



Short Communication

High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects

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OBJECTIVE: To test the hypothesis that hyperinsulinemic obese subjects would respond differently to changes in the composition of hypoenergetic diets.

DESIGN: A 4-week randomized dietary intervention trial.

SUBJECTS: Thirteen male obese hyperinsulinemic normoglycemic subjects were divided into two groups and fed hypoenergetic diets providing 80% of their resting energy expenditure (REE). One group received a high-protein diet (HP; 45% protein, 25% carbohydrates, and 30% fat as percent of dietary energy) and the other a high-carbohydrate diet (HC; 12% protein, 58 carbohydrates and 30% fat).

MEASUREMENTS: Anthropometry, body composition, fasting serum insulin and lipids, and REE were performed before and after the feeding period.

RESULTS: Weight loss was higher in the HP than HC group (8.3 ± 0.7 vs 6.0 ± 0.6 kg, $P < 0.05$). There was a decrease in body fat in both groups, whereas body water decreased significantly more in the HP group. REE decreased more in the HC than the HP group (-384.3 ± 84.6 vs -132.3 ± 51.0 kcal, $P < 0.05$). Serum total cholesterol, triglycerides and LDL cholesterol decreased significantly to a similar extent in both diet groups, while HDL cholesterol was decreased significantly only in the HP group. Mean fasting insulin decreased significantly in both diet groups and reached the normal range only in the HP group.

CONCLUSION: A low-carbohydrate (LC), HP hypoenergetic diet could be the diet composition of choice for a weight-reducing regimen in obese hyperinsulinemic subjects.

Keywords: obesity; hyperinsulinemia; diet composition; resting energy expenditure; weight loss

Introduction

There is a wide variation in insulin sensitivity in the healthy population because of differences in genetic make-up and environmental influences.¹ Obesity is the most common condition associated with insulin resistance,² and hyperinsulinemic obese individuals have been identified as a specific clinical group that require special attention in diet composition studies.^{3,4} Many research studies reported that dietary energy rather than diet composition is the determining factor in weight reducing regimens.^{5,6} However, such studies did not differentiate between obese normoinsulinemic and hyperinsulinemic subjects.

Some human studies have shown an improvement in insulin sensitivity after a high-carbohydrate (HC), high-fiber and low-fat diet,^{7,8} whereas others have not

shown any difference.^{9,10} Early studies by Grey and Kipnis¹¹ reported a significant reduction in plasma insulin levels in subjects placed on a hypocaloric low-carbohydrate (LC) diet. Tremblay¹² showed that, in obese patients, elevated dietary fat correlated with diminished insulin sensitivity. Proteins were reported in the literature to have a higher thermic effect than carbohydrates,¹³ and Skov *et al*,¹⁴ showed that weight loss on a high-protein (HP) diet was greater than on a low-protein diet in obese subjects. More recently Skov *et al*¹⁵ reported that obese subjects consuming *ad libitum* a high-protein fat-reduced diet lost weight and body fat significantly more than obese subjects consuming a high-carbohydrate similarly fat-reduced diet. However, the effect of the two diets on insulin levels was not reported. The effects of a HP, LC hypoenergetic diet on weight loss in hyperinsulinemic obese subjects has received less attention.

The aims of this study were to establish whether obese hyperinsulinemic normoglycemic subjects would respond differently to manipulations in the composition of hypoenergetic diets, and to identify certain anthropometric and metabolic changes accompanying such dietary intervention.

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Subjects and methods

Adult male obese hyperinsulinemic subjects were screened and selected for participation in the study. Criteria used for selection included adult onset obesity (body mass index (BMI) > 31, fasting insulin levels > 25 μ U/l) and normal fasting plasma glucose (76–110 mg/dl). Thirteen subjects were divided randomly into two groups (seven in the HP and six in the HC group) and fed diets containing 80% of their resting energy requirements for a period of 4 weeks. Initial mean body weight and BMI did not differ significantly between the two groups. Physical activity was assessed using a detailed activity questionnaire.

The diets were either a HP (45% protein, 25% CHO, 30% fat as percentage of energy), or a HC diet (12% protein, 58% CHO, 30% fat). Body weight, body composition, resting energy expenditure (REE), fasting insulin, glucose and plasma lipid levels were measured at the beginning and end of the study.

A 7-d rotating menu was offered. An itemized composition of both diets is displayed in Appendix I. Both diets consisted of natural foods. Recipes and menus of various food items were standardized and food items were cooked in the organoleptic kitchen of the Food Technology and Nutrition Department at the American University of Beirut. To ensure maximal compliance, the food items were catered to each subject for the duration of the study. Subjects were asked to consume the entire food basket and to record any uneaten portion or deviation from the experimental diet on a special form that was sent daily with the basket of food. All subjects attended a weekly nutrition counseling session.

Body composition was measured using bioelectrical impedance analysis (Tanita body fat analyzer, Model TBF-305, Tanita Corp, IL, USA) and REE by indirect calorimetry (The Cardiopulmonary Case Company, Sensor Medics, CA, USA). Insulin was measured by Radioimmuno-assay (kit CIS Bio International, France). Serum cholesterol was analyzed by an enzymatic colorimetric test (kit for automated analysis by

Boehringer Mannheim, catalogue no. 1447513). Serum HDL-C was also determined colorimetrically, after precipitation of LDL and VLDL with dextran sulfates (1 mg) and magnesium acetate (14.2 mg) (HDL separation tab; Union Carbide Corp., PLSNTVL, NY, 10570, for *in vitro* diagnosis). Serum LDL level was calculated by differences according to Friedwald *et al.*¹⁶ Serum triglycerides were analyzed by an enzymatic colorimetric test provided by Boehringer Mannheim (Catalogue no. 816370).

Statistical methods

Data were expressed as means \pm S.E. and were analyzed using the MSTAT software.¹⁷ Comparisons between groups based on diet composition were done by use of a two-sided Student's *t*-test for independent variables.

Results

All 13 subjects completed the study and had similar sedentary physical activity profiles. Both HP and HC groups lost weight and fat on the two hypoenergetic dietary regimens. However, the mean loss of weight was significantly higher on the HP as compared to the HC diet (Table 1, Figure 1). Median weight loss on the HP diet (8.8 kg) was higher than that on the HC diet (6.1 kg). The frequency of a weight loss of 7 kg or more was 16% in the HC group as compared to 71% in the HP group. Body composition measurements revealed a decrease in body fat in both HP and HC groups (– 7.1 \pm 0.9 vs – 6.3 \pm 0.2), respectively. The decrease in total body water in the HP group was significantly lower than the HC group (– 1.0 \pm 0.3 HP vs 0.3 \pm 0.4 HC). The initial insulin levels in both diet groups were not statistically different. At the end of the study period, insulin levels dropped

Table 1 Changes in body weight, BMI, REE and blood parameters (mean \pm S.E.) of hyperinsulinemic male subjects fed HP vs HC diet during energy restriction

	HP (n = 7)			HC (n = 6)		
	Pre \pm S.E.	Post \pm S.E.	$\Delta \pm$ S.E.	Pre \pm S.E.	Post \pm S.E.	$\Delta \pm$ S.E.
Weight (kg)	113.2 \pm 6.8	104.9 \pm 6.4	– 8.3 \pm 0.7 ^a	105.5 \pm 4.7	99.5 \pm 5.0	– 6.0 \pm 0.6 ^a
BMI (kg/m ²)	36.8 \pm 1.9	34.1 \pm 1.8	– 2.7 \pm 0.2 ^a	34.6 \pm 0.8	32.6 \pm 0.8	– 2.0 \pm 0.2 ^a
REE (kcal)	2239.1 \pm 122.9	2106.9 \pm 141.9	– 132.3 \pm 51.0 ^a	2203.8 \pm 54.6	1819.5 \pm 88.6	– 384.3 \pm 84.6 ^a
Glucose (mg/dl)	97.6 \pm 1.5	89.6 \pm 1.6	– 8.0 \pm 2.1	92.8 \pm 2.1	92.0 \pm 2.7	– 0.8 \pm 2.8
Insulin (μ U/l)	37.9 \pm 3.9	20.5 \pm 2.1	– 17.4 \pm 3.0	41.5 \pm 3.9	27.4 \pm 3.0	– 14.1 \pm 4.5
Triglyceride (mg/dl)	206.0 \pm 49.3	95.9 \pm 18.5	– 110.1 \pm 38.4	169.2 \pm 30.9	93.7 \pm 12.9	– 75.5 \pm 27.2
TC (mg/dl)	179.6 \pm 13.8	130.4 \pm 11.9	– 49.1 \pm 16.9	167.8 \pm 12.8	134.5 \pm 13.0	– 33.3 \pm 1.5
LDL-C (mg/dl)	99.7 \pm 9.5	78.4 \pm 10.4	– 21.3 \pm 13.7	94.3 \pm 11.2	72.8 \pm 11.8	21.5 \pm 5.3
HDL-C (mg/dl)	37.6 \pm 3.1	32.9 \pm 2.3	– 4.7 \pm 1.9 ^a	39.8 \pm 2.3	43.2 \pm 2.7	3.3 \pm 2.1 ^a
TC/HDL-C	5.0 \pm 0.6	4.2 \pm 0.6	– 0.9 \pm 0.6	4.2 \pm 0.2	3.2 \pm 0.4	– 1.1 \pm 0.2

^aIndicates significant difference between groups at $P < 0.05$. BMI: body mass index; REE: resting energy expenditure; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; s.e.: standard error of the mean.

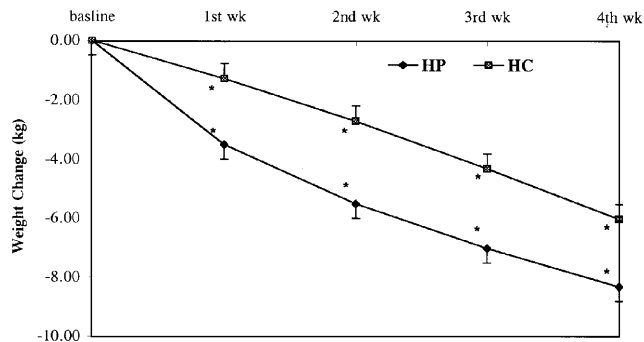


Figure 1 Effect of hypoenergetic HP vs HC diet on changes in body weight in hyperinsulinemic obese male subjects. *Significant difference between the two groups at $P < 0.05$.

significantly in both diet groups, but the degrees of reduction were not statistically different. However, the insulin levels were reduced to within the normal range (below $25 \mu\text{U/l}$) only in the HP group.

Total cholesterol, triglycerides, and LDL cholesterol decreased significantly, and to a similar extent, on both dietary manipulations. However, a statistically significant decrease was observed in HDL-cholesterol only in the HP group.

Upon completion of 4 weeks, REE measurements decreased significantly in both dietary groups, but the decrease was significantly higher in the HC group (Table 1). The mean decrease in REE in HC group remained significant after adjusting for differences in change of body weight (-22.09 ± 2.16 kcal/kg weight loss in the HP group vs -58.79 ± 5.21 kcal/kg weight loss in the HC group).

Comments

The significance of this study lies in providing evidence for a possible distinct response of obese insulin-resistant subjects, as a subgroup of the obese population, to manipulations in diet composition. Published data concentrated on studying responses to manipulations in the type of dietary carbohydrates in the diets of the obese, or on comparisons between HC and high-fat diets.¹⁸ to our knowledge studies comparing the responses of hyperinsulinemic subjects to HP vs HC hypocaloric diets have not been reported. The results of the present study showed that both diets induced significant and comparable reduction in fasting insulin levels. However subjects on the HP diet achieved levels that were within the normal range. Such a finding is in agreement with Parillo *et al.*,¹⁸ who showed that a reduction in the consumption of complex carbohydrates associated with an increase in monounsaturated fats resulted in improved peripheral insulin sensitivity. The present study also showed that the HP diet resulted in a greater weight loss than the equienergetic HC diet. Similarly, recent data¹⁵ showed that replacement of dietary carbohydrate by

protein, in an *ad libitum* fat-reduced diet improved weight loss. This could be partly explained by the higher thermogenic response observed in the HP group. The literature provides less data on energy expenditure of subjects on HP diets than on diets containing high proportions of the other two macronutrients. However, earlier reports have shown that HP diets increase both thermogenesis¹³ and 24-h energy expenditure¹⁹ as compared with HC diets, and isoenergetic substitution of a HC by a HP diet resulted in a 12% increase in energy expenditure. In our study, the difference in the REE between the HP and the HC group was of a similar magnitude of approximately 12%. The mechanism by which HP diets exert their effect could be attributed to the formation of serotonin and dopamine in peripheral tissues of animals and humans, both of which were shown to be potentially thermogenic.²⁰ Moreover, the difference in weight loss between the two diets was most evident in the first week of treatment, which may be explained by the greater water losses observed in the HP group.

Lower HDL cholesterol levels were observed on the HP diet as compared with the HC diet. This may be explained by the activation effect of HC diets on adipose tissue lipoprotein lipase (LPL).²¹ Activation of LPL has previously been shown to be positively correlated with increasing fasting HDL cholesterol concentrations.^{22,23}

Total and LDL cholesterol levels decreased to the same extent on both diets, suggesting that this reduction is probably mediated by the reduction in body weight and fat, rather than being affected by diet composition, as was also shown by Alford *et al.*²⁴

This study provides evidence supporting a favorable response to a high-protein low-energy diet in insulin resistance. We therefore conclude that in dietary management of obesity it is important to identify a subgroup of obese patients who are hyperinsulinemic and normoglycemic who might benefit from the use of a HP, LC, hypoenergetic diet, as it produces more rapid weight loss and restores insulin levels to normal.

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Appendix I

An itemized composition of the diets

Table 2 Group I (high protein)

Day	Breakfast	Lunch	Supper
1	Low-fat yoghurt, cracotte, skimmed <i>labneh</i> , low-fat cheese spread, cucumber, tomato	Chicken with rice, green salad, fruit	<i>Daoud pasha</i> (meat balls), fruit
2	Low-fat yoghurt, Arabic bread, skimmed <i>labneh</i> , low-fat cheese slices, cucumber, tomato, boiled egg	<i>Shawarma</i> (lean beef), cabbage/tomato, salad, fruit	Tuna, boiled vegetables (squash, carrots and potatoes), fruit
3	Low-fat yoghurt, cracotte, skimmed <i>labneh</i> , low-fat cheese spread, cucumber, tomato	Grilled fish with tomato sauce, <i>fattoush</i> (salad), fruit	Steak with canned vegetables, fruit
4	Low-fat yoghurt, Arabic bread, skimmed <i>labneh</i> , low-fat cheese slices, cucumber, tomato	Baked chicken with spinach and rice, fruit	Sheesh kabab, cabbage/carrot salad, fruit
5	Low-fat yoghurt, toast, skimmed <i>labneh</i> (strained yoghurt), low-fat cheese spread, cucumber, tomato, boiled egg	Mushrooms with meat, rice, fruit	Tuna, beet salad, fruit
6	Cracotte, skimmed <i>labneh</i> , low-fat cheese slices, cucumber, tomato	<i>Rosto</i> (roast beef) with canned vegetables and sauce, seasonal salad, fruit	<i>Kibbeh</i> (ground meat and parboiled wheat mix) with low-fat yogurt, fruit
7	Low-fat yogurt, Arabic bread, skimmed <i>labneh</i> , low-fat cheese spread, cucumber, tomato, boiled egg	<i>Kafta</i> (grilled ground meat and parsley) with potatoes, green bean salad, fruit	<i>Shish taouk</i> (chicken), mixed salad, fruit

Table 3 Group II (high carbohydrate)

Day	Breakfast	Lunch	Supper
1	Cracotte, <i>labneh</i> with olive oil, cheese spread, tomato, cucumber, fruit	<i>Borghul</i> (parboiled wheat), rocca salad, fruit, <i>sfouf</i>	Mushroom pie, fruits
2	Arabic bread, <i>labneh</i> with olive oil, cheese slices, cucumber, fruit	<i>Moujaddara</i> (lentils), Arabic bread, tomato/cabbage salad, fruit	Potato salad, unsweetened orange juice, cake
3	<i>Mankousheh</i> (bread with thyme and oil), yogurt, cucumber, tomato, fruit	Spaghetti with red sauce and mozzarella cheese, <i>fattoush</i> , fruit	Spinach pie, unsweetened pineapple juice, custard
4	Toasted bread slices, <i>labneh</i> , with olive oil, boiled egg, cheese spread, cucumber, tomato	Broad beans and chickpeas, lettuce/carrot salad, Arabic bread, fruit	Rice with vegetables, fruit salad
5	Arabic bread, <i>labneh</i> with olive oil, cheese slices, cucumber, tomato	Potato stew, beet salad, fruit	Cabbage pie, <i>mughli</i> (rice pudding – non dairy), unsweetened orange juice
6	Cracotte, <i>labneh</i> , thyme with olive oil, cucumber, tomato	Mexican beans, Arabic bread, mixed salad, fruit	<i>Lahm bi Ajeen</i> (meat pie), fruit salad
7	<i>Mankousheh</i> , yogurt, cucumber, tomato, fruit	<i>Nouille au curry</i> (spaghetti with mushrooms and mozzarella cheese), cabbage/carrot salad, fruit	Rice with green beans, jam with Arabic bread, unsweetened pineapple juice