ORIGINAL ARTICLE

A Low-Carbohydrate as Compared with a Low-Fat Diet in Severe Obesity

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ABSTRACT

BACKGROUND

The effects of a carbohydrate-restricted diet on weight loss and risk factors for atherosclerosis have been incompletely assessed.

METHODS

We randomly assigned 132 severely obese subjects (including 77 blacks and 23 women) with a mean body-mass index of 43 and a high prevalence of diabetes (39 percent) or the metabolic syndrome (43 percent) to a carbohydrate-restricted (low-carbohydrate) diet or a calorie- and fat-restricted (low-fat) diet.

RESULTS

Seventy-nine subjects completed the six-month study. An analysis including all subjects, with the last observation carried forward for those who dropped out, showed that subjects on the low-carbohydrate diet lost more weight than those on the low-fat diet (mean [±SD], −5.8±8.6 kg vs. −1.9±4.2 kg; P=0.002) and had greater decreases in triglyceride levels (mean, −20±43 percent vs. −4±31 percent; P=0.001), irrespective of the use or nonuse of hypoglycemic or lipid-lowering medications. Insulin sensitivity, measured only in subjects without diabetes, also improved more among subjects on the low-carbohydrate diet (6±9 percent vs. −3±8 percent, P=0.01). The amount of weight lost (P<0.001) and assignment to the low-carbohydrate diet (P=0.01) were independent predictors of improvement in triglyceride levels and insulin sensitivity.

CONCLUSIONS

Severely obese subjects with a high prevalence of diabetes or the metabolic syndrome lost more weight during six months on a carbohydrate-restricted diet than on a calorie- and fat-restricted diet, with a relative improvement in insulin sensitivity and triglyceride levels, even after adjustment for the amount of weight lost. This finding should be interpreted with caution, given the small magnitude of overall and between-group differences in weight loss in these markedly obese subjects and the short duration of the study. Future studies evaluating long-term cardiovascular outcomes are needed before a carbohydrate-restricted diet can be endorsed.

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The differences in health benefits between a carbohydrate-restricted diet and a calorie- and fat-restricted diet are of considerable public interest. However, there is concern that a carbohydrate-restricted diet will adversely affect serum lipid concentrations.[1] Previous studies demonstrating that healthy volunteers following a low-carbohydrate diet can lose weight have involved few subjects, and few used a comparison group that followed consensus guidelines for weight loss.[2,3] The reported effects of a carbohydrate-restricted diet on risk factors for atherosclerosis have varied.[2-4] We performed a study designed to test the hypothesis that severely obese subjects with a high prevalence of diabetes or the metabolic syndrome would have a greater weight loss, without detrimental effects on risk factors for atherosclerosis, while on a carbohydrate-restricted (low-carbohydrate) diet than on a calorie- and fat-restricted (low-fat) diet.

METHODS

SUBJECTS

The study was approved by the institutional review board at the Philadelphia Veterans Affairs Medical Center, and an approved consent form was signed by each subject. Inclusion criteria were an age of at least 18 years and a body-mass index (the weight in kilograms divided by the square of the height in meters) of at least 35. Exclusion criteria were a serum creatinine level of more than 1.5 mg per deciliter (132.6 μmol per liter); hepatic disease; severe, life-limiting medical illness; inability of diabetic subjects to monitor their own glucose levels; active participation in a dietary program; or use of weight-loss medications. During an enrollment period that lasted from May to November 2001, 132 subjects from the Philadelphia Veterans Affairs Medical Center were randomly assigned to either the low-carbohydrate diet or the low-fat diet, with use of a preestablished algorithm generated from a random set of numbers. We used stratified randomization, with blocking within strata, to ensure that each group would contain approximately equal numbers of women, subjects with diabetes, and severely obese subjects (body-mass index, 40 or higher). The study was not blinded.

STUDY DESIGN

The two diet groups attended separate two-hour group-teaching sessions each week for four weeks, followed by monthly one-hour sessions for five additional months; all sessions were led by experts in nutritional counseling. Subjects received a diet-overview handout, instructional nutrition labels, sample menus and recipes, and a book on counting calories and carbohydrates.[5] No specific exercise program was recommended. The subjects assigned to the low-carbohydrate diet were instructed to restrict carbohydrate intake to 30 g per day or less.[6] No instruction on restricting total fat intake was provided. Vegetables and fruits with high ratios of fiber to carbohydrate were recommended.[6] The subjects assigned to the low-fat diet received instruction in accordance with the obesity-management guidelines of the National Heart, Lung, and Blood Institute,[7] including caloric restriction sufficient to create a deficit of 500 calories per day, with 30 percent or less of total calories derived from fat.

DATA COLLECTION

The subjects' weights were measured monthly on a single calibrated scale (SRScales, SR Instruments). Other data collected at enrollment and at six months included waist size, self-reported medical history, blood pressure, and glucose and serum lipid levels, measured in blood specimens obtained after an overnight fast (Synchron LX20 Clinical Chemistry System, Beckman Coulter). Low-density lipoprotein cholesterol levels were calculated according to the Friedewald formula.[8] Serum insulin levels were measured by radioimmunoassay (Laboratory Corporation of America). Insulin sensitivity was estimated with use of the quantitative insulin-sensitivity check index as follows: $1 \div [(\text{log fasting insulin level, in microunits per milliliter}) + (\text{log fasting glucose level, in milligrams per deciliter})]$; this index has a good correlation with the results of glucose-clamp studies in obese subjects and subjects with diabetes.[9] Dietary compliance was estimated by means of a previously validated[10] instrument in which subjects are interviewed to obtain data on 24-hour recall of dietary consumption. Data were analyzed with Nutribase Management software (CyberSoft).

STATISTICAL ANALYSIS

The primary end point was weight loss at six months. Assuming a two-sided type I error of 5 percent, we estimated that we would need 100 subjects (50 per group) for the study to have 80 percent power to demonstrate a mean (±SD) weight

loss that was 5±12 kg greater in the low-carbohydrate group than in the low-fat group.[11] Given an anticipated dropout rate of 25 percent, we set the enrollment target at 135 subjects. By six months, 79 subjects remained in the study (36 in the low-fat group and 43 in the low-carbohydrate group). The primary analysis included all 132 subjects: the 79 subjects who completed the study, the 29 subjects who dropped out but had six-month data available from records of routine office visits, and the 24 subjects for whom the weight recorded at the last follow-up visit was carried forward. Since the 29 subjects whose final weight was obtained from office records were weighed on a different scale from that used in the study, we performed a second analysis that included all subjects, with base-line weights carried forward for all 53 subjects who dropped out.

For analyses of changes in dietary intake, serum lipid levels, glycemic control, and insulin sensitivity, we included all subjects, with base-line values carried forward for subjects who dropped out of the study. No interim analyses were performed.

For comparison of continuous variables between the two groups, we calculated the change from base line to six months in each subject and compared the mean changes in the two diet groups using an unpaired t-test.[12] We assessed the normality of the distribution of all variables before using the t-test. Triglyceride, insulin, and glucose levels were skewed and were therefore log-transformed for analysis. Dichotomous variables were compared by chi-square analysis.[12] Linear regression and two-way analysis of covariance models were used to correct for potentially confounding variables and to identify interactions between variables and diet-group assignment.[12] Missing waist sizes were imputed by linear extrapolation on the basis of height and weight. All P values were two-sided, and a P value of 0.05 or less was considered to indicate statistical significance. Analyses were performed with use of SPSS software (version 10.0).

RESULTS

BASE-LINE CHARACTERISTICS

Sixty-eight subjects were randomly assigned to the low-fat diet and 64 to the low-carbohydrate diet (Fig. 1). Subjects in the two groups were well matched with regard to base-line characteristics (Table 1). The subjects were severely obese at base line (Table 1), with a high prevalence of diabetes (39 percent) or the metabolic syndrome without diabetes (43 percent), as previously defined.[13]

ATTRITION

The cumulative percentage of subjects who dropped out of the study by months 1, 3, and 6 were 38, 44, and 47 percent, respectively, in the low-fat group and 25, 27, and 33 percent, respectively, in the low-carbohydrate group. Differences in attrition between groups were statistically significant by the third month (P=0.03) but were not significant at six months (P=0.10). There were no significant differences between the groups in the characteristics of the subjects who dropped out of the study (Table 2). Subjects on the low-carbohydrate diet attended more dietary counseling sessions than did the subjects on the low-fat diet (mean, 5.7±2.7 vs. 4.3 ±2.7; P=0.006).

ASSESSMENT OF DIETARY INTAKE

After six months of dietary counseling, subjects on the low-fat diet reported a decrease in caloric consumption while their macronutrient composition was close to the guidelines of the National Heart, Lung, and Blood Institute (Table 3).[7] As compared with the subjects on the low-fat diet, subjects on the low-carbohydrate diet reported a nonsignificantly greater reduction in caloric intake (P=0.33), a significantly greater decrease in the percentage of calories from carbohydrates (P<0.001), and a significantly greater increase in the percentage of calories from protein (P<0.001) and fat (P=0.004).

WEIGHT LOSS

Subjects on the low-carbohydrate diet lost more weight during the six-month study than did those on the low-fat diet (mean, −5.8±8.6 kg vs. −1.9± 4.2 kg; 95 percent confidence interval for the difference in weight loss between groups, −1.6 to −6.3; P=0.002) (Fig. 1). The difference in weight loss between the groups remained significant after adjustment for base-line variables alone (age, race or ethnic group, sex, base-line body-mass index, base-line caloric intake, and the presence or absence of hypertension, diabetes, active smoking, and sleep apnea) (P=0.002) and for base-line variables plus the number of dietary counseling sessions attended (P=0.01).

A second analysis in which we carried forward the base-line weights of subjects who dropped out of the study (i.e., assumed no weight loss in these subjects) still demonstrated greater weight loss in the low-carbohydrate group than in the low-fat group (mean, −5.7±8.6 kg vs. −1.8±3.9 kg; 95 percent confidence interval for the difference in weight loss between groups, −1.6 to −6.2; P=0.002).

As a measure of substantial weight loss, we found that a weight loss of at least 10 percent of the base-line weight occurred in 9 of 64 subjects on the low-carbohydrate diet (14 percent), as compared with 2 of 68 subjects on the low-fat diet (3 percent) (P=0.02). White subjects lost more weight than black subjects (mean, −13±19 kg vs. −5±12 kg; P=0.009), regardless of the diet-group assignment. There were no other significant differences in weight loss between the groups.

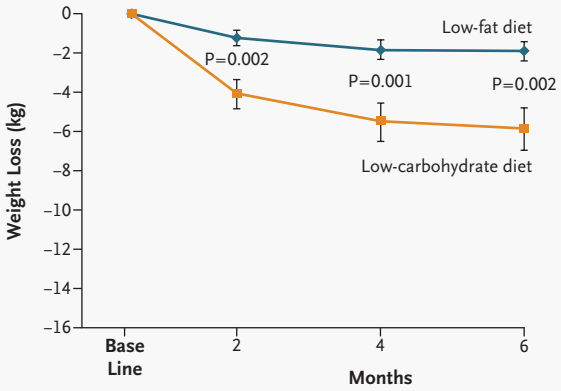

Figure 1. Mean (±SE) Decrease in Weight between Subjects on the Low-Carbohydrate Diet and Those on the Low-Fat Diet.

Weights for each time point include all 132 subjects. The number of subjects at each point for whom weights were either extracted from records or carried forward from a previous visit are given in parentheses. The standard errors have not been adjusted for these imputed values.

SERUM LIPIDS

During the six-month study, there was a greater decrease in the mean triglyceride level in the low-carbohydrate group than in the low-fat group (−20±43 percent vs. −4±31 percent, P=0.001) (Table 4). This difference remained significant after adjustment for base-line variables (P<0.001). Subjects on the low-carbohydrate diet also had a greater mean decrease in triglyceride levels whether or not they were taking lipid-lowering drugs (−25±38 percent vs. −8±35 percent with lipid-lowering drugs, P=0.01; and −16±46 percent vs. −1±25 percent without lipid-lowering drugs; P=0.04). Triglyceride levels may also be affected by medications taken for diabetes. However, in a separate analysis of subjects who were not taking either diabetes medications or lipid-lowering medications (28 on the low-fat diet and 24 on the low-carbohydrate diet), we still observed a greater reduction in the mean triglyceride level among subjects on the low-carbohydrate diet (−20±42 percent vs. 2±28 percent, P=0.001). In a model adjusted for the amount of weight lost and the base-line variables, assignment to the low-carbohydrate diet (P=0.01) and the amount of weight lost (P<0.001) were each independent predictors of a decrease in the triglyceride level. However, comparison of subjects within weight-loss strata demonstrated that this finding was limited to subjects who lost more than 5 percent of their base-line weight.

Black subjects had a smaller decrease in triglyceride levels than did white subjects (mean, −1±30 percent vs. −21±36 percent), independent of the diet-group assignment (P=0.002), but not after adjustment for base-line variables and the amount of weight lost (P=0.09).

Total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels did not change significantly during the six-month study within or between groups (Table 4). During the study, there were no changes in lipid-lowering therapy in the low-fat group, whereas two subjects on the low-carbohydrate diet started taking a statin and one stopped taking a statin.

GLYCEMIC CONTROL AND INSULIN SENSITIVITY

The mean fasting glucose level decreased more in the low-carbohydrate group than in the low-fat group at six months (−9±19 percent vs. −2±17 percent, P=0.02) (Table 4). This difference remained significant after adjustment for base-line variables (P=0.004). However, the greater reduction in serum glucose levels in the low-carbohydrate group was limited to diabetic subjects, with no significant change in the levels in nondiabetic subjects on either diet (Table 4). Assignment to the low-carbohydrate diet was no longer a significant predictor of a decrease in glucose levels after adjustment for the amount of weight lost (P=0.12). There was a trend toward a greater decrease in mean glycosylated hemoglobin values in diabetic subjects on the low-carbohydrate diet, as compared with those on the low-fat diet (P=0.06) (Table 4). By six months, seven subjects in the low-carbohydrate group had had dose reductions in oral hypoglycemic agents or insulin. In comparison, one subject in the low-fat group had a dose reduction in insulin and one subject began oral therapy.

Insulin sensitivity was measured only in subjects

Table 1. Base-Line Characteristics of the Subjects.*

Characteristic	Low-Carbohydrate Diet (N=64)	Low-Fat Diet (N=68)
Age (yr)	53±9	54±9
Body-mass index	42.9±6.6	42.9±7.7
Weight (kg)	130.0±22.7	131.8±27.3
Systolic blood pressure (mm Hg)	133±15	135±16
Diastolic blood pressure (mm Hg)	78±11	80±9
Race or ethnic group (%)		
White	42	34
Black	55	62
Hispanic	3	3
Sex (%)		
Female	20	15
Male	80	85
Diabetes mellitus (%)	41	38
Treatment for diabetes		
Sulfonylurea	11	16
Metformin	17	13
Peroxisome proliferator–activated receptor γ agonist	2	2
Insulin	9	4
Metabolic syndrome without diabetes (%)	45	41
Hypertension (%)	72	57
Antihypertensive therapy (%)	64	57
Hyperlipidemia (%)	51	50
Lipid-lowering therapy		
Statin	42	37
Gemfibrozil	3	0
Niacin	0	2
Coronary artery disease (%)	16	16
Depression (%)	33	34
Current cigarette smoking (%)	20	22
Sleep apnea (%)	27	21

* Plus–minus values are means ±SD. Because of rounding, percentages may not total 100. Race and the presence of diabetes, hypertension, coronary artery disease, depression, current smoking, and sleep apnea were all self-reported. Subjects were considered to have hyperlipidemia if they reported a total cholesterol level of more than 200 mg per deciliter (5.2 mmol per liter) or were receiving lipid-lowering therapy. There were no significant differences between groups.

without diabetes. Among these subjects, those on the low-carbohydrate diet had a greater increase in insulin sensitivity than those on the low-fat diet (6±9 percent vs. −3±8 percent, P=0.01). This difference remained significant after adjustment for base-line variables (P=0.001). In a model adjusted for the amount of weight lost and base-line variables, assignment to the low-carbohydrate diet (P=0.01) and the amount of weight lost (P<0.001) were each independent predictors of an improvement in insulin sensitivity. Comparison of subjects within weight-loss strata demonstrated a uniformly, but nonsignificantly, greater improvement in insulin sensitivity among those on the low-carbohydrate diet within each stratum.

BLOOD PRESSURE

We did not observe significant overall or between-group changes in blood pressure. Systolic and diastolic blood pressure decreased by 2 mm Hg and 1 mm Hg, respectively, in the low-carbohydrate group. In the low-fat group, both systolic and diastolic blood pressure decreased by 2 mm Hg (P=0.85 for between-group differences in the change in systolic blood pressure and P=0.70 for between-group differences in the change in diastolic blood pressure). Although many subjects were receiving antihypertensive therapy at base line (Table 1), none had a change in this therapy during the study.

ADVERSE REACTIONS

One subject on the low-carbohydrate diet was hospitalized with chest pain, which was ultimately determined to be unrelated to myocardial ischemia. One subject on the low-carbohydrate diet died from complications of hyperosmolar coma, which was thought to be due to poor compliance with drug therapy for diabetes. There was no clinically significant change in the uric acid level in either group (Table 4).

DISCUSSION

We found that severely obese subjects with a high prevalence of diabetes and the metabolic syndrome lost more weight in a six-month period on a carbohydrate-restricted diet than on a fat- and calorie-restricted diet. The greater weight loss in the low-carbohydrate group suggests a greater reduction in overall caloric intake, rather than a direct effect of macronutrient composition. However, the explanation for this difference is not clear. Subjects in this group may have experienced greater satiety on a diet with liberal proportions of protein and fat. However, other potential explanations include the simplicity of the diet and improved compliance related to the novelty of the diet.

Subjects in the low-carbohydrate group had greater decreases in triglyceride levels than did subjects in the low-fat group; nondiabetic subjects on the low-carbohydrate diet had greater increases in insulin sensitivity, and subjects with diabetes on this diet had a greater improvement in glycemic

control. No adverse effects on other serum lipid levels were observed. Most studies suggest that lowering triglyceride levels has an overall cardiovascular benefit.[14-16] Insulin resistance promotes such atherosclerotic processes as inflammation,[17] decreased size of low-density lipoprotein particles,[18] and endothelial dysfunction.[19] Impaired glycemic control in subjects with other features of the metabolic syndrome markedly increases the risk of coronary artery disease.[20] As expected, we found that the amount of weight lost had a significant effect on the degree of improvement in these metabolic factors. However, even after adjustment for the differences in weight loss between the groups, assignment to the low-carbohydrate diet predicted greater improvements in triglyceride levels and insulin sensitivity. Subjects who lost more than 5 percent of their base-line weight on a carbohydrate-restricted diet had greater decreases in triglyceride levels than those who lost a similar amount of weight while following a calorie- and fat-restricted diet.

There was a consistent trend across weight-loss strata toward a greater increase in insulin sensitivity in the low-carbohydrate group, although these changes were small and were not significant within each stratum. Although greater weight loss could not entirely account for the greater decrease in triglyceride levels and increase in insulin sensitivity in the low-carbohydrate group, we cannot definitively conclude that carbohydrate restriction alone accounted for this independent effect. Other uncontrolled variables, such as the types of carbohydrates selected (e.g., the proportion of complex carbohydrates or the ratio of carbohydrate to fiber), or other unknown variables may have contributed to this effect. In addition, more precise measurements of insulin sensitivity than we used would be needed to confirm this effect of a carbohydrate-restricted diet.

Table 2. Comparison of Base-Line Characteristics between Subjects Who Completed the Study and Those Who Dropped Out of the Study.*

Characteristic	Completed Study		Dropped Out of Study	
	Low-Carbohydrate Diet (N=43)	Low-Fat Diet (N=36)	Low-Carbohydrate Diet (N=21)	Low-Fat Diet (N=32)
Body-mass index	44±7	43±7	40±5	43±9
Age (yr)	54±9	54±10	49±9	53±9
Female sex (%)	19	19	24	9
Black race (%)	54	62	70	65
Diabetes (%)	40	33	43	44
Metabolic syndrome (%)	72	81	81	66
Antihypertensive therapy (%)	67	56	57	63
Lipid-lowering therapy (%)	44	47	38	25
Sleep apnea (%)	30	28	19	13
Current cigarette smoking (%)	16	19	29	25

* Plus–minus values are means ±SD. There were no significant differences between groups.

Table 3. Change from Base Line in the Composition of the Two Diets at Six Months.*

Variable	Base Line	P Value†	6 Months	Absolute Change	P Value†
Total calories per day		0.25			0.33
Low-fat diet	1848±1338		1576±760	−271±1260	
Low-carbohydrate diet	2090±1055		1630±894	−460±902	
Protein (% of total calories)		0.46			<0.001
Low-fat diet	16±6		16±6	1±5	
Low-carbohydrate diet	17±7		22±9	6±10	
Carbohydrate (% of total calories)		0.41			<0.001
Low-fat diet	51±14		51±15	−1±15	
Low-carbohydrate diet	49±17		37±18	−13±21	
Fat (% of total calories)		0.66			0.004
Low-fat diet	33±12		33±14	0±14	
Low-carbohydrate diet	33±14		41±16	8±18	

* Dietary macronutrient data are given as the mean (±SD) percentage of total calories on the basis of dietary recall by all 132 subjects, with base-line values carried forward for subjects who had dropped out of the study by six months. Because of rounding, percentages may not total 100.
† P values are for between-group comparisons and were calculated with use of the unpaired t-test.

Table 4. Changes from Base Line in Serum Lipid, Glucose, Glycosylated Hemoglobin, and Uric Acid Levels at Six Months.*

Variable	Base Line	P Value†	6 Months	Absolute Change	P Value†
Triglycerides (mg/dl)		0.65			0.001
Low-fat diet	176±120		169±110	−7±54	
Low-carbohydrate diet	188±176		150±171	−38±80	
Total cholesterol (mg/dl)		0.14			0.53
Low-fat diet	192±30		192±40	−1±29	
Low-carbohydrate diet	181±52		184±48	2±34	
High-density lipoprotein cholesterol (mg/dl)		0.73			0.55
Low-fat diet	41±10		40±11	−1±7	
Low-carbohydrate diet	41±11		41±10	0±5	
Low-density lipoprotein cholesterol (mg/dl)‡		0.52			0.77
Low-fat diet	118±29		121±27	3±18	
Low-carbohydrate diet	114±36		118±40	5±23	
Insulin sensitivity§		0.86			0.01
Low-fat diet	0.32±0.03		0.31±0.03	−0.01±0.03	
Low-carbohydrate diet	0.31±0.03		0.33±0.03	0.02±0.03	
Glucose level in all subjects (mg/dl)		0.61			0.017
Low-fat diet	124±47		122±46	−2±21	
Low-carbohydrate diet	128±53		117±48	−11±24	
Glucose level in nondiabetic subjects (mg/dl)		0.65			0.60
Low-fat diet	103±14		104±15	1±10	
Low-carbohydrate diet	102±14		100±11	−2±11	
Glucose level in diabetic subjects (mg/dl)		0.57			0.01
Low-fat diet	158±61		153±62	−5±31	
Low-carbohydrate diet	168±63		142±68	−26±31	
Insulin level without diabetes medication (μU/ml)		0.28			0.008
Low-fat diet	18±10		19±11	1±10	
Low-carbohydrate diet	22±20		16±14	−6±16	
Insulin level with diabetes medication (μU/ml)		0.66			0.25
Low-fat diet	36±26		36±25	0±20	
Low-carbohydrate diet	40±42		32±27	−8±30	
Glycosylated hemoglobin value in diabetic subjects (%)		0.42			0.06
Low-fat diet	7.4±1.5		7.4±1.8	0.0±1.0	
Low-carbohydrate diet	7.8±1.2		7.2±1.7	−0.6±1.2	
Uric acid (mg/dl)		0.5			0.10
Low-fat diet	6.6±1.4		6.5±1.2	−0.2	
Low-carbohydrate diet	6.3±1.4		6.4±1.4	0.1	

* Plus–minus values are means ±SD. The analysis includes all 132 subjects, with base-line values carried forward for subjects who had dropped out of the study by six months. To convert values for cholesterol to millimoles per liter, multiply by 0.02586. To convert values for triglycerides to millimoles per liter, multiply by 0.01129. To convert values for glucose to millimoles per liter, multiply by 0.05551.

† P values are for between-group comparisons and were calculated with use of the unpaired t-test.

‡ The low-density lipoprotein cholesterol level was not calculated in one subject on the low-carbohydrate diet who had a triglyceride level of more than 400 mg per deciliter (4.5 mmol per liter).

§ Insulin sensitivity was calculated only in subjects without diabetes with use of the quantitative insulin-sensitivity check index as follows: 1÷[(log fasting insulin level)+(log fasting glucose level)].

Many of our subjects were taking lipid-lowering medications and hypoglycemic agents. Although enrolling these subjects introduced confounding variables, it allowed the inclusion of subjects with the obesity-related medical disorders typically encountered in clinical practice. Analyses from which these subjects were excluded still revealed greater improvements in insulin sensitivity and triglyceride levels on a carbohydrate-restricted diet than on a fat- and calorie-restricted diet.

Our study included a high proportion of black subjects, a group previously underrepresented in lifestyle-modification studies. As compared with the white subjects, the black subjects had a smaller overall weight loss. Future studies should explore whether greater weight loss in this population can be achieved by more effective incorporation of culturally sensitive dietary counseling.

The high dropout rate in our study occurred very early and affected our findings. The very early dropout of these subjects may indicate that attrition most closely reflected base-line motivation to lose weight, rather than a response to the dietary intervention itself.

Taken together, our findings demonstrate that severely obese subjects with a high prevalence of diabetes and the metabolic syndrome lost more weight during six months on a carbohydrate-restricted diet than on a calorie- and fat-restricted diet. The carbohydrate-restricted diet led to greater improvements in insulin sensitivity that were independent of weight loss and a greater reduction in triglyceride levels in subjects who lost more than 5 percent of their base-line weight. These findings must be interpreted with caution, however, since the magnitude of the overall weight loss relative to our subjects' severe obesity was small, and it is unclear whether these benefits of a carbohydrate-restricted diet extend beyond six months. Furthermore, the high dropout rate and the small overall weight loss demonstrate that dietary adherence was relatively low in both diet groups. This study proves a principle and does not provide clinical guidance; given the known benefits of fat restriction, future studies evaluating long-term cardiovascular outcomes are needed before a carbohydrate-restricted diet can be endorsed.

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