International Journal of Obesity (2005) 1–9

0307-0565/05 $30.00
www.nature.com/ijo

ORIGINAL ARTICLE

Randomized, multi-center trial of two hypo-energetic diets in obese subjects: high- versus low-fat content

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Objective: To investigate whether a hypo-energetic low-fat diet is superior to a hypo-energetic high-fat diet for the treatment of obesity.
Design: Open-label, 10-week dietary intervention comparing two hypo-energetic (−600 kcal/day) diets with a fat energy percent of 20–25 or 40–45.
Subjects: Obese (BMI $\geqslant$30 kg/m^2) adult subjects ($n=771$), from eight European centers.
Measurements: Body weight loss, dropout rates, proportion of subjects who lost more than 10% of initial body weight, blood lipid profile, insulin and glucose.
Results: The dietary fat energy percent was 25% in the low-fat group and 40% in the high-fat group (mean difference: 16 (95% confidence interval (CI) 15–17)%). Average weight loss was 6.9 kg in the low-fat group and 6.6 kg in the high-fat group (mean difference: 0.3 (95% CI −0.2 to 0.8) kg). Dropout was 13.6% ($n=53$) in the low-fat group and 18.3% ($n=70$) in the high-fat group ($P=0.001$). Among completers, more subjects lost >10% in the low-fat group than in the high-fat group ((20.8%, $n=70$) versus (14.7%, $n=46$), $P=0.02$). Fasting plasma total, low-density lipoprotein- and high-density lipoprotein-cholesterol decreased in both groups, but more so in the low-fat group than in the high-fat group. Fasting plasma insulin and glucose were lowered equally by both diets.
Conclusions: The low-fat diet produced similar mean weight loss as the high-fat diet, but resulted in more subjects losing >10% of initial body weight and fewer dropouts. Both diets produced favorable changes in fasting blood lipids, insulin and glucose.
International Journal of Obesity advance online publication, 6 December 2005; doi:10.1038/sj.ijo.0803186

Keywords: blood lipids; lipoprotein-cholesterol; drop-out rate; low-carbohydrate diet

Introduction

The rapidly increasing prevalence of obesity is a major, global health problem because of the increased risk of serious complications such as cardiovascular disease, type 2 diabetes and some cancers.[1] Even a minor weight loss of 4–6% in obese individuals with impaired glucose tolerance is associated with a reduction of the risk of type 2 diabetes by 58% within 3–5 years.[2,3]

Successful weight loss depends upon achieving negative energy balance, and the scientific debate regarding the

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[13]NUGENOB is the acronym of the project 'Nutrient-Gene interactions in human obesity – implications for dietary guidelines' supported by the European Community (Contract no. QLK1-CT-2000-00618), see the web-site www.nugenob.org
Received 7 January 2005; revised 1 May 2005; accepted 29 May 2005

optimal macronutrient composition for the dietary treatment of obesity requires a better evidence-based fundament. Meta-analyses of intervention trials have demonstrated that *ad libitum* low-fat diets produce 3–4 kg weight loss over 3–6 months,[4] and there is some evidence to suggest that weight maintenance is easier to achieve by a fat-reduced diet than with a higher fat diet.[5] While there is little evidence to support any important difference between low-fat diets with complex and simple carbohydrates,[6] higher protein levels might improve weight loss.[7] However, very few randomized trials have been conducted, which combine energy restriction and compare different levels of energy from fat and carbohydrate. These studies have included only small numbers of obese subjects and have therefore limited statistical power to detect clinically relevant differences in weight loss and body composition.[8,9]

Dietary composition also affects risk factors for cardiovascular disease and type 2 diabetes independently of weight loss. Increasing the percentage of total energy from carbohydrate while decreasing the percentage of energy from fat may lower fasting plasma total and low-density lipoprotein (LDL)-cholesterol and also high-density lipoprotein (HDL)-cholesterol concentrations, and increase, at least initially, fasting plasma triacylglycerol concentration.[10,11] The same changes in the diet induce a lowering of fasting plasma insulin concentrations, reflecting an increase in whole-body insulin sensitivity.[12] However, it is less clear which diet composition has the most beneficial effect during hypo-energetic dieting.

The objective of this study was, in a randomized intervention trial with obese subjects from eight centers in seven European countries, to examine if a 10-week low-fat hypo-energetic diet has a more beneficial effect on body weight, body composition and concentrations of fasting plasma lipids, glucose and insulin than a high-fat hypo-energetic diet.

Subjects and methods

Protocol

The study was a randomized, parallel, two-arm, open-label 10-week dietary intervention of two hypo-energetic diets at eight sites in seven European countries: United Kingdom (England), The Netherlands, France (two centers), Spain, Czech Republic, Sweden and Denmark. The trial was part of a study of gene–nutrient interactions in the physiology and dietary treatment of obesity (see www.nugenob.org), in which it was planned to recruit 100 subjects from each center of the seven centers and 50 from one center. This would allow the study to detect 0.7 kg difference in weight loss, assuming a standard deviation (s.d.) of 4 kg, a significance P-value of 0.05 and a statistical power of 0.90.

Participants

We included 771 Caucasian Europeans (579 women). Inclusion criteria were body mass index $\geqslant 30\,kg/m^2$ and age 20–50 years. Exclusion criteria were weight change $>3\,kg$ within the 3 months before the start of the study, hypertension, diabetes or hyperlipidemia treated by drugs, untreated thyroid disease, surgically or drug-treated obesity, pregnancy, participation in other trials, alcohol or drug abuse. However, some subjects were erroneously included despite a slightly lower BMI, and slightly greater antecedent weight loss, but a sensitivity analysis was conducted to examine the importance for the outcome (see statistical analysis). Analyses evaluating whether excluding the subjects who either had an inconsistent report of previous weight stability (n=82) or failed to meet one or more of the inclusion criteria for body mass index, fasting glucose, inconsistent bioimpedance measurement, medication, menopausal status or race (n=71) gave similar results, which are not presented. Participants were recruited through the media, from waiting lists, ongoing population studies, by self-referral or referral from a general physician or other clinical units and local obesity organizations. Recruitment of subjects was undertaken from May 2001 until September 2002. The study was approved by the Ethical Committee at each of the participating centers. Volunteers were informed about the nature of the study, and written consent was obtained before study participation.

Assignment

Stratified block randomization was used with center, gender and three age groups (20–29, 30–39 and 40–50 years) as strata and a block size of 12. The randomization list was computer generated and the block size was unknown to the clinical centers. Randomization was performed by contacting the coordinating center at each allocation (see details at www.nugenob.org).

Participant flow

The flow of participants is shown in Figure 1.

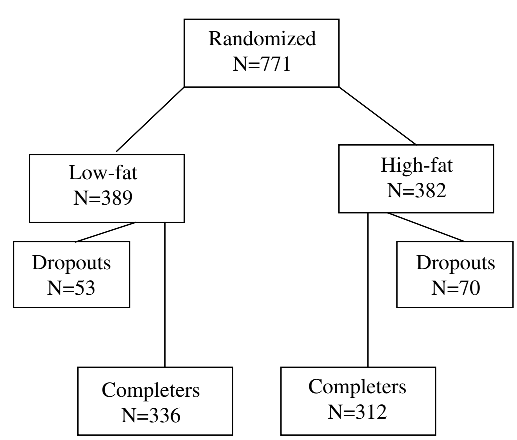

Figure 1 Flow chart describing the progress of participants throughout the trial.

Diets

The target macronutrient composition of the two diets was as follows: low-fat diet – 20–25% of total energy from fat, 15% from protein and 60–65% from carbohydrate; high-fat diet – 40–45% of total energy from fat, 15% from protein and 40–45% from carbohydrate. Both diets were designed to provide 600 kcal/day (1 kilocalorie (kcal) = 4.2 kilo joule (kJ)) less than the individually estimated energy requirement based on an initial resting metabolic rate multiplied by 1.3. Subjects were given oral and written instructions relating to these targets based on either a template (see details at www.nugenob.org) or an exchange system.[13] Instructions were also given to minimize differences between the two diets in other components such as sources and type of fat, amount and type of fiber, type of carbohydrate, fruit and vegetables, and meal frequency. Subjects were requested to abstain from alcohol consumption. Dietary advice reflected local customs, and all food items were purchased by the subjects themselves. The dietary instructions were reinforced weekly. At each session, the dietician and the participant rated compliance with the dietary advice on a scale from 1 to 5, with perfect compliance equal to 1.

A 3-day-weighed food record of two weekdays and one weekend day was performed before the study and during the last week of the intervention. One-day-weighed food records were completed in the 2nd, 5th and 7th weeks. The dietary records were analyzed using the food–nutrient database routinely used in each center.

Anthropometry and metabolic rate

Body weights were measured on calibrated scales. Waist and hip circumferences were measured with the participant wearing only non-restrictive underwear. Body height was measured with a calibrated stadiometer. The mean of three measurements was recorded for each variable. Fat mass and fat-free mass were assessed by multifrequency bioimpedance (Bodystat®; QuadScan 4000, Isle of Man, British Isles). Resting metabolic rate was measured by ventilated hood systems routinely used at each center, and a standardized validation program was used to facilitate pooling of the results from the different centers.

Biochemical analyses

Venous blood samples were drawn after an overnight fast of 12 h, following a 3-day period when subjects had been instructed to avoid excessive physical activity or alcohol consumption. Subjects rested in the supine position for 15 min before the procedure. Fasting plasma glucose and lipid concentrations were measured with standard enzymatic techniques on a COBAS FARA centrifugal spectrophotometer (Roche Diagnostica, Basel, Switzerland; glucose HK 125, ABX Diagnostics, Montpellier, France; triglycerides, Sigma, St Louis, MO, USA; total cholesterol, cholesterol 100, ABX Diagnostics Montpellier France; HDL, HDL-C, Roche, IN, USA). Fasting plasma LDL-cholesterol was calculated using the formula of Friedewald *et al.*[14] Fasting plasma insulin concentration was measured with a double-antibody radioimmunoassay (Insulin, RIA 100, Kabi-Pharmacia, Uppsala, Sweden). All biochemical analyses were conducted independently of the allocated intervention groups in core facilities at the Department of Human Biology, Nutrition Research Centre NUTRIM, Maastricht University, and Medical Laboratories Dr Stein & colleagues, Mönchengladbach, Germany.

Statistical analysis

The primary outcomes were mean weight loss and proportion of subjects who lost more than 10% of initial body weight, but we also analyzed the proportion of subjects who lost more than 5% of their initial body weight. The weight loss was calculated as the difference between the weight recorded immediately before randomization and the weight at the completion of the intervention program. Secondary outcomes were drop out, body composition, and blood lipids, insulin and glucose. Baseline differences were compared by an independent two-sample *t*-test. Differences in the changes were compared by univariate General Linear Models controlling for center and baseline value, and as appropriate with gender as covariate. To analyze changes within a group, paired samples *t*-tests were used. Variables with skewed distributions were log-transformed, and distributions were described by mean and s.d.. Testing of treatment effects on dichotomous outcomes (dropout rates and weight loss exceeding 5 and 10% of body weight) was performed by logistic regression allowing for both treatments, gender and center effects and using a robust estimation of the variance. Reasons for dropout were compared by χ^2 test. The time courses of weight loss with the two diets were compared by repeated measurement analysis in General Linear Models. A thorough analysis of the impact on the estimated effects of the dietary regimens of the missing values, owing to the absence from some of the scheduled visits at the clinics and dropout, was conducted according to the methods recently suggested by Gadbury *et al.*[15] This involved multiple imputation of the missing values and analysis by mixed linear models based on the assumption that values missing at random were conditional on the relevant observed values. In addition, a sensitivity analysis based on the assumptions of plausible deviant missing values in either direction of the results obtained was conducted. The outcomes of these analyses were essentially similar to those presented in the results section, and did not change the basis of the conclusions drawn from the results and are therefore not shown (they can be obtained on request). Statistical significance was set at $P<0.05$. The statistical software SPSS version 11.5, SAS version 8.2 and Stata version 8.0 were used.

Results

The analyses were first conducted in men and women separately, and the results were presented for each gender. However, no significant differences in outcome were found between the two genders, and they were therefore also analyzed together.

Baseline characteristics and dropouts

The two groups were well matched at randomization (Table 1). Seventy (18.3%) failed to complete the 10-week high-fat intervention and only 53 (13.6%) failed to complete the low-fat intervention ($P = 0.001$). Causes of dropout between the two groups were not statistically different and included change in personal circumstances, dislike of the diet and emerging health problems unrelated to the treatments. There were no clinically or statistically significant differences with respect to the variables listed in Table 1 between the participants who completed and those who did not, or between non-completers in the high- and the low-fat groups. The time point and the weight lost at dropout were not significantly different between the two groups.

Dietary intake

The self-reported, baseline dietary intake of the two groups was similar (Table 2). The fat energy percent during the interventions was within the targeted interval: 25% in the low-fat group and 40% in the high-fat group with a group difference of 16% (95% confidence interval (CI) 15–17%). Energy intake decreased to a slightly lower level in the low-fat group than in the high-fat group ($P = 0.023$). The fiber intake was approximately 20% higher in the low-fat group than in the high-fat group ($P < 0.001$). The percentage of energy from protein was slightly higher in the low fat diet, but total intake was not different. There was no difference between the compliance ratings for the two diets. The ratio of saturated to monounsaturated to polyunsaturated fatty acids was approximately 2:2:1 in the habitual diet and in the two intervention diets.

Body weight and body composition

Mean weight loss was 6.9 kg in the low, and 6.6 kg in the high-fat group with no group difference (mean 0.3 (95% CI −0.2 to 0.8) kg) (Table 3). The proportion of subjects who lost more than 5% was, on the low-fat diet 72.0% (242/336), and on the high-fat diet, 70.5% (220/312) ($P = 0.67$). The proportion of subjects who lost 10% or more was greater in the low (20.8%, $n = 70$) than in the high-fat group (14.7%,

Table 1 Baseline characteristics of subjects at randomization

	High fat (n = 382)		*Low fat* (n = 389)	
	Women (n = 287)	*Men* (n = 95)	*Women* (n = 292)	*Men* (n = 97)
Age (years)	37 (8)	38 (8)	36 (8)	39 (7)
Body weight (kg)	97.3 (14.8)	111.6 (16.0)	96.7 (15.0)	110.6 (18.0)
Height (m)	1.65 (0.06)	1.79 (0.07)	1.64 (0.07)	1.78 (0.07)
BMI (kg/m^2)	35.8 (5.0)	34.9 (4.5)	35.9 (4.9)	34.7 (5.1)
Fat-free mass (kg)	53.9 (5.6)	76.9 (6.9)	53.7 (5.7)	76.0 (7.9)
Fat mass (kg)	43.6 (11.1)	34.8 (10.7)	43.0 (11.1)	34.5 (11.9)
Body fat (%)	44.2 (5.1)	30.6 (5.1)	43.9 (5.0)	30.5 (5.6)
Waist circumference (cm)	103.4 (11.9)	114.6 (11.6)	103.4 (12.2)	114.0 (12.5)
Hip circumference (cm)	121.2 (10.5)	114.9 (8.0)	120.6 (10.5)	115.2 (9.8)
Resting metabolic rate (kcal/day)	1740 (226)	2151 (323)	1744 (251)	2119 (304)

BMI = body mass index. Values are means (s.d.).

Table 2 Compositions of the habitual diet, the low- and the high-fat diets of the obese subjects

	Habitual (n = 745[a]) (562 women, 185 men)	*High fat* (n = 370[a])[b] (278 women, 92 men)	*Low fat* (n = 377[a])[b] (284 women, 93 men)
Energy intake (kcal/day)			
Women	2029 (550)	1514 (258)	1447 (258)
Men	2675 (838)	1928 (312)	1900 (442)
All	2187 (691)	1620 (327)	1561 (371)[c]
% of total energy from fat			
Women	36 (7)	40 (5)	24 (5)
Men	37 (8)	40 (6)	26 (5)
All	36 (8)	40 (5)	25 (5)[c]
% of total energy from carbohydrate			
Women	46 (8)	43 (5)	57 (5)
Men	44 (9)	42 (6)	56 (6)
All	45 (9)	43 (5)	57 (6)[c]
% of total energy from protein			
Women	17 (4)	17 (3)	18 (3)
Men	16 (3)	17 (2)	18 (2)
All	17 (4)	17 (3)	18 (3)[c]
% of total energy from alcohol[d]			
Women	1 (3)	0.1 (0.4)	0.2 (0.8)
Men	3 (5)	0.4 (1.1)	0.5 (1.5)
All	2 (4)	0.2 (0.7)	0.4 (2.0)[c]
Dietary fiber (g/day)			
Women	17 (7)	18 (6)	22 (7)
Men	21 (9)	23 (7)	26 (9)
All	18 (8)	19 (7)	23 (8)[c]

The composition of the habitual diet is based on a mean of a 3-day-weighed food record. The intervention diets are based on a mean of 1-day-weighed food records conducted in the 2nd, 5th and 7th weeks and a 3-day-weighed record in the last week of the 10-week intervention. Values are means (s.d.). [a]A small proportion of subjects did not complete the dietary records. [b]All values for dietary intake during both interventions were statistically different from the habitual values. [c]Significantly different from the high-fat diet. [d]The % of total amount of energy from alcohol were non-normally distributed. The habitual median and 5th and 95th percentiles were 0.0 (0.0–9.3) %. During the intervention the % of total amount of energy from alcohol were 0.0 (0.0–1.3) % in the high- versus 0.0 (0.0–2.3) % in the low-fat group. These values were tested by non-parametric tests.

Table 3 Baseline and 10-week measurements of body weight and body composition in subjects completing the intervention

	High fat (235 women, 77 men)[a]		*Low fat (251 women, 85 men)*[a]		*Difference in mean change*[b]
	Baseline	*Decrease*	*Baseline*	*Decrease*	*(95% CI)*[c]
Body weight (kg)					
Women	97.4 (14.9)	6.1 (3.4)	96.7 (15.2)	6.7 (3.1)	—
Men	110.9 (14.7)	8.2 (3.4)	110.3 (17.6)	7.6 (4.0)	—
All	100.7 (16.0)	6.6 (3.5)	100.2 (16.9)	6.9 (3.4)	−0.3 (−0.8 to 0.2)
BMI (kg/m^2)					
Women	35.8 (5.0)	2.2 (1.2)	35.8 (4.9)	2.5 (1.1)	—
Men	34.9 (4.3)	2.6 (1.1)	34.5 (4.8)	2.4 (1.3)	—
All	35.6 (4.9)	2.3 (1.2)	35.5 (4.9)	2.5 (1.2)	−0.1 (−0.4 to 0.04)
Fat mass (kg)					
Women	43.6 (11.2)	4.9 (3.2)	43.1 (11.3)	5.4 (2.9)	—
Men	34.7 (10.0)	5.5 (6.2)	33.9 (11.3)	5.5 (3.6)	—
All	41.4 (11.6)	5.0 (4.1)	40.8 (12.0)	5.4 (3.1)	−0.5 (−1.0 to 0.1)
Fat-free mass (kg)					
Women	54.0 (5.7)	1.3 (2.3)	53.6 (5.8)	1.3 (2.4)	—
Men	76.3 (6.4)	2.8 (6.1)	76.3 (7.9)	2.0 (2.2)	—
All	59.5 (11.3)	1.6 (3.7)	59.4 (11.7)	1.5 (2.3)	0.1 (−0.3 to 0.6)
Waist circumference (cm)					
Women	103.3 (12.1)	5.5 (4.6)	103.4 (12.3)	5.5 (7.0)	—
Men	114.1 (10.4)	7.7 (3.9)	113.6 (12.3)	7.8 (4.6)	—
All	106.0 (12.6)	6.0 (4.5)	105.9 (13.1)	6.1 (6.5)	−0.1 (−0.9 to 0.8)
Hip circumference (cm)					
Women	121.0 (10.8)	4.5 (3.7)	120.5 (10.6)	5.2 (5.7)	—
Men	114.1 (7.8)	4.3 (3.4)	114.8 (8.9)	4.1 (3.3)	—
All	119.3 (10.5)	4.5 (3.6)	119.0 (10.5)	4.9 (5.2)	−0.5 (−1.2 to 0.2)

BMI = body mass index; CI = confidence interval. Baseline values and decreases are means (s.d.). [a]During the study, 70 and 53 subjects dropped out of the high- and low-fat group, respectively. [b]Mean difference in change is calculated by subtracting the mean decrease in the high-fat group from the mean decrease in the low-fat group. [c]The 95% CIs are adjusted for center, gender and baseline value.

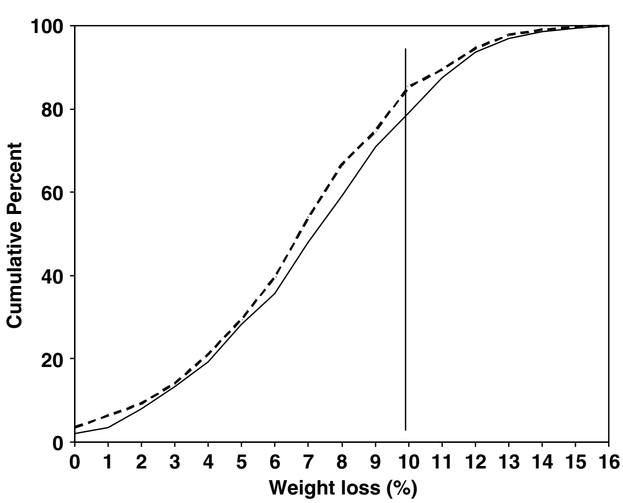

Figure 2 Cumulative percentage weight loss during the 10-week intervention for the 648 subjects completing the 10-week intervention. The black line represents the low (n = 336) and the dotted line the high-fat diet (n = 312). On the x-axis, 0 represents a weight increase, 1 represents a weight loss of <1%, 2 represents a weight loss of <2%, and so on. The vertical line indicates the definition of the outcome of losing >10% of initial body weight, which was significantly different in the two groups (P = 0.02).

n = 46; P = 0.02) (Figure 2). There was no difference in the time course of weight loss during the 10 weeks between the groups (Figure 3). The changes in fat-free mass, fat mass, waist and hip circumference were not statistically different between the groups. In the intention-to-treat analysis, based on the principle of 'last observation carried forward' showed there was a 6.1% reduction of body weight in the low-fat group versus 5.4% in the high-fat group.

Plasma lipids, glucose and insulin

The reduction of mean fasting plasma total cholesterol was 7.4% in the low versus 5.3% in the high-fat group (mean difference 2.2 (95% CI 0.4–4.0)%, P = 0.016) (Table 4). Fasting plasma LDL-cholesterol was lowered by 7.8% in the low versus 4.7% in the high-fat group (mean difference 3.3 (95% CI 0.8–5.8)%, P = 0.01). In the low-fat group, mean fasting plasma HDL-cholesterol was reduced by 7.3%, and by 2.4% in the high-fat group (mean difference 4.1 (95% CI 1.9–6.2)%, P<0.001). Mean fasting plasma triacylglycerol was lowered by 4.8% in the low and by 16.7% in the high-fat group (mean difference 5.7 (95% CI −0.5–11.8)%, P = 0.07). There was no difference in the change between the two diets

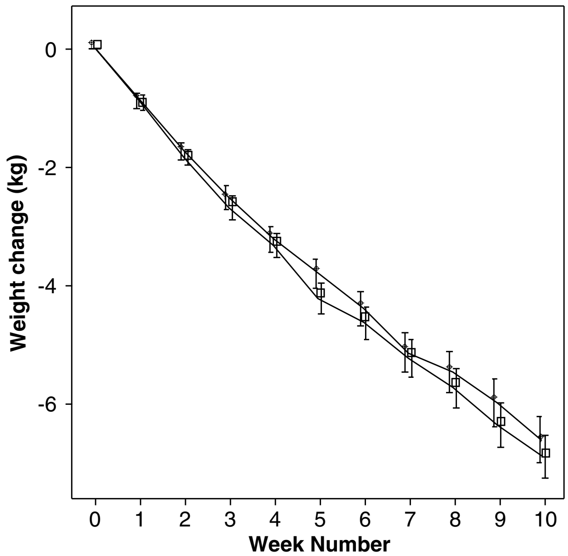

Figure 3 Mean weight change with 95% confidence interval for the 648 subjects completing the 10-week intervention on the low-fat diet (open squares, $n=336$) or the high-fat diet (filled squares, $n=312$). In weeks 1–9, the number of body weights recorded was less than 648.

in LDL/HDL ratio (mean difference 0.02 (95% CI −0.09 to 0.11)%). Fasting plasma insulin and glucose concentrations were lowered similarly by both diets.

Discussion

This 10-week randomized trial of two hypo-energetic diets with either low- or high-fat content, involving 771 obese subjects from eight centers in seven European countries, demonstrates that the two diets were not very different in producing a clinically significant weight loss in both women and men. There were however, in the low-fat group, fewer dropouts and a higher proportion of subjects who lost more than 10% of their initial body weight, than in the high-fat group. Fasting plasma total, LDL- and HDL-cholesterol were lowered more in the low-fat group, whereas fasting plasma insulin and glucose decreased equally in the two groups.

To minimize misreporting,[16–18] we carefully trained subjects in completing weighed food records. In order to prevent bias introduced by the enthusiasm of the dietician providing the intervention,[8] careful attention was paid to standardizing the delivery method of the dietary programs.

Table 4 Baseline and 10-week measurements of fasting plasma variables in subjects completing the intervention

	High fat (235 women, 77 men)[a]		*Low fat (251 women, 85 men)*[a]		*Difference in mean change*[b]
	Baseline	*Decrease*	*Baseline*	*Decrease*	*(95% CIs)*[c]
Plasma cholesterol (mmol/l)					
Women	4.85 (0.93)	0.20 (0.54)	4.92 (0.87)	0.32 (0.61)	—
Men	5.03 (0.92)	0.41 (0.57)	5.01 (0.83)	0.48 (0.68)	—
All	4.90 (0.93)	0.25 (0.55)	4.94 (0.86)	0.36 (0.63)	0.10 (0.02 to 0.18)
Plasma triacylglycerol (mmol/l)[d]					
Women	1.04 (0.83)	0.12 (0.67)	1.02 (0.52)	0.01 (0.39)	—
Men	1.49 (0.91)	0.40 (0.79)	1.19 (0.55)	0.13 (0.43)	—
All	1.15 (0.87)	0.19 (0.71)	1.06 (0.53)	0.04 (0.41)	−0.09 (−0.16 to (−0.03))
Plasma LDL-cholesterol (mmol/l)					
Women	3.24 (0.82)	0.11 (0.49)	3.28 (0.80)	0.21 (0.54)	—
Men	3.41 (0.75)	0.24 (0.51)	3.53 (0.78)	0.42 (0.62)	—
All	3.28 (0.81)	0.14 (0.50)	3.34 (0.80)	0.26 (0.57)	0.11 (0.03 to 0.18)
Plasma HDL-cholesterol (mmol/l)					
Women	1.16 (0.30)	0.05 (0.17)	1.19 (0.31)	0.11 (0.18)	—
Men	0.96 (0.22)	0.00 (0.14)	0.94 (0.21)	0.00 (0.14)	—
All	1.11 (0.29)	0.04 (0.16)	1.12 (0.31)	0.08 (0.18)	0.04 (0.02 to 0.07)
Plasma insulin (μU/ml)[d]					
Women	10.2 (6.8)	0.74 (6.1)	9.5 (5.0)	1.1 (4.1)	—
Men	12.0 (5.7)	2.7 (5.1)	10.9 (7.2)	1.5 (6.7)	—
All	10.7 (6.6)	1.2 (5.9)	9.9 (5.7)	1.2 (4.9)	0.3 (−0.5 to 1.0)
Plasma glucose (mmol/l)					
Women	5.32 (0.67)	0.07 (0.44)	5.29 (1.00)	0.11 (0.47)	—
Men	5.74 (0.62)	0.37 (0.51)	5.71 (1.21)	0.17 (0.54)	—
All	5.43 (0.68)	0.14 (0.48)	5.39 (1.07)	0.12 (0.49)	−0.01 (−0.08 to 0.05)

BMI = body mass index; CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein. Baseline values and decreases are mean (s.d.). [a]During the study, 70 and 53 subjects dropped out of the high- and low-fat group, respectively. [b]Mean difference in change is calculated by subtracting the mean decrease in the high-fat group from the mean decrease in the low-fat group. [c]The 95% CIs are adjusted for center, gender and baseline value. [d]Plasma triacylglycerol and plasma insulin were non-normally distributed. The baseline median and 5 and 95 percentiles for total plasma triacylglycerol were 0.92 (0.42–2.71) mmol/l in the high-fat group versus 0.95 (0.46–2.05) mmol/l in the low-fat group and for plasma insulin 9.5 (2.7–21.2) μU/ml versus 8.6 (2.3–20.2) μU/ml, respectively.

Based on the differences between fat and carbohydrate in digestibility and thermogenic effect, and interactions between diet composition and exercise, it has been suggested that low-fat diets are superior to higher fat diets in producing a weight loss.[19,20] Short-term test meal studies with calorie for calorie comparisons suggest that carbohydrate is more satiating than fat and that overeating may be more likely with a high-fat diet because of the higher energy density and greater sensory pleasure.[21,22] The present study demonstrates that these potential differences produced by energy-fixed diets with various fat and carbohydrate contents do not translate into overall weight loss differences, but may contribute to explain why more subjects lost >10% of the initial body weight in the low-fat group. However, it is important to stress that the study duration of only 10 weeks was relatively short in the course of a weight management program, and diet palatability and tolerability might have more important influence on weight loss outcome in long-term studies.

Other studies suggest that diets high in protein and fat, but with very low carbohydrate contents, might be more satiating, and produce better weight loss than low-fat diets with normal protein content.[4] However, it is very likely that the high protein content rather than the high-fat content is responsible for the weight loss effect with these diets.[7] Our results suggest that a larger proportion of obese subjects achieve a major weight loss, that is, more than 10%, and fewer will drop out on the low-fat diet. This is in line with previous *ad libitum* studies,[4–6] and suggests that energy from carbohydrate are slightly more satiating than those from fat also under conditions with a fixed energy deficit.

We did find a slightly greater reduction in energy intake in the low- compared with the moderate-fat group, which may be attributed to a greater satiating effect of the low-fat diet. The difference of 60 kcal/day during a 10-week period corresponds to a difference in weight loss of ~0.54 kg,[23] which is within the 95% CI of the difference in weight loss among completers (−0.2–0.8 kg). The slightly lower weight loss in the high-fat diet may also be explained by the contrast with subjects' expectations regarding dietary weight loss regimens, and the challenge of providing an acceptable high-fat diet. This may also explain the lower rate of dropout in the low-fat diet group. In this study, a larger weight loss has been achieved than in most other studies. The intervention package included prescribed energy intake based upon an individually measured resting metabolic rate in contrast to others who used a fixed energy intake target.[7,8] A tailored dietary program was used, in contrast to one other study, which used a limited menu cycle,[6] and a high level of support was offered to the subjects.

The effect of the diets on blood lipids was as expected from other studies.[8,24] The slight reduction observed in HDL-cholesterol is very likely owing to the negative energy balance at the time of measurement. The effect of diet *per se* on HDL-cholesterol cannot be seen before the subject are weight stable. In previous studies, the undesirable reduction in HDL-cholesterol brought about by a low-fat diet had returned to baseline concentration by 6 months.[8] Other studies with smaller subject numbers showed either a limited[7] or no effect.[6] The decrease in the blood lipids is primarily a result of the weight loss *per se*. The present study additionally demonstrates that both diets have beneficial effects on blood lipids.

This study shows that when intensive support is given, dietary advice of a hypo-energetic high-fat diet adhered to during 10 weeks is almost as effective as a low-fat diet in producing weight loss. However, more subjects lost >10% of initial body weight on the low fat diet and fewer dropped out. Both diets produced beneficial changes in the fasting blood lipid profile, plasma insulin and glucose.

Acknowledgements

The study was supported by the European Community (Contract no. QLK1-CT-2000-00618). The funding organization had no role in the preparation of the manuscript.

Conflict of interest

None of the authors have any conflict of interest.

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