Nutrition 28 (2012) 1016–1021

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes

Talib A. Hussain M.B., Ch.B., R.C.G.P. [a], Thazhumpal C. Mathew M.Sc., Ph.D., F.R.C.Path. [b], Ali A. Dashti M.Sc., Ph.D. [b], Sami Asfar M.B., Ch.B., M.D., F.R.C.S., F.A.C.S. [c], Naji Al-Zaid B.Sc., Ph.D. [d], Hussein M. Dashti M.D., Ph.D., F.I.C.S., F.A.C.S. [c,*]

[a] Al Shaab Family Medicine Medical Center, Ministry of Health, Kuwait
[b] Department of MLS, Faculty of Allied Health Sciences, Health Sciences Center, Kuwait University, Kuwait
[c] Department of Surgery, Faculty of Medicine, Health Sciences Center, Kuwait University, Kuwait
[d] Department of Physiology, Faculty of Medicine, Health Sciences Center, Kuwait University, Kuwait

ARTICLE INFO

Article history:
Received 13 June 2011
Accepted 16 January 2012

Keywords:
Obesity
Body mass index
Blood glucose
Lipid profile
Ketogenic diet
Low-calorie diet

ABSTRACT

Objective: Effective diabetic management requires reasonable weight control. Previous studies from our laboratory have shown the beneficial effects of a low-carbohydrate ketogenic diet (LCKD) in patients with type 2 diabetes after its long term administration. Furthermore, it favorably alters the cardiac risk factors even in hyperlipidemic obese subjects. These studies have indicated that, in addition to decreasing body weight and improving glycemia, LCKD can be effective in decreasing antidiabetic medication dosage. Similar to the LCKD, the conventional low-calorie, high nutritional value diet is also used for weight loss. The purpose of this study was to understand the beneficial effects of LCKD compared with the low-calorie diet (LCD) in improving glycemia.
Methods: Three hundred and sixty-three overweight and obese participants were recruited from the Al-Shaab Clinic for a 24-wk diet intervention trial; 102 of them had type 2 diabetes. The participants were advised to choose LCD or LDKD, depending on their preference. Body weight, body mass index, changes in waist circumference, blood glucose level, changes in hemoglobin and glycosylated hemoglobin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, uric acid, urea and creatinine were determined before and at 4, 8, 12, 16, 20, and 24 wk after the administration of the LCD or LCKD. The initial dose of some antidiabetic medications was decreased to half and some were discontinued at the beginning of the dietary program in the LCKD group. Dietary counseling and further medication adjustment were done on a biweekly basis.
Results: The LCD and LCKD had beneficial effects on all the parameters examined. Interestingly, these changes were more significant in subjects who were on the LCKD as compared with those on the LCD. Changes in the level of creatinine were not statistically significant.
Conclusion: This study shows the beneficial effects of a ketogenic diet over the conventional LCD in obese diabetic subjects. The ketogenic diet appears to improve glycemic control. Therefore, diabetic patients on a ketogenic diet should be under strict medical supervision because the LCKD can significantly lower blood glucose levels.

Introduction

The current increase in the rate of type 2 diabetes is quite alarming. During the past three decades, the prevalence of this disease in the middle-aged has almost doubled [1]. According to reports by the World Health Organization, approximately 170 million people worldwide have diabetes and this figure is expected to reach to 366 million by 2030 [2]. A similar trend in the increase of type 2 diabetes has been observed in the Gulf region, especially in Kuwait [3,4].

The risk of diabetes is strongly associated with obesity, and even a modest weight loss has been reported to substantially decrease the diabetic risk. According to statistics from the US Center for Disease Control and Prevention, 55% of diabetic patients are obese and 85% are overweight [5]. In several previous

* Corresponding author. Tel.: +965-2498-6226; fax: +965-2531-9597.
E-mail address: dashticlinic@gmail.com (H. M. Dashti).

0899-9007/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.nut.2012.01.016

Table 1
Recommended and restricted food in a low-carbohydrate ketogenic diet and a sample low-calorie diet

Recommended food in low-carbohydrate ketogenic diet	
Proteins	fish: tuna, sardine prawns, shrimps, lobster meat; kebabs; sausages; minced poultry; chicken; eggs; cheese: full-fat cheese
Vegetables/fruits	spinach, watercress, eggplant, parsley, mulberry, coriander, mint, artichoke, okra, cabbage, mushroom, avocado, leek, carrot, radish, celery, cauliflower, green pepper, lettuce, cucumber, tomato, 10–15 olives/d, lemon, strawberry 6/d, avocado, berries 10/d
Oil	olive oil (5 tbsp, added to salad), flax seed oil
Restricted food in low-carbohydrate ketogenic diet	flour, potato, macaroni spaghetti, noodles, bread, rice, sugar, sweets, honey, cakes, all fruit juices, all soft drinks
Sample 2200-calorie low-calorie diet	
Breakfast	coffee with caffeine (12 oz); cottage cheese 1% fat (1.5 cup); cream, fluid, half and half (1 tbsp); fruit cocktail (0.5 cup)
Morning snack	medium apple with peel, medium banana (1 each)
Lunch	medium apple with peel (1 each); bread whole wheat slice (2 each); cheddar cheese (2 in.^{3}); mayonnaise (tuna salad, 0.15 cup); turkey breast/white meat (3 oz)
Afternoon snack	Bread slice rye 7 grain (2 each); jelly: any fruit flavor (4 tsp); peanut butter (2 tbsp)
Dinner	chicken breast/white meat (4 oz); rice: white cook steamed (1.5 cups); low-calorie thousand island dressing (salad); Kraft mayonnaise (4 tbsp); croutons (cook cuts bred into small cubes) plain (0.25 cup); 1 small garden salad with tomato, onion

studies, we have shown that a low-carbohydrate ketogenic diet (LCKD) is quite effective in decreasing body weight [6–13]. The LCKD has a low-carbohydrate content (20–30 g/d) that causes ketosis and mimics the physiologic state of fasting [6].

Before the advent of exogenous insulin, dietary modification was the main therapy for diabetes. However, the diet recommendations during that time were completely different from the current low-fat, high-carbohydrate dietary recommendations for patients with diabetes [14,15]. For example, Dr. Elliot Joslin's Diabetic Diet in 1923 consisted of meats, poultry, fish, clear soups, gelatin, eggs, butter, olive oil, coffee, and tea, providing approximately 5% of energy from carbohydrates, 20% from protein, and 75% from fat [16]. During that time, a diabetic diet with a similar composition was advocated by Dr. Frederick Allen [17].

In a previous study from our laboratory, we quite convincingly showed the beneficial effects of a ketogenic diet in obese diabetic subjects [9]. Furthermore, in recent studies in an animal model of diabetes, we showed that the LCKD has a significant beneficial effect on ameliorating the diabetic state and helping to stabilize hyperglycemia [11,13]. From the results of these studies, we recommended that the LCKD may be effective in diabetes management by improving glycemia and decreasing the need for medication.

The present study, therefore, is a continuation of our previous studies in diabetic patients and experimental diabetic animals. The main purpose of the therapeutic plan of this study was to evaluate the effects of administering a low-calorie diet (LCD) and an LCKD for 24 wk in improving glycemia and decreasing the need for diabetic medication in overweight and obese patients with type 2 diabetes.

Materials and methods

Participants

In this study, the participants were recruited from the Al-Shaab Family Medicine Medical Center, Kuwait. The participants were included in this study if they were at least 18 y old, had a body mass index higher than 25 kg/m^2 and a fasting serum glucose level higher than 125 mg/dL (>6.9 mmol/L). Patients with evidence of renal insufficiency, liver disease, or unstable cardiovascular disease by history, physical examination, and laboratory tests were excluded from the study. All participants provided written informed consent, and the study was approved by Kuwait University.

Intervention

The participants were given detailed information on the LCKD and LCD during their initial visit. They were then advised to take choose an LCD or an LCKD, depending on their preference. Initially, participants in the LCKD group were instructed to follow the LCKD as individuals or in small groups, with an initial goal of ~20 g/d of carbohydrate. The list of recommended and restricted foods in the LCKD is presented in Table 1.

The participants were given previous reports on the LCKD from our laboratory, a handout, and a handbook [6–13] concerning the type and amount of foods

Table 2
Baseline values of different physical and biochemical parameters monitored in diabetic and non-diabetic subjects consuming an LCD or an LCKD

	Total	Diabetic		Non-diabetic	
		LCD	LCKD	LCD	LCKD
Age	37.2 ± 0.4	45.1 ± 1.1	39.2 ± 0.7	34.8 ± 0.7	36.8 ± 0.6
Weight	96.0 ± 0.9	95.7 ± 2.0	104.0 ± 2.1	91.0 ± 1.6	95.7 ± 1.3
Fasting blood sugar	6.3 ± 0.1	9.0 ± 0.6	9.1 ± 0.3	5.3 ± 0.1	5.4 ± 0.1
Triacylglycerols	1.8 ± 0.1	2.5 ± 0.2	2.2 ± 0.1	1.5 ± 0.1	1.7 ± 0.1
Total cholesterol	5.3 ± 0.1	5.5 ± 0.2	5.7 ± 0.1	5.0 ± 0.1	5.2 ± 0.1
LDL	3.0 ± 0.1	3.4 ± 0.2	3.4 ± 0.1	2.7 ± 0.1	2.8 ± 0.1
HDL	1.0 ± 0.0	1.0 ± 0.1	1 ± 0.1	1.1 ± 0.0	1.0 ± 0.0
Uric acid	303.2 ± 4.0	328.5 ± 12.0	307.8 ± 9.0	284.8 ± 7.0	311.8 ± 6.4
Creatinine	75.0 ± 0.8	76.7 ± 2.9	74.2 ± 1.6	76.1 ± 1.6	74.2 ± 1.1
Urea	4.5 ± 0.1	4.7 ± 0.2	5.0 ± 0.2	4.4 ± 0.1	4.4 ± 0.1
Waist circumference	110.2 ± 0.6	113 ± 1.7	115.3 ± 1.2	107.7 ± 1.1	108 ± 0.9
HbA1c	7.9 ± 0.1	8.2 ± 0.3	7.8 ± 0.1		
Body mass index	37.3 ± 0.3	36.3 ± 0.5	40.0 ± 0.7	36.0 ± 0.6	37.2 ± 0.5

HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LCD, low-calorie diet; LCKD, low-carbohydrate ketogenic diet; LDL, low-density lipoprotein
Data are expressed as mean ± SE

they could eat and the types of food that should be avoided. Initially, the participants were allowed to eat unlimited amounts of meats, poultry, fish, and eggs. In addition, the participants were asked to take 2 cups of salad vegetables per day, hard cheese (100–120 g), and limited amounts of cream, olives, and lemon juice. Although fats and oils were allowed, the participants were instructed not to take *trans*-fats. Antidiabetic medications were decreased with the diet initiation. In general, the insulin doses were halved and the sulfonylurea doses were halved or discontinued. The participants also were instructed to take a standard multivitamin/multimineral tablet and drink approximately six to eight glasses of water daily.

The participants returned every other week for 24 wk for further counseling on diet and medication. When a participant neared half the weight loss goal or developed cravings, he or she was advised to increase the carbohydrate intake by approximately 5 g/d each week as long as the weight loss continued. The participants could choose 5-g carbohydrate portions from one of the following foods each week: salad vegetables, low-carbohydrate vegetables, hard or soft cheese, nuts, or low-carbohydrate snacks. The participants in the LCD group were given appropriate guidelines and a sample LCD menu of 2200 calories is presented in Table 1.

The initial dose of some antidiabetic medications was decreased to half in the LCKD group at the beginning of the dietary program. The antidiabetic medication dosage was modified based on twice-daily glucometer measurements and hypoglycemic episodes, and diuretic and other antihypertensive medication adjustments were based on the orthostatic symptoms, blood pressure, and lower extremity edema.

Measurements

The participants were given written instructions on how to complete the food records. All participants completed the take-home food record according to the directions. These food records were collected at the beginning of the study and at weeks 2, 8, 12, 16, 20, and 24.

The anthropometric and vital sign measurements and assessments for hypoglycemic episodes and other symptomatic side effects were performed every other week. Weight was measured on a standardized digital scale while the participant was wearing light clothes and without shoes. Blood pressure was measured after the participant had been seated quietly without talking for 3 min. Hypoglycemic episodes and symptomatic side effects were assessed by direct questioning of the participant.

Blood specimens were collected after the participant had fasted overnight at weeks 0, 4, 8, 12, 16, 20, and 24. The following serum tests were performed in the hospital laboratory using standardized methods: complete blood cell count and lipid, liver, and renal profiles.

For statistical analysis of the data, a paired *t* test was used to determine the statistical significance between weeks 1 and 24 in the different groups and an independent *t* test was used to analyze the significance between the LCD and LCKD groups using SPSS 16 (SPSS, Inc., Chicago, IL, USA). The method used in this study for estimating the treatment effects was with completers only, rather than an intent-to-treat analysis.

Results

Three hundred sixty-three participants were enrolled in the study and completed the 24 wk of follow-up. Adherence to the two dietary programs was discussed with the participants and recorded. Adequate food records were available to determine each participant's adherence to the dietary program (data not shown). Among the 363 participants, 86 were men (23.7%) and 277 were women (76.3%). Among the men, 28 were diabetic and 58 were non-diabetic; among the women, 74 were diabetic and 203 were non-diabetic. In total, 102 participants were diabetic and 261 were non-diabetic. Concerning diet, 143 (27 men and 116 women) of the 363 participants were on a low-calorie diet, whereas 220 (59 men and 161 women) were on a ketogenic diet. In the LCD group, 24 participants (16.8%) were diabetic, whereas in the LCKD group 78 (35.5%) were diabetic. The baseline values of the clinical parameters examined are listed in Table 2.

Effect on body weight, body mass index, and waist circumference

There was a significant difference ($P < 0.0001$) in the body weight, body mass index, and waist circumference of the diabetic and non-diabetic participants in the LCD and LCKD groups compared with their initial (week 1) and final (week 24) measurements (Fig. 1A, Table 3). The effectiveness of the LCKD over the LCD is quite evident in Figure 1A, which shows the percentage of weight loss in the different groups.

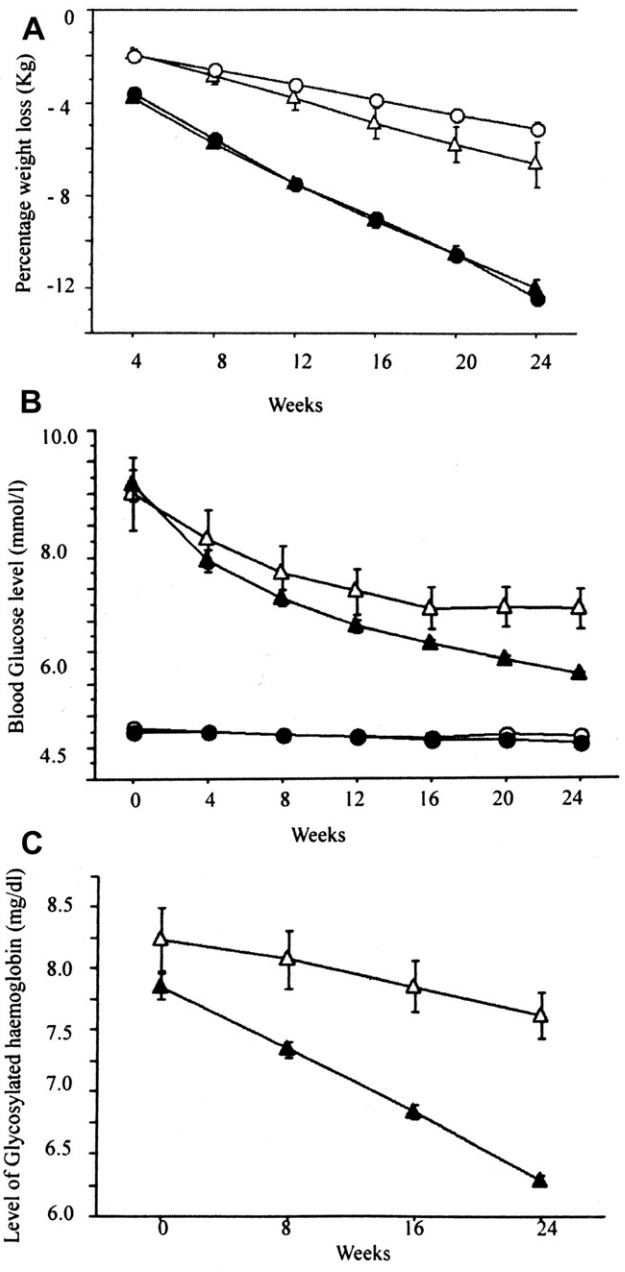

Fig. 1. Changes in the percentage of body weight (A), blood glucose level (B), and level of glycosylated hemoglobin (C) in diabetic and non-diabetic subjects after the administration of a low-calorie diet or a low-carbohydrate ketogenic diet for 24 wk. A significant difference ($P < 0.0001$) in body weight was noticed in the low-calorie and low-carbohydrate ketogenic diet groups compared with their initial (week 1) and final (week 24) measurements. The ketogenic diet was more effective than the low-calorie diet. The blood sugar level significantly decreased in the two groups. The effectiveness of the low-carbohydrate ketogenic diet was much greater ($P < 0.0001$) in the diabetic group on the low-carbohydrate ketogenic diet than on the low-calorie compared with week 1 and week 24 blood glucose levels. In the diabetic group, the glycosylated hemoglobin level significantly decreased with the low-carbohydrate ketogenic diet compared with the two diets. Black circles, ketogenic and non-diabetic; black triangles, ketogenic and diabetic; white circles, low calorie andnon-diabetic; white triangles, low calorie and diabetic.

Table 3
Effect of an LCD and an LCKD on body weight, body mass index, and waist circumference in diabetic and non-diabetic subjects

Group	Initial, mean ± SD	Week 24, mean ± SD	Change (%)	P^*
Body weight (kg)				
Diabetic and LCD	95.71 ± 9.56	89.02 ± 5.97	−7.0	<0.0001
Diabetic and LCKD	104.01 ± 18.89	91.56 ± 17.45	−12.0	<0.0001
$P^\dagger$	0.005	0.275	<0.001	
Non-diabetic and LCD	91.01 ± 17.77	86.38 ± 17.08	−5.1	<0.0001
Non-diabetic and LCKD	95.71 ± 15.58	83.87 ± 14.82	−12.4	<0.0001
$P^\dagger$	0.024	0.026	<0.001	
Body mass index (kg/m^2)				
Diabetic and LCD	36.31 ± 2.63	33.87 ± 2.75	−6.7	<0.0001
Diabetic and LCKD	39.84 ± 6.40	35.05 ± 5.90	−12.0	<0.0001
$P^\dagger$	0.001	0.180	<0.001	
Non-diabetic and LCD	35.97 ± 6.06	34.14 ± 5.86	−5.1	<0.0001
Non-diabetic and LCKD	37.19 ± 5.73	32.59 ± 5.40	−12.4	<0.0001
$P^\dagger$	0.097	0.026		
Waist circumference (cm)				
Diabetic and LCD	113.92 ± 8.43	109.94 ± 9.07	−3.5	<0.0001
Diabetic and LCKD	115.27 ± 10.45	106.81 ± 9.83	−7.3	<0.0001
$P^\dagger$	0.563	0.168	<0.001	
Non-diabetic and LCD	107.72 ± 11.58	104.72 ± 11.00	−2.8	<0.0001
Non-diabetic and LCKD	108.74 ± 10.50	102.10 ± 9.36	−6.1	<0.0001
$P^\dagger$	0.455	0.041	<0.001	

LCD, low-calorie diet; LCKD, low-carbohydrate ketogenic diet
* Significance between weeks 1 and 24 by paired *t* test.
† Significance between LCD and LCKD groups by independent *t* test.

Effect on blood glucose and glycosylated hemoglobin levels

Although the initial dose of some antidiabetic medications was decreased to half and some were discontinued at the beginning of the dietary program in the LCKD group, the blood sugar level significantly decreased in the two groups (Fig. 1B,C). However, the effectiveness of the LCKD was much greater ($P < 0.0001$) in the diabetic LCKD group than in the LCD group compared with the initial (week 1) and final (week 24) blood glucose levels. Similarly, the glycosylated hemoglobin (HbA1c) level significantly decreased with the LCKD compared with the two diets in the diabetic group (Fig. 1C).

Effect on lipid profile

The effects of the LCD and LCKD on the lipid profile of diabetic and non-diabetic participants are shown in Figure 2. Diabetic and non-diabetic participants in the LCKD group showed a significant decrease ($P < 0.0001$) in triglycerides, total cholesterol, and low-density lipoprotein levels, whereas the

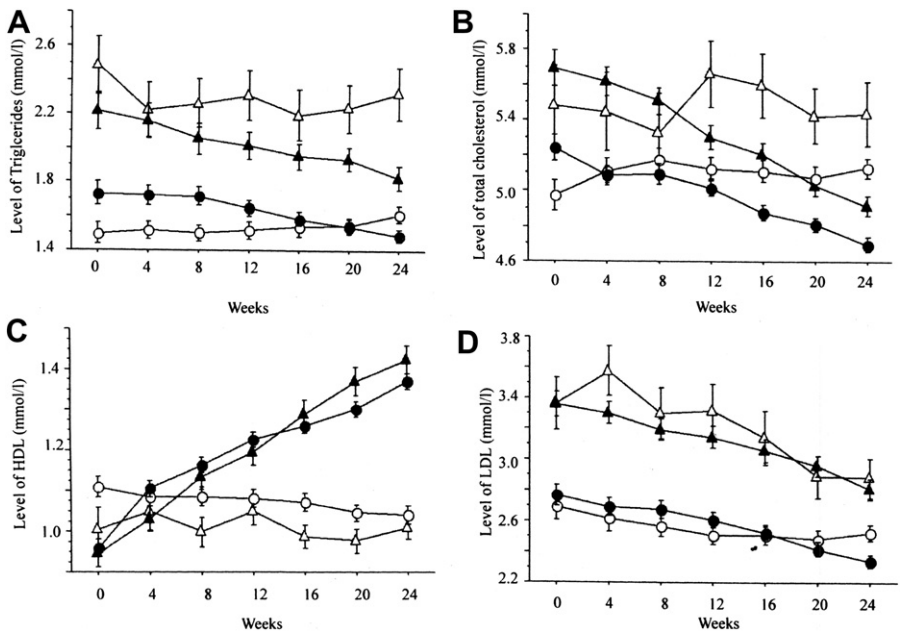

Fig. 2. Changes in the lipid profile in diabetic and non-diabetic subjects after the administration of a low-calorie diet or a ketogenic diet for 24 wk. Diabetic and non-diabetic participants in the low-calorie ketogenic diet group showed a significant decrease ($P < 0.0001$) in triglycerides (A), total cholesterol (B), and LDL (D) levels, whereas the HDL level (C) was significantly ($P < 0.0001$) increased. Black circles, ketogenic and non-diabetic; black triangles, ketogenic and diabetic; HDL, high-density lipoprotein; LDL, low-density lipoprotein; white circles, low calorie and non-diabetic; white triangles, low calorie and diabetic.

high-density lipoprotein level was significantly ($P < 0.0001$) increased (Fig. 2).

Changes in urea, uric acid, and creatinine levels

Urea levels were significantly increased for the two diet groups in diabetic and non-diabetic participants (Fig. 3A). Interestingly, the uric acid level increased in the LCD group, whereas it decreased in the LCKD group (Fig. 3B). A similar change was noted for the creatinine level (Fig. 3C).

Discussion

The effect of carbohydrate restriction on type 2 diabetes was previously examined in our laboratory [9]. We found that the body weight, body mass index, and levels of blood glucose, total cholesterol, low-density lipoprotein cholesterol, triglycerides, and urea were significantly decreased from week 1 to week 56 ($P < 0.0001$). Conversely, the level of high-density lipoprotein cholesterol was increased significantly ($P < 0.0001$). These changes were more significant in subjects with a high blood glucose level as compared with those with a normal blood glucose level. Furthermore, we found that the cardiac protective and ultrastructural changes in the cardiac muscles of laboratory rats that were fed normal, high-carbohydrate, and low-carbohydrate ketogenic diets [10]. We convincingly showed the therapeutic and protective effects of the LCKD in a diabetic rat model [11,13].

The present results showed that, in addition to its therapeutic value, an LCKD is safe to use for a longer period in obese diabetic subjects. Other investigators reported that HbA1c improved to a greater degree with an LCKD over 1 y compared with a low-fat, calorie-restricted diet [18,19]. Our results are in agreement with the previous similar studies carried out by other investigators [20–22]. Furthermore, very LCKDs have not been found to have an adverse effect on glucose metabolism or insulin resistance [23–25]. Also, the prolonged administration of very LCKDs has been reported to not cause any chronic dehydration [26].

In the present 6-months' dietary intervention, the LCKD resulted in a significant improvement of glycemia, as measured by the fasting glucose and HbA1c levels in patients with type 2 diabetes. More importantly, this improvement was observed after some antidiabetic medications had been decreased to half in the LCKD group. The present data showed that the participants in the two dietary programs exhibited decreases in body weight.

Several recent studies have indicated that an LCKD is effective in improving glycemia. A few studies have shown that, in non-diabetic individuals, LCKDs are more effective than higher-carbohydrate diets at improving fasting serum glucose [27–31] and insulin [19,31–33] and at improving insulin sensitivity as measured by the homeostasis model [5,6].

Furthermore, other investigators have reported that antidiabetic medications were decreased in some participants of the dietary program [19,21,22]. Based on the theoretical effects of the LCKD [34], the observed effects of the diet on body water by bioelectric impedance [35] and practical experience with the diet [35], the continuation of antidiabetic medication in patients who are on an LCKD should be cautiously monitored. Until we learn more about using LCKDs, the medical monitoring for hypoglycemia, dehydration, and electrolyte abnormalities is imperative in patients taking antidiabetic or diuretic medications.

Although body weight decreased significantly in these 102 diabetic participants, the mean weight loss was less compared with what we observed in participants consuming an LCKD in a similar previous trial (−12.0 kg) [35]. Because the diabetic participants had a higher baseline mean weight than the participants consuming an LCKD in our previous trial, this translates into an even more dramatic disparity in the percentage of change in body weight. It should be noted that in the present study, most participants were taking insulin and/or oral hypoglycemic agents that are known to induce weight gain

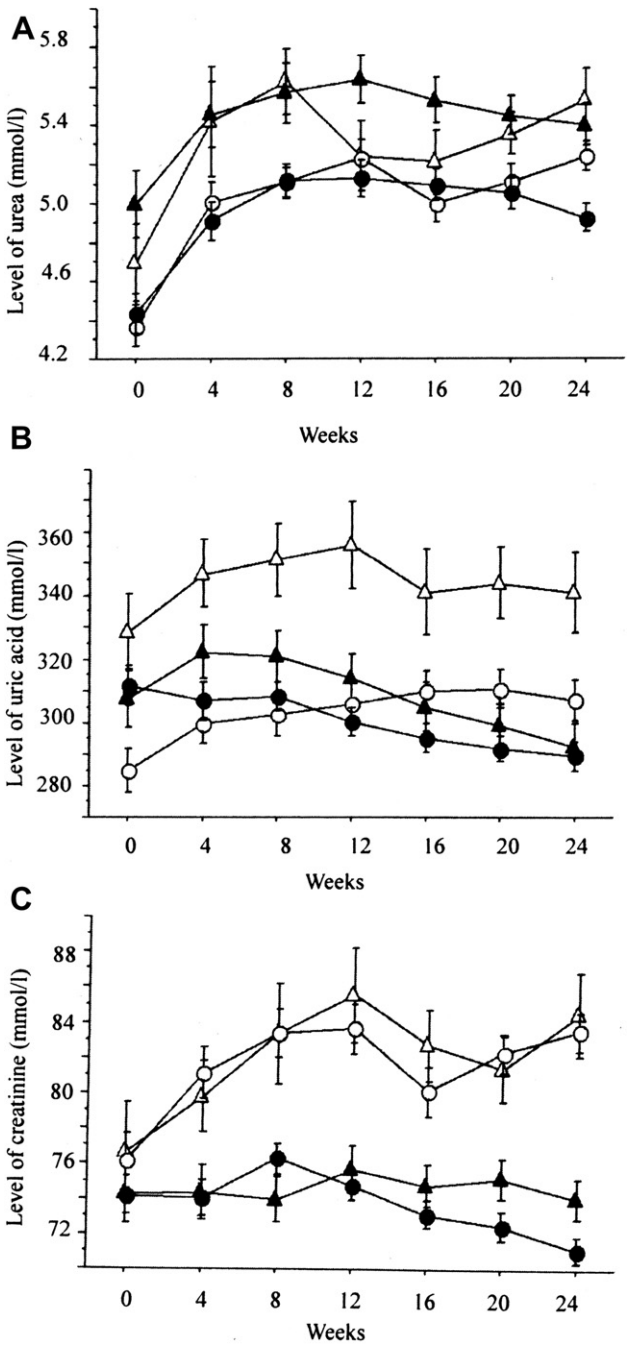

Fig. 3. Changes in the levels of urea (A), uric acid (B), and creatinine (C) after the administration of a low-calorie diet or a ketogenic diet for 24 wk in diabetic and non-diabetic subjects. Urea levels were significantly increased in the two diet groups in diabetic and non-diabetic participants. Uric acid level increased in the low-calorie diet group but decreased in the low-carbohydrate ketogenic diet groups. A similar change was noticed for the creatinine level. Black circles, ketogenic and non-diabetic; black triangles, ketogenic and diabetic; white circles, low calorie and non-diabetic; white triangles, low calorie and diabetic.

[36–38]. Moreover, these same agents, particularly insulin, inhibit ketosis, which is strived for in the earliest phases of the LCKD. Although it remains unclear whether ketones actually play a role in weight loss on the LCKD, previous research in non-diabetic patients has shown a positive correlation between the level of ketonuria and a success in weight loss [39]. The main limitations of our study are its small sample and short duration.

Conclusion

In summary, the LCKD had significant positive effects on body weight, waist measurement, serum triacylglycerols, and glycemic control in participants with type 2 diabetes. Most impressively, there was an improvement in HbA1c despite the small sample and short duration of follow-up, and this improvement in glycemic control occurred after the antidiabetic medications had been decreased substantially in participants using the LCKD program. Further studies are necessary to examine the optimal adjustments, particularly for antidiabetic medications and diuretic agents, to avoid the possible complications of hypoglycemia and dehydration because the LCKD can be very effective at lowering blood glucose. Diabetic patients who use this diet should be under close medical supervision or capable of adjusting their medication as required.

Acknowledgments

The authors thank Mr. Joseph E Gomez, Department of Community Medicine, Faculty of Medicine, Kuwait University for advice and assistance in the statistical analysis of the data.

References

[1] Fox CS, Pencina MJ, Meigs JB, Vasan RS, Levitzky YS, D'Agostino RB Sr. Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham heart study. Circulation 2006;113:2914–8.
[2] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes. Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047–53.
[3] Abdella N, Al Arouj M, Al Nakhi A, Al Assoussi A, Moussa M. Non-insulin-dependent diabetes in Kuwait: prevalence rates and associated risk factors. Diabetes Res Clin Pract 1998;42:187–96.
[4] Abdella N, Al Nakhi A, Al Arouj M, Al Assoussi A, Moussa M. Impact of the 1997 American Diabetes Association criteria on classification of glucose tolerance among Kuwaitis below 50 years of age. Acta Diabetol 1999;36:133–40.
[5] Campbell RK. Type 2 diabetes: where we are today: an overview of disease burden, current treatments, and treatment strategies. J Am Pharm Assoc 2009;49:S3–9.
[6] Dashti HM, Bo-Abbas YY, Mathew TC, Hussein T, Behbehani A, Khoursheed M, et al. Ketogenic diet modifies the risk factors for heart disease in obese patients. Nutrition 2003;19:901–2.
[7] Dashti HM, Mathew TC, Hussein T, Asfar SK, Behbehani AI, Al-Sayer HM, Al-Zaid NS. Long term effects of ketogenic diet in obese subjects. Exp Clin Cardiol 2004;9:200–5.
[8] Dashti HM, Al-Zaid NS, Mathew TC, Al- Mouzawi M, Talib H, Asfar SK, Behbehani AI. Long term effects of ketogenic diet in obese subjects with high cholesterol level. Mol Cell Biochem 2006;286:1–9.
[9] Dashti HM, Mathew TC, Khadada M, Al- Mouzawi M, Talib H, Asfar SK, et al. Beneficial effects of ketogenic diet in obese diabetic subjects. Mol Cell Biochem 2007;302:249–56.
[10] Al-Zaid NS, Dashti H, Mathew TC, Juggi JS. Low carbohydrate ketogenic diet enhances cardiac tolerance to global ischemia. Acta Cardiol 2007;62:381–9.
[11] Al-Khalifa A, Mathew TC, Al-Zaid NS, Mathew E, Dashti H. Therapeutic role of low carbohydrate ketogenic diet in diabetes. Nutrition 2009;25:1177–85.
[12] Dashti HM, Mathew TC. Prevention of obesity using low carbohydrate ketogenic diet. Kuwait Med J 2009;41:3–12.
[13] Al-Khalifa A, Mathew TC, Al-Zaid NS, Mathew E, Dashti H. Low carbohydrate ketogenic diet prevents the induction of diabetes using streptozotocin in rats. Exp Toxicol Pathol 2011;63:663–9.
[14] Klein S, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, Clark NG, American Diabetes Association, North American Association for the Study of Obesity, American Society for Clinical Nutrition. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies. A statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. Am J Clin Nutr 2004;80:257–63.
[15] Arora SK, McFarlane SI. The case for low carbohydrate diets in diabetes management. Nutr Metab (Lond) 2005;2:6.
[16] Osler W, McCrae T. The principles and practice of medicine. New York: Appleton and Co; 1923.
[17] Allen FM, Stillman E, Fitz R. Total dietary regulation in the treatment of diabetes: monograph no. II. New York: Rockefeller Institute for Medical Research; 1919.
[18] Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. Ann Intern Med 2004;140:778–85.
[19] Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003;348:2074–81.
[20] Gannon MC, Nuttall FQ. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. Diabetes 2004;53:2375–82.
[21] Boden G, Sargrad K, Homko C, Mozzoli M, Stein TP. Effect of a low-carbohydrate diet on appetite, blood glucose levels, and insulin resistance in obese patients with type 2 diabetes. Ann Intern Med 2005;142:403–11.
[22] Nielsen JV, Jonsson E, Nilsson AK. Lasting improvement of hyperglycaemia and bodyweight: low-carbohydrate diet in type 2 diabetes. A brief report. Ups J Med Sci 2005;10:179–83.
[23] Cutler DL, Gray CG, Park SW, Hickman MG, Bell JM, Kolterman OG. Low-carbohydrate diet alters intracellular glucose metabolism but not overall glucose disposal in exercise-trained subjects. Metabolism 1995;44:1264–70.
[24] Bisschop PH, de Metz J, Ackermans MT, Endert E, Pijl H, Kuipers F, et al. Dietary fat content alters insulin-mediated glucose metabolism in healthy men. Am J Clin Nutr 2001;73:554–9.
[25] Bisschop PH, Pereira Arias AM, Ackermans MT, Endert E, Pijl H, Kuipers F, et al. The effects of carbohydrate variation in isocaloric diets on glycogenolysis and gluconeogenesis in healthy men. J Clin Endocrinol Metab 2000;85:1963–7.
[26] Volek JS, Gómez AL, Kraemer WJ. Fasting and postprandial lipoprotein responses to a low-carbohydrate diet supplemented with n-3 fatty acids. J Am Coll Nutr 2000;19:383–91.
[27] Yancy WS Jr, Vernon MC, Westman EC. Brief report: a pilot trial of a low-carbohydrate, ketogenic diet in patients with type II diabetes. Metab Syndr Relat Disord 2003;1:239–44.
[28] The Atkins trial kit handbook: a simple guide to doing Atkins. Ronkonkoma, NY: Atkins Nutritionals; 2001.
[29] Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 1974;32:77–97.
[30] Sharman MJ, Gomez AL, Kraemer WJ, Volek JS. Very low-carbohydrate and low-fat diets affect fasting lipids and postprandial lipemia differently in overweight men. J Nutr 2004;134:880–5.
[31] Volek JS, Sharman MJ, Gomez AL, DiPasquale C, Roti M, Pumerantz A, Kraemer WJ. Comparison of a very low-carbohydrate and low-fat diet on fasting lipids, LDL subclasses, insulin resistance, and postprandial lipemic responses in overweight women. J Am Clin Nutr 2004;23:177–84.
[32] Meckling KA, O'Sullivan C, Saari D. 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. J Clin Endocrinol Metab 2004;89:2717–23.
[33] Volek JS, Sharman MJ, Love DM, Avery NG, Gomez AL, Scheett TP, Kraemer WJ. Body composition and hormonal responses to a carbohydrate-restricted diet. Metabolism 2002;51:864–70.
[34] Denke MA. Metabolic effects of high-protein, low-carbohydrate diets. Am J Cardiol 2001;88:59–61.
[35] Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. Ann Intern Med 2004;140:769–77.
[36] Vernon MC, Mavropoulos J, Yancy WS Jr, Westman EC. Brief report: clinical experience of a carbohydrate-restricted diet: effect on diabetes mellitus. Metab Syndr Relat Disord 2003;1:233–8.
[37] UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes, UKPDS 33. Lancet 1998;352:837–53.
[38] Purnell JQ, Hokanson JE, Marcovina SM, Steffes MW, Cleary PA, Brunzell JD. Effect of excessive weight gain with intensive therapy of type I diabetes on lipid levels and blood pressure: results from the DCCT. Diabetes Control and Complications Trial. JAMA 1998;280:140–6.
[39] Westman EC, Yancy WS, Edman JS, Tomlin KF, Perkins CE. Effect of six-month adherence to a very-low-carbohydrate diet program. Am J Med 2002;113:30–6.