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Carbohydrate Restriction, as a First-Line Dietary Intervention, Effectively Reduces Biomarkers of Metabolic Syndrome in Emirati Adults[1,2]

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Abstract

The prevalence of diabetes mellitus (DM) in the United Arab Emirates is among the highest world-wide. Metabolic syndrome (MetS) predisposes individuals to DM; therefore, dietary interventions targeting MetS biomarkers are a high priority. We evaluated whether a carbohydrate-restricted diet (CRD) could effectively be used as a first-line therapy intervention in adult Emirati to improve the characteristics of MetS. A total of 39 participants (14 men, 25 women) 18–50 y, classified with MetS, followed a CRD (20–25% carbohydrate, 50–55% fat, 25–30% protein energy distribution). After 6 wk, 19 participants were randomly switched to the AHA diet (55% carbohydrate, 25–30% fat, 15–20% protein) whereas 20 participants continued with the CRD diet for an additional 6 wk. Fasting plasma lipids, 24-h dietary recalls, body composition, anthropometrics, blood pressure (BP), glucose, insulin, and plasma markers of inflammation were measured at baseline, wk 6, and wk 12. Dietary analysis indicated high compliance. At wk 6, the CRD ($n = 39$) resulted in decreased body weight (−13%), waist circumference (−4.5%), body fat (−10.6%), and plasma triglycerides (TG) (−38.7%) ($P < 0.001$). Significant decreases in LDL cholesterol, BP, glucose, insulin, and inflammatory markers and increases in adiponectin ($P < 0.05$) also occurred. After 12 wk, positive changes persisted for all participants, independent of diet. However, body weight and plasma TG and insulin were lower in the CRD ($P < 0.05$) group than in the CRD + AHA group. Results from this study suggest that a 6-wk CRD can effectively be used as a first-line diet therapy to rapidly improve features of MetS and cardiovascular risk in adult Emirati. J. Nutr. 139: 1–10, 2009.

Introduction

Metabolic syndrome (MetS)[6] is a clustering of metabolic abnormalities characterized by abdominal obesity, dyslipidemia [elevated apolipoprotein B, high triglyceride (TG), elevated small, dense LDL particles, and low HDL-cholesterol (HDL-C)], hypertension, insulin resistance, hyperglycemia, and a systemic proinflammatory state (1). To facilitate clinical diagnosis of high-risk individuals, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) has identified 5 main criteria: waist circumference (WC) >102 cm for men and >88 cm for women; TG ≥150 mg/dL (1.69 mmol/L); HDL-C <40 mg/dL (1.04 mmol/L) for men and <50 mg/dL (1.29 mmol/L) for women; blood pressure (BP) ≥130/85 mm Hg; and fasting glucose ≥100 mg/dL (5.55 mmol/L). When 3 of 5 identified characteristics are present, a diagnosis of MetS is made (1).

The age-adjusted prevalence of MetS among United Arab Emirates (UAE) citizens was reported to be >42% using the NCEP ATP III or International Diabetes Federation criteria (2,3). These results may explain the high rate of diabetes mellitus (DM) in this country that is 2-fold higher than the United States (4,5). During the previous 4 decades, UAE underwent rapid development that led to the growth of environmental health problems such as obesity, MetS, and DM (2–4,6), which may be related to poor diet and physical inactivity.

Because individuals with MetS, with or without insulin resistance, are more prone to develop DM and cardiovascular disease (CVD) (7), the NCEP ATP III has emphasized a therapeutic lifestyle and dietary modification as the first-line approach in the treatment of MetS and insulin resistance. These modifications can significantly reduce body weight and thus improve many of the clinical criteria associated with diabetes and MetS (8).

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[6] Abbreviations used: BP, blood pressure; CRD, carbohydrate-restricted diet; CRD + AHA group, 6-wk carbohydrate-restricted diet followed by a 6-wk conventional low-fat diet as prescribed by the AHA; CRP, C-reactive protein; CVD, cardiovascular disease; DM, diabetes mellitus; HDL-C, HDL-cholesterol; HOMA, homeostatic model assessment; ICAM-1, intercellular adhesion molecule-1; IL-6, interleukin-6; LDL-C, LDL-cholesterol: LSD, least significant differences test; MetS, metabolic syndrome; MCP-1, monocyte chemoattractant protein-1; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; TC, total cholesterol; TG, triglyceride; TNFα, tumor necrosis factor-α; UAE, United Arab Emirates; WC, waist circumference.

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Traditionally, diets that are low in fat, particularly saturated fat, have been used to promote weight loss and improve atherogenic dyslipidemia (9). A meta-analysis of clinical trials showed that low-fat diets produced positive outcomes on plasma lipids, mainly plasma total cholesterol (TC) and LDL-cholesterol (LDL-C) (10). However, recent data from clinical trials have shown that carbohydrate-restricted diets (CRD) produced greater weight loss compared with other traditional dietary interventions (11). CRD have been shown to reduce fasting glucose (12) and insulin (13) and BP (14) and improve atherogenic dyslipidemia, mainly lipoprotein particle size (15), associated with MetS (16). In fact, CRD have been shown to uniquely target traditional, as well as many emerging, markers of MetS, arguing for the idea of a common carbohydrate-sensitive mechanism underlying the syndrome (15,16). Proinflammatory cytokines, such as C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor-α (TNFα), can subsequently lead to insulin resistance, impaired glucose tolerance, and accelerated development of MetS and type-2 DM (17) Furthermore, low adiponectin concentration is associated with insulin resistance (18). CRD have been used to improve circulating adipokines (19) and proinflammatory markers (20) that are strongly associated with CVD (21).

Our aim in this study was to determine the effect of a CRD, followed by the conventional low-fat diet prescribed by the AHA, on the clinical features of MetS and on inflammation markers and adiposity hormones associated with CVD among Emirati adults. We hypothesized that a CRD would improve clinical markers of MetS and that switching to an AHA diet would maintain these improvements. To our knowledge, this is the first nutritional intervention study conducted in the UAE that explores this particular area of research. The results provide important information on the efficacy of dietary modification among individuals with MetS.

Methods and Participants

Participants. This study was conducted at Tawam hospital affiliated with Johns Hopkins Medicine International in the city of Al-Ain, Abu Dhabi Emirate, UAE. We recruited Emirati men and women, aged 18–50 y, and diagnosed with MetS using the NCEP ATP III criteria. Exclusion criteria were: pregnancy and lactation, thyroid problems, use of cholesterol-lowering medication, type-2 DM or fasting blood glucose >126 mg/dL (6.9 mmol/L), stroke or heart disease, and liver and renal disease. Written and word-of-mouth advertisement for the MetS screening program was circulated among the hospital Emirati employees and their relatives, UAE University, and Faculty of Medicine and Higher College of Technology students, in addition to random governmental schools and institutions in Al-Ain.

All human protocols were approved by the Institutional Review Board of the University of Connecticut and the Human Research and Ethics Committee, Faculty of Medicine and Health Science, UAE University. All participants signed an informed consent form written in Arabic before participating in the study.

Study design. The study was conducted at Tawam hospital, one of the major tertiary hospitals in the UAE that is affiliated with Johns Hopkins Medicine International and the Faculty of Medicine and Health Sciences, UAE University.

The study design was a randomized, controlled, interventional trial. We recruited 227 overweight/obese adults aged 18–50 y to screen for MetS. Ninety-two volunteers had the NCEP III criteria for MetS; all were invited to participate in the dietary intervention, but only 56 agreed and signed the consent form. Enrolled participants were carefully matched by age and gender and randomized to either a CRD (20–25% carbohydrate) for 12 wk or to a 6-wk CRD followed by a 6-wk conventional low-fat diet as prescribed by the AHA. This group was referred to as the CRD + AHA group. Of those, 17 did not finish the study for personal reasons, including failure to comply with the diet, lack of motivation, or travel plans. Thirty-nine (14 male and 25 female) volunteers completed the study, 20 in the CRD group and 19 in the CRD + AHA group. Although we had high attrition, the number of participants who completed the study gave us enough power to detect significant differences in the measured variables as previously reported (15,16).

Diet. This was a free-living study in which no food was provided to participants. Registered dietitians met with the participants at baseline and every 2 wk until the end of the study to instruct and educate them how to comply with the CRD or the conventional AHA diets. Participants were also instructed to accurately complete 24-h dietary recalls. Each participant was given written dietary education materials to reinforce the dietary principles covered during the meeting sessions. Carefully prepared brochures with recipes and other pertinent information were given to the participants when they signed the consent form.

The CRD was designed to provide ~20–25% of energy from carbohydrates, ~25–30% of energy from protein, and ~50–55% of energy from fat (mainly monounsaturated fatty acids and PUFA with restriction of saturated fat). There were no guidelines or instruction regarding energy consumption; however, specific guidelines were given to educate participants about the definition of carbohydrate-restricted foods, the type of fat to be consumed, and recipes. Food choices included moderate amounts of lean lamb, beef, poultry meat, fish, and eggs; a moderate amount of low-fat cheese; 200 mL of low-fat milk or plain yogurt; unlimited amount of low-carbohydrate vegetables and salad dressing; 1–2 fruits per day; 250 g of legumes; and 100 g of nuts and seeds. Restricted foods were starchy vegetables, rice, pasta, breads, cereals, simple sugars, sweets and desserts, honey, syrups, sugar-based drinks, regular soda, and fruit juices.

In contrast, the conventional low-fat AHA diet was designed to provide ~50–55% of energy from carbohydrate, ~15–20% from protein, and ≤30% from fat (<10% from saturated fat and 20% from monounsaturated fatty acids and PUFA). Standard AHA exchange lists were used to ensure a constant energy and macronutrient balance. Foods were categorized into exchanges of fruits, vegetables, meats, low-fat dairy products, whole-grain carbohydrates, and fats. Participants were encouraged to consume a specified number of items from each group depending on the participant's last energy intake after 6 wk of CRD to avoid differences in energy between the 2 diets. Participants were instructed to limit fat (mainly saturated fat), simple sugars, and sugar-containing food items such as candies, desserts, or regular soda drinks.

Dietary assessment. To check dietary compliance, phone calls were made twice per week. Participants were encouraged to call the dietitian after working hours if there were any dietary concerns regarding shopping, recipes, restaurant menus, and other diet-related questions. The 24-h dietary recalls were obtained at baseline and wk 1, 6, and 12. Dietary recalls were analyzed by the same dietitian who interviewed the subjects and who was familiar with the type of food consumed in the region. Dietary intake was analyzed using the Nutritional Data System 8.0. Specific recipes and food preparation associated with UAE culture were included into the Data System for a more accurate dietary intake. During the intervention, we confirmed the absence of ketosis using ketostix reagent strips (Bayer).

Anthropometrics and BP. Weight, height, and BMI were measured using a professional digital body composition analyzer scale/stadiometer (TANITA–Body Composition Analyzer TBF-215). WC was measured midway between the lowest rib and iliac crest to the nearest 0.1 cm using a flexible tape over 1 layer of loose, light clothing.

BP (systolic and phase-V diastolic) was measured on the right arm using a validated electronic sphygmomanometer (CRITICARE Systems, model 506 DXNT2 series) with the participant seated following a 10-min rest. Three separate recordings were made and the mean was used.

Body composition/dual-energy X-ray absorptiometry scan. Body mass and body composition were measured in the morning after an overnight fast. Body mass was recorded to the nearest 100 g on a calibrated digital scale with participants wearing only underwear. Whole-body and regional body composition was assessed using a state-of-the-art fan-beam dual-energy X-ray absorptiometry (Prodigy, Lunar Advance). Analyses were performed by the same technician who had no knowledge of the treatment groups.

Blood collection. After 12 h of fasting, blood was collected from an antecubital vein to isolate serum and plasma using EDTA tubes. Plasma was immediately centrifuged at 2000 × *g* for 20 min. Preservatives (1 mL/L sodium azide, 1 mL/L phenylmethylsulphonyl fluoride, and 5 mL/L aprotinin,) were added after separation from RBC. Plasma was then divided into aliquots and frozen at −80°C for measuring insulin, adiponectin, and inflammatory cytokines.

Serum electrolytes, urea, and creatinine. Serum electrolytes, urea, and creatinine were measured using the SYNCHRON Clinical System at Tawam Hospital's laboratory department.

Serum lipids and glucose. Serum TC, direct LDL-C, HDL-C, TG, and glucose were measured in samples from fasting participants at Tawam Hospital's laboratory using the UniCel DxC 600/800 system and SYNCHRON Systems Multi Calibrator.

Homeostasis model assessment. The homeostasis model assessment (HOMA) (22) was used to calculate insulin resistance according to the following equation: HOMA insulin resistance = fasting insulin (μU/mL) × fasting glucose (mmol/L) ÷ 22.5.

Adiponectin and intercellular adhesion molecule-1. Intercellular adhesion molecule-1 (ICAM-1) and adiponectin were measured in samples from fasting participants in duplicate in the same assay using the Human CVD Panel 1 Lincoplex kit. Samples were diluted 1:100 and simultaneously quantified using Antibody-Immobilized beads and Luminex × MAP technology. All assays were conducted on the same day to decrease variability. The CV was between 2 and 6%. The sensitivity for ICAM-1 and adiponectin were 9.0 ng/L and 56.0 ng/L, respectively as previously reported (23).

Insulin, TNFα, IL-6, and MCP-1. Plasma insulin, TNFα, IL-6, and MCP-1 concentrations were measured in duplicate in the same assay in samples from fasting participants using the Human Cytokine Lincoplex kit based on Luminex × MAP technology (Linco Research). All assays were conducted on the same day to decrease variability. The CV was between 3 and 6%. The sensitivities for this assay were 0.66, 1.12, and 1.29 ng/L, respectively.

Statistical analyses. Repeated-measures ANOVA was used to determine diet and time effects on macronutrients, fatty acids, sugar, fiber, cholesterol, plasma lipids, body composition, BP, glucose, insulin, inflammatory cytokines, and adiponectin. Each individual's response to the intervention over time was the repeated measure (baseline, wk 6, and wk 12) and CRD compared with CRD + AHA, the between-subject factors. A *P*-value of <0.05 was considered significant. The least significant differences test (LSD) was used as a post hoc test when time × diet was significant. SPSS version 13.0 for Windows was used to perform the statistical analyses and the data values are reported as means ± SD.

Results

Diet composition

The typical diet of Emirati people consists of fish, eggs, rice, bread, dates and other fruits, yogurt, vegetables (including tomato, carrots, green leafy vegetables, and others), and wheat flour that is used to prepare desserts and meat wraps. They had no difficulty adapting to the CRD, which was followed by eliminating the rice and bread from their diets and reducing the intake of yogurt and milk and consuming only 1 fruit per day to comply with 25% of energy from carbohydrate.

Results from dietary analysis of the habitual intake and intervention diets are presented in **Table 1**. Total energy intake was reduced by 37% for both dietary groups and the groups did not differ even at the end of the study when participants were following 2 different diets. Percent energy from carbohydrate was reduced ($P < 0.01$) from baseline to wk 1 and 6, because all the participants were consuming the CRD at wk 6. Similarly, at 6 wk, increases in the percent of energy from fat ($P < 0.001$) and protein ($P < 0.0001$) were observed when all participants were consuming the CRD diet (Table 1). As designed, when participants ($n = 19$) changed to the CRD + AHA diet, there were significant differences in percent of energy from macronutrients. At 12 wk, participants ($n = 20$) who continued consuming the CRD had lower energy intake from carbohydrate ($P < 0.01$) and higher energy intake from protein ($P < 0.01$) and fat ($P < 0.01$) than the CRD + AHA group (Table 1). Dietary fiber intake was reduced over time from 37 to 26% in both groups from baseline, with no significant difference between the 2 groups (Table 1) ($P < 0.0001$). Total sugar intake was significantly reduced over time at wk 6 for all participants consuming the CRD. However, at wk 12, the CRD + AHA group consumed significantly more total sugar (113.6 ± 26.4 g) compared with the CRD group (88.7 ± 20.9 g). Added sugar was reduced over time in both groups from baseline to wk 6 and 12, with no differences between groups indicating dietary compliance in volunteers from the CRD + AHA group. Dietary cholesterol did not change between baseline and wk 6 when all participants were consuming the CRD. The CRD + AHA group decreased cholesterol intake as prescribed and dietary cholesterol intake was less than in the CRD group at wk 12 ($P < 0.05$).

TABLE 1 Dietary intake of participants consuming a carbohydrate restricted diet for 12 wk (CRD) or a CRD diet for 6 wk and AHA diet for 6 wk (CRD + AHA)[1]

Variable	Habitual	Wk 1	Wk 6	Wk 12	*P*-value (time effect)
Total energy, *kJ/d*					
CRD	19061 ± 459	12099 ± 3921	10929 ± 2544	10740 ± 2452	<0.0001
CRD + AHA	18194 ± 6454	10257 ± 2914	10057 ± 2080	10075 ± 2180	
Carbohydrate, *%en*					
CRD	51.9 ± 5.2	22.7 ± 3.1	23.5 ± 2.5	24.9 ± 2.3*	<0.0001
CRD + AHA	52.5 ± 8.8	24.1 ± 3.0	23.4 ± 2.8	52.5 ± 2.3	
Fat, *%en*					
CRD	34.7 ± 5.2	53.1 ± 5.1	50.5 ± 3.7	48.3 ± 3.6*	<0.0001
CRD + AHA	35.4 ± 7.5	51.0 ± 3.5	46.8 ± 7.2	28.8 ± 1.9	
Protein, *%en*					
CRD	14.5 ± 2.9	26.4 ± 2.9	27.2 ± 2.7	27.9 ± 2.7*	<0.0001
CRD + AHA	14.9 ± 2.5	26.9 ± 3.0	28.3 ± 2.3	18.8 ± 2.0	
Dietary fiber, *g/d*					
CRD	36.9 ± 15.7	29.1 ± 9.0	25.1 ± 6.3	25.1 ± 5.6	<0.0001
CRD + AHA	38.3 ± 17.7	27.5 ± 10.0	23.0 ± 7.2	28.8 ± 7.7	
Dietary fiber, *g/d*					
CRD	36.9 ± 15.7	29.1 ± 9.0	25.1 ± 6.3	25.1 ± 5.6	<0.0001
CRD + AHA	38.3 ± 17.7	27.5 ± 10.0	23.0 ± 7.2	28.8 ± 7.7	
Total sugar, *g/d*					
CRD	224.3 ± 81.8	84.2 ± 15.8	79.0 ± 24.0	88.7 ± 20.9*	<0.001
CRD + AHA	196.6 ± 69.4	78.0 ± 21.8	80.2 ± 13.4	113.6 ± 26.4	
Cholesterol, *mg/d*					
CRD	665 ± 276	904 ± 302	905 ± 170	882 ± 236*	<0.0001
CRD + AHA	740 ± 428	761 ± 280	714 ± 175	377 ± 198	

[1] Values are means ± SD, *n* = 20 (CRD) or 19 (CRD + AHA). Data were analyzed using repeated-measures ANOVA. The LSD test was used when time × diet was significant, $P < 0.05$. *Different from CRD + AHA, $P < 0.001$.

There was a decrease ($P < 0.0001$) in the absolute amount of dietary carbohydrate when all participants were consuming the CRD from an initial 570 g/d to 150 g/d at wk 6 for all participants (**Fig. 1**). Although the actual consumption of carbohydrate differed between the CRD and CRD + AHA groups at wk 12 ($P < 0.01$), the CRD + AHA group was still consuming 43% less carbohydrate than at baseline (326 g/d compared with 567 g/d). Despite the increment in the percent of energy from fat in the CRD group, the absolute fat intake was reduced significantly. At baseline, fat intake was 172 g and was reduced to 141 g at wk 6 for all participants. However, the intake of fat at wk 12 differed, with the CRD group consuming 139 g/d and the CRD + AHA group 79 g/d ($P < 0.01$) (Fig. 1). The intake of protein for both groups tended to increase ($P = 0.058$) from baseline to 6 wk for all participants from 161 to 176 g/d. At the end of the intervention (12 wk) and after the change in diet for the CRD + AHA group, protein intake was 177 g/d for the CRD group and 112 g/d for the CRD + AHA group ($P < 0.01$) (Fig. 1).

There was a 25% increase in the percent of saturated fat from baseline to wk 6 in both groups (**Table 2**). However, there was a decrease in the CRD + AHA group at wk 12 compared with baseline or to the CRD group ($P < 0.01$). There was a 47% increase in the intake of monounsaturated fat as a percent of total energy for both groups compared with baseline ($P < 0.001$). Monounsaturated fat intake did not differ between the CRD and CRD + AHA groups at wk 12 (Table 2). There was a 15% increase in energy from PUFA over time ($P < 0.001$). However, the CRD + AHA group consumed less energy as PUFA at wk 12 ($P < 0.01$). Despite the increment in the percentage of energy from fat in the CRD group, absolute saturated, monounsaturated, and polyunsaturated fat intakes were less than at baseline in both the CRD + AHA and the CRD groups ($P < 0.001$). The intakes of SFA, monounsaturated fatty acids, and PUFA at wk 12 were lower in the CRD + AHA group than in the CRD group ($P < 0.001$).

Clinical measures

Anthropometrics, body composition, and BP. Participants in the CRD group lost 8.4% of body weight from baseline to 12 wk compared with the CRD + AHA group, who lost 5.9% of body weight (**Table 3**). Furthermore, BMI was reduced in both the CRD and the CRD + AHA groups ($P < 0.001$) (Table 3). Both body weight and BMI differed between groups at the end of the intervention.

Both groups experienced significant reduction from baseline in WC. We analyzed the data for men and women separately, because this is one of the characteristics of MetS that varies with gender. Both men and women had significant reductions in WC from baseline at wk 6 and 12, independent of dietary group (Table 3). Similarly, both groups experienced reductions in body fat and trunk fat ($P < 0.0001$). These variables did not differ between the groups. Systolic and diastolic BP were reduced significantly over time, with no differences between groups.

There were no changes in serum electrolytes or creatinine over time or between groups (data not shown). However, serum urea concentrations increased from 3.94 ± 1.49 mmol/L at baseline to 5.15 ± 2.19 mmol/L at wk 6 for all participants. However, values were still within normal ranges according to Tawam Hospital guidelines (normal range, 2.5–6.7 mmol/L). At wk 12, urea concentrations did not differ between the CRD (4.2 ± 1.8 mmol/L) and CRD + AHA (4.3 ± 1.8 mmol/L) groups,

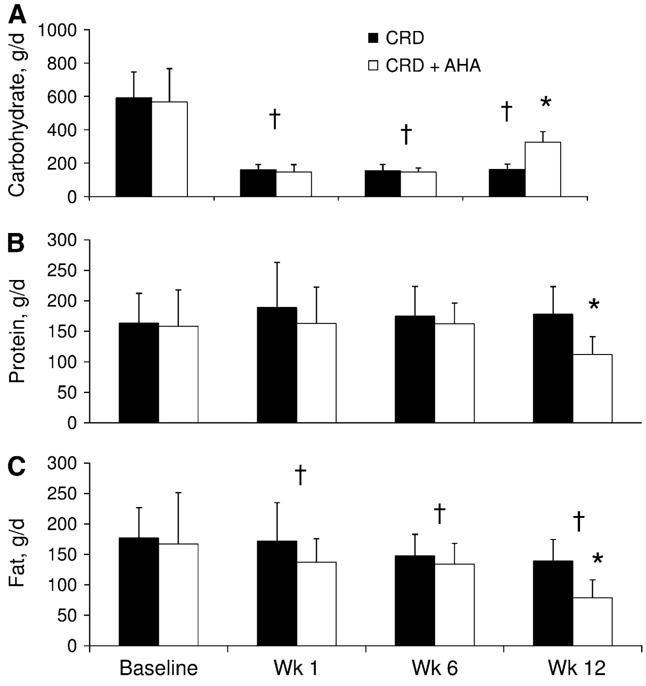

FIGURE 1 Intakes of carbohydrate, fat, and protein from baseline to 12 wk in participants following the CRD and participants consuming the CRD + AHA diet (CRD for 6 wk and AHA for 6 wk). Values are means ± SD, *n* = 20 (CRD) or 19 (CRD + AHA). †Different from baseline, $P < 0.0001$; *different from CRD, $P = 0.01$.

indicating that plasma urea concentrations returned to baseline in the CRD group.

Plasma lipids and glucose, insulin, and HOMA. From baseline to wk 12, the CRD group as well as the CRD + AHA group had significant reductions in TC (−6.6%, −3.7%) and LDL-C (−5.3%, −2.6%), respectively, without differences between groups (**Table 4**). However, the decrease in plasma TG was greater in the CRD group (−27.6%) compared with the CRD + AHA group (−20.1%). Because the NCEP ATP III guidelines for HDL-C differ between men and women, we analyzed these data separately. Compared with baseline, HDL-C had not changed at wk 6 or 12 in men or women in either group (Table 4).

Plasma glucose was reduced from baseline to wk 12 in the CRD and CRD + AHA groups with no difference between groups. In contrast, plasma insulin was reduced more in the CRD group (−30.9%) compared with the CRD + AHA group (−10.7%) (Table 4). Results for insulin resistance as measured by HOMA were similar (data not shown).

Although both dietary interventions improved insulin resistance and characteristics of MetS, CRD reduced body weight, TG, and insulin more than CRD + AHA. After 6 wk of consuming the CRD, 38 individuals had a decrease in WC, 36 had a reduction in plasma TG, 30 had a reduction in systolic BP, and 29 had reduced blood glucose (**Fig. 2**). HDL cholesterol increased only in 16 participants; 15 had a reduction whereas 7 had no change (data not shown).

MetS status. At wk 6, 31% of the participants (7 mean and 5 women) classified with MetS remained while only 15% participants (4 men and 2 women) remained with this classification at wk 12. These results show the effectiveness of both diets in decreasing the markers of MetS.

Inflammation markers. Plasma adiponectin increased relative to baseline in both groups at wk 6 and this increase continued to wk 12 ($P < 0.05$) without a difference between the groups (**Table 5**).

Plasma CRP, TNFα, ICAM-1, and MCP-1 were reduced ($P < 0.01$) both at wk 6 when all participants were consuming the CRD and at wk 12, with no difference between groups (Table 5).

TABLE 2 SFA, monounsaturated fatty acid, and PUFA intakes as % energy and g/d of participants consuming a CRD for 12 wk (CRD group) or a CRD diet for 6 wk and AHA diet for 6 wk (CRD + AHA group)[1]

Variable	Habitual	Wk 1	Wk 6	Wk 12	*P*-value (time effect)
SFA,[2] *%en*					
CRD	10.8 ± 2.5	14.1 ± 2.7	14.6 ± 2.6	13.9 ± 2.3*	<0.0001
CRD + AHA	10.5 ± 2.9	14.7 ± 2.6	13.6 ± 2.7	8.5 ± 1.3	
Monounsaturated fatty acids, *%en*					
CRD	12.6 ± 3.4	23.2 ± 4.6	21.5 ± 2.9	21.4 ± 3.3	<0.0001
CRD + AHA	12.3 ± 3.6	22.6 ± 2.6	19.2 ± 5.3	18.1 ± 5.5	
PUFA, *%en*					
CRD	8.6 ± 2.9	11.8 ± 4.2	10.7 ± 3.4	9.3 ± 3.8*	<0.0001
CRD + AHA	8.3 ± 3.2	9.9 ± 2.9	10.1 ± 3.0	7.5 ± 1.7	
SFA, *g/d*					
CRD	54.8 ± 16.6	46.1 ± 23.7	41.7 ± 8.5	40.1 ± 12.4*	<0.0001
CRD + AHA	50.6 ± 24.1	39.3 ± 10.3	36.5 ± 7.7	23.1 ± 6.1	
Monounsaturated fatty acids, *g/d*					
CRD	64.4 ± 22.1	75.3 ± 29.9	63.6 ± 18.0	61.4 ± 17.1*	<0.0001
CRD + AHA	61.8 ± 39.7	60.3 ± 17.0	58.7 ± 17.1	28.8 ± 8.7	
PUFA, *g/d*					
CRD	44.6 ± 18.6	37.8 ± 18.6	31.7 ± 14.5	26.9 ± 13.9*	<0.0001
CRD + AHA	41.4 ± 22.9	27.7 ± 13.1	28.8 ± 12.6	20.6 ± 6.4	

[1] Values are means ± SD, *n* = 20 (CRD) or 19 (CRD + AHA). Data were analyzed using repeated-measures ANOVA. The LSD test was used when time × diet was significant. *Different from CRD + AHA, $P < 0.001$.

TABLE 3 Body weight, WC, body composition, and BP of participants consuming a CRD for 12 wk (CRD group) or a CRD diet for 6 wk and AHA diet for 6 wk (CRD + AHA group)[1]

Variable	Baseline	Wk 6	Wk 12	*P*-value (time effect)
Body weight, *kg*[2]				
CRD	102.8 ± 24.2	97.2 ± 23.4	94.2 ± 23.3*	<0.00001
CRD + AHA	91.4 ± 20.0	87.0 ± 18.7	86.0 ± 18.5	
BMI, kg/m^2				
CRD	38.7 ± 7.6	36.1 ± 6.4	35.0 ± 6.6*	<0.0001
CRD + AHA	33.5 ± 6.0	31.8 ± 5.9	31.5 ± 5.8	
WC, *cm*				
Men (*n* = 14)				
CRD	117.1 ± 9.8	109.0 ± 13.3	106.4 ± 13.1	<0.0001
CRD + AHA	111.7 ± 14.5	106.2 ± 14.8	104.9 ± 15.7	
Women (*n* = 25)				
CRD	104.9 ± 7.7	100.8 ± 8.1	98.1 ± 8.2	<0.0001
CRD + AHA	100.1 ± 11.6	96.5 ± 10.9	95.0 ± 10.4	
Body fat, *kg*				
CRD	46.2 ± 8.6	42.7 ± 8.7	40.7 ± 8.9	<0.0001
CRD + AHA	39.3 ± 8.36	36.5 ± 9.1	35.1 ± 9.2	
Trunk fat, *kg*				
CRD	22.4 ± 6.7	19.8 ± 4.8	18.5 ± 4.5	<0.0001
CRD + AHA	20.0 ± 3.3	17.3 ± 3.5	16.6 ± 3.5	
Systolic BP, *mm Hg*				
CRD	137.7 ± 9.0	126.2 ± 5.3	124.3 ± 6.5	<0.0001
CRD +AHA	137.6 ± 16.7	125.9 ± 11.4	124.6 ± 4.8	
Diastolic BP, *mm Hg*				
CRD	84.8 ± 10.3	79.8 ± 12.9	77.3 ± 5.3	<0.001
CRD + AHA	85.2 ± 9.5	78.6 ± 7.6	75.8 ± 6.6	

[1] Values are means ± SD, *n* = 20 (CRD) or 19 (CRD + AHA). Data were analyzed using repeated-measures ANOVA. The LSD test was used when time × diet was significant. *Different from CRD + AHA, $P < 0.001$.

In contrast, IL-6 was unchanged throughout the intervention (Table 5).

Discussion

In this study, we demonstrated that using CRD as a first line of therapy to improve the clinical markers of the MetS and to decrease inflammation was effective in a population of Emirati adults. We also demonstrated that a lower fat intervention with lower carbohydrate intake than their habitual diet maintained the positive effects of a CRD on MetS features and the inflammatory response in this population.

Effect of the dietary intervention on the parameters of MetS. The initial dietary intervention approach among Emirati adults produced considerable improvements in the clinical markers of MetS. Further, as assessed by dietary records, all participants adhered with their dietary plan. During the first phase of the dietary treatment when CRD was introduced to all participants, there were no specific instructions regarding energy restriction, yet energy intake was significantly reduced from baseline to wk 6 by ~37%. The reduction in energy intake resulted in body weight reduction consistent with results from other studies using CRD (14,24,25).

At wk 6, 20 participants continued with CRD and 19 were instructed to follow the conventional CRD + AHA diet by changing the macronutrient composition of the diet without changing the caloric intake achieved at wk 6. By the end of wk 12, a high compliance with the dietary guidelines was observed in both groups. With the continuous reduction in energy intake, the CRD group experienced an overall 8.4% decrease in body weight, whereas the CRD + AHA group experienced a lower, yet significant, 5.9% reduction in body weight. It has been reported that CRD is excellent for weight loss, especially during short periods of time, compared with other conventional diets (14,15). Some researchers argue that increased weight loss with CRD could be due to ketosis. However, the amount of carbohydrate prescribed in this study was not restricted enough to produce ketosis (as confirmed by use of ketone kits). Samaha et al. (12) reported that CRD resulted in greater weight loss than did a low-fat diet over a period of 6 mo. Yet this was suggested to be due to a greater reduction in overall energy intake with CRD. However, in our study, both groups consumed a similar amount of energy at wk 12; thus, energy intake cannot be related to the extent of weight loss in participants consuming the CRD. Data from other studies detected greater weight loss with a CRD compared with low-fat diets despite similar energy intake among groups (26,27). Accordingly, the macronutrient distribution, mainly the increment in carbohydrate intake among CRD + AHA dieters, may have played a role in the efficiency of weight loss.

Efficacy of weight reduction diets is evaluated through the power of reducing body fat, particularly abdominal fat. Participants from both groups experienced significant losses of body fat and, most importantly, of abdominal fat, which is a major determinant of MetS (28). The loss of abdominal fat was associated with great reductions in WC and was similar in both groups. These results were expected, because the CRD used in this study is not a ketogenic diet (<100 g carbohydrate), which would be expected to increase the demand for gluconeogenesis because of the low energy and carbohydrate availability and thus increase the loss of body fat mass (29). Buchholz and Schoeller (30) averaged results from 10 studies of low-carbohydrate, but

TABLE 4 Plasma TC, LDL-C, HDL-C, and glucose of participants consuming a CRD for 12 wk (CRD) or a CRD diet for 6 wk and AHA diet for 6 wk (CRD + AHA)[1]

Variable	Baseline	Wk 6	Wk 12	*P*-value (time effect)
TC, *mmol/L*				
CRD	5.73 ± 1.11	5.44 ± 1.04	5.35 ± 1.10	<0.001
CRD + AHA	5.96 ± 1.01	6.08 ± 1.09	5.74 ± 0.99	
LDL-C, *mmol/L*				
CRD	4.18 ± 0.91	4.09 ± 0.93	3.96 ± 0.98	<0.05
AHA	4.19 ± 0.84	4.53 ± 0.98	4.08 ± 0.89	
HDL-C, *mmol/L*				
Men, *n* = 14				
CRD	0.83 ± 0.13	0.82 ± 0.15	0.89 ± 0.13	NS[2]
AHA	1.00 ± 0.14	1.01 ± 0.19	0.97 ± 0.21	
Women, *n* = 25				
CRD	1.05 ± 0.16	1.03 ± 0.13	1.00 ± 0.16	NS
AHA	1.12 ± 0.26	1.30 ± 0.26	1.16 ± 0.15	
TG, *mmol/L*				
CRD	1.23 ± 0.68	0.84 ± 0.44	0.89 ± 0.56*	<0.0001
AHA	1.59 ± 0.76	0.84 ± 0.44	1.27 ± 0.67	
Glucose, *mmol/L*				
CRD	5.60 ± 0.63	5.05 ± 0.61	4.79 ± 1.15	<0.001
AHA	5.54 ± 0.50	5.00 ± 0.87	4.97 ± 0.52	
Insulin, *mmol/L*				
CRD	114.4 ± 59.8	92.2 ± 44.2	79.1 ± 38.6*	<0.001
AHA	84.0 ± 37.6	71.1 ± 38.6	75.0 ± 40.8	
HOMA				
CRD	2.89 ± 1.44	2.04 ± 1.08	1.61 ± 0.88*	<0.001
AHA	2.03 ± 0.94	1.61 ± 1.00	1.63 ± 0.89	

[1] Values are means ± SD, $n = 20$ (CRD) or 19 (CRD + AHA). Data were analyzed using repeated-measures ANOVA. The LSD test was used when time × diet was significant. *Different from CRD + AHA, $P < 0.001$.

[2] NS, Nonsignificant, $P > 0.05$.

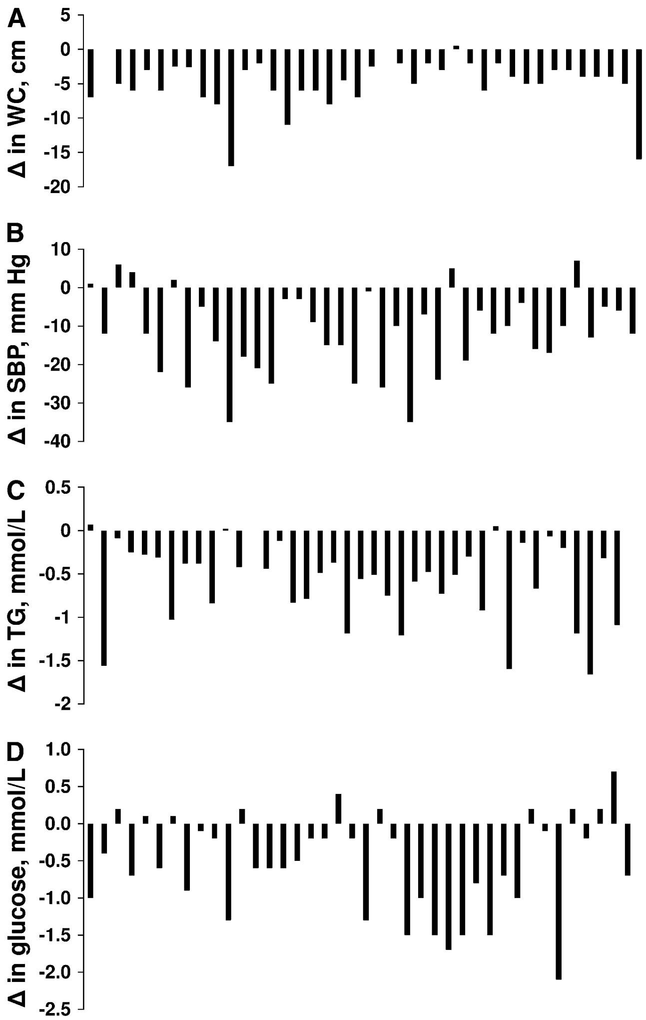

FIGURE 2 Individual changes in WC (*A*), systolic BP (*B*), plasma TG (*C*), and plasma glucose (*D*) after 6 wk of participants ($n = 39$) consuming the CRD. Bars are organized to represent the same participant for the 4 measured parameters.

not ketogenic, diets and reported no effect on 24-h energy expenditure. This result was supported by Brehm et al. (31), who reported no differences in estimated total energy expenditure between groups that consumed a CRD or low-fat diet, especially if the CRD used was not a ketogenic diet.

Lower insulin concentrations promote free fatty acids mobilization from body fat storage (32). When healthy, normal-weight men consumed a CRD consisting of 8% energy from carbohydrate (46 g/d), insulin was significantly reduced and this was positively correlated with reductions in body fat mass (33). However, we did not detect further reduction in body fat mass in the CRD group despite the lower plasma insulin compared with the CRD + AHA group. Again, this could be due to the ketogenic diet used in this particular study (33).

Prior studies have indicated that CRD consistently reduce fasting TG and increase HDL-C compared with a low-fat diet (11–16). The main reason behind using a CRD as an initial dietary intervention was to correct low HDL-C and reduce high TG associated with MetS. This was partially accomplished as demonstrated by the reduction in plasma TG with a greater reduction in the CRD group. It has been reported that CRD increases HDL-C concentration compared with conventional diets (16). Nevertheless, our results show that HDL-C remained constant for all participants over time. This is consistent with previous findings by Sharman et al. (34), who reported no change in serum HDL-C with both low-fat and very low-carbohydrate hypoenergetic diets among overweight healthy men. It is unknown why HDL-C remained unchanged in this population. It could be due to genetic predisposition to low HDL-C despite dietary interventions.

Most health practitioners are cautious with the use of CRD due to possible adverse effects on blood lipids (35). Our data do not support such concerns, because significant reductions in TC as well as LDL-C concentrations were observed consistent with previous studies (17,35). Despite the higher intake of dietary cholesterol, there was no effect on plasma TC or LDL-C concentration in either group. Results from our laboratory have shown that dietary cholesterol did not affect atherogenic LDL particles, independent of response classification (36). The reduction in TC and LDL-C may be explained by the reduction in absolute intake of saturated fat (10) during the intervention. Despite the increment in the percentage of fat intake, actual mean intake in g/d decreased from baseline by ~22% (36 g fat reduction) in the CRD group and by ∼53% (89 g fat reduction) in the CRD + AHA group. Saturated fat was also reduced by 28 and 54% in CRD and CRD + AHA consumers, respectively. Another dietary factor that might have contributed to the lowering of LDL-C is the high amount of dietary fiber consumed by Emirati participants (37). Consistent with previous studies (38), weight loss had a great impact in reducing serum LDL-C. Both groups in our study experienced a significant reduction in weight by wk 12.

TABLE 5 HOMA and plasma adiponectin, CRP, sICAM, TNFα, and IL-6 of participants consuming a CRD for 12 wk (CRD group) or a CRD diet for 6wk and AHA diet for 6 wk (CRD + AHA group)[1]

Variable	Baseline	Wk 6	Wk 12	*P*-value (time effect)
Adiponectin, *mg/L*				
CRD	9.53 ± 4.15	10.71 ± 4.35	10.29 ± 4.08	<0.05
AHA	9.63 ± 4.86	11.17 ± 3.64	11.21 ± 4.23	
CRP, *mg/L*				
CRD	6.4 ± 4.5	6.1 ± 4.5	5.9 ± 4.3	<0.05
AHA	6.4 ± 5.4	4.4 ± 5.8	4.5 ± 5.6	
TNFα, *mg/L*				
CRD	6.1 ± 3.8	5.1 ± 3.8	4.7 ± 3.5	<0.05
AHA	10.1 ± 7.4	9.7 ± 6.8	9.2 ± 5.9	
Il-6, *pg/L*				
CRD	2.77 ± 1.69	2.66 ± 2.09	2.77 ± 2.23	NS[2]
AHA	1.98 ± 1.25	1.89 ± 1.33	1.82 ± 1.02	
ICAM-1, *mg/L*				
CRD	0.13 ± 0.04	0.11 ± 0.03	0.11 ± 0.05	<0.05
AHA	0.13 ± 0.04	0.10 ± 0.04	0.11 ± 0.03	
MPC-1, *μg/L*				
CRD	161.7 ± 83.1	150.6 ± 77.5	155.0 ± 68.0	<0.05
AHA	224.3 ± 88.8	200.9 ± 71.7	203.5 ± 76.9	

[1] Values are means ± SD, $n = 20$ (CRD) or 19 (CRD + AHA). Data were analyzed using repeated-measures ANOVA. There were no group or interactions effects.

[2] NS, Nonsignificant, $P > 0.05$.

The accumulated evidence indicates that insulin resistance is an important pathogenic factor for MetS (1). Our results show that HOMA was reduced over time in both groups, although more so for the CRD group. Our laboratory has reported a similar effect of CRD on insulin resistance in overweight men (25,33).

Effect of the dietary intervention on inflammation markers. Several studies showed that the sensitive marker of systemic inflammation, CRP, is released by the liver in response to inflammation associated with obesity and MetS (39). CRP has also been considered a strong clinical marker of CVD (21). On the other hand, TNFα and IL-6 are mostly produced by the adipose tissue and mainly regulate CRP production. Both TNFα and IL-6 have been linked to CVD (40). In our study, both CRP and TNFα were significantly reduced over time in both groups. The reductions in body weight and body fat mass may have improved plasma levels of inflammatory biomarkers in all participants. These results are consistent with previous reports (41).

In contrast, IL-6 did not change from baseline to wk 12 in either group. This was an unexpected result, because IL-6 has often been reduced following a weight loss (42). Ziccardi et al. (43) studied a multidisciplinary program, which included diet, exercise, and behavioral counseling, designed for weight loss in 56 healthy obese women. After 1 y, women lost at least 10% of their initial body weight and experienced a significant reduction in IL-6. However, IL-6 reduction could have been due to either diet or exercise. Other studies with much greater weight loss have shown no change in IL-6 (44). In studies utilizing either CRD or low-fat diets, there were no changes in IL-6 despite weight loss (45). There are also other factors that can elevate circulating IL-6, such as psychological stress (46).

Obesity is positively associated with disturbed endothelial function (47). Impaired endothelial function can be assessed by measuring the level of molecules secreted by the endothelium, such as sICAM1. Evidence shows that these molecules decrease after weight loss (48). In our study, participants in both groups experienced a significant reduction in sICAM-1 following 6 wk of CRD. This reduction persisted for both groups at the end of the intervention, possibly due to the decreased body weight.

Adipocytokines, including adiponectin and MCP-1, are produced by adipose tissue. Adiponectin decreases with obesity, whereas MCP-1 increases. Both have been shown to contribute to insulin resistance (49,50). A recent study by Madsen et al. (51) on the effect of weight loss bariatric surgery on obese women reported the need for >10% of weight loss to effectively improve adiponectin levels. The study did not refer to any type of diet or sport program during the 3-y period. Nevertheless, the current study shows a significant increment in adiponectin with <10% weight loss. Participants also significantly reduced their MCP-1 concentration. There are limited dietary intervention studies on the effect of CRD and low-fat on adiponectin and MCP-1. Thus, we suggest that weight reduction especially in the abdominal area produced by either diet improved circulating levels of adiponectin and MCP-1.

Our study demonstrates that a short term of carbohydrate restriction followed by a low-fat diet was effective in improving clinical markers of MetS over a 12-wk period. However, CRD was more effective at improving MetS characteristics, including body weight, fasting serum TG, and insulin resistance. It is also important to note that those participants consuming the CRD + AHA diet for 6 additional weeks were consuming 43% less carbohydrate in g/d compared with baseline and this may have contributed to the sustained improvements achieved with the initial CRD in some of the markers of MetS. Thus, in principle, a moderate restriction in carbohydrate with limitation in saturated fat appears to be safe and beneficial for Emirati individuals with MetS.

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