effects on blood glucose control in NIDDM patients (2–5).

We postulate that it could be possible to reconcile the deleterious effects of high-carbohydrate diets observed in some recent studies (in patients with severe forms of glucose intolerance) with the beneficial effects demonstrated in the past (in diabetic patients with mild glucose intolerance). The aim of our study was to compare the effects of a high-carbohydrate diet on blood glucose control and plasma lipids in NIDDM patients with either mild glucose intolerance (treated with diet alone) or more severe glucose intolerance (treated with oral hypoglycemic drugs).

RESEARCH DESIGN AND METHODS

— Eighteen patients with NIDDM (fasting blood glucose >7.8 mmol/l on repeated occasions) were studied. All patients were free of diabetic complications and renal or liver diseases. Aside from hypoglycemic treatment, none of the patients were taking any drugs known to affect carbohydrate or lipid metabolism. Patients were divided into two groups on the basis of the hypoglycemic treatment: diet alone or diet plus glibenclamide. In patients treated with glibenclamide, the drug was started after failure of diet treatment (fasting blood glucose >10 mmol/l and HbA_{1c} >8.5% for >6 months). Both groups were composed of nine patients who were comparable for age (47.6 ± 3.8 vs. 50.4 ± 4.4 years), BMI (24.7 ± 1.5 vs. 24.6 ± 0.9 kg/m^2), diabetes duration (6.2 ± 2.0 vs. 7.7 ± 1.5 years), and level of HbA_{1c} (7.5 ± 0.1 vs. 7.4 ± 0.1%). All subjects gave informed consent to participate in the study. The experimental protocol was approved by the ethical committee of the Medical School of the Federico II University in Naples.

Patients were hospitalized in the metabolic ward for the entire duration of the study. All patients, irrespective of their hypoglycemic treatment, were randomly assigned to either a high-carbohydrate/low–monounsaturated fatty acid (MUFA)/low-fiber diet or a low-carbohydrate/high-MUFA/low-fiber diet. At the end of the first dietary period, they

From the Institute of Internal Medicine and Metabolic Diseases (M.P., A.V.C., A.A.R., G.R.), Medical School, University of Naples Federico II, Naples; and the Institute of Food Science and Technology (R.G.), Italian National Research Council, Avellino, Italy.

Address correspondence and reprint requests to Gabriele Riccardi, MD, Associate Professor, Institute of Internal Medicine and Metabolic Disease, University of Naples Federico II, Via S. Pansini 5, 80131, Naples, Italy.

Received for publication 30 May 1995 and accepted in revised form 14 December 1995.

MUFA, monounsaturated fatty acid.

Table 1—*Diet composition*

	Low-carbohydrate	High-carbohydrate
Carbohydrate	40	60
Monodisaccharides	15	14
Polysaccharides	25	46
Fat	40	20
Saturated	7	5
Monounsaturated	29	13
Polyunsaturated	4	2
Protein	20	20
Fiber (g/day)	24	24
Cholesterol (mg/day)	250	250

Data are % energy (except for fiber and cholesterol).

were crossed over to the other diet without any washout. Each dietary period lasted 15 days. Five patients in the group treated with glibenclamide and four patients in the group treated with diet alone started the study with the high-carbohydrate/low-MUFA/low-fiber diet. In the group taking hypoglycemic drugs, the dosage of the drug was maintained constant throughout the study (glibenclamide, mean dosage 13.1 ± 0.9 mg/day).

The compositions of the diets are shown in Table 1. The increase in carbohydrate in the high-carbohydrate diet was obtained by consuming larger amounts of starchy foods, especially bread. The increase in fat in the low-carbohydrate diet was achieved by increasing the consumption of olive oil (rich in monounsaturated fat).

On day 15 of each dietary period, blood samples for glucose, insulin, cholesterol, triglycerides, and HDL cholesterol assessment were collected from each patient after a 12- to 14-h overnight fast. On the same day, glucose and insulin were also measured 2 h after lunch. Plasma insulin was assayed by radioimmunoassay (intrassay coefficient of variation 4.1%). HDL cholesterol was assayed by precipitation method; plasma glucose, cholesterol, and triglyceride were measured by standard enzymatic colorimetric methods (Boehringer Mannheim, Mannheim, Germany).

All data are presented as means ± SE. Differences between the two dietary treatments were evaluated by the paired Student's *t* test, while differences between the two groups were evaluated by unpaired *t* test. The level of statistical significance was set at $P = 0.05$ (two tailed).

RESULTS — The palatability of the two diets was very good, and all patients were able to comply with the menus administered. No effect of diet sequence on the results was observed.

Body weight did not change during the two dietary periods in either the group treated with diet alone (65.3 ± 1.0 vs. 65.1 ± 0.9 kg) or the group treated with diet plus glibenclamide (65.1 ± 0.8 vs. 65.4 ± 1.0 kg).

Fasting plasma glucose concentrations were similar after the high- and low-carbohydrate diet in both groups (6.5 ± 0.3 vs. 6.7 ± 0.5 mmol/l and 7.4 ± 0.9 vs. 7.7 ± 0.9 mmol/l). Conversely, a significant increase in postprandial plasma glucose levels was observed after the high-carbohydrate diet only in the group treated with diet plus glibenclamide (95% CI 0.5–4.5 mmol/l; $P < 0.05$); no significant difference in postprandial blood glucose levels between the two diets was recorded in the group treated with diet alone (95% CI −0.8 to 2.3 mmol/l) (Table 2). Similarly, postprandial plasma glucose concentration during the high-carbohydrate diet (but not during the low-carbohydrate diet) was significantly higher in the group on glibenclamide than in the group on diet alone (13.6 ± 1.4 vs. 9.7 ± 0.9 mmol/l, $P < 0.05$).

Fasting insulin concentrations were similar after the high- and low-carbohydrate diet in both groups (48 ± 12 vs. 54 ± 12 pmol/l and 72 ± 12 vs. 54 ± 6 pmol/l). On the other hand, a significant increase in postprandial insulin levels was observed after the high-carbohydrate diet only in the group treated with diet alone (95% CI 22.2–91.2 pmol/l, $P < 0.01$). Conversely, in the group treated with diet plus glibenclamide, no significant difference in postprandial plasma insulin levels was observed between the two diets (95% CI −2.6 to 52.0 pmol/l) (Table 2).

In comparison to the low-carbohydrate diet, the high-carbohydrate diet also induced a significant increase in fasting plasma triglyceride concentrations in both groups (1.36 ± 0.2 vs. 1.12 ± 0.2 mmol/l, $P < 0.05$, and 1.40 ± 0.3 vs. 1.14 ± 0.1 mmol/l, $P < 0.05$), while plasma cholesterol levels did not change after either diet (5.1 ± 0.3 vs. 5.1 ± 0.3 mmol/l and 4.4 ± 0.2 vs. 4.4 ± 0.3 mmol/l) both in the group treated with diet alone and in the group treated with diet plus oral hypoglycemic drugs. HDL cholesterol concentrations were also similar at the end of the two dietary periods in both groups (1.0 ± 0.05 vs. 1.0 ± 0.05 mmol/l and 1.1 ± 0.05 vs. 1.1 ± 0.10 mmol/l).

Table 2—*Postprandial plasma glucose and insulin concentrations*

	Diet group		Glibenclamide group	
	Low-carbohydrate	High-carbohydrate	Low-carbohydrate	High-carbohydrate
Blood glucose (mmol/l)	8.9 ± 0.6	9.7 ± 0.9	11.0 ± 1.8*	13.6 ± 1.4
Plasma insulin (pmol/l)	192 ± 28†	248 ± 32	202 ± 24	226 ± 19

Data are means ± SE. $n = 9$ for both the diet group and the glibenclamide group. *$P < 0.02$; †$P < 0.01$ vs. high carbohydrate.

DISCUSSION — This study demonstrates that the high-carbohydrate diet has different effects on glucose control in NIDDM patients with different degrees of severity of glucose intolerance.

In the last years, several groups have compared the effects of high- and low-carbohydrate diets in NIDDM patients but have obtained contrasting results in relation to glucose metabolism

(2–8). An explanation for this discrepancy comes from this study, which shows that the different metabolic characteristics of the patients (in relation to a more or less pronounced glucose intolerance) can influence the metabolic effects of a high-carbohydrate diet. In patients with less severe glucose intolerance (who could be treated with diet alone), a higher carbohydrate intake produces a compensatory increase in pancreatic insulin secretion, which allows plasma glucose levels to remain unchanged (6). By contrast, in patients with more severe glucose intolerance (with a grossly impaired insulin secretory reserve, who therefore require hypoglycemic drugs), the compensatory increase in the insulin response to a higher carbohydrate intake does not occur, and this determines the increase in blood glucose levels (2,3).

The effects of a high-carbohydrate diet on plasma lipoproteins are less influenced by the degree of glucose intolerance. In fact, the high-carbohydrate diet induced in both groups of patients a similar increase in plasma triglyceride values, while it did not influence plasma cholesterol or HDL cholesterol concentrations. This confirms that a moderately higher fat content in the diabetic diet is not deleterious for lipoprotein metabolism as long as unsaturated fats, but not saturated fats, are increased (9,10).

In conclusion, the effects of a high-carbohydrate diet on blood glucose control in NIDDM patients differ according to the severity of their glucose intolerance. Therefore, the most appropriate carbohydrate content in the diet should be decided for each patient according to a number of relevant metabolic parameters, i.e., body weight, levels of plasma cholesterol, plasma triglyceride, etc. (1). Among these parameters, the degree of glucose intolerance should also be considered.

Acknowledgments— This work was supported in part by the Italian National Research Council Grant 91.00226.PF41: target project Prevention and Control of Disease Factors, subproject Nutrition.

We gratefully acknowledge R. Scala for linguistic revision.

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