Clinical Efficacy of Two Hypocaloric Diets That Vary in Overweight Patients With Type 2 Diabetes

Comparison of moderate fat versus carbohydrate reductions

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Approximately 80% of patients with type 2 diabetes are overweight/obese (1), and weight loss is the mainstay of treatment for these individuals. However, there is growing controversy as to whether reduced-fat or reduced-carbohydrate diets are best suited for this purpose, and results (2–8) in nondiabetic subjects suggest that lower carbohydrate diets are similarly or more efficacious in improving weight, triglycerides, and HDL cholesterol. There are no published randomized studies evaluating the role of dietary macronutrients with respect to weight loss and cardiovascular risk improvement in patients with type 2 diabetes. Thus, we randomized diet-treated patients with type 2 diabetes to hypocaloric diets, moderately restricted in either carbohydrate or fat, to determine whether weight loss or metabolic improvement differed as a function of macronutrient composition.

RESEARCH DESIGN AND METHODS — A total of 29 patients with diet-treated type 2 diabetes were recruited from the San Francisco Bay area. All subjects gave written informed consent. Inclusion criteria included BMI 27–36 kg/m^2, fasting plasma glucose concentration 7.2–8.3 mmol/l, no use of antihyperglycemic medications, and stable weight for 3 months. Subjects on antihypertensive or cholesterol-lowering drugs or aspirin were allowed to continue their medications.

Insulin-mediated glucose uptake was quantified by a modification (9) of the insulin suppression test as originally described (10) and validated (11). In this test, a 180-min infusion of somatostatin (0.27 μg/m^2 per min), insulin (25 mU/m^2 per min), and glucose (250 mg/m^2 per min) yields similar steady-state insulin concentrations in all subjects but different steady-state plasma glucose (SSPG) concentrations; the higher the SSPG, the more insulin resistant the individual. Only those who qualified as insulin resistant (12–14) were eligible to proceed. These subjects had plasma glucose and insulin concentrations measured hourly during a standardized 8-h meal tolerance test. Daylong glucose and insulin concentrations were calculated as the area under the curve of nine samples. Lipid and lipoprotein concentrations were determined using the Vertical Auto-Profile II test, as previously described (16), on fasting blood samples (triglycerides averaged from two fasting samples).

Subjects were randomized to one of two equally hypocaloric (−750 kcal/day) diets: *1*) 60% carbohydrate, 25% fat, and 15% protein; or *2*) 40% carbohydrate, 45% fat, and 15% protein. Both diets restricted saturated fat to ≤7% of total calories, so the calorie difference between the two diets was made up of a combination of carbohydrate and mono- and polyunsaturated fats. Resting calorie requirements were calculated via the Harris Benedict equation (17) and an activity factor, and subjects were instructed not to change their activity level during the study. Subjects received 2 h of nutritional education utilizing the 2003 *Exchange Lists for Meal Planning*. The dietary interventions lasted 16 weeks; subjects prepared their own food and returned to the General Clinical Research Center at weekly intervals for a weight check and a 15–20–min visit with the study dietitian to review food diaries. Compliance with assigned diet was estimated by entering food diary records from the entire study period into Esha Food Processor (version 8.0; Esha, Portland, OR). The hypocaloric diet was followed by 2 weeks of weight maintenance, after which baseline measurements were repeated. The macronutrient composition of the final meal tolerance test was congruent with assigned diet.

Student's *t* tests or χ^2 analyses were used for between-group comparisons. Within-group comparisons utilized paired Student's *t* tests or, for daylong glucose and insulin values, two-way ANOVA, with hour and pre- versus post-diet as the factors. Triglycerides and area-under-the-curve insulin values were log-transformed for analyses. Other variables were distributed normally. $P < 0.05$ was considered statistically significant. Pearson's correlations were performed to assess the relationship between weight loss and change in each metabolic variable. Multiple linear regression models for each metabolic variable included weight loss, dietary assignment, and an interaction term.

RESULTS — All subjects completed the study. Table 1 depicts demographic and metabolic characteristics of the two

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Abbreviations: SSPG, steady-state plasma glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Clinical and metabolic data pre– and post–weight loss intervention*

	60% carbohydrate diet (n = 15)			40% carbohydrate diet (n = 14)		
	Pre	Post	P*	Pre	Post	P*
Age (years)	56 ± 7	—	—	57 ± 7	—	—
Sex (male/female)	9/6	—	—	8/6	—	—
Race (Caucasian/ Hispanic/Asian/Black)	10/1/4/0	—	—	12/1/1/0	—	—
BMI (kg/m^2)	31.0 ± 2.4	28.6 ± 2.4	<0.001	31.4 ± 2.4	29.6 ± 2.9	<0.001
Weight (kg)	90 ± 15.2	83.0 ± 1.2	<0.001	95 ± 16.6	89.1 ± 16.3	<0.001
Waist (cm)	105 ± 10	99 ± 10	<0.001	108 ± 7	103 ± 7	0.02
SSPG (mmol/l)	14.9 ± 3.1	11.0 ± 3.8	0.002	15.1 ± 3.1	12.8 ± 3.3	0.005
Fasting glucose (mmol/l)	7.8 ± 0.8	6.6 ± 0.8	<0.001	7.5 ± 1.0	6.6 ± 0.7	0.004
Daylong glucose (mg/dl × 8 h)	1,169 ± 171	981 ± 131	<0.005	1,147 ± 210	977 ± 142	0.008
Daylong insulin (uU/ml × 8 h)	472 ± 303	404 ± 299	0.021	490 ± 269	374 ± 324	0.023
Systolic blood pressure (mmHg)	129 ± 12	124 ± 10	0.11	128 ± 17	123 ± 16	0.24
Diastolic blood pressure (mmHg)	78 ± 7	73 ± 7	0.03	75 ± 7	74 ± 8	0.47
Total cholesterol (mmol/l)	4.32 ± 0.88	4.27 ± 1.03	0.67	4.71 ± 0.88	4.53 ± 1.11	0.57
Triglycerides (mmol/l)†	1.92 ± 0.86	1.37 ± 0.54	0.007	2.47 ± 0.84	1.95 ± 1.42	0.008
HDL cholesterol (mmol/l)	0.98 ± 0.16	1.03 ± 0.18	0.29	0.98 ± 0.21	1.03 ± 0.24	0.56
LDL cholesterol (mg/dl)	2.74 ± 0.78	2.74 ± 0.91	0.53	3.00 ± 0.72	2.87 ± 0.88	0.59
LDL particle size (sec)	111.9 + 4.1	113.6 + 3.6	0.07	111.8 + 4.8	112.9 + 5.1	0.53

Data are means ± SD unless otherwise indicated. Between-group comparisons (unpaired Student's t test) of all variables yielded no statistically significant differences ($P > 0.20$ for all comparisons). *Paired Student's t test. †Log values for triglycerides and daylong insulin were used in all comparisons.

groups at baseline and following the period of weight loss. Baseline characteristics between groups did not differ significantly. Reported macronutrient consumption in the 60% vs. the 40% carbohydrate group, respectively, was 52 vs. 43% carbohydrate ($P < 0.0001$), 18 vs. 19% protein ($P = 0.31$), 29 vs. 38% total fat ($P = 0.006$), and 8 vs. 9% saturated fat ($P = 0.31$).

There was no significant difference in the amount of weight loss, with decreases of 7.0 ± 4.7 kg in the 60% carbohydrate group and 5.9 ± 3.5 kg in the 40% carbohydrate group. Variables that decreased significantly in each dietary group (Table 1) included SSPG, fasting and daylong plasma glucose, daylong insulin, and fasting triglycerides. Between-group comparisons of change in all metabolic variables were not statistically significant.

The more weight lost, the greater were the decreases in SSPG ($r = 0.72$, $P < 0.0001$) and fasting plasma glucose ($r = 0.57$, $P = 0.002$), daylong plasma glucose ($r = 0.40$, $P = 0.03$), insulin ($r = 0.44$, $P = 0.018$), and fasting triglyceride concentrations ($r = 0.38$, $P = 0.050$). There were no interactions between dietary assignment and weight loss with respect to change in metabolic variables.

CONCLUSIONS — We believe that this is the first study to evaluate the effect of moderate variations in relative amounts of dietary fat and carbohydrate on glycemic control and cardiovascular disease risk factors in patients with type 2 diabetes. The results indicated that moderate weight loss (~7%) led to significant improvements in insulin sensitivity, plasma glucose, insulin, and triglyceride concentrations. The changes in these metabolic variables were significantly associated with the amount of weight lost, with no interaction with diet. We have previously demonstrated in similarly obese, insulin-resistant, nondiabetic subjects that the 40% carbohydrate hypocaloric diet led to similar weight loss but greater reductions in daylong insulin, triglycerides, and small-dense LDL cholesterol compared with the 60% carbohydrate diet (8). Others have published similar results (2–7), and it is not clear why we could not replicate our earlier findings in this population of patients with type 2 diabetes. One possibility is that the differences in amount of fat and carbohydrate actually consumed were less than planned. The results of this study suggest that the impact of moderate variations in macronutrient composition in calorie-restricted diets in patients with type 2 diabetes is less powerful than the beneficial effects of weight loss, per se, a conclusion that needs to be confirmed in a larger study.

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