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Effects of a high-protein/low carbohydrate versus a standard hypocaloric diet on adipocytokine levels and insulin resistance in obese patients along 9 months

Daniel Antonio de Luis *, Olatz Izaola, Rocio Aller, Beatriz de la Fuente, Rosario Bachiller, Enrique Romero

Center of Investigation of Endocrinology and Nutrition, Medicine School and Dept Endocrinology and Nutrition, Hospital Clinico Universitario, University of Valladolid, Valladolid, Spain

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ABSTRACT

Objective: Recent dietary trials and observational studies have focused on the effects of diet on health outcomes such as improvement in levels of surrogate biomarkers. The aim of our study was to examine the changes in weight, adipocytokines levels and insulin resistance after a high-protein/low carbohydrate hypocaloric diet vs. a standard hypocaloric diet during an intervention of 9 months.

Subjects and methods: 331 obese subjects were randomly allocated to one of two diets for a period of 9 months. Diet HP (n = 168) (high-protein hypocaloric diet) consisted in a diet of 1050 cal/day, 33% of carbohydrates, 33% of fats and 34% of proteins. Diet S (n = 163) (standard protein hypocaloric diet) consisted in a diet of 1093 cal/day, 53% carbohydrates, 27%fats, and 20% proteins.

Results: With the diets HP and S, BMI, weight, fat mass, waist circumference, waist-to-hip ratio, systolic blood pressure, total cholesterol, LDL-cholesterol, insulin and HOMA decreased. The decrease at 9 months of (BMI: -2.6 ± 1.3 kg/m^2 vs. -2.1 ± 1.2 kg/m^2:$p < 0.05$), weight (-8.4 ± 4.2 kg vs. -5.0 ± 4.1 kg: $p < 0.05$), fat mass (-5.1 ± 4.1 kg vs. -3.4 ± 4.2 kg: $p < 0.05$), systolic blood pressure (-5.1 ± 7.1 mmHg vs. -3.1 ± 2.1 mmHg: $p < 0.05$), (insulin levels -4.0 ± 4.8 UI/L vs. -2.2 ± 2.4 UI/L; $p < 0.05$) and HOMA (-0.8 ± 1.0 units vs. -0.3 ± 1.0 units; $p < 0.05$) was higher in diet HP than Diet S. With both diets, leptin levels decreased.

Conclusion: A high-protein/low carbohydrate hypocaloric diet shows a higher weight loss, insulin and HOMA-R decreased after 9 months than a standard hypocaloric diet. The improvement in adipokine levels was similar with both diets.

1. Introduction

The prevalence of obesity is increasing worldwide, and there is a growing body of evidence that obesity-associated cardiovascular disease (CVD) morbidity and mortality are also increasing, mediated by increases in the risks for hypertension, type 2 diabetes, insulin resistance, and dyslipidemia (Aranceta, Perez Rodrigo, & Serra Majem, 1998). Recent studies have suggested no major differences between the effects of various dietary approaches, including between low-carbohydrate and low-fat diets on body weight outcomes (Castaneda-Gonzalez, Bacardi Gascon, & Jimenez, 2011; Hu, Mills, Yao, et al., 2012; Nordmann, Nordmann, Briel, et al., 2006). However, other studies have reported that very low-carbohydrate ketogenic diets and the Mediterranean diet are superior to low-fat diets in reducing body weight (Bueno, de Melo, de Oliveira, et al., 2013; Nordmann, Suter-Zimmermann, Bucher, et al., 2011). In terms of the cardiometabolic outcomes, some dietary types have shown more beneficial effects than others. Compared with low-fat diets, low-carbohydrate diets have shown beneficial effects on lipid profile, such as triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) levels (Castaneda-Gonzalez et al., 2011; Hu, Mills, Yao, et al., 2012; Nordmann, Nordmann, Briel, et al., 2006).

Adipose tissue is considered an active secretory organ, sending out and responding to signals that modulate appetite, insulin sensitivity, energy expenditure, inflammation and immunity. Adipocytokines are proteins produced mainly by adipocytes (Matsuda, Shimomura, & Sata, 2002). These molecules have been shown to be involved in the pathogenesis of the metabolic syndrome and cardiovascular disease. Dietary patterns are associated with fluctuations in certain adipokine levels. In a recently published article, the Mediterranean, low-fat, and low carbohydrate diets were associated with decreased levels of leptin, retinol-binding protein 4, and vaspin, whereas adiponectin levels tended to increase throughout the intervention (Bluher, Rudich, Kloting, et al., 2012). Recent dietary trials and observational studies

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* Corresponding author at: Executive Director of Center of Investigation of Endocrinology and Nutrition, Medicine Schooll, Valladolid University, C/Los perales 16 Simancas 47130, Valladolid, Spain. Tel.: +34 983420000; fax: +34 0983423514.
E-mail address: dadluis@yahoo.es (D.A. de Luis).

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have focused on the effects of diet on health outcomes such as improvement in levels of surrogate biomarkers, obesity status, and reduction in the incidence of chronic diseases. Low-carbohydrate diet trials have also been shown to have favorable effects on weight control, cardiovascular parameters, and adipokine levels (Bradley, Spence, Courtney, et al., 2009; Ruth, Port, Shah, et al., 2013), similar to those of the Mediterranean diet (Esposito, Maiorino, Ciotola, et al., 2009; Esposito, Pontillo, Di Palo, et al., 2003; Fragopoulou, Panagiotakos, Pitsavos, et al., 2010; Hermsdorff, Zulet, Abete, et al., 2009; Mantzoros, Williams, Manson, et al., 2006), although the association has been less clear in studies of high-carbohydrate diets (Claessens, van Baak, Monsheimer, et al., 2009; Kasim-Karakas, Tsodikov, Singh, et al., 2006; Kitabchi, McDaniel, Wan, et al., 2013).

The aim of our study was to examine the changes in weight, adipocytokines levels and insulin resistance after a high-protein/low carbohydrate hypocaloric diet vs. a standard hypocaloric diet during an intervention of 9 months.

2. Subjects and methods

2.1. Subjects and procedures

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving patients were approved by the HCUVA ethics committee. A sample of 331 obese non-diabetic outpatients was enrolled in a prospective way. These patients were recruited in a nutrition clinic unit. All participants provided informed consent to a protocol approved by the local ethical review boards. Inclusion criteria were body mass index >30. Exclusion criteria included history of cardiovascular disease or stroke during the previous 24 months, total cholesterol >200 mg/dl, triglycerides >250 mg/dl, blood pressure >140/90 mmHg, fasting plasma glucose >110 mg/dl, as well as the use of metformin, sulphonylurea, thiazolidinedions, insulin, glucocorticoids, antineoplastic agents, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and psychoactive medications.

Basal fasting glucose, c-reactive protein (CRP), insulin, insulin resistance (HOMA-R), total cholesterol, LDL-cholesterol, HDL-cholesterol, plasma triglycerides concentration and adipokines (leptin, adiponectin, resistin and visfatin) levels were measured within the start of the trial and repeated after three months of both dietary intervention. Weight, height, a tetrapolar bioimpedance and blood pressure measures were realized within the start of the trail and repeated 9 months of intervention. These measures were realized at same time of the day (morning).

2.2. Procedure

331 obese subjects were randomly allocated to one of two diets for a period of nine months. Diet HP (n = 168) (high-protein hypocaloric diet) consisted in a diet of 1050 cal/day, 33% of carbohydrates (86.1 g/day), 33% of fats (39.0 g/day) and 34% of proteins (88.6 g/day). The distribution of fats was; 23.5% of saturated fats, 63.8% of monounsaturated fats and 12.6% of polyunsaturated fats. Cholesterol was 215 mg/day, and dietary fiber was 21 g/day. Diet S (n = 163) (standard protein hypocaloric diet) consisted in a diet of 1093 cal/day, 53% carbohydrates (144.3 g/day), 27% fats (32.6 g), and 20% proteins (55.6 g/day). The distribution of fats was; 20.9% of saturated fats, 67.4% of monounsaturated fats and 11.6% of polyunsaturated fats. Cholesterol was 195 mg/day, and dietary fiber was 22 g/day. Consumption of alcohol was not allowed. The exercise program consisted of an aerobic exercise at least 3 times per week (60 min each). The adherence of these diets was assessed each 7 days with a phone call by a dietitian in order to improve compliment of the calorie restriction and macronutrient distribution. National composition food tables were used as reference (Mataix & Mañas, 2003).

2.3. Anthropometric measurements and blood pressure

Blood pressure was measured twice after a 10 minutes rest with a random zero mercury sphygmomanometer, and averaged (Omrom, LA, CA). Body weight was measured to an accuracy of 0.1 Kg and body mass index computed as body weight/(height^2). Waist (narrowest diameter between xiphoid process and iliac crest) and hip (widest diameter over greater trochanters) circumferences to derive waist-to-hip ratio (WHR) were measured, too. Tetrapolar body electrical bioimpedance was used to determine body composition with an accuracy of 50 g (Lukaski & Johnson, 1985). The same investigator measured patients and controls. Precautions taken to insure valid BIA measurements were; no alcohol within 24 hours of taking the test, no exercise or food for four hours before taking the test.

3. Assays

CRP was measured by immunoturbimetry (Roche Diagnostics GmbH, Mannheim, Germany), with a normal range of (0–7 mg/dl) and analytical sensitivity 0.5 mg/dl. Serum total cholesterol and triglyceride concentrations were determined by enzymatic colorimetric assay (Technicon Instruments, Ltd., New York, N.Y., USA), while HDL cholesterol was determined enzymatically in the supernatant after precipitation of other lipoproteins with dextran sulfate–magnesium. LDL cholesterol was calculated using Friedewald formula. Plasma glucose levels were determined by using an automated glucose oxidase method (Glucose analyser 2, Beckman Instruments, Fullerton, California). Insulin was measured by RIA (RIA Diagnostic Corporation, Los Angeles, CA) with a sensitivity of 0.5 mUI/L (normal range 0.5–30 mUI/L) (Duart, Arroyo, & Moreno, 2002), and the homeostasis model assessment for insulin resistance (HOMA) were calculated using these values (Mathews, Hosker, & Rudenski, 1985).

A single blood sample was obtained from each patient in tubes containing ethylenediaminetetraacetic acid (EDTA) in each visit of the study. Plasma samples were obtained after proper centrifugation. Samples were stored at −80 °C until hormone profiling. Plasma hormone levels were evaluated using the multiplex Biorad© 10 plex assay following manufacturer's instructions (Bio-Rad®, Hercules, CA). This system allows for quantitative measurement of different hormones, while consuming a small amount of biological material; resistin, leptin, visfatin and adiponectin. Limits of detection were as follows (pg/ml): leptin (1.8), resistin (1.4), visfatin (1.5) and adiponectin (3.8).

4. Statistical analysis

Sample size was calculated to detect differences over 3 kg in body weight with 90% power and 5% significance (n = 160, in each diet group). The results were expressed as average ± standard deviation. The distribution of variables was analyzed with Kolmogorov–Smirnov test. Quantitative variables with normal distribution were analyzed with a two-tailed Student's-t test. Non-parametric variables were analyzed with the Wilcoxon test. In order to retain a prescribed family wise error rate α in our analysis involving more than one comparison, Bonferroni correction method was used. Qualitative variables were analyzed with the chi-square test, with Yates correction as necessary, and Fisher's test. A p-value <0.05 was considered significant.

5. Results

Three hundred and thirty one patients gave informed consent and were enrolled in the study. The mean age was 50.1 ± 13.2 years and the mean BMI 35.4 ± 5.3, with 25.7% males and 74.3% females. All patients completed the 9-month follow-up period without drop-outs in both branches (diet HP vs. diet S). Sex distribution was similar in groups, males (27.9% vs. 23.3%) and females (72.1% vs. 76.7%).