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Comparison of a Low-Fat Diet to a Low-Carbohydrate Diet on Weight Loss, Body Composition, and Risk Factors for Diabetes and Cardiovascular Disease in Free-Living, Overweight Men and Women

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Overweight and obese men and women (24–61 yr of age) were recruited into a randomized trial to compare the effects of a low-fat (LF) *vs.* a low-carbohydrate (LC) diet on weight loss. Thirty-one subjects completed all 10 wk of the diet intervention (retention, 78%). Subjects on the LF diet consumed an average of 17.8% of energy from fat, compared with their habitual intake of 36.4%, and had a resulting energy restriction of 2540 kJ/d. Subjects on the LC diet consumed an average of 15.4% carbohydrate, compared with habitual intakes of about 50% carbohydrate, and had a resulting energy restriction of 3195 kJ/d. Both groups of subjects had significant weight loss over the 10 wk of diet intervention and nearly identical improvements in body weight and fat mass. LF subjects lost an average of 6.8 kg and had a decrease in body mass index of 2.2 kg/m^2, compared with a loss of 7.0 kg and decrease in body mass index of 2.1 kg/m^2 in the LC subjects. The LF group better preserved lean body mass when compared with the LC group; however, only the LC group had a significant decrease in circulating insulin concentrations. Group results indicated that the diets were equally effective in reducing systolic blood pressure by about 10 mm Hg and diastolic pressure by 5 mm Hg and decreasing plasminogen activator inhibitor-1 bioactivity. Blood β-hydroxybutyrate concentrations were increased in the LC only, at the 2- and 4-wk time points. These data suggest that energy restriction achieved by a very LC diet is equally effective as a LF diet strategy for weight loss and decreasing body fat in overweight and obese adults. (*J Clin Endocrinol Metab* 89: 2717–2723, 2004)

OBESITY IS THE most common metabolic condition in industrialized nations and is reaching epidemic proportions in North American men, women, and children (1). According to Statistics Canada (2) 48% of Canadians between the ages of 20 and 64 yr are overweight [body mass index (BMI) $>$ 25]. Results from the National Health and Nutrition Examination Survey suggest the prevalence of overweight and obesity in the United States is as high as 64%. As disturbing as these numbers are in adults, an even more alarming finding is that a growing number of children are developing severe obesity early in life. In one study, 37% of children aged 2–11 yr were considered overweight in 1999 with half of these being considered obese (BMI $\geq$ 30, according to the Statistics Canada National Longitudinal Survey of Children and Youth: Childhood Obesity, October 2002). Factors contributing to these changes include social and physiological factors resulting in a relative increase in energy intake compared with energy expenditure. Obesity, particularly visceral fat accumulation, is associated with dyslipidemia, impaired glucose tolerance, and insulin resistance, which, in turn, are risk factors for the development of the metabolic syndrome, type II diabetes mellitus, and cardiovascular disease. Several estimates put the economic cost of obesity and overweight at well over 100 billion U.S. dollars per year (1, 3). Effective lifestyle strategies are required to both prevent and treat overweight in the world's population.

In addition to absolute energy use, there are a number of studies, in both the pediatric and adult populations, that suggest that diet composition plays an important role in both weight loss and maintenance of weight changes (4–7). Although prevailing opinion, including "Canada's Food Guide to Healthy Eating" and the U.S. Department of Agriculture's "Food Guide Pyramid," promote a diet with 30% or less energy from fat, 15–20% energy from protein, and 50–55% energy from complex carbohydrates, for the general population. However, the appropriateness of this strategy for prevention of obesity has not been clearly documented. Despite a decrease from approximately 40% of energy from fat in the U.S. diet in 1965, to 34% in 1991, the incidence of obesity actually increased (8). We have previously shown that in adult overweight women, a low-carbohydrate (LC) hypocaloric diet can promote efficient weight loss and improvements in body composition and lipid profile while maintaining glucose tolerance (9). The present investigation was initiated to extend our earlier observations by directly comparing a conventional energy-restricted, low-fat (LF) diet to an equivalent energy-restricted LC diet in an overweight group of men and women.

Subjects and Methods

Subjects

Forty overweight, healthy adult volunteers (10 males and 30 females) were recruited from the Guelph community via poster and newspaper

Abbreviations: BIA, Bioelectrical impedance analysis; BMI, body mass index; HDL, high-density lipoprotein; LC, low-carbohydrate; LDL, low-density lipoprotein; LF, low-fat; PAI-1, plasminogen activator inhibitor-1.

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advertisements between December 2000 and April 2001. Approval for this study was granted by the Human Subjects Committee of the University of Guelph, and all subjects gave their informed, written consent to participate. Criteria for admission included a BMI of more than 25 with the potential for weight loss of 9 kg or more without becoming underweight (BMI < 20), sufficient energy intake as based on habitual diet (>4000 kJ/d), and strong personal motivation. Two subjects had BMIs close to the cutoff; however, both of these subjects had high body fat (>30%) as measured by bioelectrical impedance analysis (BIA) and thus were considered suitable weight loss subjects. Subjects were ineligible if they were on medications known to affect blood glucose, blood lipids, or blood pressure. Individuals with obesity secondary to clinically diagnosed endocrine disease were also excluded. To maintain objectivity, data concerning biochemical parameters were not unblinded to identify subjects until after all samples had been analyzed. As such, diagnosis of diabetes type II, hypertriglyceridemia, or hypercholesterolemia were not made at study entry but rather at study completion (see *Results* and *Discussion*). Subjects identified at study completion in one of these three categories were referred to their physicians for follow-up. Participants recorded at least 7 d of diet records before commencing the study diets. Before initiation of the study, subjects were randomly assigned, on entry, to consume an energy restricted, LF diet (control) or energy-restricted, LC diet for 10 wk. Baseline characteristics of the two experimental groups are shown in Table 1. The groups were comparable in terms of sex distribution, age, weight, height, and BMI.

Experimental diets

All study subjects were provided with journals, recipe ideas, information on how to keep accurate food records, and detailed food composition lists to assist with compliance. Subjects met weekly with one of the study coordinators for weight measurements and diet consultation. The goal of the LC diet was to restrict carbohydrates to 50–70 g/d. This was achieved by gradually restricting carbohydrate intake from 100 g on d 0 to 50–70 g by d 5. The restriction in carbohydrates resulted in concomitant energy restriction such that females achieved daily intakes of 5020–6690 and males 5860–9200 kJ/d. Subjects on the control diet (LF) were energy-restricted to achieve the same average energy restriction as the LC group. Subjects maintained detailed food diaries and exercise logs through the entire 10-wk period. Participants were instructed not to change their activity/exercise programs for the duration of the study. Food records were collected periodically, without prior announcement, throughout the 10-wk period to monitor compliance and ensure that energy intakes were similar between the two diet groups. Food records were analyzed using FoodWorks 3 (The Nutrition Company, Long Valley, NJ). When necessary, the intakes of LF subjects were adjusted through nutritional counseling to achieve matching energy intakes for the two experimental groups. Recommendations for food choices for the LC group were essentially as we have previously described (9). Briefly, this included limiting intake of breads, pastas, rice, and desserts, eliminating intake of deep-fried foods, dried fruit, candy, sweetened soft drinks, and sugar and increased consumption of vegetables, lean meats, eggs, and nuts. Subjects on the LF regimen were instructed to eliminate high-fat dairy products and substitute with no-fat or LF alternatives, to increase intake of fruits, vegetables, whole-grain breads, and pastas and to eliminate fried foods, cream sauces, and high-fat/sugar cakes, pastries, chocolate, and candy. They were also asked to reduce use of oil products in cooking. As with LC subjects, LF subjects were encouraged to consume lean meats as alternatives to high-fat meat products. Weekly counseling sessions were held to instruct subjects in both groups on appropriate dietary choices to meet the energy and fat or carbohydrate restriction.

Weight, blood pressure, and body composition analysis

Weight was measured weekly, in similar clothing without shoes, to the nearest quarter kilogram using an electronic scale and tape measure to estimate the subjects' weight (kilograms) and height (centimeters), respectively. Weights were communicated to the subjects but not analyzed statistically until wk 6. Blood pressure was measured while the subject was sitting in a chair after a 5-min rest period, using a digital, self-inflating cuff. Measurements were taken in duplicate and averaged. For the purposes of this study, borderline hypertension was defined as a systolic blood pressure between 130 and 139 mm Hg, and diastolic blood pressure between 85 and 89 mm Hg. Hypertension was defined as systolic blood pressure more than 140 mm Hg and/or diastolic pressure 90 mm Hg or more (10). Body composition was estimated at baseline, wk 6, and wk 10 by BIA (Bodystat 1500; Bodystat, Inc., Tampa, FL) as we have previously described (9). To decrease dehydration, which could complicate the BIA measures, subjects were instructed to refrain from consumption of alcohol and caffeine and to avoid exhaustive exercise 24 h before the measurements were to take place. Subjects were encouraged to take in as much water as possible in the 2 d leading up to the measurements, and all subjects attempted to void immediately before the BIA.

Blood collection and analyses

After an overnight fast of at least 12 h, venous blood was collected into vacutainers containing EDTA [for triglyceride, β-hydroxybutyrate, and insulin assays], trisodium citrate [for plasminogen activator inhibitor-1 (PAI-1) assay], and no anticoagulant [for total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and glucose assays]. Plasma and serum were separated by centrifugation at 1500 × *g* for 15 min, and aliquots were stored in plastic tubes at 4 C or −20 C until analysis.

Lipids

Total cholesterol levels were estimated using the Infinity Cholesterol Reagent (Sigma procedure no. 401; Sigma, St. Louis, MO) using calibrators (Cholesterol Calibrator no. C 0284; Sigma) to create a standard curve from 0.6–10.4 mM. Baseline samples from two subjects who had dropped out of the study served as internal controls for assays performed at different times or in different plates. Two microliters of thawed serum samples, calibrators, controls, and blanks were each pipetted in triplicate on a 96-well plate. All samples from the same subject were on the same plate. Two hundred microliters of reagent were added

TABLE 1. Baseline and wk-10 characteristics of study population

	LF		LC	
	Baseline	wk 10	Baseline	wk 10
Average age (yr)	43.2		41.2	
Age range	27–61		24–56	
Female subjects	12		10	
Male subjects	4		5	
BMI (kg/m^2)	32.2 ± 0.9^a	30.0 ± 0.9^b	32.2 ± 1.5^a	30.1 ± 1.6^b
BMI range	27.5–41	25.2–38.1	25.6–47.2	23.6–46.1
Total body weight (kg)	92.3 ± 3.0^a	85.5 ± 3.0^b	91.0 ± 4.5^a	84.0 ± 4.4^b
Fat weight (kg)	34.8 ± 2.1^a	29.4 ± 2.2^b	33.3 ± 3.1^a	29.2 ± 3.2^b
Fat weight (%)	37.8 ± 1.8^a	34.1 ± 1.9^b	36.1 ± 2.1^a	33.6 ± 2.1^b
Lean weight (kg)	57.4 ± 2.7^a	56.4 ± 2.6^{a,b}	57.5 ± 3.0^a	55.6 ± 2.9^b
Lean weight (%)	62.2 ± 1.9^a	66.1 ± 2.0^b	63.7 ± 2.1^a	66.9 ± 2.2^b

Values are means ± SEM. *Values in a row not sharing a letter* are statistically different, $P < 0.05$.

to each well, and the plates were incubated for 5 min at 37 C, mixed, and read at 540 nm on a microplate reader (Molecular Devices). HDL cholesterol was separated from the other cholesterol fractions using HDL precipitating reagent (Sigma procedure no. 352-7) and HDL cholesterol calibrators (no. H 8020; Sigma) with a standard curve from 0.1–2 mM using a 540-nm filter. LDL cholesterol was calculated using the equation LDL cholesterol = (total cholesterol − HDL cholesterol) − (triglycerides/5), provided that triglyceride levels were below 4.5 mM. triglycerides were analyzed using the Infinity Triglycerides Reagent (Sigma procedure no. 343) using calibration standards (glycerol standard no. G 1394; Sigma) and a standard curve from 0.5–5.7 mM. All samples were analyzed in triplicate at 540 nm using the same protocol as described above for cholesterol measures.

Glucose

Glucose was analyzed using the Glucose (Trinder) Reagent (Sigma procedure no. 315) using calibrators (glucose standard no. 16-300; Sigma Diagnostics) and standard curve from 2–27 mM. Diluted serum samples (1:4 with distilled water) were examined in triplicate on a 96-well plate using controls and blanks as described for lipid measures and were read at 490 nm on a microplate reader.

Insulin and PAI-1

Plasma insulin was measured at baseline and 10 wk into the intervention diets. Insulin values for each subject were determined in duplicate and averaged for each time point using the Coat-A-Count Insulin Kit (TKIN5, Diagnostic Products Corp., Los Angeles, CA) and Cobra II Auto-Gamma Counter (Packard, Albertville, MI). A calibration curve was prepared using insulin standards and control samples provided with the kit. The intraassay coefficient of variation was 4–8%, and interassay coefficient of variation was 6–9%. Cross-reactivity with proinsulin was 9%. Values are presented as μIU/mL plasma.

PAI-1 functional enzyme activity was measured by bioimmunoassay according to the manufacturer's instructions (Chromolize PAI-1; Biopool International, Inc., Ventura, CA). Blood samples taken at baseline and 10 wk intervention were examined in duplicate and values reported in IU/mL where one unit (U) of PAI-1 activity is defined as the amount of PAI-1 that inhibits 1 IU of the International Standard for tissue plasminogen activator. A standard curve was prepared from 0–50 IU/mL using commercial standards.

β-Hydroxybutyrate

Methodology for assay of the ketone, D(-)3-hydroxybutyrate, was based on the original method of Williamson *et al.* (11) with modifications as we have previously described (9). Briefly, blood plasma from heparinized tubes was thawed on ice, diluted, and precipitated with perchloric acid and precipitate removed by centrifugation. One hundred microliters of supernatant were diluted with 1 ml reagent buffer (200 mM glycine, 150 mM hydrazine sulfate, pH 9.8, 500 mM of the oxidized form of nicotinamide adenine dinucleotide) and 10 μl of 1:4 enzyme (β-hydroxybutyrate dehydrogenase; Sigma Chemicals, Mississauga, Ontario, Canada). After incubation at 37 C for 1 h, samples were read on a fluorometer (excitation wavelength, 340 nm; emission, 455 nm). Samples were analyzed in duplicate and ketone concentrations were estimated by comparing with a standard curve from 10–540 μM.

Results

There were initially 20 subjects enrolled in each experimental group; LF, 16 females, 4 males; LC, 15 females, 5 males. There were no differences in the age, sex, weight, or BMI distribution between the two groups at randomization. Over the course of the study, four subjects dropped out of the LF group and five dropped out of the LC group (all female). Reasons for leaving the study included scheduling conflicts with blood collection, vacation plans, or noncompliance as evidenced at weekly counseling sessions and/or review of diet records. No subjects reported significant side effects in either treatment group. The details of the baseline and wk-10 characteristics of the subjects completing all 10 wk of the study are shown in Table 1.

BMI decreased by approximately 2 kg/m^2 with both control (LF) and test (LC) diet interventions (Table 1). Total body weight decreased by 6.8 kg in the LF group and by 7.0 kg in the LC group over the 10-wk period. There was no difference in the pattern of weight loss over time between the two groups. Significant losses in fat weight were observed in both groups (LF, −5.4 kg; LC, −4.1 kg), but a significant decrease in lean mass (−1.9 kg) was observed only in subjects on the LC diet. Despite a greater loss of lean mass in the LC subjects compared with the LF subjects, both groups had similar improvements in body composition in terms of percentage of body fat and percentage of lean mass when controlling for total body weight changes (Table 1).

Macro- and micronutrient compositions of the habitual and intervention diets as recorded in daily diaries from each of the subjects are shown in Table 2. The average intake over at least a 7-d consecutive period was used for each subject at two time points during the 10-wk study, in addition to habitual intake before study entry. Because these interventions were both initiated to promote weight loss in overweight subjects, each intervention diet had reduced energy compared with the habitual diets. The average energy restriction over the 10-wk protocol was 2540 kJ for the LF group and 3195 kJ for the LC group. Each of these resulted in a statistically significant difference from the habitual intake and there was no difference between the diets in terms of level of energy restriction. Although total protein intake (grams) did not change for subjects on the LC diet, because total energy decreased there was a net increase in the proportion of energy coming from protein in this group. Changes in protein intake were not significant for the LF group, and the LF group did not differ from the LC group at either baseline or after the 10-wk intervention period. Total fat intake did not change for subjects on the LC group but for LF subjects decreased by approximately 50 g/d producing a decrease in the percentage of energy from a habitual diet of 36.4% to an average of 17.8%. LF subjects consumed lower levels of all three classes of fatty acids and cholesterol compared with their habitual diets. The LC group consumed similar levels of fatty acids to their habitual diets but also consumed 250 mg of additional cholesterol not seen in their habitual diets (Table 2). The largest dietary change for the LC group was a substantial decrease in carbohydrate intake by 228 g/d. This decrease included both complex carbohydrates as well as simple sugars. In contrast, there was a significant increase in carbohydrate consumption by the LF group (+13 g/d). The decrease in carbohydrate-rich foods was associated with a 50% decrease in fiber intake on the LC diet.

The intake of several micronutrients was altered by the interventions. Common changes in intake between the LF and LC protocols included a decrease in daily calcium (LF, −147 mg/d; LC, −139 mg/d), decrease in daily sodium (LF, −728 mg/d; LC, −1095 mg/d), and decrease in daily riboflavin (LF, −0.4 mg/d; LC, −0.9 mg/d) intake. Changes unique to the LF diet were a decrease in vitamin E (−2.2 mg/d) and an increase in vitamin C (+38 mg/d). Habitual folate intakes were higher in the LC group than the

TABLE 2. Diet composition of baseline habitual diets and LF and LC intervention diets

	LF baseline	LF intervention	LC baseline	LC intervention
Energy (kJ)	8617 ± 414^{a}	6077 ± 255^{b}	9616 ± 600^{a}	6421 ± 353^{b}
Protein (g)	82.4 ± 4.0^{a,b}	70.9 ± 4.1^{a}	88.6 ± 25.1^{a,b}	100.6 ± 10.5^{b}
Protein (% energy)	16.0 ± 0.8^{a}	19.5 ± 1.1^{a,b}	15.4 ± 1.3^{a}	26.2 ± 1.4^{b}
Fat total (g)	80.9 ± 4.9^{a}	28.8 ± 2.6^{b}	90.8 ± 7.9^{a}	94.6 ± 3.9^{a}
Fat (% energy)	36.4 ± 2.2^{a}	17.8 ± 1.6^{b}	35.6 ± 2.7^{a}	55.5 ± 3.9^{c}
SFAs (g)	29.2 ± 1.8^{a}	9.0 ± 1.1^{b}	30.3 ± 3.1^{a}	33.9 ± 1.5^{a}
MUFAs (g)	28.6 ± 2.3^{a}	9.5 ± 0.9^{b}	32.6 ± 3.3^{a}	37.3 ± 2.0^{a}
PUFAs (g)	13.4 ± 1.1^{a}	5.9 ± 0.4^{b}	16.8 ± 1.6^{a}	13.7 ± 1.2^{a}
Cholesterol (mg)	293 ± 18^{a}	162 ± 22^{b}	308 ± 34^{a}	556 ± 42^{c}
Carbohydrate (g)	251 ± 13^{a,b}	225 ± 9^{a}	287 ± 26^{b}	59 ± 3^{c}
Carbohydrate (% energy)	49.0 ± 2.7^{a}	61.9 ± 2.5^{b}	50.0 ± 0.8^{a}	15.4 ± 0.2^{c}
Sugars	23.8 ± 4.6^{a}	20.5 ± 3.2^{a}	22.6 ± 7.1^{a}	1.4 ± 0.6^{b}
Fiber (g)	17.8 ± 1.2^{a}	20.3 ± 1.5^{a}	19.8 ± 1.5^{a}	8.9 ± 0.8^{b}
Alcohol (g)	1.3 ± 0.4^{a}	3.0 ± 0.9^{a}	5.7 ± 2.7^{b}	7.2 ± 2.6^{b}
Calcium (mg)	864 ± 64^{a}	717 ± 47^{b}	873 ± 79^{a}	734 ± 61^{b}
Potassium (mg)	2906 ± 138^{a}	2933 ± 164^{a}	3318 ± 221^{a}	2268 ± 184^{b}
Sodium (mg)	3213 ± 166^{a}	2485 ± 119^{b}	3731 ± 339^{a}	2636 ± 143^{b}
Iron (mg)	15.4 ± 1.5^{a}	15.0 ± 1.4^{a}	16.7 ± 1.6^{a}	9.7 ± 0.8^{b}
Magnesium (mg)	283 ± 16^{a,b}	298 ± 17^{a}	305 ± 18^{a}	228 ± 20^{b}
Zinc (mg)	10.9 ± 0.7^{a}	9.0 ± 0.6^{a}	11.8 ± 1.0^{a}	11.6 ± 0.8^{a}
Vitamin A (RE)	1191 ± 140^{a,b}	1074 ± 120^{b}	1886 ± 346^{a}	1251 ± 150^{a,b}
Vitamin C (mg)	127 ± 15^{a}	165 ± 17^{b}	167 ± 18^{b}	85 ± 13^{a}
Vitamin D (IU)	101 ± 13^{a}	108 ± 14^{a}	93 ± 24^{a}	29 ± 6^{b}
Vitamin E (mg)	6.4 ± 0.6^{a}	4.2 ± 0.5^{b}	7.5 ± 0.8^{a}	8.3 ± 1.6^{a}
Vitamin K (μg)	42 ± 6.3^{a,b}	51 ± 9^{a,b}	36 ± 8^{a}	77 ± 14^{b}
Thiamin (mg)	1.7 ± 0.1^{a,b}	1.5 ± 0.1^{a,b}	1.9 ± 0.2^{a}	1.0 ± 0.1^{b}
Riboflavin (mg)	2.1 ± 0.1^{a}	1.7 ± 0.1^{b}	2.4 ± 0.3^{a}	1.5 ± 0.1^{b}
Niacin (mg)	23 ± 2^{a}	24 ± 2^{a}	28 ± 4^{a}	22 ± 3^{a}
Folate (μg)	318 ± 21^{a,b}	337 ± 21^{a}	451 ± 64^{c}	244 ± 19^{b}
Vitamin B_6 (mg)	1.7 ± 0.1^{b}	1.9 ± 0.2^{a,b}	2.4 ± 0.3^{a}	1.4 ± 0.1^{b}
Vitamin B_{12} (μg)	4.8 ± 0.9^{a}	3.4 ± 0.4^{a}	9.5 ± 3.1^{a}	5.8 ± 0.6^{a}

Values are means ± SEM. *Values in a row not sharing a letter* are statistically different, $P < 0.05$. SFA, Saturated fatty acids; MUFAs, monosaturated fatty acids; PUFAs, polyunsaturated fatty acids; RE, retinol equivalents.

LF group, which resulted in a significant decrease in folate intake for the LC group on the intervention diet (Table 2.) Alcohol intakes, although still relatively low, were statistically higher in the LC subjects both at baseline and with the intervention; however, the diets themselves were not associated with a change in alcohol consumption (Table 2). Other dietary intake changes unique to the LC diet included: lower potassium (−1050 mg/d), lower iron (−7 mg/d), lower magnesium (−77 mg/d), lower vitamin C (−82 mg/d), lower vitamin D (−64 mg/d), lower thiamin (−0.9 mg/d), lower vitamin B_6 (−1.0 mg/d), and an approximate doubling of vitamin K intake (+41 μg/d).

Twelve of 31 subjects completing all 10 wk of the study had some form of abnormal blood pressure at baseline. The group results indicated that both diets were equally effective in reducing systolic blood pressure by about 10 mm Hg and diastolic blood pressure by 5 mm Hg.

PAI-1 bioactivity, as a risk factor for cardiovascular disease (12–14), was similar in both groups of subjects at baseline and significant improvements were observed for both groups after 10 wk of diet intervention. The magnitude of the decrease in PAI-1 appeared larger for the LF group, but this was not statistically different from the change observed in the LC group. Total cholesterol values at baseline indicated that six subjects in each diet category had hypercholesterolemia (>6.2 mM) and six more had borderline hypercholesterolemia (5.2–6.2 mM). After 10 wk, significant improvements in total cholesterol values were only observed in the LF group. Group results indicated that total and LDL cholesterol levels were unchanged from baseline in LC subjects, whereas total cholesterol decreased by 1.6 mM and LDL cholesterol by 1.3 mM in LF subjects. LF subjects also showed a significant decrease (−0.3 mM) in HDL cholesterol and LC subjects a significant increase (+0.14) in HDL cholesterol. Group results indicated that both LC and LF groups saw a decrease of 0.4 mM in total triglyceride values over the intervention period.

Nine subjects (seven in the LC group and two in the LF group), by definition, had impaired fasting glucose (>6.1 mM) at baseline and at least one other time point in the study. In fact, five of these individuals would be diagnosed as type II diabetic (>7.0 mM) using fasting plasma glucose as the lone indicator. Thus, 30% of subjects had some form of impaired glucose tolerance before starting the study diets, and none of these subjects was aware of their abnormal metabolism at study entry. Although individual results suggested some improvements in glucose control, group results indicated that there was no significant decrease in fasting serum glucose for either LF or LC interventions. However, fasting insulin levels were significantly lower after 10 wk of the LC diet, but not the LF diet. This resulted in a significant decrease in the insulin to glucose ratio for the LC group after diet intervention (Table 3). There was no change in fasting glucose or insulin to glucose ratio for the LF subjects.

Blood concentration of β-hydroxybutyrate was measured at baseline and at 2-wk intervals in all subjects (Fig. 1). There was no change in β-hydroxybutyrate concentration over time in the LF group. There was an increase is circulating β-

TABLE 3. Blood pressure and blood biochemistry at baseline and after 10 wk intervention with LC or LF hypocaloric diets in men and women

	LF baseline	LF intervention	LC baseline	LC intervention
Systolic blood pressure (mm Hg)	121.3 ± 1.5^a	110.1 ± 2.2^b	124.8 ± 2.6^a	114.6 ± 1.8^b
Diastolic blood pressure (mm Hg)	77.9 ± 3.1^a	72.9 ± 2.5^b	77.7 ± 3.8^a	71.6 ± 3.2^b
PAI-1 activity (IU/ml)	27.7 ± 10^a	8.2 ± 3.9^b	30.1 ± 8.5^a	16.2 ± 7.9^b
Total cholesterol, mg/dl (mM)	228 ± 14^a	166 ± 10^b	230 ± 12^a	232 ± 11^a
	(5.90 ± 0.35)	(4.30 ± 0.25)	(5.94 ± 0.31)	(6.00 ± 0.28)
LDL cholesterol, mg/dl (mM)	165 ± 13^a	113 ± 9^b	169 ± 11^a	170 ± 10^a
	(4.26 ± 0.33)	(2.93 ± 0.23)	(4.38 ± 0.28)	(4.40 ± 0.26)
HDL cholesterol, mg/dl (mM)	52 ± 3^a	44 ± 3^b	49 ± 2^a	55 ± 3^c
	(1.34 ± 0.08)	(1.14 ± 0.07)	(1.27 ± 0.06)	(1.41 ± 0.08)
Triacylglycerol, mg/dl (mM)	134 ± 24^a	100 ± 10^b	136 ± 22^a	96 ± 17^b
	(1.51 ± 0.27)	(1.13 ± 0.11)	(1.54 ± 0.25)	(1.08 ± 0.19)
LDL:HDL ratio	3.2^{a,b}	2.6^c	3.4^a	3.1^b
TAG:HDL ratio	1.1^a	1.0^b	1.2^a	0.7^c
Insulin (μIU/ml)	20.9 ± 1.3^{a,b}	20.2 ± 1.5^{a,b}	23.7 ± 2.7^a	16.9 ± 1.9^b
Serum glucose, mg/dl (mM)	98 ± 8^a	88 ± 3^a	113 ± 12^a	104 ± 10^a
	(5.42 ± 0.47)	(4.90 ± 0.17)	(6.30 ± 0.66)	(5.79 ± 0.58)
Insulin:glucose ratio	3.85^a	4.12^a	3.76^a	2.91^b

Values are means ± SEM. *Values in a row not sharing a letter* are statistically different, $P < 0.05$.

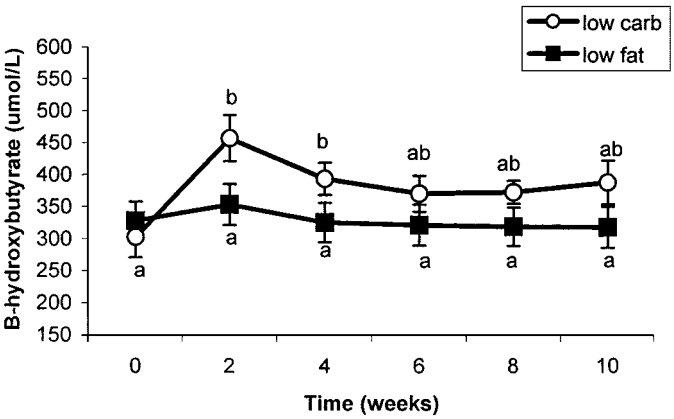

FIG. 1. β-Hydroxybutyrate levels in blood of subjects on experimental diets. Fasting blood samples were collected and analyzed as described in *Subjects and Methods*. Values at each time point are group averages with *error bars* as SEM. *Values not sharing a letter* are statistically different ($P < 0.05$). *Open circles* are subjects on the LC diet, and *solid squares* are subjects on the LF experimental diet.

hydroxybutyrate at the 2- and 4-wk time points in the LC group that remained numerically higher for the remainder of the study but not statistically different from the high at 2–4 wk or baseline. There were no statistical differences between the LC and LF subjects after wk 4.

Discussion

The outcomes in our study population suggest that either a LF or a LC energy-restricted diet is an effective means for short-term weight loss in overweight adults. Dietary compliance was assessed by interview and diet records and for the LC correlated well with early rises in blood β-hydroxybutyrate. Energy restriction alone predicted a weight loss of 5.5. and 6.9 kg, respectively, in the LF and LC groups, which was close to the observed values of 6.8 and 7 kg for the same groups. Slight differences, particularly for LF subjects might be explained by underreporting of habitual diets, as the subjects became better able to estimate their intakes and keep better food records as the trial proceeded. BMI was improved in both groups of subjects, and this was largely attributed to a decrease in fat mass. Although both groups also experienced losses in lean mass, this was only significant in the LC group, suggesting that a LF diet regimen with sufficient protein may better preserve lean mass. A recent study by Brehm *et al.* (15) using dual-energy x-ray absorptiometry to measure body composition showed a similar effect of carbohydrate restriction, *vs.* a LF diet on lean mass at 3 months intervention.

Although weight loss, macronutrient distribution, and improvements in body composition were similar between our study and that of Brehm *et al.*, there were major differences in outcomes suggested to determine risk for cardiovascular disease, the metabolic syndrome, and diabetes type II. In general, we saw additional improvements in blood pressure and triglycerides not observed in this other study, whereas they observed improvements in cholesterol concentrations in both groups of subjects and we observed this only in the LF group (15). The decrease in triglycerides we observed in this mixed gender population is very similar to what we previously reported in younger women on a LC diet (9). In our previous study, we also saw a decrease in total and LDL cholesterol in subjects on the LC diet. However, the current study was of longer duration, and although there appeared to be improvements at the 6-wk time point, these differences had evaporated by the 10-wk mark. This suggests that changes in LDL cholesterol may be transient. Our LF diet was less than 18% fat energy, which is considerably lower than the LF diets reported by others where increases in triglycerides were sometimes reported (16). The very LF level may also be responsible for the decrease in HDL cholesterol seen in our study and similar to the results of other LF diet intervention studies. Despite a slight decrease in HDL cholesterol in this group, the ratios of total cholesterol and LDL cholesterol to HDL cholesterol were all improved in both diet groups as was the ratio of triglyceride to HDL cholesterol, all indicators of cardiovascular disease risk reduction. Our conclusion is that factors other than macronutrient composition must dominate in determining circulating triglyceride levels because the LC and LF differed so extremely in macronu-

trient content and yet resulted in identical triglyceride changes.

In addition to being energy deficient relative to habitual diets, both the LF and LC diet restrictions resulted in major changes in micronutrient intake. In the short term, decreases in sodium intake may contribute to the improvements in blood pressure observed in both diet groups. If either of these diet patterns were to be pursued in the longer term, issues of calcium and vitamin E nutriture could become important in the LF regimen and calcium, magnesium, iron, vitamin D, folate, and B_6 intakes relevant to those consuming a very LC diet. Dietary inadequacy can be tolerated in the short term to achieve weight loss goals, but maintenance diets must include the right balance of micronutrients to promote optimal health. Thus, the long-term impacts of these diet strategies on biochemical parameters and markers of disease risk need to be evaluated.

With respect to glucose control, there were no significant changes in the LF group; however, on an individual basis, there were a number of subjects whose fasting glucose values improved over the study period. Mean insulin values were in the normal range for both diet groups at baseline and after 10 wk of intervention. Only the LC group showed a significant decrease in circulating insulin that translated into a significant decrease in insulin to glucose ratio, a possible indicator of insulin sensitivity. In our previous study of subjects on a LC diet, we did not observe a decrease in fasting insulin levels or in oral glucose tolerance (9). However, it should be noted that subjects in the current study had significantly higher insulin levels at baseline than did our subjects in the previous study. In fact, in the previous study, the starting and finishing insulin values and plasma glucose values were both lower than the finishing values in the current study (9). It is perhaps not surprising that the more severe the insulin resistance (high insulin and high glucose), the more likely the subjects are to benefit from weight loss.

Interestingly, PAI-1 levels decreased in both diet groups, which we would predict reduces cardiovascular disease risk. In other studies, PAI-1 levels have been correlated with insulin levels and glucose disposal (17, 18); however, there was no correlation between these variables in the current study. The only blood marker that correlated with PAI-1 in the current study (regardless of diet group) was circulating triglyceride levels consistent with what other researchers have found (14, 19).

Because the biochemical analyses were done blind, subjects were notified only at the end of the study about biochemical values that recommended clinical follow-up. The fact that 30% of our study subjects had abnormal glucose values and many more had abnormal lipid profiles at baseline, without being aware of their situation, is alarming. Furthermore, *post hoc* examination of the baseline characteristics of the study subjects, including blood chemistry, showed that five subjects had at least three criteria for diagnosis of metabolic syndrome (National Institutes of Health, 2001; www.nih.gov) and seven more had at least two criteria fulfilled. Because we did not have data on waist circumference, it is likely that our estimates for metabolic syndrome and those at high risk, are underestimates of the real frequency in this population. Thus, despite our subjects' belief that they were overweight/obese but otherwise healthy, this was an inaccurate description for many of the subjects. Better screening of adults to prevent diabetes type II, cardiovascular disease, and the metabolic syndrome and to promote early dietary and physical activity interventions is clearly needed.

In conclusion, hypoenergetic diets of widely differing macronutrient concentration are feasible strategies for promoting short-term weight loss and improvements in chronic disease risk markers in overweight and obese men and women. A LF regimen may be preferred when reduction of blood cholesterol is a primary goal, whereas the LC regimen may be more appropriate when improvement in insulin sensitivity is the target. Either strategy promotes loss of fat weight and improvements of similar magnitude in blood pressure, and triglycerides, both of which can be seen as additional benefits to chronic disease risk reduction in addition to weight loss itself.

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