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CLINICAL RESEARCH

Restoration of Normal Insulinemia and Insulin Sensitivity in Hyperinsulinemic Normoglycemic Men by a Hypoenergetic High Monounsaturated Fat Diet

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Abstract

Purpose: *To test the hypothesis that the macronutrient composition of hypoenergetic diets is an important consideration in weight-reducing regimens of hyperinsulinemic normoglycemic obese subjects.*

Design: *A 4-week randomized dietary intervention trial.*

Subjects and Methods: *Sixteen male obese hyperinsulinemic normoglycemic subjects were recruited and 15 completed the study. The participants were divided into two groups and fed hypoenergetic diets providing 80% of their resting energy expenditure (REE). One group received a high carbohydrate diet (HC) (60% carbohydrate, 20% fat, 20% protein as a percentage of dietary energy) and the other group received a high monounsaturated fat diet (HM) (35% carbohydrate, 45% fat and 20% protein). Anthropometry, body composition, REE, serum glucose, insulin and lipid analyses were performed before and after the feeding period.*

Results: *The subjects on the HC diet achieved comparable weight loss but without restoration of normoinsulinemia and insulin sensitivity. Fasting insulin levels, insulin to glucose ratio, and Homeostatic Model & Assessment Index decreased to normal ranges and were significantly lower in the HM group as compared with the HC group. Similarly, insulin sensitivity score (Mffm/I) increased significantly on the HM diet. Waist circumference measurements showed a significantly higher decrease on the HM than HC diet, whereas body weight, percentage body fat, glucose, plasma lipids, and REE decreased to the same extent whether subjects were fed the HC or HM diet.*

Conclusions: *In this study, feeding a HM diet was more effective than a HC diet for restoring normoinsulinemia and insulin sensitivity. Therefore, hyperinsulinemic normoglycemic obese subjects may benefit from a diet lower in carbohydrates and higher in monounsaturated fats for decreasing cardiovascular disease risk factors while achieving the desired weight reduction.*

Keywords: obesity, hyperinsulinemia, insulin sensitivity, monounsaturated fats, resting energy expenditure, weight loss.

INTRODUCTION

Hyperinsulinemia, whether in diabetic or non-diabetic subjects, has been associated with a number of cardiovascular risk factors such as hyperglycemia, hypertension, dyslipidemia,

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and a central fat distribution [1]. The role of diet composition in ameliorating hyperinsulinemia has been the subject of controversy, particularly in relation to the optimal ratio of carbohydrate to fat in the diet [2, 3]. Some scientists claim that increased fat in the diet contributes to several chronic diseases [4]; whereas others contend that certain types of fat, such as monounsaturated fats, are beneficial, and may protect against diseases [5]. A number of studies have shown an association between high dietary fat intakes and insulin resistance in both animals [6] and humans [7]. Reviewed by Lovejoy *et al.* [8], certain classes of fatty acids were suggested to have a more deleterious effect on insulin action than others. In animals, consumption of saturated and polyunsaturated fat was reported to induce severe insulin resistance, whereas monounsaturated fats and omega-3 fatty acids from fish oils may actually be helpful [9]. In humans, a cross-sectional population study of over 4000 healthy individuals found that fasting insulin levels were positively associated with the percentage of saturated fat in plasma and inversely associated with the percentage of monounsaturated fat [10]. Taken as a whole, Lovejoy *et al.* noted that there is a strong suggestion that specific dietary fatty acids influence insulin resistance and increase the risk of type 2 diabetes mellitus [8].

In relation to insulin, the literature suggests a situation similar to that seen with fats when high carbohydrate (HC) diets are used. Several studies reported an increase in insulin sensitivity with HC high fiber diets [11]; whereas other studies demonstrated a negative effect of HC diets on peripheral insulin action [12].

With respect to weight loss, some studies have demonstrated that hypocaloric HC and high fat diets cause similar weight loss [8]. Nevertheless, other studies have shown greater weight loss after consumption of a high monounsaturated fatty acid (HM) diet [13]. Data from credible intervention studies on the role of dietary macronutrients on insulin action and obesity were recently reported as still needed [14].

Traditionally, weight-reducing regimens grouped the obese as one population who require a balanced energy-restricted diet with exercise to achieve weight loss. The body was considered as energy blind where energy restriction rather than diet composition was the only important factor considered for achieving weight loss [15]. Attention has not been given to whether the obese subjects were hyper- or normoinsulinemic, and hence the macronutrient composition of the recommended diet was similar for all the obese.

We have recently proposed that obese non-diabetic subjects with concomitant hyperinsulinemia should be treated as a subgroup of the obese population who deserve special dietary intervention strategies, which take into consideration, in addition to successful weight loss, lowering hyperinsulinemia and improving cardiovascular risk factors. Male hyperinsulinemic obese subjects showed a greater weight loss and normalization of insulinemia when fed high protein compared with HC hypoenergetic diets [16].

The present study was undertaken to test the hypothesis that manipulations in the ratio of carbohydrate to monounsaturated fatty acids within the macronutrient composition of a hypoenergetic diet, in favor of monounsaturated fatty acids and without changing the protein content, will reduce the hyperinsulinemia and insulin resistance in obese hyperinsulinemic normoglycemic men, while achieving the desired weight loss.

SUBJECTS AND METHODS

Subjects

Thirty-four male obese subjects aged 18–48 years who responded to public advertisements were screened for fasting serum insulin and blood glucose levels. Individuals with diabetes, hyperglycemia or other endocrine disorders, and subjects who were smokers or under current medical therapy were excluded from the study. None of the volunteers participated in any regular exercise.

Sixteen male obese hyperinsulinemic normoglycemic subjects aged 19–48 years (mean age 28.6 years) were selected to participate. The criteria used for selection included adult onset obesity (body mass index $>31\,\mathrm{kg\,m^{-2}}$, fasting insulin levels $>25\,\mu\mathrm{U\,ml^{-1}}$, and normal fasting plasma glucose 76–110 $\mathrm{mg\,dl^{-1}}$). The subjects were divided randomly into two groups, fed either a HC or a HM diet. The protocol was approved by the University Research Board and all volunteers gave written informed consent.

Study Protocol

The two groups were fed either a HC or HM hypoenergetic diet containing 80% of their resting energy expenditure (REE) for a period of 4 weeks.

One group received a HC diet [60% carbohydrate, 20% fat (9% saturated fat, 4% monounsaturated fatty acids, 7% polyunsaturated fatty acids), and 20% protein as a percentage of dietary energy] and the other a HM diet [35% carbohydrate, 45% fat (10% saturated fat, 30% monounsaturated fatty acids, 5% polyunsaturated fatty acids), and 20% protein]. The dietary content of mono- and polyunsaturated fatty acids in the diet was assessed using Nutritionist Pro software [17]. The HM diet in this study was not a ketogenic diet as its carbohydrate content was 35% and the subjects consumed between 156 and 238 g carbohydrates per day.

A 7-day rotating menu was offered. Both HC and HM diets consisted of natural foods. Recipes and menus of various food items were standardized and the food was cooked in the organoleptic kitchen of the Nutrition and Food Science Department at the American University of Beirut (Appendix). 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 any deviation from the experimental diet. For that purpose, a special form was offered daily with the basket of food. All subjects attended a weekly nutrition counseling session and were requested not to exercise for the duration of the study.

REE

To assess each individual's energy needs and changes in energy expenditure induced by the diets, REE was measured, after a rest period of equal duration (30 min), for all subjects at the beginning and at the end of the study by indirect calorimetry using a metabolimeter (Sensor Medics, Cardiopulmonary Care Company, California, USA).

Anthropometry and Body Composition

Body weight, waist and hip circumferences were measured at the beginning, weekly, and at the end of the study period. Body composition was measured using dual-energy X-ray absorptiometry (DEXA). The amount of loss from fat and fat-free mass in subjects on both diets seems to be underestimated by DEXA. This could be due to the underestimation of fat mass by DEXA in subjects with a body weight greater than 100 kg. DEXA manufacturers acknowledge this problem in subjects weighing over 100 kg as the scan field of the machine might not cover the entire body of the obese subject [18]. Another problem is the decrease in the accuracy of DEXA estimates of body fat as body thickness increases [19].

Blood Parameters

Glucose, insulin and lipid levels were measured at the beginning and end of the study. Serum samples were analyzed for glucose using an ultraviolet test based on the hexokinase/G6p-DH assay (provided by Boehringer Mannheim, cat. no. 1 447 513). Insulin was measured by

radioimmunoassay (kit CIS Bio International, France). In addition to fasting insulin levels, changes in insulin sensitivity were determined using the Homeostatic Model of Assessment Index (HOMA-IR) [20], the insulin to glucose (I/G) ratio [21], and the newly developed score for insulin sensitivity index (ISI) which includes fasting insulin and fasting triglyceride levels [22]. The use of a score which included fasting insulin and fasting triglycerides, rather than fasting insulin alone, was reported to be best at predicting insulin sensitivity. The score was calculated according to the following equation: $Mffm/I = \exp[2.63 - 0.28\ln(\text{insulin}) - 0.31\ln(\text{TAG})]$, where: M = glucose disposal rate; *ffm* = fat-free mass; $Mffm/I$ = insulin sensitivity index corrected for fat-free mass divided by average insulin; TAG = fasting triglycerides. An ISI ≤ 6.3 M $\text{mU}^{-1} \cdot \text{l}^{-1}$ defined individuals with insulin resistance.

Serum cholesterol was analyzed using an enzymatic colorimetric test (Boehringer Mannheim, cat. no. 1 447 513). Serum high-density lipoprotein-cholesterol (HDL-C) was also determined colorimetrically, after precipitation of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) with dextran sulfate (1 mg) and magnesium acetate (14.2 mg) (HDL separation tab; Union Carbide Corp.). The serum LDL level was calculated by differences, according to Friedwald *et al.* [23]. Serum triglycerides were analyzed by an enzymatic colorimetric test provided by Boehringer Mannheim (cat. no. 816 370).

Statistical Analysis

Data are presented as means $\pm$ standard error of the mean (SE). Comparison between two groups based on diet composition was performed by a two-sided student's t-test for independent variables. All analyses were performed using Statistical Packages for the Social Sciences (SPSS, Chicago, IL, USA). Data were considered to be significant at $p < 0.05$.

RESULTS

Fifteen male obese hyperinsulinemic normoglycemic subjects (eight in the HC group and seven in the HM group) completed the study and had similar sedentary physical activity profiles for the duration of the experiment.

Both the HC and HM groups lost weight and fat on the two hypoenergetic dietary regimens (Fig. 1, Table 1). The difference in mean loss of weight was not statistically different between the HM and HC diets. The frequency of a weight loss of 7.0 kg or more was 50% in the HC group as compared with 100% in the HM group.

Waist circumference decreased on both the HC and HM diets following the period of 4 weeks of energy restriction. The decrease was of a greater magnitude and significantly different on the HM diet than on the HC diet.

At the end of 4 weeks, a statistically significant decrease in REE was observed in the HC group. The decrease in REE following the HM diet was not statistically significant.

Indicators of insulin sensitivity and insulin resistance were affected by diet composition (Table 2). In the HM group as compared with the HC group, a higher and statistically significant decrease in fasting insulin levels, I/G ratio, and HOMA-IR and an increase in insulin sensitivity score were induced. This resulted in normalization of insulin levels in the HM subjects only. The fasting insulin levels in the HC group did not normalize to below 25 $\mu\text{U}\,\text{m}^{-1}$. Similarly, the I/G ratio did not normalize to below 4.0 in the HC group. The insulin sensitivity score ($Mffm/I$) significantly increased to a level above 6.3 on the HM diet alone; indicating normalization of insulin sensitivity.

The glucose, total serum cholesterol, and triglyceride levels decreased to the same extent whether the subjects were fed the hypoenergetic HC or HM diets (Table 2).

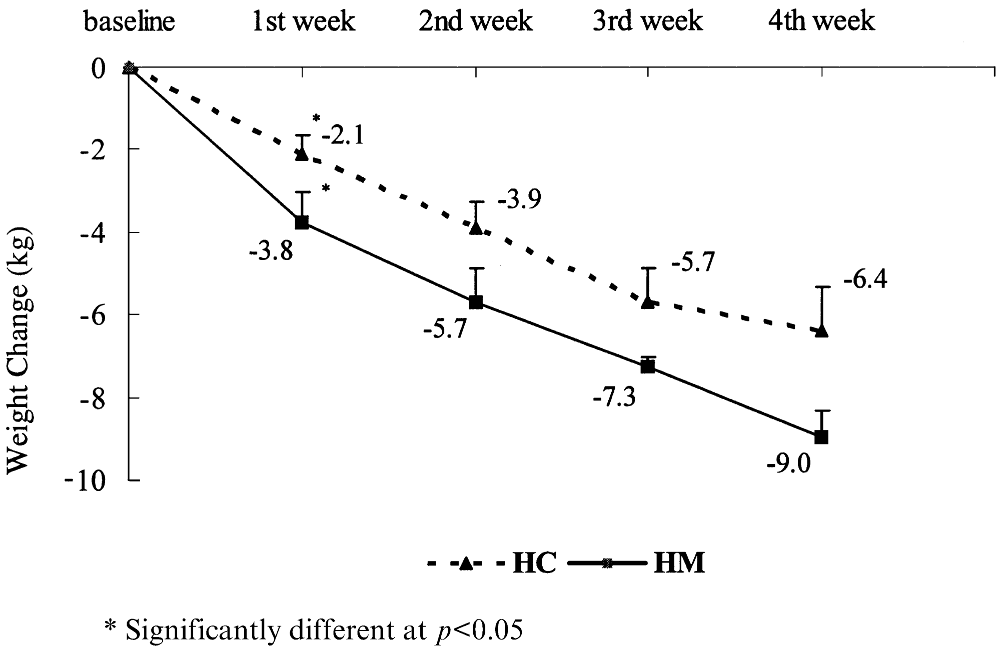

FIG. 1. Effects of hypoenergetic high carbohydrate vs. high monounsaturated fat diet on changes in body weight in hyperinsulinemic obese subjects.

TABLE 1. Changes in whole body composition (mean ± standard error) in males on a high carbohydrate (HC) or a high monounsaturated fat (HM) hypoenergetic diet

	HC ($n=8$)			HM ($n=7$)		
	Pre	Post	Δ	Pre	Post	Δ
Weight (kg)	110.7 ± 2.6^{x}	104.3 ± 3.1^{x}	-6.4 ± 1.1	113.0 ± 4.9^{y}	104.0 ± 4.9^{y}	-9.0 ± 0.8
BMI ($kg\,m^{-2}$)	35.2 ± 0.9^{x}	33.2 ± 1.0^{x}	-2.1 ± 0.4	34.8 ± 1.6^{y}	32.0 ± 1.6^{y}	-2.8 ± 0.2
Waist (cm)	110.7 ± 2.1^{x}	106.8 ± 2.0^{x}	-3.9 ± 0.9^{a}	111.8 ± 6.0^{y}	104.9 ± 6.5^{y}	-6.9 ± 0.9^{a}
WHR	0.92 ± 0.02	0.91 ± 0.01	0.01 ± 0.01	0.92 ± 0.03^{y}	0.90 ± 0.00^{y}	-0.03 ± 0.01
REE	2293.3 ± 66.5^{x}	2052.4 ± 28.8^{x}	-240.9 ± 68.8	2504.0 ± 206.0	2200.4 ± 121.6	-303.6 ± 130.1
FM (kg)	34.8 ± 1.8^{x}	31.5 ± 1.7^{x}	-3.2 ± 1.0	33.4 ± 3.3^{y}	30.77 ± 3.2^{y}	-2.6 ± 0.9
% fat	31.4 ± 1.3	30.2 ± 1.2	-1.2 ± 0.7	29.2 ± 1.8	29.2 ± 1.7	$5.0 \times 10^{-2} \pm 0.7$

BMI, body mass index; WHR, waist to hip ratio; REE, resting energy expenditure; FM, fat mass measured by duel-energy x-ray absorptiometry.
[x,y,a]Values in the same row with the same superscript are significantly different at $p < 0.05$.

DISCUSSION

It is generally acknowledged that diet plays an essential role in both insulin resistance and obesity. However, the optimal macronutrient composition for achieving both goals of reducing hyperinsulinemia and achieving weight loss, remain unresolved. The disagreement centers mainly on the fat to carbohydrate ratio and more recently on the type of fat in the diet. The aim of the present study was to investigate the use of monounsaturated fats in hypoenergetic diets for lowering hyperinsulinemia in obese normoglycemic subjects. Two hypoenergetic diets which varied in the percentage energy from monounsaturated fat were tested.

The difference in weight loss and fat loss between the HC and HM groups did not differ significantly. This is in agreement with previous studies which could not elucidate that total

TABLE 2. Selected clinical characteristics (mean ± standard error) before and after weight loss in males on a high carbohydrate (HC) or a high monounsaturated fat (HM) hypoenergetic diet

	HC ($n=8$)			HM ($n=7$)		
	Pre	Post	Δ	Pre	Post	Δ
Glucose	93.9 ± 2.6^{x}	85.5 ± 2.0^{x}	-8.4 ± 3.0	95.9 ± 3.5	89.0 ± 4.9	-6.9 ± 4.8
TC (mg dl^{-1})	218.8 ± 11.7^{x}	171.3 ± 14.1^{x}	-47.5 ± 6.1	193.4 ± 14.0	166.3 ± 16.4	-27.1 ± 16.4
HDL-C (mg dl^{-1})	41.5 ± 6.9^{x}	34.9 ± 2.0	-6.6 ± 1.4	37.6 ± 2.4	34.7 ± 2.4	-2.9 ± 2.9
TC/HDL-C	5.4 ± 0.5	5.0 ± 0.5	-0.4 ± 0.2	5.2 ± 0.4	4.9 ± 0.5	-0.4 ± 0.3
TG(mg dl^{-1})	131.5 ± 22.6	100.9 ± 11.1	-30.6 ± 15.6	166.0 ± 29.2^{y}	112.7 ± 20.1^{y}	-53.3 ± 18.7
Insulin (μU l^{-1})	31.7 ± 1.4	27.5 ± 2.2^{b}	-4.1 ± 1.9^{a}	34.5 ± 3.2^{y}	14.8 ± 4.3^{by}	-19.6 ± 3.9^{a}
Insulin/glucose	6.1 ± 0.2	5.8 ± 0.5^{b}	-0.3 ± 0.5^{a}	6.5 ± 0.7^{y}	2.8 ± 0.6^{by}	-3.7 ± 0.7^{a}
HOMA-IR	7.4 ± 0.5^{x}	5.8 ± 0.5^{x}	-1.6 ± 0.5^{a}	8.2 ± 0.8^{y}	3.6 ± 1.3^{y}	-4.6 ± 1.1^{a}
Mffm/I	4.9 ± 0.3^{x}	5.4 ± 0.4^{x}	0.5 ± 0.1^{a}	4.4 ± 0.2^{y}	6.7 ± 0.6^{y}	2.3 ± 0.6^{a}

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HOMA-IR, Homeostatic Model of Assessment Index.
Mffm/I = exp[2.63 − 0.28ln(fasting insulin) − 0.31ln(fasting triglycerides)]
[x,y,a,b]Values in the same row with the same superscript are significantly different at $p < 0.05$.

body fat differed significantly in response to low or high fat hypoenergetic diets [15]. However, the striking point in this study is that subjects who consumed the HC diet for 4 weeks lost 6.4 kg but were still hyperinsulinemic and had a larger waist circumference than those who consumed the HM diet. High insulin, insulin resistance and waist circumference are major risk factors for cardiovascular diseases.

In this study, a significant reduction in waist circumference and a remarkable decrease in fasting plasma insulin levels, I/G ratio, HOMA-IR, and increase in *Mffm/I* insulin sensitivity score accompanying the HM diet as compared with the HC dietary regimen was observed. This result demonstrated that the high HM diet was superior in terms of lowering insulin levels and improving insulin sensitivity, hence normalizing insulin levels, whereas the HC diet maintained hyperinsulinemia albeit of weight loss. Similar results were obtained by Hwalla *et al.* [16] where the hyperinsulinemia of obese subjects was improved upon consuming a high protein diet, whereas the HC diet did not return the insulin levels back to normal [24]. Garg *et al.* [13] also indicated that diets providing 55% of total energy requirements as carbohydrates resulted in an increase in insulin and glucose levels, as compared with diets high in monounsaturated fatty acids. The mechanism underlying the decrease in insulin levels was explained as possibly due to a decline in the circulating free fatty acids (FFA) following a reduction in fat mass, especially abdominal fat in the HM group, as seen by the greater and significant decrease in waist circumference in this group. Similarly, Slabber and coworkers [25] suggested that the improvement in insulin might be attributed to the increase in insulin clearance at the beginning of the intervention period, and that diet composition *per se*, and not the weight loss, improved hyperinsulinemia. The HM diet is also a low carbohydrate diet, which results in less stimulation of insulin secretion.

Another possibility explaining the lowering of insulin levels may be linked to the hypertrophic pancreatic ß-cells, which are characteristic of obesity. With weight reduction, a decrease in ß-cell mass will be incurred, resulting in a decrease in insulin [26]. The greater magnitude of weight loss in the HM group could in part explain the enhanced insulin sensitivity supported by previous studies [27, 28]. In the present study, HM diets resulting in enhanced insulin sensitivity possibly mediate their effects through improving blood glucose control [8]. Some studies assert that improvement in glycemic control is independent of diet composition [29], whereas others are in agreement with the present result. Low and colleagues [30] demonstrated that a high monounsaturated fatty acid content of the diet induces improvement in control of non-insulin-dependent diabetes mellitus (NIDDM) patients as compared with a diet high in carbohydrate content.

As for the lipid profile, a small decrease in HDL-C levels was observed in both the HM and HC groups, However, the decrease was greater under the HC dietary regimen. The data of Gumbiner *et al.* [31] are in accordance with this observation, as they reported a smaller magnitude of reduction in HDL-C in subjects consuming a HM hypocaloric diet as compared with a HC diet. It is important to note that weight loss results in a lowering of HDL-C; and it was reported that for every kilogram decrease in body weight, HDL-C decreases by 0.007 $\mathrm{mmol\,l^{-1}}$ for subjects actively losing weight [5]. Total cholesterol levels decreased similarly on both the HM and HC diets, which is in agreement with Bonanome and coworkers [32] and Thomsen *et al.* [33], who showed similar cholesterol levels in subjects on HC vs. HM diets in NIDDM patients. The weight loss rather than differences in the macronutrient composition most probably mediated the reduction in total cholesterol. The total cholesterol to HDL-C ratio decreased in a similar manner in both groups, but there was slightly more decline under the HM group as it normalized below 5. Heilbronn and colleagues [29] reported similar results in NIDDM subjects; as diets high in monounsaturated fat lowered the total cholesterol to HDL-C ratio more than the HC diet.

A greater reduction in triglyceride levels was observed in the HM group than in the HC group, this was observed in earlier studies showing that dietary fatty acid composition affects the fatty acid composition of VLDL-triglyceride [34], and alterations in composition of VLDL and in the enzymes involved in its catabolism are two mechanisms involved in the hypotriglyceridemic effect of HM diets [35]. Oleic acid has also been found to cause a reduction in triglyceride levels, possibly through increasing the removal of triacylglycerol [36]. Moreover, olive oil has been found to promote gastrointestinal secretions and stimulate stomach emptying, thereby increasing the rate of supply of fatty acids to the enterocytes [37], thus accelerating the rate of digestion and absorption and faster rate of entry of chylomicrons into the circulation. This implies that the long-term use of olive oil may cause up-regulation of the enterocytes' ability to process dietary triacylglycerol and synthesize chylomicrons [38]. HC diets are known for their hypertriglyceridemic effect [39]. Down-regulation of muscle lipoprotein lipase (LPL) activity by HC diets was reported as the mechanism underlying the rise in triglyceride levels [40].

This study provides additional data on the importance of diet composition, in weight-reducing regimens, for obese hyperinsulinemic subjects. The normalization of insulinemia with HM diets, combined with our previous reports on a similar effect with high protein hypoenergetic diets constitute preliminary data which needs to be pursued in studies with a larger number of subjects and for a longer duration of 7–8 weeks. The study provides evidence suggesting that hyperinsulinemic normoglycemic obese subjects may constitute a subgroup of the obese population who may benefit from a diet lower in carbohydrates and higher in monounsaturated fats for restoring normoinsulinemia and achieving the desired weight reduction.

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REFERENCES

[1] Després JP. Insulin resistance: influence of diet and exercise. Symposium on 'Reducing cardiovascular disease risk: today's achievements and tomorrow's opportunities'. Proc Nutr Soc 2000; 59: 427.

[2] Daly ME, Vale C, Walker M *et al.* Dietary carbohydrates and insulin sensitivity: a review of the evidence and clinical implications. Am J Clin Nutr 1997; 66: 1072–85.

[3] Hung T, Sievenpiper JL, Marchie A *et al.* Fat versus carbohydrate in insulin resistance, obesity, diabetes and cardiovascular disease. Curr Opin Clin Nutr Metab Care 2003; 6: 165–76.

[4] Grundy SM. The optimal ratio of fat-to-carbohydrate in the diet. Annu Rev Nutr 1999; 19: 325–41.

[5] Kris-Etherton PM, Pearson TA, Wan Y *et al.* High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. Am J Clin Nutr 1999; 70: 1009–15.
[6] Storlein LH, Tapsell LC, Calvert GD. Role of dietary factors: macronutrients. Nutr Rev 2000; 58: S7–S9.
[7] Lovejoy JC, Windhauser MM, Rood JC, de la Bretonne JA. Effect of a controlled high-fat versus low-fat diet on insulin sensitivity and leptin levels in African-American and Caucasian women. Metabolism 1998; 47: 1520–4.
[8] Lovejoy JC, Champagne CM, Smith SR *et al.* Relationship of dietary fat and serum cholesterol ester and phospholipid fatty acids to markers of insulin resistance in men and women with a range of glucose tolerance. Metabolism 2001; 50: 86–9.
[9] Storlien LH, Jenkins AB, Chisholm DJ *et al.* Influence of dietary fat composition on development of insulin resistance in rats: relationship to muscle triglyceride and ω-3 fatty acids in muscle phospholipid. Diabetes 1991; 40: 280–9.
[10] Folsom AR, Ma J, McGovern PG, Eckfeldt JH. Relation between plasma phospholipid saturated fatty acids and hyperinsulinemia. Metabolism 1996; 45: 223–8.
[11] Fukagawa NK, Anderson JW, Hageman G *et al.* High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. Am J Clin Nutr 1990; 52: 524–8.
[12] Brand-Miller JC, Colagiuri S. Evolutionary aspects of diet and insulin resistance. World Rev Nutr Diet 1999; 84: 74–105.
[13] Garg A, Bantle JP, Henry RR *et al.* Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA 1994; 271: 1421–8.
[14] Storlein LH, Higgins JA, Thomas TC *et al.* Diet composition and insulin action in animal models. Br J Nutr 2000; 83 (Suppl.): S85–90.
[15] Golay A, Allaz A-F, Ybarra J *et al.* Similar weight loss with low-energy food combining or balanced diets. Int J Obs Relat Metab Disord 2000; 24: 492–6.
[16] Hwalla Baba N, Torbay N, Sawaya S *et al.* High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. Int J Obes 1999; 23: 1202–6.
[17] Nutritionist Pro Software, version 1.2, 2002. San Bruno, CA: First Data Bank (www.firstdatabank.com).
[18] Heymsfield SB, Allison DB, Wang Z-M *et al.* Evaluation of total and regional body composition. In: Bray GA., Bouchard C., James WPT (eds) Handbook of Obesity. New York: Marcel Dekker, 1998, 41.
[19] Van Loan MD, Mayclin PL. Body composition assessment: dual-energy X-ray absorptiometry (DEXA) compared to reference methods. Eur J Clin Nutr 1992; 46: 125–30.
[20] Matthews DR, Hosker JP, Rudenski AS *et al.* Homeostatic model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985; 28: 412–19.
[21] Spritzer PM, Poy M, Wiltgen M *et al.* Endocrine metabolic features in hirsute patients with PCOS or idiopathic hirsutism: the influence of obesity. Proceedings of the Annual Meeting of the Endocrine Society (ENDO' 98), New Orleans, USA, 1998, abstract P1-364, 196.
[22] McAuley KA, Williams SM, Mann JI *et al.* Diagnosing insulin resistance in the general population. Diabetes Care 2001; 24: 460–4.
[23] Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18: 499.
[24] Torbay N, Hwalla Baba N, Sawaya S *et al.* High protein vs high carbohydrate hypoenergetic diet in treatment of obese normoinsulinemic and hyperinsulinemic subjects. Nutr Res 2002; 22: 587–98.
[25] Slabber M, Barnard HC, Kuyl JM *et al.* Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females. Am J Clin Nutr 1994; 60: 48–53.
[26] Oglivie RF. The Islands of Langerhans in 19 cases of obesity. J Pathol 1933; 37: 473.
[27] Laakso M, Uusitupa M, Takala J *et al.* Effects of hypocaloric diet and insulin therapy on metabolic control and mechanisms of hyperglycemia in obese non-insulin-dependent diabetic subjects. Metabolism 1988; 37: 1092–100.
[28] Friedman JE, Dohm GL, Legget-Frazier N *et al.* Restoration of insulin responsiveness in skeletal muscle of morbidly obese patients after weight loss: effect on muscle glucose transport and glucose transporter GLUT4. J Clin Invest 1992; 89: 701–5.
[29] Heilbronn LK, Noakes M, Clifton PM. Effect of energy restriction, weight loss, and diet composition on plasma lipids and glucose in patients with type 2 diabetes. Diabetes Care 1999; 22: 889–95.
[30] Low CC, Grossman EB, Gumbiner B. Potentiation of effects of weight loss by monounsaturated fatty acids in obese NIDDM patients. Diabetes 1996; 45: 569–75.
[31] Gumbiner B, Low CC, Reaven PD. Effects of a monounsaturated fatty acid-enriched hypocaloric diet on cardiovascular risk factors in obese patients with type 2 diabetes. Diabetes Care 1998; 21: 9–15.
[32] Bonanome A, Visonà A, Lusiani L *et al.* Carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus: effects of a low-fat, high-carbohydrate diet vs a diet high in monounsaturated fatty acids. Am J Clin Nutr 1991; 54: 586–90.
[33] Thomsen C, Rasmussen O, Christiansen C *et al.* Comparison of the effects of a monounsaturated

fat diet and a high carbohydrate diet on cardiovascular risk factors in first degree relatives to type-2 diabetic subjects. Eur J Clin Nutr 1987; 52: 818–23.
[34] Ruiz-Gutiérrez V, Morgado N, Prada JL *et al.* Composition of human VLDL triacylglycerol after ingestion of olive oil and high oleic sunflower oil. J Nutr 1998; 128: 570–6.
[35] McNamara DJ. Dietary fatty acids, lipoproteins, and cardiovascular disease. Adv Food Nutr Res 1992; 36: 253.
[36] Montalto MB, Bensadoun A. Lipoprotein lipase synthesis and secretion: effects of concentration and type of fatty acids in adipocyte cell culture. J Lipid Res 1993; 34: 397–407.
[37] Kafatos A, Comas GE. Biological effect of olive oil in human health. In: Kiritsakis A (ed.) Olive Oil. Champaign, IL: American Oil Chemists Society, 1990, 157.
[38] Roche HM, Zampelas A, Knapper JME *et al.* Effect of long-term olive oil dietary intervention on postprandial triacyglycerol and factor VII metabolism. Am J Clin Nutr 1998; 68: 552–60.
[39] Blades B, Garg A. Mechanisms of increase in plasma triacylglycerol concentrations as a result of high carbohydrate intakes in patients with non-insulin-dependent diabetes mellitus. Am J Clin Nutr 1995; 62: 996–1002.
[40] Kiens B, Essen-Gustausson B, Gad P, Lithell H. Lipoprotein lipase activity and intra-muscular triglyceride stores after long-term high fat and high-carbohydrate diets in physically trained men. Clin Physiol 1987; 7: 1.

APPENDIX

An Itemized Composition of the Diets

Group 1. High Carbohydrate Hypoenergetic Diet

Days	Breakfast	Lunch	Supper
1	French toast, cottage cheese, cucumber, tomato	Spaghetti and tomato sauce, mozzarella, salad (lettuce, cucumber, tomato), fruit (apple)	Bread white soft and spinach, pineapple juice (unsweetened), custard *** 2 tsp corn oil added**
2	Bread white soft, cottage cheese, cucumber, tomato	Lentils and rice, cabbage and tomato salad, fruit (orange)	Potato boiled, tomato, lettuce, cucumber, canned pineapple juice (unsweetened) *** 8 tsp corn oil added**
3	Bread white soft, cottage cheese, cucumber, tomato	Lima beans and rice, mixed salad (lettuce, tomato, cucumber), fruit (apple)	Turkeyslice and French toast, canned pineapple juice (unsweetened) *** 4 tsp corn oil added**
4	Bread white soft, yogurt, cucumber, tomato	Rice, boiled potato, lean meat beef boiled, fruit (orange)	Bread white soft, cottage cheese, canned orange juice *** 6 tsp corn oil added**
5	French toast, cottage cheese, boiled egg, low fat cheese spread, tomato, cucumber	Pasta and tomato sauce, salad (tomato, lettuce, cucumber), fruit (orange)	Bread white soft, beef, yogurt, fruit (apple) *** 2 tsp corn oil added**
6	Bread white soft, yogurt, cucumber, tomato	Beans boiled, salad (lettuce, cucumber, tomato, onion)	Bread white soft, tuna, fruit cocktail juice *** 5 tsp corn oil added**
7	French toast, cottage cheese, cucumber, tomato	Peas and carrot stew with white rice, fruit (orange)	French toast, cottage cheese, fruit (apple) *** 4 tsp corn oil added**

Group 2. High Monounsaturated Fat (HM) Hypoenergetic Diet

Days	Breakfast	Lunch	Supper
1	Cottage cheese, French toast, tomato	Chicken breast with white rice, salad (tomato, lettuce, cucumber), fruit (apple)	Tuna in water, French toast, orange juice *** 14 tsp olive oil added**
2	Bread white soft, cottage cheese, cucumber, fruit	Beef cooked, green beans, salad (lettuce, tomato, cucumber), fruit (apple)	Kidney beans, bread white soft, fruit (orange) *** 14 tsp olive oil added**
3	French toast, cottage cheese, boiled egg, tomato	Chicken breast, baked potatoes and corn, cabbage salad, tomato	Low fat feta cheese, French toast, canned pineapple juice *** 12 tsp olive oil added**
4	Bread white soft, cottage cheese, tomato, cucumber	Beef cooked and white rice, salad (tomato, cucumber, lettuce), fruit (orange)	Green beans in olive oil, fruit (apple) *** 16 tsp olive oil added**
5	French toast, cottage cheese, cucumber	Chicken breast, baked potatoes, cabbage salad, fruit (apple)	Turkey slices, yogurt, French toast, orange juice *** 16 tsp olive oil added**
6	Bread white soft, cottage cheese, tomato, fruit (orange)	Broiled fish fillet, boiled squash, carrots, green salad (lettuce, tomato), fruit (apple)	Kibbeh (ground lean meat beef and parboiled wheat mix), yogurt, fruit (apple) *** 19 tsp olive oil added**
7	Bread white soft, cottage cheese, tomato	Chicken breast stewed, noodles, raw sweet green pepper, corn boiled, salad (cabbage, carrots), fruit (apple)	Chicken breast stewed, salad (lettuce, tomato, cucumber), pineapple juice *** 17 tsp olive oil added**