Body Composition and Hormonal Responses to a Carbohydrate-Restricted Diet

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The few studies that have examined body composition after a carbohydrate-restricted diet have reported enhanced fat loss and preservation of lean body mass in obese individuals. The role of hormones in mediating this response is unclear. We examined the effects of a 6-week carbohydrate-restricted diet on total and regional body composition and the relationships with fasting hormone concentrations. Twelve healthy normal-weight men switched from their habitual diet (48% carbohydrate) to a carbohydrate-restricted diet (8% carbohydrate) for 6 weeks and 8 men served as controls, consuming their normal diet. Subjects were encouraged to consume adequate dietary energy to maintain body mass during the intervention. Total and regional body composition and fasting blood samples were assessed at weeks 0, 3, and 6 of the experimental period. Fat mass was significantly ($P \leq .05$) decreased (-3.4 kg) and lean body mass significantly increased (+1.1 kg) at week 6. There was a significant decrease in serum insulin (-34%), and an increase in total thyroxine (T_4) (+11%) and the free T_4 index (+13%). Approximately 70% of the variability in fat loss on the carbohydrate-restricted diet was accounted for by the decrease in serum insulin concentrations. There were no significant changes in glucagon, total or free testosterone, sex hormone–binding globulin (SHBG), insulin-like growth factor-I (IGF-I), cortisol, or triiodothyronine (T_3) uptake, nor were there significant changes in body composition or hormones in the control group. Thus, we conclude that a carbohydrate-restricted diet resulted in a significant reduction in fat mass and a concomitant increase in lean body mass in normal-weight men, which may be partially mediated by the reduction in circulating insulin concentrations.

THE POPULARITY of diets with the common theme of restricting intake of carbohydrate while increasing protein and fat has increased in recent years. Surprisingly few scientific studies have examined the physiologic effects of carbohydrate-restricted diets. Extreme restriction of carbohydrate results in a metabolic state of ketosis and these diets are commonly refered to as "ketogenic diets." The most common application of ketogenic diets is for weight loss. Several studies have documented that very low carbohydrate diets result in greater weight loss compared to isoenergetic diets higher in carbohydrate,[1-6] yet few studies have examined the effects on body compostion.

To our knowledge, only 4 studies have assessed body composition responses to a carbohydrate-restricted diet.[1,7-9] These studies involved hypoenergetic diets in a small number of obese subjects. Nevertheless, they indicate that a carbohydrate-restricted diet low in energy results in body composition changes that favor loss of fat mass and preservation (perhaps even increases) in lean body mass. The mechanism(s) explaining the greater fat loss and preservation of lean body mass on carbohydrate-restricted diets remain unclear. The regulation of lipolysis/lipogenesis and protein synthesis/degradation is heavily influenced by the endocrine system. For example, insulin is a potent inhibitor of lipolysis at physiological contrations,[10] whereas cortisol, thyroid hormones, and glucagon stimulate lipolysis. Protein balance is influenced by stimulatory (eg, testosterone, insulin-line growth factor-I) and inhibitory (eg, cortisol, glucagon) hormones. In turn, carbohydrate-restricted diets have been shown to decrease circulating concentrations of insulin[11-15] and triiodothyronine (T_3),[13,15-18] and increase glucagon,[13,14] catecholamines,[11,12] growth hormone,[14,15] and cortisol.[12] However, the relationship among changes in hormones and changes in body composition on a carbohydrate-restricted diet have not been investigated.

The primary purpose of this study was to examine total and regional body composition changes on a very low carbohydrate diet and to relate these changes to circulating concentrations of hormones. We chose to study normal-weight men because of the potential confounding affects of metabolic and hormonal aberrations prevalent in overweight individuals (eg, insulin resistance). We hypothesized that the carbohydrate-restricted diet would result in decreased fat mass and increased lean body mass and that these responses would be partially explained by decreased concentrations of insulin.

MATERIALS AND METHODS

Experimental Design

The study design involved a group of normal-weight men that switched from their habitual diet (48% carbohydrate) to a very low carbohydrate diet (8% carbohydrate) for 6 weeks. Body composition was assessed and 2 consecutive 12-hour fasting blood samples were collected at weeks 0, 3, and 6 of the diet intervention. A separate control group of normal-weight men was recruited to establish reliability of the dependent variables. Control subjects continued to follow their habitual diet and performed the same experimental tests as the intervention subjects.

Subjects

Twenty healthy men free of metabolic and endocrine disorders volunteered to participate. Twelve subjects volunteered to switch from their habitual diet to a carbohydrate-restricted diet for 6 weeks (mean ± SD; age, 36.7 ± 11.6 years; body mass, 79.2 ± 8.3 kg; percent fat, 20.5 ± 6.2%) and the remaining 8 subjects served as controls (age, 35.0 ± 13.0 years; body mass, 85.4 ± 12.8 kg; percent fat, 22.2 ± 9.0%). The subjects had not lost or gained weight in the previous year, were not

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adhering to special diets or regular consumers of nutritional supplements, and habitually consumed between 19% and 43% of energy as fat (assessed via a 7-day food diary). All subjects were nonsmokers, and not currently taking any medication known to affect the hormones measured in this study. Subjects were moderately active performing a variety of different aerobic and weight-training routines, but none were competitive athletes. In the carbohydrate-restricted diet group, 1 subject was sedentary, 5 performed regular aerobic exercise (2 to 4 times/wk for 20 to 60 minutes), and 6 performed a combination of aerobic exercise (3 to 5 times/wk for 15 to 90 minutes) and resistance exercise (2 to 6 times/wk for 45 to 120 minutes). Subjects were required to maintain their current level of physical activity during the study. All subjects were informed of the purpose and possible risks of this investigation prior to signing an informed consent document approved by the institutional review board.

Dietary Intervention

The aim of the intervention diet was to reduce carbohydrate intake to 5% to 10% of energy. The diet was designed so that fat comprised approximately 60% of energy with no restrictions on the type of fat from saturated and unsaturated sources or cholesterol levels. The actual diets consumed were mainly comprised of beef (eg, hamburger, steak), poultry (eg, chicken, turkey), fish, oils, cheese, eggs, various nuts/seeds and peanut butter, vegetables, salads with low-carbohydrate dressing, protein powder, and water or low-carbohydrate diet drinks. Foods avoided or consumed infrequently included fruits and fruit juices, most dairy products (with the exception of hard cheeses and heavy cream), breads, cereals, beans, rice, desserts/sweets, or any other foods containing significant amounts of carbohydrate. A portion of the foods consumed during the intervention diet (≈30% to 40% of total energy) were provided to subjects during weekly meetings to review compliance with the registered dietitian. These foods included pumpkin seeds, roasted cheese, low-carbohydrate bars, shakes, and bake mix (Atkins Nutritionals, Inc, Hauppauge, NY) and protein powders (Super Whey Fuel and Fuel Plex Lite, Twin Laboratories, Hauppauge, NY). Subjects were also provided with a daily multivitamin/mineral complex (Daily One Caps With Iron, Twin Laboratories).

Each subject received individual dietary instruction weekly on how to consume meals within the specified nutrient goals and to assess compliance. Subjects were provided with a packet outlining specific lists of appropriate foods, recipes, and sample meal plans that were compatible with their individual preferences and the nutrient profile goals of the intervention diet. Food measuring utensils and scales were provided to all subjects prior to the study to assist in the estimation of portion sizes of foods and beverages. Subjects kept records each day of the experiment (7 days during baseline and 42 days during the very low carbohydrate diet) and the control group kept 7-day records during weeks 1 and 6. All recorded days were analyzed for nutrient content (Nutritionist V, Version 2.3, N-Squared Computing, First Databank Division, The Hearst Corporation, San Bruno, CA). Subjects were also provided with log sheets to record any physical activity performed during the experimental period.

Body Composition

Total and regional body composition was assessed using dual-energy x-ray absorptiometry (DXA) with a total-body scanner (Prodigy, Lunar Corp, Madison, WI) that uses a constant potential x-ray source of 76 kVp and a cerium filter that produces dual-energy peaks of 38 and 62 keV. Soft tissue mass, which is comprised of fat mass and lean body mass, is measured pixel-by-pixel as a beam of photons penetrate the subjects' body. Subjects remained motionless in the supine position for approximately 6 minutes while the scanning arm of the DXA passed over their body from head to toe in parallel 1-cm strips. Percent body fat from the DXA testing was subsequently calculated as fat tissue mass divided by the total soft tissue mass plus the estimated bone mineral content. Regional analyses of the trunk, arm, and leg regions were automatically calculated according to anatomical landmarks by the computer software. All analyses were performed by the same technician using computer algorithms (software version 2.17.008). Quality assurance was assessed by analyzing a phantom spine provided by the company and daily calibrations were performed prior to all scans using a calibration block provided by the manufacturer. Intraclass correlation coefficients ($r \geq 0.98$) were obtained for bone mineral content, lean body mass, and fat mass from repeated scans on a group of men and women in our laboratory.

Blood Collection and Analyses

Fasting blood samples were obtained on 2 separate days at weeks 0, 3, and 6 after a 12-hour overnight fast and abstinence from alcohol and strenuous exercise for 24 hours. Subjects reported to the laboratory between 7 AM and 9 AM, rested quietly for 10 minutes in the supine position, and blood was obtained from an antecubital vein with a 20-gauge needle and Vacutainers (Becton Dickinson, Franklin Lakes, NJ). Within 15 minutes, whole blood was centrifuged (1,200 × *g* for 15 minutes at 10°C) and the resultant serum or plasma divided into aliquots. A comprehensive metabolic screening profile was performed that assessed serum glucose, albumin, total protein, minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, iron), renal function (blood urea nitrogen [BUN], uric acid, creatinine, bilirubin), and liver function (alkaline phosphatase [AP], alanine aminotransferase, asparate aminotransferase, gamma glutamyl transferase [GGT], lactate dehydrogenase). Fasting serum β-hydroxybutyrate concentrations were enzymatically determined in duplicate using a commercially available kit (Sigma Diagnostics, St Louis, MO) and spectrophotometric analysis (Spectronic 601, Milton Roy Co, Rochester, NY). Intra-assay variance was 0.9%. Serum insulin concentrations were determined in duplicate using an enzyme-linked immunosorbent assay (ELISA; Diagnostic Systems Laboratory, Webster, TX) with a sensitivity of 1.8057 pmol · L^{-1} and an intra-assay variance of 5.5%. Thyroid function tests included determination of triiodothyronine (T_3) uptake using a solid phase ^{125}I radioimmunoassay (RIA) and total thyroxine (T_4) concentrations using an ELISA kit with a sensitivity of 2.322 nmol · L^{-1}. Intra-assay variance was 2.62%. The free T_4 index was calculated as total T_4 multiplied by the percent T_3 uptake. Cortisol concentrations were determined in duplicate serum samples using an enzyme immunosorbent assay (EIA; Diagnostic Systems Laboratory) with a sensitivity of 2.76 nmol · L^{-1} and an intra-assay variance of 4.9%. Testosterone concentrations were determined in duplicate serum samples using an EIA kit with a sensitivity of 0.14 nmol · L^{-1} and an intra-assay variance of 2.5%. Insulin-like growth factor-I (IGF-I) concentrations were determined in duplicate serum samples using an ELISA with a sensitivity of 0.004 nmol · L^{-1} and an intra-assay variance of 5.5%. Sex hormone binding globulin (SHBG) concentrations were determined in duplicate serum samples using a competetive ^{125}I RIA with a sensitivity of 5.0 nmol · L^{-1} and an intra-assay variance of 14.2%. Glucagon concentrations were determined in duplicate plasma samples using a double antibody ^{125}I RIA with a sensitivity of 3.7 pmol · L^{-1}. Absorbances for all ELISA and EIA samples were read on a multilabel counter (Wallac1420 Victor, Wallac Oy, Turku, Finland).

Statistical Analyses

Two fasting samples were obtained for each blood variable and the mean of these 2 values used for statistical analysis. An analysis of variance (ANOVA) with repeated measures was used to evaluate changes in body composition and hormones over time. When a significant *F* value was achieved, the Fisher's least significant difference (LSD) test was used to locate the pairwise differences between means. Relationships among the percent changes in hormones and body com-

Table 1. Daily Intake of Dietary Energy and Nutrients

	Low-Carbohydrate Group (n = 12)		Control Group (n = 8)	
	Habitual Diet (week 0)	Low-Carbohydrate (week 6)	Habitual Diet (week 0)	Habitual Diet (week 6)
Energy (MJ)	10.63 ± 2.47	9.77 ± 1.57	9.16 ± 2.27	8.16 ± 1.46
Protein (g)	113 ± 40	176 ± 45*	88 ± 19	80 ± 23
Protein (%)	17 ± 4	30 ± 5*	16 ± 1	16 ± 2
Carbohydrate (g)	306 ± 100	46 ± 10*	330 ± 119	283 ± 49
Carbohydrate (%)	48 ± 10	8 ± 3*	58 ± 8	58 ± 7
Fat (g)	91 ± 31	157 ± 27*	62 ± 17	56 ± 18
Fat (%)	32 ± 8	61 ± 4*	26 ± 8	26 ± 7
SFA (g)	31 ± 12	56 ± 11*	19 ± 7	16 ± 5
SFA (%)	14 ± 4	25 ± 2*	12 ± 5	11 ± 4
MUFA (g)	27 ± 11	57 ± 12*	14 ± 5†	15 ± 10
MUFA (%)	12 ± 4	25 ± 3*	8 ± 2	9 ± 4
PUFA (g)	12 ± 6	24 ± 5*	9 ± 2	9 ± 7
PUFA (%)	6 ± 2	11 ± 2*	6 ± 1	5 ± 3
Cholesterol (mg)	332 ± 126	741 ± 254*	132 ± 12	155 ± 85
Alcohol (%)	3 ± 3	1 ± 2	0 ± 0	0 ± 1

NOTE. Values are mean ± SD.
Abbreviations: SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.
*$P \leq .05$ *v.* corresponding week 0 value.

position were examined using Pearson's product-moment correlation coefficients. The level of significance was set at $P \leq .05$.

RESULTS

Dietary Intake

Daily intakes of dietary energy and nutrients are presented in Table 1. All dietary nutrients were significantly different during the carbohydrate-restricted diet with the exception of dietary energy and alcohol consumption. Dietary protein, fat, and cholesterol were significantly greater and dietary carbohydrate was significantly lower (8% of total energy) during the carbohydrate-restricted diet. There were no significant changes in dietary nutrient intake in the control group. Data from exercise logs indicated that there were no changes in physical activity patterns of subjects.

Total and Regional Body Composition

Compared to body mass at week 0 (79.2 ± 8.3 kg), there was a small but significant decrease in body mass at weeks 3 (77.5 ± 7.7 kg) and 6 (77.0 ± 7.5 kg). There was no change in body mass in the control group (85.4 ± 12.8 to 85.8 ± 12.0 kg). Total and regional body composition responses are presented in Table 2 and Fig 1. Although the decrease in body mass was small (-2.2 kg), there was a significant decrease in total body percent fat at week 3 that significantly decreased further at week 6. Fat mass was significantly decreased at week 3 (-1.7 kg) and continued to decrease at week 6 (-3.3 kg). Soft tissue lean body mass significantly increased at week 6 (+1.1 kg). This same pattern of change in body composition (decreased fat mass and increased lean body mass) was observed for the arm, leg, and trunk regions as well. There were no significant changes in bone mineral content. There were no significant changes in total and regional body composition in the control group.

Metabolic Responses

Serum β-hydroxybutyrate concentrations were significantly increased at week 3 (+427%) and remained significantly elevated at week 6 (+279%) in the carbohydrate-restricted group. All subjects demonstrated β-hydroxybutyrate concentrations above 0.20 mmol · L^{-1} indicating compliance with the carbohydrate-restricted diet. All changes in the metabolic screening profile were small to moderate and within normal expected values for both the carbohydrate-restricted and control groups. There were significant decreases in serum AP (-10.3), carbon dioxide (-10%) and GGT (-18%), and significant increases in BUN (+43%), the BUN/creatinine ratio (+45%), and chloride (+3%) after the carbohydrate-restricted diet.

Hormonal Responses

There were no significant changes in any hormones in the control group (Table 3). After the carbohydrate-restricted diet, there was a significant decrease in serum insulin concentrations at week 3 (-19.4%) and week 6 (-34.2%). After 6 weeks of the carbohydrate-restricted diet there was also a significant increase in total T_4 (+10.8%) and the free T_4 index (+12.5%). There were no significant changes in glucagons, testosterone, SHGB, cortisol, IGF-I, or T_3 uptake. The only hormone significantly correlated with change in body composition was insulin. Using the week 6 data, the percent change in insulin was significantly related to the change in total and regional fat mass (r = -0.738 to -0.819) and percent fat (r = -0.709 to -0.836) (Fig 2).

DISCUSSION

The primary objective of this study was to examine how healthy normal-weight men respond to a carbohydrate-restricted diet and to examine the relationships with potential changes in the circulating hormonal mileue. Subjects consumed

Table 2. Total and Regional Percent Fat, LBM, FM, and BMC Responses to a 6-Week Carbohydrate-Restricted Diet

	Low-Carbohydrate Group (n = 12)				Control Group (n = 8)		
	Week 0	Week 3	Week 6	Percent Δ	Week 0	Week 6	Percent Δ
Total							
%Fat	20.5 ± 6.2	18.8 ± 5.5*	16.9 ± 5.0*†	−17.6%	22.1 ± 9.0	22.0 ± 9.8	−0.5%
LBM (kg)	60.4 ± 5.6	60.2 ± 5.0	61.5 ± 5.2*†	+1.8%	62.9 ± 5.5	63.3 ± 5.4	+0.6%
FM (kg)	16.7 ± 5.9	15.0 ± 5.4*	13.4 ± 4.8*†	−24.6%	19.9 ± 9.9	19.9 ± 10.4	0.0%
BMC (kg)	3.4 ± 0.4	3.3 ± 0.4	3.3 ± 0.4	−2.9%	3.5 ± 0.3	3.5 ± 0.3	0.0%
Arms							
%Fat	13.5 ± 6.0	12.0 ± 5.3*	9.8 ± 5.1*†	−27.4%	15.8 ± 8.5	15.4 ± 9.5	−2.5%
LBM (kg)	8.2 ± 0.8	8.2 ± 0.9	8.2 ± 0.8	0.0%	8.2 ± 1.0	8.1 ± 0.8	−1.2%
FM (kg)	1.4 ± 0.7	1.2 ± 0.6*	1.0 ± 0.5*†	−28.6%	1.7 ± 1.0	1.7 ± 1.2	0.0%
BMC (kg)	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.0%	0.5 ± 0.1	0.5 ± 0.0	0.0%
Legs							
%Fat	20.1 ± 5.5	18.7 ± 5.3*	17.1 ± 4.7*†	−14.9%	20.7 ± 8.5	20.5 ± 8.6	−1.0%
LBM (kg)	19.9 ± 2.3	19.7 ± 2.2	20.5 ± 2.3*†	+3.0%	21.7 ± 2.3	21.8 ± 2.1	+0.5%
FM (kg)	5.4 ± 1.8	4.9 ± 1.8*	4.5 ± 1.5*†	−16.7%	6.3 ± 3.1	6.2 ± 2.9	−1.6%
BMC (kg)	1.3 ± 0.2	1.3 ± 0.2	1.3 ± 0.2*†	0.0%	1.4 ± 0.1	1.4 ± 0.1	0.0%
Trunk							
%Fat	23.9 ± 7.5	21.8 ± 6.7*	19.6 ± 6.1*†	−18.0%	26.1 ± 10.4	25.9 ± 11.8	−0.8%
LBM (kg)	28.1 ± 3.0	28.0 ± 2.4	28.6 ± 2.5*†	+1.8%	28.9 ± 2.3	29.3 ± 2.8	+1.4%
FM (kg)	9.4 ± 3.6	8.3 ± 3.1*	7.4 ± 2.9*†	−21.3%	11.3 ± 5.8	11.4 ± 6.3	+0.9%
BMC (kg)	1.1 ± 0.1	1.1 ± 0.1	1.0 ± 0.2*†	−9.1%	1.1 ± 0.1	1.1 ± 0.1	0.0%

NOTE. Values are mean ± SD.
Abbreviations: LBM, soft tissue lean body mass; FM, fat mass; BMC, bone mineral content.
*$P \leq .05$ *v.* corresponding week 0 value.
†$P \leq .05$ *v.* corresponding week 3 value.

a diet that consisted of 8% carbohydrate (<50 g/d), 61% fat, and 30% protein. Adaptation to this carbohydrate-restricted diet resulted in a significant decrease in percent body fat and increase in lean body mass. Serum insulin was significantly decreased and serum total T_4 increased. The decrease in serum insulin resulting from the reduction in carbohydrate was associated with the decrease in serum insulin. The contribution of other circulating metabolites (eg, ketone bodies) and hormones (eg, thyroid hormones) in mediating the changes in fat mass and lean body mass on a carbohydrate-restricted diet remain unclear.

Similar to our prior work,[19] a significant decrease in body

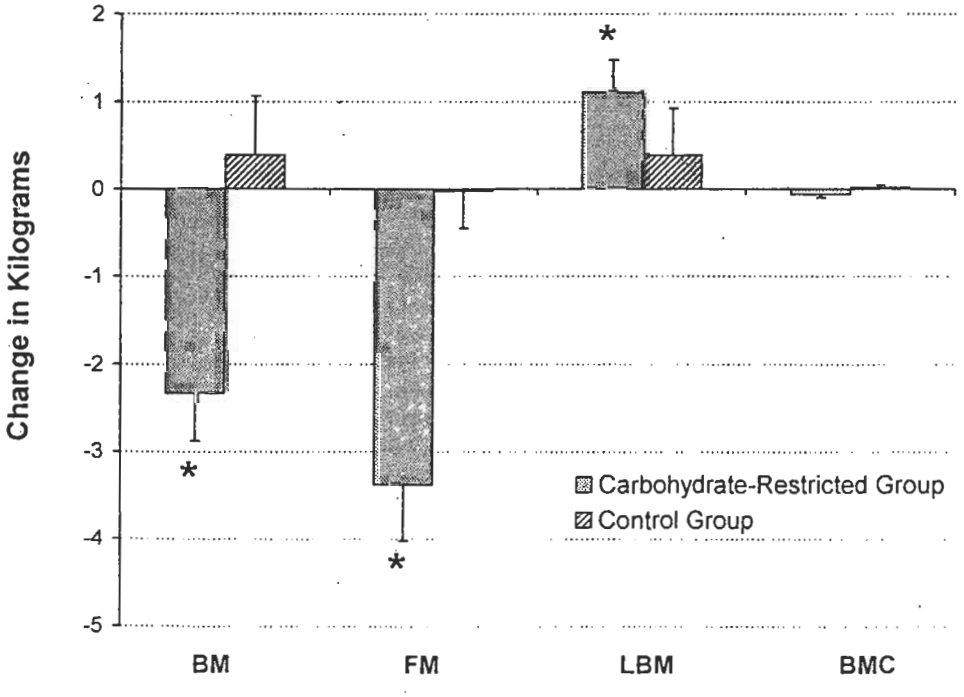

Fig 1. Changes in body composition after a 6-week carbohydrate-restricted diet. BM, body mass; FM, fat mass; LBM, lean body mass; BMC, bone mineral content. *$P \leq .05$ from week 0 to week 6.

Table 3. Hormonal Responses to a 6-Week Carbohydrate-Restricted Diet

	Low-Carbohydrate Group (n = 12)			Control Group (n = 8)	
	Week 0	Week 3	Week 6	Week 0	Week 6
Insulin (pmol · L^{-1})	23.7 ± 16.3	19.1 ± 12.2*	15.6 ± 8.9*	21.5 ± 6.7	24.3 ± 9.9
Glucagon (pmol · L^{-1})	25.9 ± 10.4	25.8 ± 4.9	30.3 ± 8.7	16.2 ± 3.6	17.0 ± 4.1
Total testosterone (nmol · L^{-1})	20.7 ± 8.1	19.8 ± 7.8	20.3 ± 10.1	22.7 ± 7.1	22.5 ± 6.9
Cortisol (nmol · L^{-1})	618 ± 326	513 ± 105	515 ± 247	332 ± 83	382 ± 98
SHBG (nmol · L^{-1})	42.8 ± 32.0	34.8 ± 22.2	38.3 ± 28.7	23.0 ± 7.9	21.6 ± 5.0
IGF-I (nmol · L^{-1})	30.0 ± 8.7	30.6 ± 14.0	30.4 ± 8.5	32.5 ± 17.4	35.0 ± 17.2
T_3 uptake (%)	32.6 ± 2.5	32.9 ± 2.9	32.4 ± 2.5	31.7 ± 1.2	31.6 ± 1.2
Total T_4 (nmol · L^{-1})	59.2 ± 11.5	64.5 ± 10.1	66.4 ± 12.2*	57.0 ± 8.1	56.5 ± 5.8
Free T_4 index	19.2 ± 3.4	21.1 ± 3.5*	21.6 ± 4.6*	18.2 ± 2.2	17.8 ± 1.4

NOTE. Values are mean ± SD.

Abbreviations: SHBG, sex hormone–binding globulin; IGF, insulin-like growth factor; Free T_4 index, total T_4 × T_3 uptake.

*$P \leq .05$ *v* corresponding week 0 value.

weight occurred during the carbohydrate-restricted diet (-2.2 kg) despite encouragement to consume more food to maintain weight, which has also been reported in previous free-living low-carbohydrate diet interventions:[20,21] The small but nonsignificant reduction in voluntary dietary energy intake may have been due to fewer food choices, the higher satiety value of fat and protein,[22] or the anorectic effect of ketosis.[23] The cumulative effect of the small reduction in dietary energy of 0.86 MJ/d (205 kcal/d) over 6 weeks would be predicted to result in a 1.1-kg weight loss, about half of the observed 2.2-kg decrease in body mass. Notable was the composition of weight loss. The entire loss in body weight was from fat and there was a significant increase in soft tissue lean body mass. These changes occurred despite no alteration in each subject's exercise pattern.

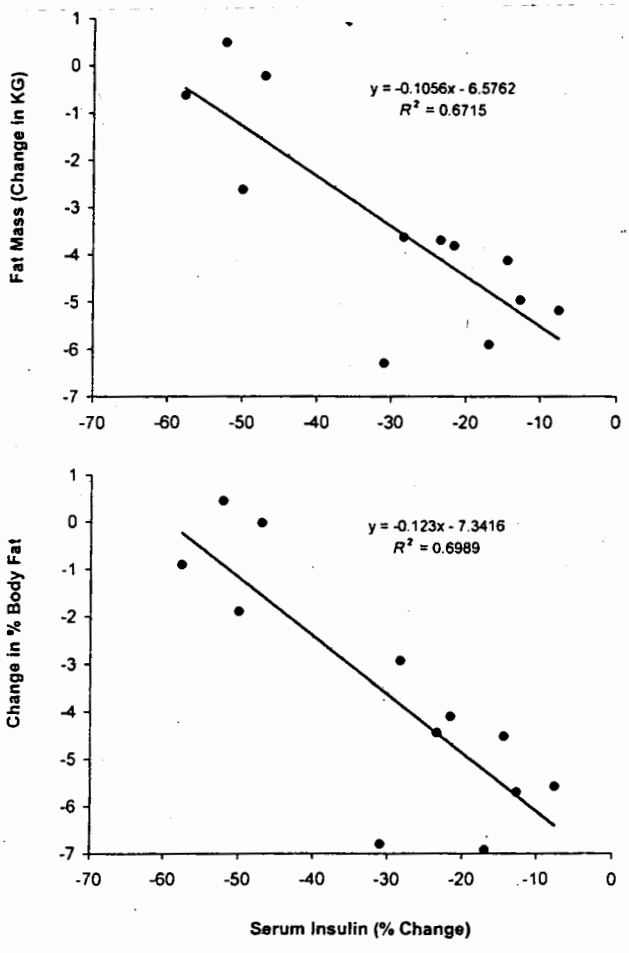

Fig 2. Correlation between the percent change in insulin concentrations and the change in total body fat mass (top) and percent fat (bottom) in response to a 6-week carbohydrate-restricted diet.

A greater loss of fat and preservation of lean body mass has also been shown with very low-carbohydrate diets. Benoit et al[7] compared the effects of fasting and a hypoenergetic (1,000 kcal/d) very low carbohydrate diet (4% carbohydrate, 82% fat) on weight loss and body composition assessed via total body potassium counting (K^{40}) in obese men. Weight loss was 9.6 kg after 10 days of fasting and 6.6 kg after 10 days of the very low carbohydrate diet. Lean body mass was decreased 6.2 kg after fasting; however, the very low carbohydrate diet only resulted in a 0.2-kg decrease in lean body mass. Young et al[1] compared the effects of 3 isoenergetic (1,800 kcal/d), isoprotein (115 g/d) diets containing varying carbohydrate contents (30, 60, and 104 g/d) on weight loss and body composition assessed via underwater weighing in obese men. After 9 weeks on the 30-g, 60-g, and 104-g carbohydrate diets, weight loss was 16.2, 12.8, and 11.9 kg and fat accounted for 95%, 84%, and 75% of the weight lost, respectively. These results should be interpreted cautiously given the low number of subjects (3 per group) and lack of control for physical activity. More recently, Willi et al[8] examined the effects of a hypoenergetic (645 to 725 kcal/d) very low carbohydrate (25 g/d) diet on weight loss and body composition assessed via DXA in obese adolescents aged 12 to 15 years. After 8 weeks, body mass significantly decreased (-15.4 kg) and lean body mass increased (+1.4 kg), although this was not significant. In line with our body composition results, these studies indicate that a very low carbohydrate diet results in body composition changes that favor loss of fat mass and greater preservation of lean body mass.

The significant decrease in fat mass indicates that adipose tissue mobilization was upregulated on the carbohydrate-restricted diet, which is also supported by the elevated β-hydroxybutyrate concentrations. Inhibition of lipolysis occurs at

relatively low concentrations of insulin with a half-maximal effect occurring at a concentration of 12 pmol · L^{-1} and a maximal effect at a concentration of about 200 to 300 pmol · L^{-1}.[10] The significant reduction in insulin from 23.7 to 15.6 pmol · L^{-1} may have been permissive to mobilization of body fat on the carbohydrate-restricted diet. Although a cause and effect relationship cannot be established, it is interesting to note that there was a significant correlation between the decrease in insulin concentrations and the decrease in body fat on the carbohydrate-restricted diet (Fig 2). We ackowledge the limitations associated with measuring circulating concentrations of hormones, which do not necessarily reflect changes in hormone biosynthesis/secretion or receptor uptake and signal induction. Thus, other hormones that affect lipid metabolism that were either not measured (eg, growth hormone, epinephrine) or not correlated to the change in fat mass (eg, cortisol, glucagon) may have also contributed to the proportionally large decrease in fat mass.

The significant increase in lean body mass on the carbohydrate-restricted diet was not expected. Infusions of β-hydroxybutyrate (the major ketone in the circulation) have been shown to reduce proteolysis during starvation.[24] Young et al[1] compared 3 isocaloric (1,800 kcal/d), isoprotein (115 g) diets differing in carbohydrate content (30, 60, and 104 g) consumed for 9 weeks in obese men. The diet with the lowest amount of carbohydrate (30 g/d) was associated with increased ketones, greater fat loss, and greater nitrogen retention and preservation of lean tissue compared to the diets with more carbohydrate. The overall effect of elevated ketones on nitrogen retention must be considered in the context of other stimulatory (eg, growth hormone, testosterone, insulin) and inhibitory (eg, cortisol, catecholamines) hormones that regulate protein balance. We hypothesize that elevated β-hydroxybutyrate concentrations may have played a minor role in preventing catabolism of lean tissue on the carbohydrate-restricted diet but other anabolic hormones were likely involved (eg, growth hormone).

Similar to our prior study,[25] we observed a significant decrease in fasting insulin responses after the carbohydrate-restricted diet. Decreases in resting insulin concentrations have been reported in response to 3 to 4 days of a low-carbohydrate diet high in fat.[11-15] The mechanism for such a response probably resides in the greater reliance on fat oxidation induced by dietary carbohydrate restriction[9] and subsequent reduced requirement for insulin to assist in glucose uptake. The significant increase in total T_4 and the free T_4 index was unexpected. Other studies have reported decreases in T_3 and no change in T_4 in response to reducing carbohydrate.[13,15,17,18] However, carbohydrate-restricted very low calorie diet caused less of a decline in T_3 than a carbohydrate-rich very-low calorie diet.[26] In the present study, the nonsignificant change in T_3 uptake suggests that T_3 and T_4 binding proteins were not affected by carbohydrate restriction. Thus, the significant increase in total T_4 may represent an increase in the biologically active hormone available to cells. This interpretation should be made with caution since we did not directly measure concentrations of free T_3 or T_4 nor did we measure metabolic rate in these subjects.

All the subjects adapted well to the restricted-carbohydrate diet and there were no adverse responses in any of the biochemical variables measured. Similar to data from our prior carbohydrate-restricted diet study,[19] there was a significant increase in serum BUN concentrations and the BUN/creatinine ratio, whereas creatinine concentrations remained stable. A disproportionate rise in BUN relative to creatinine is not indicative of renal stress. The increased BUN was probably due to a greater amount of dietary protein available for hepatic catabolism leading to increased urea formation during the carbohydrate-restricted diet. Krehl et al[22] observed progressively higher BUN concentrations in healthy men consuming a low-carbohydrate diet that was gradually increased in protein so that the protein to fat ratio was raised in increments from 30%:70% to 70%:30%.

In summary, a 6-week carbohydrate-restricted diet resulted in a favorable response in body composition (decreased fat mass and increased lean body mass) in normal-weight men. Our results indicate that endocrine adaptations may partially mediate the acclerated fat loss, in particular the decrease in circulating insulin concentrations. Further study of the metabolic and hormonal adaptations associated with carbohydrate-restricted diets is warranted considering the potential for favorable effects on body composition, especially given the widespread frequency of obesity in the United States.[27]

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