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CLINICAL RESEARCH

Short-Term Carbohydrate-Restricted Diet for Weight Loss in Severely Obese Women

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Abstract
Background Weight loss in bariatric pre-surgery period reduces surgical complications, surgery time, blood loss, and length of hospital stay. Carbohydrate-restricted diets have been used as an alternative for weight loss. We tested the efficacy of a low-calorie carbohydrate-restricted diet (RD) for short-term weight loss in women with severe obesity and evaluate its metabolic effects in relation to a conventional low-calorie diet (CD).
Methods The subjects received a 1,200-kcal diet with or without carbohydrate restriction for a period of 1 week in the hospital. Nineteen obesity class III women were distributed into two groups: experimental (n=10) and control (n=9). The following variables were assessed at the beginning and end of the study: anthropometric measurements, body composition, resting energy expenditure, substrate oxidation, and biochemical tests.
Results Compared with CD, RD led to larger weight loss (2.6 and 4.4 kg, respectively; p=0.01) and waist circumference reduction (p<0.01). Among the assessed biochemical indicators, only plasma and urine acetone levels were different (p<0.01); higher values were found in the experimental group with no symptoms and other diet-related complaints. There was also a significant decrease in triglycerides and carbohydrate oxidation, as well as a significant enhancement in lipid oxidation in the RD group.
Conclusion Short-term RD was more efficient than CD regarding quick weight loss and waist circumference reduction, which may favor gastroplasty. Also, RD did not lead adverse metabolic effects.

Keywords Low-carbohydrate diet · Weight loss · Ketosis · Morbid obesity

Abbreviations

RD	low-calorie carbohydrate-restricted diet
CD	conventional low-calorie diet
HCFMRP-USP	Clinical Hospital, School of Medicine of Ribeirão Preto, University of São Paulo
BMI	body mass index
AC	arm circumference
WC	waist circumference in the navel
WC1	waist circumference 10 cm above the WC
WC2	waist circumference 20 cm above the WC
HOMA-IR	homeostasis model assessment-insulin resistance
SD	standard deviation
REE	resting energy expenditure
FM	fat mass
LM	lean mass
RQ	respiratory quotient
TEV	total energy value

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Introduction

Obesity, which is currently considered a severe health problem, affects 400 million adults worldwide [1, 2]. In Brazil, the latest estimates reveal a prevalence of 40% overweight and obese individuals in the adult population [3]. In 2003, approximately 606,000 Brazilian adults were estimated to be morbidly obese [4].

Known as a chronic multifactorial disease with genetic basis, class III obesity or severe obesity is caused by excess fat tissue accumulation and leads to many serious comorbidities [5, 6]. Treatment of this condition is of utmost importance.

The conservative treatment for obesity comprises the combination of a low-calorie diet therapy with increased physical activity and nutritional education. The unsuccessful outcome of these measures in the morbidly obese and even the difficulty in maintaining weight loss when the treatment is efficacious reinforce the need for alternative therapeutic approaches that favor the desired energy balance. These strategies consist mainly in pharmacotherapy and obesity surgery [7].

Between 2000 and 2006 in Brazil, there was a sevenfold rise in the number of bariatric surgeries performed by the Brazilian Public Health System, known as Unified Health System. Indeed, the number of such surgical procedures increased from 353 to 2528 in the above mentioned period [4]. The main objective of bariatric surgery is to achieve substantial reduction in weight and comorbidities along with significant improvement in the patient's quality of life [8].

A 10-15% weight loss prior to surgery can significantly decrease the risk of respiratory or cardiovascular complications in the obese with obstructive sleep apnea [9]. Various studies have demonstrated that a 10% weight loss preoperatively has such beneficial effects as shorter surgery time, fewer complications, less blood loss, shorter length of hospital stay, and marked improvement in long-term weight loss [10–12]. A large number of surgeons have included this preoperative weight loss in the criteria for indication of bariatric surgery. Diets promoting quick weight loss in the pre-surgical period can aid obese patients in satisfying the conditions required for gastroplasty.

Researchers and scientists have long debated on which diet promotes the most satisfactory weight loss and whether such a diet really exists. Low-carbohydrate diets have been used as an alternative for weight loss. Studies have shown that these diets lead to larger weight loss compared with conventional low-fat, low-calorie diets [13, 14].

Special dietary interventions, such as carbohydrate-restricted diets, can be employed as a punctual strategy to stimulate quick initial weight loss. Low-carbohydrate diets with slightly larger protein intake can have beneficial effects on the weight and lipid profile compared with diets involving a high level of carbohydrates, and weight loss can be maintained for 2 years [15]. There are additional benefits like improvement in glycemic control and triglyceride levels, not to mention the advantages associated with weight loss [16, 17].

The present study tested the efficacy of a low-calorie carbohydrate-restricted diet (RD) for short-term weight loss and evaluated its metabolic outcome in class III obesity women. Results were compared with data obtained from morbidly obese females on a conventional low-calorie diet (CD).

Subjects and Methods

Subjects

Twenty obese women were selected for this investigation, one of which dropped out before the end of the study. For inclusion, participants had to be female, have a body mass index (BMI) larger than 40 kg/m^2, and be aged between 20 and 50 years. Exclusion criteria were diabetes mellitus, use of diuretics, and other exclusion criteria for bariatric surgery.

Participants were selected by the Bariatric Surgery Group, which follows patients prior to hospital admission. Selection was aided by the psychologist responsible for the group. Individuals that met the bariatric surgery criteria as well as the inclusion criteria of the present study, between November 2007 and August 2008, were chosen.

This study was approved by the Research Ethics Committee of Clinical Hospital, School of Medicine of Ribeirão Preto, University of São Paulo (HCFMRP-USP), Brazil.

Study Design

This is a prospective experimental study carried out at HCFMRP-USP between December 2007 and September 2008.

Patients were admitted for an 8-day stay in the Metabolic Unit (Nutrology Division) of the above mentioned hospital and followed by the multiprofessional healthcare team of the unit. Participants were divided into two groups, namely experimental and control, and received the experimental or control diet for seven consecutive days. The experimental group received a 1,200 kcal diet with 45 g carbohydrate (15%), 105 g protein (35%), and 67 g lipid (50%), designated RD. The control group was placed on a 1,200-kcal conventional diet composed by 171 g carbohydrate (54%), 74 g protein (23%), and 32 g lipid (23%), designated CD. Both diets were fractionated into six daily meals.

The participants were evaluated at days 1 and 8. All the evaluations were performed at 7 a.m., after night rest and

12-h fasting. A requirement of the study was that the subjects consumed everything they were offered.

A questionnaire for assessment of the diet received during the investigation period was applied in order to verify the acceptance of the diet by the participants and the presence of symptoms associated with it. The questionnaire consisted of two questions. One of the questions assessed diet acceptance by means of a five-score scale varying from very bad to very good. The other question evaluated the presence of the following symptoms: hunger, dizziness, nausea, tiredness, weakness, cephalalgia, intestinal constipation, or any other gastrointestinal symptoms worthy of mention. The questionnaire also offered extra lines for additional comments. Patients were questioned about the existence of symptoms on a daily basis.

Body Measurements and Indirect Calorimetry

Body weight, BMI, circumferences (arm, waist, and hip), electric bioimpedance (lean mass, fat mass, and total body water), and indirect calorimetry (resting energy expenditure and substrate oxidation) were measured at days 1 and 8.

Participants were weighed (in kilogram) in the morning, after fasting and urination, wearing light clothes but no shoes. An electronic platform scale Filizola® with a capacity of 300 Kg and 0.2 Kg precision was employed. The BMI was calculated by dividing the body weight (kilogram) by the square of the height (meter square). A 2-m metallic, non-extendable tape measure with a 0.1 cm precision was used to measure circumferences. Arm circumference (AC) was measured at the midpoint between the olecranon process of the ulna and the acromial process of the scapula. Due to the difficulty in measuring the midpoint between the iliac crest and the last rib, waist circumference was measured at three distinct locations: in the navel (WC), 10 cm above the WC (WC1), and 20 cm above the WC (WC2), with the tape measure placed horizontally. The hip circumference (HC) was obtained in the horizontal plane, around the largest circumference observed at the buttock level.

The corporal composition evaluation method regarded as a gold standard is by DXA (dual energy X-ray absorptiometry), however, since the patients in the study exceeded maximum weight limit (120 kg), the electric bioimpedance method was used instead. Eletric bioimpedance (*Bioeletric Impedance Analysis of Body Composition*) was accomplished using a *Biodynamics* BIA 450 apparatus. After 12-h fasting, the patient was placed in supine position with legs spread apart and parallel arms positioned away from the trunk. A mobile calorimeter *Vmax 29 Sensor Medics*® (Sensor Medics Corporation, Yorba Linda, CA, USA) was employed for indirect calorimetry measurements. To obtain resting energy expenditure (REE) values, in kilocalorie/day, the values of oxygen consumption (Vo_2) and carbon dioxide production (Vco_2) measured by indirect calorimetry were applied to the Weir's formula [18]. The estimated substrate oxidation (glucose and lipid) was calculated from the values of Vo_2 and Vco_2 applied to the formula according to Frayn [19], whereas protein oxidation was calculated according to Schutz [20].

Biochemical Indicators and Assay Methods

Fasting blood samples were collected for analysis of total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, fasting glucose, albumin, total proteins, baseline insulin, plasma acetone, and venous gasometry. Urine (24 h) was also collected at days 1 and 8, to assess urine acetone and nitrogen.

Fasting glucose levels, albumin, and total protein were determined in a multichannel automatic analyzer. Baseline insulin was measured by radioimmunoassay soon after blood sample collection. Concentrations of total cholesterol, triglycerides, and HDL cholesterol were determined by a colorimetric and enzymatic method, and low-density lipoprotein (LDL) cholesterol was calculated by the Friedewald's formula [21]. Resistance to insulin was assessed by the homeostasis model assessment-insulin resistance (HOMA-IR) index [22]. Both plasma and urine acetone were obtained by gas chromatography (GC-2014 Shimadzu Chromatograph), using the headspace technique [23]. The micro-Kjeldahl method [24] was employed for estimation of total nitrogen levels in the urine samples.

Statistical Analysis

Data listed in the tables are presented as the mean and standard deviation (SD). To assess the differences in the variables between the two groups at day 1 (initial time) and within the groups (paired samples), the generalized linear model with random effects (random and fixed effects) was used. This model is applied to data analysis where the variables concerning the same individual are grouped, but the supposition that observations within the same group are independent is not adequate [25]. For this model to be employed, it is necessary that its residues have normal distribution with mean value equal to zero and constant variance. When this requirement was not met, a transformation was employed for the response variable (logarithmic or Box-Cox on data). Model adjustment was accomplished by means of the PROC MIXED procedure of the *software* SAS® 8.0.

To verify the difference in the variables between groups (non-paired samples), the Wilcoxon test was utilized (implemented in the software R) [26], since data did not present normality even after the application of transformations. The significance level was set at 5% ($p<0.05$) for all the analyses.

Table 1 Baseline characteristics of the experimental and control groups

Variable	Experimental group		Control group		*p* value
	n=10		*n*=9		
	Mean	SD	Mean	SD	
Weight (kg)	142.00	26.70	135.80	14.80	0.51
BMI (kg/m^2)	54.40	9.60	51.10	4.70	0.26
FM (kg)	70.30	18.10	65.60	9.30	0.50
LM (kg)	71.70	9.00	70.30	6.00	0.54
Total body water (L)	51.90	7.00	50.60	4.00	0.48
REE (kcal/d)	2,272.00	275.50	2,463.00	431.80	0.18
AC (cm)	45.00	5.70	46.90	3.50	0.29
WC (cm)	139.40	15.10	136.50	10.60	0.60
WC1 (cm)	131.50	13.60	128.50	11.40	0.55
WC2 (cm)	123.50	12.30	121.90	12.50	0.70
HC (cm)	152.70	20.40	143.80	5.60	0.09
Total cholesterol (mg/dl)	182.30	33.80	160.10	35.90	0.07
Triglycerides (mg/dl)	161.20	70.00	124.60	46.70	0.09
HDL cholesterol (mg/dl)	40.30	6.80	39.70	6.70	0.76
LDL cholesterol (mg/dl)	108.90	24.80	95.60	30.90	0.16
Fasting glucose (mg/dl)	88.70	6.00	83.60	8.10	0.11
Albumin (g/dl)	4.20	0.30	4.10	0.20	0.32
Total protein (g/dl)	7.30	0.30	6.70	0.30	0.17
Baseline insulin (μIU/ml)	16.40	11.60	17.30	15.20	0.80
HOMA-IR	3.63	2.66	3.70	3.57	0.60
Plasma acetone (mg/dl)	0.20	0.10	0.20	0.10	0.54
Urine acetone (mg in 24 h)	8.20	10.30	3.70	6.30	0.58

SD standard deviation, *BMI* body mass index, *FM* fat mass, *LM* lean mass, *REE* resting energy expenditure, *AC* arm circumference, *WC* waist circumference, *WC1* waist circumference 10 cm above navel, *WC2* waist circumference 20 cm above navel, *HC* hip circumference. There was no statistical difference ($p<0.05$)

Results

The anthropometric measurements, body composition, biochemical parameters (Table 1), and mean age were similar in both groups. The mean ages in the experimental and control groups were 35 (SD=8) and 32 (SD=8) years, respectively.

A comparison between the two groups in terms of body weight ($p=0.01$), BMI ($p=0.01$), and waist circumferences (WC, WC1, and WC2; $p<0.01$) at days 1 and 8 revealed significant differences. There was a larger reduction in these variables in the experimental group (Table 2) compared with the control. The mean weight loss in the experimental and control groups were 4.4 kg (3.1% of the body weight) and 2.6 kg (1.9% of the body weight), respectively. There were no significant differences between the groups in terms of the variables AC and HC. The fat mass (FM), lean mass (LM), and total water, determined by bioimpedance, were not statistically different in the two groups, either.

Symptoms and other diet-related complaints were not reported during the study period. The diets were considered good or very good by the majority of the participants (80% experimental group and 89% control group). However, on the last day of the investigation and after participants had completed the final questionnaire (concerning the diet received during the study period), most of the subjects in the control group (67%) stated that they felt hungry, in contrast to the experimental group, where 40% reported hunger. No other symptom was reported.

As for biochemical data, only urine and plasma acetone levels were significantly different ($p<0.01$) between the groups, and the RD diet led to a larger increase in these levels compared with CD (Table 3). The remaining biochemical parameters (total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, fasting glucose, albumin, total protein, baseline insulin, and the HOMA-IR index) of the two groups did not differ significantly, although the variables total cholesterol, triglycerides, and fasting glucose decreased in both groups. LDL cholesterol reduced in the experimental group only, without statistical significance.

Analysis of the results within each group (paired samples) showed that only the experimental group presented significantly ($p=0.02$) reduced triglycerides (Table 4).

Venous gasometry revealed normal results in both groups: pH between 7.32 and 7.42, HCO_3 ranging between 24 and 29 mmol/L, and base excess (BE) from 0 to ±4 mmol/L. The experimental group had mean values of pH=7.35, HCO_3=

Table 2 Analysis of anthropometric data of the experimental and control groups at days 1 and 8

Variable	Experimental group (n=10)					Control group (n=9)					p value
	Day 1		Day 8		Mean variation	Day 1		Day 8		Mean variation	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		
Weight (kg)	142.00	26.60	137.50	26.20	−4.40*	135.80	14.80	133.30	14.50	−2.60*	0.01
BMI (kg/m^2)	54.40	9.60	52.70	9.40	−1.70*	51.10	4.70	50.20	4.60	−1.00*	0.01
AC (cm)	44.90	5.70	44.20	5.70	−0.70	46.90	3.50	46.40	3.40	−0.50	0.34
WC (cm)	139.40	15.10	134.90	13.50	−4.60*	136.50	10.60	135.20	10.40	−1.30*	<0.01
WC1 (cm)	131.50	13.60	128.40	14.00	−3.10*	128.50	11.40	127.10	10.90	−1.30*	<0.01
WC2 (cm)	123.50	12.30	120.60	12.20	−2.90*	121.90	12.50	120.70	11.90	−1.10*	<0.01
HC (cm)	152.70	20.40	150.20	20.20	−2.50	143.80	5.60	143.20	5.80	−0.60	0.06
FM (kg)	70.30	18.10	67.80	17.70	−2.50	65.60	9.30	63.90	8.80	−1.70	0.46
LM (kg)	71.70	9.30	69.70	9.20	−1.90	70.30	5.90	69.40	6.10	−0.90	0.13
Water (L)	51.90	7.20	49.20	7.00	−2.70	50.60	4.00	49.90	4.40	−0.70	0.19

SD standard deviation, BMI body mass index, *AC* arm circumference, *WC* waist circumference, *WC1* waist circumference 10 cm above navel, *WC2* waist circumference 20 cm above navel, *HC* hip circumference, *FM* fat mass, *LM* lean mass, *REE* resting energy expenditure

Variation: day 8-day 1

* $p<0.05$, statistically significant difference

26.48, and BE=0.09 at day 1; and pH=7.35, HCO_3=26.42, and BE=0.58 at day 8. The control group presented mean values of pH=7.36, HCO_3=25.69, and BE=0.09 at day 1; and pH=7.34, HCO_3=25.24, and BE=−0.51 at day 8.

The REE of the two groups and within the same group were not statistically different. However, there was a larger mean reduction in the control group (269.70 kcal) compared with the experimental group (51.11 kcal; Table 4).

In the experimental group, there was significant lowering of Vco_2, respiratory quotient (Vco_2/Vo_2), and glucose oxidation, as well as significant enhancement in lipid oxidation. For the control group, there was significant

Table 3 Analysis of the biochemical data of the experimental and control groups at days 1 and 8

Variable	Experimental group					Control group					p value
	n=10					n=9					
	Day 1		Day 8		Mean variation	Day 1		Day 8		Mean variation	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		
Total cholesterol (mg/dL)	182.30	33.80	164.20	29.20	−18.10	160.10	35.90	155.80	30.50	−4.30	0.22
Triglycerides (mg/dL)	161.20**	70.00	116.90**	35.30	−44.30	124.60	46.70	110.90	47.50	−13.70	0.15
HDL cholesterol (mg/dL)	40.30	6.80	40.10	7.00	−0.20	39.70	6.70	37.30	7.30	−2.30	0.17
LDL cholesterol (mg/dL)	108.90	24.80	101.00	26.70	−7.90	95.60	30.90	96.30	24.10	0.80	0.62
Fasting glucose (mg/dL)	88.70	6.00	85.00	7.20	−3.70	83.60	8.10	82.70	7.60	−0.90	0.34
Albumin (g/dL)	4.20	0.30	4.30	0.20	0.10	4.10	0.20	4.20	0.20	0.10	0.49
Total protein (g/dL)	7.30	0.30	7.40	0.40	0.10	6.70	0.30	6.90	0.60	0.20	0.53
Baseline insulin (μIU/mL)	16.40	11.60	15.50	9.40	−0.90	17.30	15.20	20.40	13.80	3.20	0.60
HOMA-IR	3.63	2.66	3.30	2.07	−0.33	3.70	3.57	4.15	3.00	0.45	0.55
Plasma acetone (mg/dL)	0.20	0.10	0.70	0.30	0.60*	0.20	0.10	0.30	0.20	0.10*	<0.01
Urine acetone (mg in 24 h)	8.20	10.30	72.50	49.00	64.30*	3.70	6.30	6.40	9.90	2.80*	<0.01

SD standard deviation

Variation: day 8-day 1

* $p<0.05$, statistically significant difference between groups

** $p<0.05$, statistically significant difference within the groups

Table 4 Variables measured by indirect calorimetry (REE, Vo_2, Vco_2, and RQ) and substrate oxidation prior to and after the diet, in the experimental and control groups

Variable	Experimental group					Control group					*p* value
	n=10					*n*=9					
	Day 1		Day 8		Mean variation	Day 1		Day 8		Mean variation	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		
REE (kcal/Day)	2,272.00	275.50	2,220.90	270.50	−51.11	2,462.90	431.70	2,193.20	419.50	−269.70	0.27
Vo_2 (mL/min)	330.00	40.40	324.50	40.00	−5.50	350.40*	46.60	309.30*	49.00	−41.11	0.09
Vco_2 (mL/min)	251.00*	30.00	238.50*	29.40	−12.50	298.00	114.50	275.10	139.70	−22.89	0.84
Respiratory quotient (RQ)	0.80*	0.03	0.73*	0.03	−0.02	0.83	0.20	0.88	0.40	0.04	0.54
Glucose oxidation (g/day)	78.20*	56.40	17.60*	69.00	−60.60	303.70	576.60	347.20	851.70	43.54	0.60
Lipid oxidation (g/day)	162.60*	34.30	176.70*	37.00	14.08	106.80	185.50	65.30	308.20	−41.50	0.59
Protein oxidation (g/day)	89.10	20.00	98.10	8.20	8.97	62.90	19.40	55.40	13.80	−7.56	0.08

REE resting energy expenditure, *SD* standard deviation

Variation: day 8-day 1

* $p<0.05$, statistically significant difference within the groups

$p<0.05$, there was no statistically significant difference between groups

reduction in Vo_2, without significant alteration in the other parameters (Table 4).

Discussion

The results of the present study demonstrate that patients receiving a low-calorie carbohydrate-restricted diet achieved larger weight loss than those on a conventional low-calorie diet.

Low-carbohydrate diets seem to be effective for weight loss, although this has long been a controversial topic [27]. In some investigations, the majority of which with ad libitum intake diet, have shown larger weight loss at 3 and 6 months in individuals receiving a low-carbohydrate diet [17, 28]. Another study confirmed that there is spontaneous reduction in energy intake with carbohydrate restriction only (5-10% of total energy value) [27]. In the present investigation, which assessed short-term effects, there was significant decrease in the weight of the subjects on RD, compared with CD.

There are evidences that the low-carbohydrate diet results in quick weight loss because of enhanced energy expenditure via ketogenesis [29], or simply by appetite suppression due to high protein content [30]. Researchers believe that this weight loss occurs because of the combination of limited food choice with the satiety promoted by the large amount of protein in the diet [14].

The fact that high protein content is satiating and that ketosis has an anorectic effect can account for suppressed appetite [31]. Protein is more satiating than carbohydrate and fat in the short- and long-term, and it seems to have an effect on thermogenesis, thereby affecting saciety [32].

A 2-year follow-up study compared the use of a low-carbohydrate diet (with ad libitum energy intake but restricted carbohydrate consumption of 20 g for 2 months, followed by a gradual rise to 120 g), a low-fat diet (1,500 kcal/day for women and 1,800 kcal/day for men, 30% fat), and the Mediterranean diet (1,500 kcal/day for women and 1,800 kcal/day for men, 35% fat, hazelnuts, and olive oil as the main source of fat). The authors concluded that the low-carbohydrate diet was more efficient for weight loss (mean of 4.7 kg). However, regarding waist circumference, there was significant reduction in the three groups, with no statistical differences among them [17]. In the present investigation, the significant decrease in the waist circumference measures (WC, WC1, and WC2) in the experimental group indicates that RD has some kind of effect on fat accumulation in the abdominal region, compared with CD.

Authors have reported significantly reduced waist circumference values for the carbohydrate-restricted diet in follow-up studies lasting over 6 months [33]. A 5% decrease in waist circumference (from 130 to 123 cm) and a mean reduction of 4.4 cm were observed in studies using the low-carbohydrate diet [16, 34]. In the present investigation,

1-week energy restriction led to a 3% decrease in waist circumference in the case of the experimental group.

Other authors have associated the weight loss obtained with carbohydrate-restricted diets with water loss, glycogen depletion, and increased ketone secretion into urine [35]. The present investigation revealed a significant rise in plasma and urine acetone for the experimental group. Nevertheless, there were no differences between the two groups in terms of body composition (FM, LM, and water), despite the larger water loss observed in the experimental group.

Some studies evaluating REE before and after weight loss achieved by means of low-calorie diets or obesity surgery have reported a 15-25% reduction in this variable. However, researchers are not certain whether the lower REE is due to decreased fat and fat-free mass or if the metabolically active tissues adapt and use energy more efficiently [36].

There were no significant differences in the REE, determined by indirect calorimetry in the present investigation, of the two groups, so this variable cannot account for weight loss. However, compared with the experimental group (51 kcal), the control group presented larger reduction in REE (270 kcal) at the end of the diet. One possible explanation would be that the control group adapted to the diet more satisfactorily and the fact that the different chemical composition of the RD hindered such adaptation in the case of the experimental group. The short-term use of RD might be beneficial since the experimental group virtually maintained the REE measured at the beginning of the study.

There were no differences between the two groups regarding the respiratory quotient (Vco_2/Vo_2), also determined by indirect calorimetry. Nevertheless, the experimental group presented larger protein oxidation (RQ=0.80) at the beginning and enhanced lipid oxidation at the end (RQ=0.73), according to the reference RQ values for substrate oxidation [18]. There were no changes in the respiratory quotients of the control group at days 1 and 8, and there was larger protein oxidation both at the beginning and end of the experiment (RQ=0.83 and 0.88, respectively). The enhanced lipid oxidation observed for the experimental group at the end of RD can be attributed to the induction of ketogenesis, the mechanism of action of this diet. All the carbohydrates are broken into glucose, which is the preferential metabolic fuel of the body tissues. Excess energy consumption (as protein, lipid, or carbohydrate) results in fat accumulation via lipogenesis. However, low-carbohydrate diets stimulate fat oxidation, using fatty acids and ketone bodies (including acetone) as fuel, to meet energy requirements, thereby inducing weight loss [27, 37].

Lipid oxidation produces ketone bodies, which are the result of short-chain fatty acid cleavage. These ketone bodies can be metabolized for energy production. The level of ketone bodies increases in fasting individuals, where fat oxidation is thereby stimulated to furnish energy [31].

The rise in plasma and urine acetone levels observed for the experimental group can be justified by induction of ketosis upon daily intake of less than 50 g of carbohydrate [38].

Another study has demonstrated that the level of plasma ketone bodies was also higher for the carbohydrate-restricted diet compared with the conventional diet (balanced quantities of macronutrients) up to the eighth week. After this period, there was a decrease in plasma ketone levels, which remained slightly larger than values obtained with the conventional diet until the end of the 24th week [39].

There still is a lot of discussion on the role played by ketone bodies on the mechanisms of weight loss taking place in low-carbohydrate diets. Animal models suggest that circulating ketone bodies have a direct effect on appetite by increasing satiety [31]. In agreement with this suggestion, the present study also showed fewer complaints concerning hunger in the experimental group (40%) compared with the control (67%).

Despite the elevated ketone levels (especially in the urine) detected after follow-up of a carbohydrate-restricted diet, literature reports do not mention any consequent deleterious effects [39]. The same results have been demonstrated in the present investigation, since no ketosis-related symptoms were reported by the participants.

Studies have shown that insulin resistance is reduced with the low-carbohydrate diet, possibly due to the lower glucose availability of the diet [27]. In the present study, three patients on RD presented with hyperinsulinemia at day 1, two of which had reduced insulin levels at day 8. Nevertheless, in the CD group, two patients had hyperinsulinemia at the beginning and no improvement at day 8; a third participant, with no hyperinsulinemia at day 1, presented higher insulin levels at the end of CD.

Analysis of the lipid profile revealed that only triglycerides reduced significantly in the experimental group, in accordance with studies reporting a decrease in triglycerides along with a rise in HDL cholesterol in carbon-restricted diets at 6 and 12 months, compared with the conventional diet [27, 40].

Low-carbohydrate consumption leads to lower glucose levels and, consequently, lower insulin levels, thereby reducing lipoprotein lipase and enhancing hormone-sensitive lipase. This promotes triglyceride hydrolysis and increases the amount of free fatty acids. Elevated free fatty acid levels enhance lipid oxidation, as demonstrated by the RQ value close to 0.7. The free fatty acids are captured by the liver and preferentially deviated from triglyceride esterification to mitochondrial oxidation to acetyl-CoA, resulting in lower triglyceride levels. Acetyl-CoA accumulation, exceeding the capacity of mitochondrial oxidation, produces ketone bodies [41].

Studies have suggested that low-carbohydrate diets and elevated protein levels are responsible for subclinical chronic metabolic acidosis [35], which is in contrast with the results of the present investigation. Indeed, ketosis was not detected in the patients enrolled in this study, as observed from the normality of the results obtained from venous gasometry measurements.

Neither the short nor the long-term consumption of a low-carbohydrate diet results in deleterious metabolic effects, as evidenced by maintenance of adequate glycemic control and relatively low values for conventional cardiovascular risk factors [42]. In the present work, the use of RD for 7 days did not lead to any biochemical alterations either, except for plasma and urine acetone levels; nevertheless, no patients presented with any symptoms related to ketosis.

Indeed, there are studies demonstrating the beneficial effects of the low-carbohydrate diet. An investigation comparing this diet with a conventional one (containing elevated quantity of carbohydrate), for 19 weeks, revealed the cardiac protective effect of the carbohydrate-restricted diet, with enhanced tolerance to global ischemia [43].

Furthermore, the quick weight loss provided by the low-carbohydrate diet has led surgeons to increasingly prescribe it before obesity surgery in order to minimize surgical difficulties and reduce the risk of liver trauma and blood loss [44]. The combination of a carbohydrate-restricted diet with a program of physical activity can safely help patients to achieve weight loss and improve their biochemical profile [29].

The inadequacy of the carbohydrate-restricted diet from a nutritional viewpoint is critical. This diet may be deficient in micronutrients since it restricts the intake of such foods as fruits, grains, and other sources of fiber [35]. However, no energy-restricted diet meets all the nutritional requirements, either. Dietary inadequacy can be tolerated in the short-term so that quick weight loss can be achieved, but for these diets to be maintained they must include the right balance of micronutrients so as to ensure optimal health [45].

Future studies to increase the knowledge about this dietary intervention should be accomplished. A longer follow-up of the metabolic effects of carbohydrate restriction in patients with different levels of obesity should be carried out. It should also be very interesting to look at how diabetics respond to this restrictive diet with their tendency towards central obesity.

In conclusion, the short-term low-calorie carbohydrate-restricted diet is efficient for quick weight loss and reduction of abdominal anthropometric measures of class III obese females, compared with the conventional low-calorie diet, thus favoring bariatric surgery. There are no relevant adverse metabolic effects, even though there is a rise in plasma and urine acetone levels.

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