EFFECTS OF A LOW-CARBOHYDRATE DIET ON WEIGHT LOSS AND CARDIOVASCULAR RISK FACTORS IN OVERWEIGHT ADOLESCENTS

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Objectives To compare the effects of a low-carbohydrate (LC) diet with those of a low-fat (LF) diet on weight loss and serum lipids in overweight adolescents.

Design A randomized, controlled 12-week trial.

Setting Atherosclerosis prevention referral center.

Methods Random, nonblinded assignment of participants referred for weight management. The study group (LC) (n = 16) was instructed to consume <20 g of carbohydrate per day for 2 weeks, then <40 g/day for 10 weeks, and to eat LC foods according to hunger. The control group (LF) (n = 14) was instructed to consume <30% of energy from fat. Diet composition and weight were monitored and recorded every 2 weeks. Serum lipid profiles were obtained at the start of the study and after 12 weeks.

Results The LC group lost more weight (mean, 9.9 ± 9.3 kg vs 4.1 ± 4.9 kg, $P < .05$) and had improvement in non-HDL cholesterol levels ($P < .05$). There was improvement in LDL cholesterol levels ($P < .05$) in the LF group but not in the LC group. There were no adverse effects on the lipid profiles of participants in either group.

Conclusions The LC diet appears to be an effective method for short-term weight loss in overweight adolescents and does not harm the lipid profile. *(J Pediatr 2003;142:253-8)*

The prevalence of overweight and obesity, defined as body mass index (BMI, kg/m^2) >95th percentile, has more than doubled among children and adolescents in the past three decades.[1,2] Data suggest that BMI distribution from natural probability samples between 1970 and 1994 showed little or no difference at the lower percentiles but increasing differences at higher percentiles.[3-5] Thus the heaviest children and adolescents are becoming markedly heavier. Long-term follow-up of obese pediatric patients into adulthood has shown that those who were most overweight as children were most likely to become obese as adults.[6-9]

Sequelae of obesity in the adolescent population include immediate biochemical abnormalities or disease including dyslipidemia, insulin resistance, impaired glucose tolerance, and type 2 diabetes mellitus.[10,11] Increased body fat mass in adolescents also is associated with major psychosocial difficulties, including isolation, depression, low self-esteem, and development of eating disorders.[12]

Considering the increasing prevalence of childhood and adolescent obesity, evaluations of new approaches to manage this problem are warranted. For example, very-low–carbohydrate (ketogenic), low-carbohydrate (LC) and low-fat (LF) diets have been shown to be effective and well tolerated in promoting short-term weight loss in both children and adults.[13-15] Potential advantages of the LC diet include increased protein sparing, greater

BMI	Body mass index
LC	Low-calorie
LF	Low-fat
PSMF	Protein-sparing modified fast
TC	Total cholesterol
TG	Triglycerides

See editorial, p 225.

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Table I. Baseline measurements stratified by group

Variable	LC (n = 16)	LF (n = 14)
Age (y)	14.4 ± 1.9	15.0 ± 1.8
Height (in)	63.4 ± 2.4	65.3 ± 5.2
(cm)	161.0 ± 6.1	165.9 ± 13.2
Weight (lb)	202.6 ± 32.7	219.0 ± 60.0
(kg)	92.1 ± 14.9	99.5 ± 27.3
BMI (kg/m^2)	35.4 ± 5.0	35.6 ± 5.8
Lipid values		
TC (mg/dL)	196.9 ± 37.5	183.0 ± 40.1
LDL-C (mg/dL)	133.3 ± 43.9	117.5 ± 29.2
HDL-C (mg/dL)	43.8 ± 9.8	42.8 ± 8.9
TG (mg/dL)	119.3 ± 43.8	109.9 ± 37.8
Non–HDL-C (mg/dL)	148.4 ± 38.9	143.1 ± 37.6

P = not significant for all LC versus LF.

lipolysis, and increased palatability. There is evidence that circulating ketones promote nitrogen sparing, thus maintaining lean body mass.[16]

One ketogenic diet that has gained popular appeal is the "Atkins Diet."[17] The recommended diet does not restrict fats or energy. Westman et al[18] successfully evaluated such a diet in adults. Sharman et al[19] demonstrated no harm to the lipid profile in adults on a ketogenic diet. Volek et al[20] demonstrated decrease in adiposity with maintenance of lean body mass on a meal plan that was 8% carbohydrate. To our knowledge, no controlled studies of such a diet with regard to weight loss, effects on serum lipids, or side effects have been reported in the pediatric literature.[21-25]

The purpose of this study was to compare the effects of a LC diet with self-selected energy intake to a LF diet with self-selected energy intake on weight loss in overweight adolescents and to examine the effects of these diets on serum lipids. We hypothesized that an energy-unrestricted, very-LC diet without restriction of fats would result in more weight loss compared with a LF diet over a 12-week period. We further hypothesized that this diet would increase cardiovascular risk as assessed by the serum lipid profile.

METHODS

With the use of an institutional review board–approved protocol, participants were recruited from patients 12 to 18 years of age who were referred to the Center for Atherosclerosis Prevention of Schneider Children's Hospital by their pediatricians for weight management. All participants resided in the New York City suburban area. Patients who had primary obesity with a BMI >95th percentile for age were screened and referred for random assignment. As the 95th percentile for age cutoff is the usually recognized standard for diagnosing overweight and obesity, and studies have shown that above this BMI percentile adolescents have a significantly higher risk for death caused by obesity,[10] these participants were believed to be most able to benefit from the intervention. Patients were excluded from participation if they exhibited any of the following: any chronic disease affecting growth, diabetes mellitus, familial hypercholesterolemia, clinically diagnosed psychological disorders, any chronic medication use, abnormal thyroid, kidney, or liver function tests, or abnormalities in the complete blood count. Enrollment occurred over a period of 1 year. Nine patients were approached but declined to consent. The reasons for refusal were concerns that the LC diet was unhealthy (3 of 9) and concerns that they would be unable to maintain a LC diet (6 of 9).

After informed consent was obtained, 39 patients were enrolled and randomly assigned into 2 diet treatment groups, the LC diet group (n = 20) and the LF diet group (n = 19).

THE INTERVENTION

The adolescents in the LC group were prescribed a diet that consisted of a daily intake of no more than 20 g/day of carbohydrate and an ad lib intake of protein, fat, and energy for the initial 2 weeks. For weeks 3 through 12, carbohydrate was increased to 40 g daily by adding additional nuts, fruits, and whole grains. Participants were advised to consume a minimum fluid intake of 50 oz per day, a multivitamin supplement containing 100% of the recommended dietary allowances for age, and a potassium chloride table salt substitute. Fiber supplements were prescribed when symptoms of constipation occurred.

The LF group was instructed to eat a diet consisting of <40 g/d of fat, with 5 servings of starch per day and an ad libitum intake of fat-free dairy foods, fruits, and vegetables for 12 weeks. A serving of starch was defined as a portion containing 15 g of carbohydrate per serving, and the consumption of whole grains was encouraged. Juices and sweetened beverages were omitted from the meal plan. A multivitamin supplement containing 100% of the recommended dietary allowances of vitamins and minerals for age and sex was recommended. Both diets shared a "stoplight" meal plan design with 3 categories of foods, as suggested by Epstein and Squires.[26] The contents of the food categories were designed by the investigators to correspond to the desired macronutrient content of each respective meal plan. Both groups were instructed to monitor urinary ketones daily with urine reagent strips, and these logs were reviewed biweekly with an investigator. Subjects in both groups were recommended to perform 30 minutes of aerobic exercise 3 times per week, although they were not requested to record their exercise.

The LF diet was used as the comparison diet because it is consistent with standard-of-care for the treatment of pediatric obesity and has been documented as a successful method of intervention.[15,27,28] In fact, most expert groups recommend LF diets with elimination of simple sugars and reduction of starches and complex carbohydrate and self-selected energy intake for weight control. We have been using this diet in our weight management program in clinical and research practice for more than 10 years, with both weight loss and lipid profile improvement.[15]

The 12-week duration of the study was chosen because previous studies have shown that significant effects of dietary

Table II. Mean self-selected macronutrient intake by group

Group	LC (n = 11)	LF (n = 11)	*P*
Energy (kcal/day)	1830 ± 615	1100 ± 297	.03
Carbohydrate (% total energy consumed)	8.0 ± 7.6	56.1 ± 25	.02
(g/d)	36.7 ± 35	154.2 ± 70	
Fat (% total energy consumed)	59.6 ± 10	12.3 ± 1.6	.001
(g/day)	121.2 ± 20	15.0 ± 2.0	
Saturated fat (% total energy consumed)	22.0 ± 16	6.8 ± 6.3	.001
(g/day)	44.7 ± 33	8.3 ± 7.6	
Cholesterol (mg/day)	667 ± 216	164 ± 57	.005

Table III. Changes in lipid parameters after 12 weeks, by group

Group	N	TC (mg/dL)	LDL-C (mg/dL)	HDL-C (mg/dL)	TG (mg/dL)	Non–HDL-C (mg/dL)
LC	12	–3.7 ± 18.0†	3.8 ± 13†	3.8 ± 7.2†	–48.3 ± 29.0*	–26.0 ± 22.3*
LF	14	–17.3 ± 15.8*	–25.1 ± 25.3*	1.8 ± 7.7†	–5.9 ± 70.0†	–13.6 ± 13.4*
P value (LC vs LF)		NS	.006	NS	.07	.036

NS, Not significant.
*$P < .05$ from baseline.
†$P > .05$ from baseline.

management on the serum lipid profile can be demonstrated as early as 6 weeks, and many previous investigators have successfully used 12 weeks as the cutoff for determining these effects.[29-31]

Measures

Anthropometric assessment included baseline and biweekly measurements for a period of 12 weeks. Weights were recorded on a triple-beam balance scale and heights measured by a statiometer, with participants gowned and in bare feet. BMI was calculated from recorded heights and weights and compared with reference data of the National Center of Health Statistics of the Centers for Disease Control to compute *Z* scores.[32] Laboratory assessment included baseline and 12-week assays of fasting total cholesterol (TC), triglyceride (TG) levels, HDL cholesterol (HDL-C), calculated LDL cholesterol (LDL-C), and non–HDL-C, glucose, urea nitrogen, creatinine, urea nitrogen/creatinine ratio, total protein, albumin, total bilirubin, alkaline phosphatase, AST, ALT, and electrolyte levels. Lipid determinations were performed in a laboratory with documented coefficient of variance for TC of <3%, as recommended.[33]

Dietary adherence was monitored at baseline and biweekly by a registered dietician. Adolescents and parents were instructed in the accurate completion of consecutive 3-day food records that included 2 weekdays and 1 weekend day. Food record nutrient calculations were performed with the use of the Nutrient Data System for Research software, version 4.01, developed by the Nutrition Coordinating Center, University of Minnesota.[34] The macronutrients analyzed were energy, fat, carbohydrate, protein, cholesterol, and saturated, monounsaturated, and polyunsaturated fatty acids.

Data Analysis

Two-tailed Student *t* tests were used to compare the serum lipid values. Kruskal-Wallace nonparametric tests were used to compare preintervention and postintervention weight, BMI, and BMI *Z* scores. Values of $P < .05$ were taken to be statistically significant. Participants who failed to complete at least 4 successive visits were excluded from final analysis and are reported as dropouts. The final results are taken from all 30 patients who reported compliance with the prescribed diet and completed at least 8 of the 12 weeks of the study period (LC = 16, LF = 14). One subject in each group did not return to the laboratory for follow-up lipid studies; 5 participants in the LF and 3 participants in the LC group did not return their detailed diet histories. Analyses were conducted to determine whether differences existed between groups on baseline measures of age, height, weight, and BMI. In addition, lipid levels between groups were examined.

RESULTS

As can be seen in Table I, no significant differences were detected between the groups on any of the baseline measurements.

None of the patients in the LF group had ketonuria during the study. All patients in the LC group had ketonuria on most days; on average, ketonuria developed in the LC

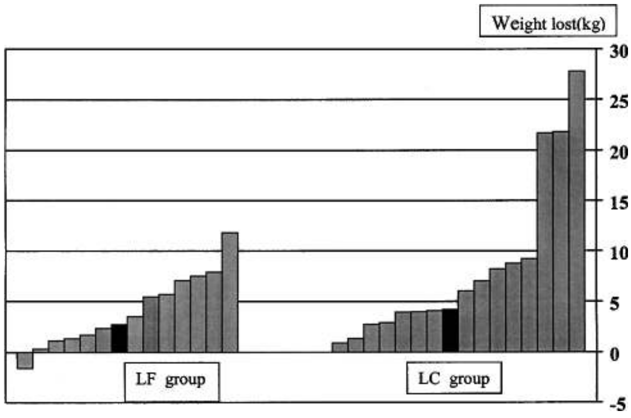

Figure. Each subject's weight loss from baseline to follow-up. Each *bar* represents one subject; *black bar* is the median.

group by the third day. No quantitative assessment of degree of ketosis was done.

An analysis with all 39 randomly assigned subjects who returned for at least 1 follow-up visit showed an average decline in BMI of 2.4 ± 2.7 kg/m^2 and 1.2 ± 1.6 for the LC and LF groups, respectively (P = .1, not significant). Of those considered for final analysis, adolescents in the LC group lost 9.9 ± 9.3 kg compared with 4.1 ± 4.9 kg for teens in the LF group (P < .04). The average BMI improvement noted at the end of the 12-week trial was significantly better in the LC group compared with the LF group (3.3 ± 3.0 kg/m^2 vs 1.5 ± 1.7, P < .05). The Figure shows the weight lost for each individual patient who completed at least 8 weeks of the intervention. In the LC group, every patient lost some weight. Eight of 16 subjects in the LC group lost more than 1 kg/wk compared with 4 of 14 in the LF group (P < .05). Analysis of weight differences with BMI T-scores used to adjust for age and sex showed a significantly greater change in the LC group than in the LF group (change in Z = –0.196 ± 0.14 vs –0.144 ± 0.27, P = .04).

On average, participants in the LC group reported consuming more energy compared with those in the LF group (Table II). The LC group reported significantly more fat and significantly less carbohydrate intake than the LF group (both P < .0001). The LC group ate more saturated fat and more cholesterol than the LF group (P < .0001) and significantly more of these macronutrients than recommended.[35-37] The changes in observed serum lipids are shown in Table III. Participants in the LF group realized a significant decrease in LDL-C, whereas those adolescents in the LC group did not. Serum TG values decreased significantly from baseline in the LC group. Of greatest importance for both groups, none of the lipid parameters measured worsened significantly. Review of compiled laboratory values at the conclusion of the intervention did not reveal any abnormalities in serum electrolytes or in liver or kidney function.

The dropout rate did not differ significantly between groups (LC: 4 of 20, LF: 5 of 19). In fact, no patient in either group failed to complete the intervention because of untenable side effects such as fatigue, headache, or severe nausea. The most frequent complaints voiced by continuing participants were constipation or diarrhea (3 of 16) and headache (2 of 16) in the LC group and fatigue in the LF group (2 of 14). The most common reasons for discontinuing the study in the LC group were discomfort with the idea of consuming mostly energy from fat (2 of 4), noncompliance (1 of 4), and failure to return for follow-up visits and inability to be reached by telephone (1 of 4). For the LF group, the most common reasons for discontinuing the diet were limited food choices (2 of 5), noncompliance (2 of 5), and failure to return for follow-up and inability to be reached by telephone (1 of 5).

DISCUSSION

These data suggest that adolescents randomly assigned to a LC diet were more likely to have greater weight loss over a 12-week period than teens treated on a LF diet and that the LC group lost more weight despite a higher reported energy intake. The results are consistent with previous studies describing the effectiveness of LC diets in promoting weight loss.[13,14,18] Whereas the previously studied LC diets were very-low–energy diets, ranging from 800 to 1200 kcal/day, our study is unique in that our participants reportedly consumed between 1500 and 2500 kcal/day and were able to lose significant amounts of weight. Furthermore, our participants ate significantly more fat and cholesterol than participants in previously studied LC diets. Contrary to our hypothesis, the diet did not appear to harm their lipid profiles over a 12-week period. Previous studies show that increasing dietary fat and cholesterol worsens the serum lipid profile and increases cardiovascular risk in adolescents in a mixed diet; this was not observed in any of our participants. Furthermore, although standard LF diets have been shown to reduce serum HDL levels,[37] the LC diet was associated with an increase in serum HDL. Also, although serum TG levels were reduced in both groups, reductions were greater in the LC group.

We recognize that the LDL-C improved from baseline in the LF group, whereas it did not improve in the LC group. The non–energy-restricted LC diet may not be appropriate for individuals whose primary pathology is an elevated LDL-C, such as those with heterozygous or homozygous familial hypercholesteremia; for those adolescents, we continue to recommend the National Cholesterol Education Program (NCEP) step 1 and step 2 diets.[36] However, for those in whom obesity is the chief complaint and who have either normal lipid profiles or lipid profiles with abnormalities primarily regarding TG or HDL, such as those with familial combined hyperlipidemia, this may be a diet plan with considerable advantages. The effects of this diet on adolescents with familial combined hyperlipidemia need to be further evaluated.

Most of the literature on ketogenic and LC diets has concentrated on very-low–energy diets, also known as protein-sparing modified fasts (PSMF). The results of these studies, however, have been equivocal. Willi et al[13] reported increased weight loss in obese adolescents on a PSMF and showed that the weight lost was predominately fat and not lean body mass. Suskind et al,[21] in an uncontrolled trial, also reported good results with a PSMF. However, other researchers have reported no advantage in weight loss in appropriately controlled ketogenic and non–ketogenic- modified fasts.[14,22] For example, Golay et al[22] found no difference in weight loss between low-energy diets that were 15% carbohydrate or 45% carbohydrate, although neither of those diets resulted in ketogenesis. Proserpi et al[23] compared an ad libitum high-fat diet with an ad libitum, high-carbohydrate diet and found no difference in energy expenditure between the groups and increased fat storage in the high-fat group. Again, the LC group in this protocol had 26% of food energy coming from carbohydrate intake, a proportion not low enough to promote ketogenesis.[23] Luscombe et al[24] reported that a diet with a low glycemic index increased HDL levels. Dietz et al[25] reported increased nitrogen losses in a very-low–calorie protein plus fat diet when compared with an isocaloric protein plus glucose diet, but these effects were observed during energy restriction of 3-month duration.

A non–energy-restricted LC meal plan may be more effective than a very-low–calorie diet because of increased palatability and better maintenance of the metabolic rate as the result of higher caloric intake. Studies show that weight loss as the result of severe caloric restriction is associated with reduction in resting energy expenditure.[38,39] Also, allowing a higher caloric intake lessens the concern of decreased growth velocity. Dietz et al[40] reported decreased growth velocity in a balanced calorie deficit diet over a period of 4 to 6 months, and although the mechanism of growth velocity reduction is unknown, energy restriction alone has been implicated. Epstein et al,[41] however, reported no decrease in linear growth with weight loss caused by moderate energy restriction. The mechanism for increased weight loss in the LC group remains obscure. The higher caloric intake among LC participants may ameliorate the metabolic response to caloric restriction seen in very-low–energy diets. Increased serum insulin is known to promote lipogenesis, and some of the known sequelae of low insulin states, such as lowered TG,[42] were observed in the LC group. Perhaps insulin production or insulin activity is affected by LC dieting. This question requires further study.

Studies have shown that in the presence of a glucose fast, the body metabolizes ketone bodies in preference to glucose for its energy needs (Randle cycle).[43] These ketone bodies are incompletely metabolized and excreted through the urine, breath, and stool in the form of the energy-containing compounds acetoacetate, β-hydroxybutyrate, and acetone.[44] Excretion of energy through ketone bodies may allow for weight loss, while consuming a higher amount of energy than the standard weight reduction diets, which, when not associated with severe energy restriction, do not result in a significant loss of ketone bodies.[45] To evaluate the plausibility of this mechanism, it would be necessary to quantify ketone body loss from the skin, breath, and urine, which is beyond the scope of this trial. Urinary ketone strips offer qualitative but not quantitative information and do not correlate completely with serum acetoacetate and do not test for β-hydroxybutyrate.[46,47] We were therefore unable to correlate lost weight or improved lipids with degree of ketosis. Further studies would be helpful to evaluate the relation of the degree of ketosis to success on the diet.

The use of urine ketone sticks may also improve dietary adherence. Adolescents on LC diets using these sticks daily receive immediate feedback as to whether they are following the meal plan correctly and thus are more able to directly observe the biological effects of the intervention. Although the LF participants were also asked to use urine ketone sticks, they did not see any changes in the readings, even with perfect compliance.

The use of recorded food records, although commonly reported in the literature, has had its validity called into question, with correlation of intake reported by food records to that of calculations with doubly weighted water reported as low as 50% in some trials.[48] Although both groups had their diets analyzed by the same technique, and every effort was made to encourage accurate reporting including regular probing for missing items, it is possible that the LC group, told that they could eat as much fat as they wanted beforehand, reported more accurately than the LF group. Differential underreporting can neither be confirmed nor denied from our existing data.

Furthermore, although we gave identical exercise instructions to both groups, we did not document the exercise that occurred in each group. This raises the possibility that there might be a difference in exogenous energy expenditure between the groups.

We recognize that the long-term maintenance of weight loss in any diet protocol is an important issue. At the Center for Atherosclerosis Prevention, after the induction phase of 12 weeks of weight loss, we suggest a 12-week period of weight maintenance in the LC group, adding back low glycemic index carbohydrate into the diet in 15-g/d increments until a weight balance is reached. There is evidence that recidivism to weight loss can be reduced if energy balance after weight loss is maintained.[49] After 12 weeks of maintenance, we allow patients to lose more weight for another 12-week period if they desire. At this point, 8 patients in the LC group and 1 patient in the LF group have completed 1-year follow-up. None of the 9 patients has gained back the significant weight he or she lost. The fact that 8 of the 9 patients that we were able to follow for 1 year were from the LC group suggests that a LC, moderate–fat and protein diet may be easier for adolescents to follow than a LF diet.

This is a preliminary study with a few limitations. The outpatient setting in which the study was conducted made it challenging to enforce compliance with diet plans and exercise as well as to measure dietary intake. The study was designed to compare weight loss and cardiovascular risk in the short term; our long-term results, although appearing successful, must be considered as anecdotal, and further long-term follow-up studies must be conducted to confirm these findings. Future directions in LC diet research include better definitions of the mechanisms involved in the increased weight loss and maintenance of the lipid profile as well as establishing long-term safety and efficacy with follow-up studies.

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