Metabolic and weight-loss effects of a long-term dietary intervention in obese patients[1–3]

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ABSTRACT

Background: Obesity is a chronic disease that has become one of the most serious health problems in Western society.

Objective: We assessed the long-term effects of an energy-restricted diet combined with 1 or 2 daily meal replacements on body weight and biomarkers of disease risk in 100 obese patients.

Design: Phase 1 consisted of a 3-mo, prospective, randomized, parallel intervention study of 2 dietary interventions to reduce weight. The energy-restricted diet (5.2–6.3 MJ/d) consisted of conventional foods (group A) or an isoenergetic diet with 2 meals and 2 snacks replaced daily by energy-controlled, vitamin-and-mineral-supplemented prepared foods (group B). Phase 2 consisted of a 24-mo, case-control, weight-maintenance study with an energy-restricted diet and 1 meal and 1 snack replaced daily for all patients.

Results: Total weight loss (as a percentage of initial body weight) was 5.9 ± 5.0% in group A and 11.3 ± 6.8% in group B ($P < 0.0001$). During phase 1, mean weight loss in group B ($n = 50$) was 7.1 ± 3.5 kg, with significant reductions in plasma triacylglycerol, glucose, and insulin concentrations ($P < 0.0001$). Group A patients ($n = 50$) lost an average of 1.3 ± 2.2 kg with no significant improvements in these biomarkers. During phase 2, both groups lost on average an additional 0.07% of their initial body weight every month ($P < 0.01$). During the 27-mo study, both groups experienced significant reductions in systolic blood pressure and plasma concentrations of triacylglycerol, glucose, and insulin ($P < 0.01$).

Conclusion: These findings support the hypothesis that defined meal replacements can be used for successful, long-term weight control and improvements in certain biomarkers of disease risk. *Am J Clin Nutr* 1999;69:198–204.

KEY WORDS Weight loss, biomarkers, disease risk, meal replacements, obesity, humans

INTRODUCTION

Persons with a body mass index (in kg/m^2) >27 have significant increases in age-related mortality (1, 2). Morbidity also increases because of the obesity-induced incidence of diabetes, coronary artery disease, and hypertension (3, 4). Clinical studies have suggested that minimal, sustained weight loss can reduce or eliminate these obesity-related disorders (3–8). Unfortunately, long-term outcome data show that most persons who lose weight regain the weight lost within 5 y (9) and that in those with abnormal biomarkers at the beginning of weight loss, these disease-associated risk factors are reestablished (9).

More recent evidence indicates that dietary interventions lasting 2 y that include the use of energy-controlled, nutrient-dense meal replacements remain a viable, practical, safe, and effective alternative to pharmacologic intervention (10). McCarron et al (11) found that patients who ate nutritionally balanced, prepackaged meals received greater clinical benefits and nutritional completeness and showed better compliance than did those following a self-selected food plan. Reductions in body weight were also associated with improvements in biomarkers of disease and obesity-related comorbidities (11). However, this study was limited in duration to 10 wk.

The present study was designed to test the hypothesis that meal replacements are a useful tool for sustained weight loss and that minimal, sustained weight loss will maintain improvements in biomarkers of disease risk. The study was 27 mo in duration and consisted of 2 phases. The first 3-mo phase was designed to test the efficacy of 2 modes of energy restriction on body weight loss and associated measures of obesity risk factors for disease, eg, blood pressure and plasma, triacylglycerol, glucose, and insulin concentrations. The second phase included the same patients for an additional 24 mo of weight maintenance to further test the hypothesis that moderate, sustained weight loss could sustain the improvements in the obesity risk factors for disease.

SUBJECTS AND METHODS

Subjects

The study patients were referred to the Obesity Center at the University Hospital of Ulm for obesity management. All patients

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had been treated by the referring practitioner with energy-restricted diets for ≥3 mo. Dissatisfaction with the degree of weight loss was the primary reason for transfer to the University Center.

The study was carried out according to the principles of the Helsinki Declaration and the protocol was approved by the Freiburg Ethics Committee International (Freiburg, Germany). Participants were informed that the purpose of the first phase of the study (phase 1) was to compare 2 diet plans for their ability to promote weight loss, whereas the purpose of the second phase of the study (phase 2) was to evaluate a single diet plan for long-term weight maintenance and improvement in blood indexes, eg, glucose homeostasis and blood lipid profiles associated with disease.

Exclusion criteria

Individuals with a history or presence of significant disease, endocrine disorders, psychiatric diseases, alcohol or drug abuse, or abnormal laboratory test results of clinical significance were excluded. In addition, women were excluded if they were lactating, pregnant, or wished to become pregnant.

Inclusion criteria

Patients were men and women aged >18 y whose body mass indexes were >25.0 and ≤40.0 and who gave their informed consent to participate. Patients indicated their willingness to be randomly assigned to study groups and to follow the program protocol, which included monthly hospital visits for physical examinations and review of diet records. One hundred patients met the inclusion criteria, agreed to be randomly assigned to study groups, and adhered to the study protocol.

Study design

The study was divided into 2 phases. Phase 1 (3 mo of weight loss) was a randomized, parallel intervention trial in which patients were randomly assigned to 1 of 2 dietary treatments (group A or B) by a computer-generated identification number. In phase 2 (24 mo of weight loss and weight maintenance), all patients were prescribed the same diet. Patients were analyzed according to their original group assignment. The patients were encouraged to maintain their usual level of physical activity throughout both phases of the study.

Dietary intervention

The dietary intervention during phase 1 was structured such that a staff nutritionist explained the diet plan in detail and counseled participants by using personalized sample menus and recipes and instruction in maintenance of a food diary. Throughout the study, patients were prescribed a balanced diet providing 5.2–6.3 MJ/d (1200–1500 kcal/d) and 19–21% of energy as protein, 48–54% of energy as carbohydrate, and 25–34% of energy as fat. Three meals (breakfast, lunch, and dinner) and 2 snacks (1 between breakfast and lunch and 1 between lunch and dinner) were recommended. The nutritionist provided monthly, personalized instructions by using food exchange lists and food diaries to equalize the prescribed energy intakes between groups A and B. Individual preferences for various food items were integrated into the diet plan.

During phase 1, the 3-mo weight-loss period, group A was prescribed a diet in which all meals and snacks were prepared from self-selected, conventional foods. Group B was prescribed similar self-selected diets, except that 2 of the 3 main meals (breakfast, lunch, or dinner) were replaced with meal-replacement shakes, soups, or hot chocolate (Slim•Fast; Slim•Fast Foods Company, West Palm Beach, FL). Each meal replacement contained 0.84–1.05 MJ energy, 14.0–17.0 g protein, 27.0–33.5 g carbohydrate, 5.0–6.6 g fat, and 4.5–6.5 g fiber and was supplemented with essential vitamins and minerals. In place of snacks, patients were provided with 2 nutrition snack bars (Slim•Fast) per day containing 0.38–0.46 MJ energy, 1.4–1.7 g protein, 16.1–18.1 g carbohydrate, 2.4–3.9 g fat, and 1.1 g fiber.

In phase 2, all patients were seen monthly and continued to receive the same instructions while following their food plans. The energy content of the prescribed diet was the same in both groups, and all patients were instructed to replace one meal and one snack with the energy-controlled, nutrient-dense meal and snack replacements.

Dietary records

At the initial visit, patients were instructed on food selection, meal portion control, and recording of daily dietary intakes. Accurate daily recording was stressed and daily food diaries were maintained for 7 consecutive days during the 2-wk period before each visit. Food quantities were recorded by using household measurements. Records were reviewed with each patient and analyzed monthly by the nutritionist. Nutrient calculations were carried out by using the German Food Code BLS and the NUTRILOG program (GiV, Göttingen, Germany).

Data collection

At each monthly visit, anthropometric data, blood pressure, and side effects were recorded. Weight measurements to the nearest 0.1 kg were taken by using the same precision scale with patients dressed only in underwear. Waist and hip circumferences were measured to the nearest 0.5 cm by using a nonstretchable tape measure. Waist circumference was measured midway between the lower rib margin and the iliac crest; hip circumference was measured at the widest point of the trochanter and buttocks area. The waist-to-hip circumference ratio was calculated. Blood pressure was measured on the upper right arm by using a mercury column manometer to the nearest 5 mm Hg at 0800 with the patient in a supine position and after the patient had rested for ≥10 min. Measurements were made at each visit under similar conditions. At baseline, 3 mo, and every 12 mo thereafter, blood samples were taken at ≈0800, ≥10 h after the previous meal. Biochemical measurements were done by standard methods in the Department of Clinical Chemistry at University Hospital.

Statistics

Comparisons of baseline values between the 2 groups, within a sex, were calculated by using a two-sample *t* test (12). Values are given as means ± SDs, unless stated otherwise. For phase 1, a linear regression model was fit for percentage weight change and absolute body weight with sex and group as covariates. The sex-by-group interaction was also considered. Treatment group was the only significant predictor of percentage weight change and absolute body weight.

For all secondary outcome variables, a two-sample *t* test was used to compare the 2 groups. A paired *t* test was also used to test whether there were significant changes from baseline to 3 mo for each group within a sex (12).

Generalized estimating equations [GEEs (13, 14)] were used to analyze phase 2 of the study. An unstructured, working corre-

lation matrix was assumed for the GEE algorithm for all outcomes except percentage weight change, for which a compound, symmetric structure was assumed. GEEs are a method of analyzing longitudinal data that do not rely on distributional assumptions. Furthermore, they give robust estimates of parameters and their SEs. For each outcome of interest, a GEE model was fit with sex, group, time, and baseline outcome as main effects and all interactions between sex, group, and time. All outcomes were measured at 3, 15, and 27 mo with the exception of anthropometric characteristics, which were measured monthly.

Thirty-seven patients did not complete phase 2 of the trial. If these dropouts were informative, then regression estimates may have been biased. Because all patients completed phase 1 of the study, a linear regression model for percentage weight change at 3 mo with sex, group, and dropouts (dropouts are defined as those who did not complete phase 2) as main effects was built. There was no significant difference in weight loss at 3 mo between dropouts and those who completed both phases of the study. Because dropping out did not appear to depend on relative success or failure in phase 1 of the study, the phase 2 analyses were performed on an available case basis.

RESULTS

Fifty patients were randomly assigned to group A (control group) and 50 patients to group B (meal-replacement group). Baseline characteristics of the 100 study patients are given in **Table 1**. There were no significant differences between the 2 groups in sex distribution, age, body weight, or body mass index.

TABLE 1
Clinical characteristics of subjects enrolled in the control group (group A) and the meal-replacement group (group B)[1]

	Group A		Group B	
	Women (n = 41)	Men (n = 9)	Women (n = 38)	Men (n = 12)
Age (y)	46.8 ± 11.2	45.5 ± 12.0	44.3 ± 9.8	46.5 ± 9.5
Body weight (kg)	90.6 ± 9.4	101.7 ± 12.3	89.1 ± 12.1	103.7 ± 12.9
BMI (kg/m^2)	33.9 ± 3.0	33.1 ± 4.1	33.1 ± 4.1	33.0 ± 3.7
Waist-to-hip ratio	0.87 ± 0.09	0.95 ± 0.12	0.86 ± 0.10	0.95 ± 0.09
SBP (mm Hg)	140 ± 14	136 ± 12	137 ± 15	142 ± 14
DBP (mm Hg)	83 ± 7	81 ± 4	81 ± 6	83 ± 5

[1] $\bar{x}$ ± SD. SBP, systolic blood pressure; DBP, diastolic blood pressure. There were no significant differences between groups.

Phase 1

Weight changes

All 100 patients completed phase 1 of the study and body weight was reduced in both groups after 3 mo (**Table 2**). In group A, men lost 1.1 ± 2.6 kg and women lost 1.2 ± 2.1 kg; in group B, men lost 8.4 ± 3.9 kg and women lost 6.8 ± 3.3 kg (two-sample t test). After 3 mo, women in group A and men and women in group B had significantly lower body weights than at baseline ($P < 0.001$). Between-group differences by sex were significant only for women: women in group B lost significantly more weight than did women in group A ($P < 0.001$). The combined mean body weight loss for group A (41 women, 9 men) was 1.3 ± 2.2 kg, whereas that for group B (38 women, 12 men) was 7.1 ± 3.5 kg ($P < 0.001$).

Food diaries

At baseline, reported energy intakes were 7.52 ± 0.85 and 7.59 ± 0.35 MJ/d for groups A and B, respectively. At the end of phase 1, reported energy intakes were 6.96 ± 0.36 and 6.17 ± 0.18 MJ/d. Although there was a trend for decreased energy intake by group and sex, reductions in energy intake were significant only for men in group B.

Baseline fat intakes for groups A and B were 37.6% and 36.0% of energy intake, respectively. At the end of phase 1, estimated fat intake was reduced to 32.9% in group A and 26.4% in group B (both $P < 0.05$).

Biomarkers for disease risk

Changes in key biomarkers for disease risk as they related to changes in body weight for women and men are shown in Table 2. Although body weight loss in women in group A was significant, there were no significant changes in biomarkers with the exception of serum cholesterol, which decreased by 0.2 mmol/L. In contrast, women in group B had a 5-fold greater weight loss than women in group A and showed significant improvements in plasma triacylglycerol, blood glucose, and insulin concentrations.

Men in group A showed no significant changes in weight or biomarkers. Men in group B, on the other hand, experienced significant weight loss and concomitant reductions in plasma triacylglycerol, blood glucose, and insulin concentrations. In addition, both women and men in group B experienced a significant improvement in systolic blood pressure.

Phase 2

Weight changes

During the next 24 mo (phase 2), patient attrition occurred and at the end of this phase 37 patients had dropped out. These patients (19 in group A and 18 in group B) withdrew because of clinical events (n = 6), social or domestic events (n = 7), unwillingness to comply with the protocol (n = 13), or unknown reasons (n = 11). The clinical events were 4 surgical interventions (2 bone fractures, 1 tendon rupture, and 1 inguinal hernia) and 2 infectious diseases (1 respiratory and 1 urinary tract infection).

No reported adverse events were attributable to the dietary regimen. Patient complaints included headache (n = 10), loss of hair (n = 4), abdominal discomfort (diarrhea, gas, and constipation; n = 7), back pain (n = 3), depressed mood (n = 2), cold intolerance (n = 2), and influenza syndrome (n = 32). These complaints were transient.

The mean body weight of the patients remaining at each milestone measurement is reported in **Table 3**. No significant sex differences were found with GEEs; hence, the phase 2 data were combined in Table 3. Both groups experienced additional weight loss over the 24 mo, with time as a significant covariate. In group A, body weight was reduced from 91.4 ± 11.6 to 85.0 ± 11.8 kg and in group B from 85.5 ± 13.4 to 82.2 ± 13.4 kg. On average, both groups lost weight at the rate of 0.07 ± 0.03% ($P < 0.01$) of their initial body weight every month from 3 to 27 mo. For those 63 patients who completed the 27-mo study, this equaled an additional weight loss of 4.2 ± 3.7 kg for group A and 3.0 ± 6.4 kg for group B. There was also a significant group effect ($P < 0.0001$) during phase 2. Group B lost and maintained an average of 5.34% more of their body weight than did group A. There was no group-by-time interaction.

TABLE 2
Anthropometric and biochemical measurements in obese subjects during phase 1 of treatment with an energy-restricted diet (5.2–6.3 MJ)[1]

	Women		Men	
	Baseline	3 mo	Baseline	3 mo
Body weight (kg)				
Group A	90.6 ± 9.4	89.4 ± 10.4[2]	101.7 ± 12.3	100.5 ± 13.0
Group B	89.1 ± 12.1	82.3 ± 12.0[2,3]	104.1 ± 13.1	95.2 ± 13.1[2]
Waist-to-hip ratio				
Group A	0.87 ± 0.09	0.85 ± 0.13	0.95 ± 0.12	0.95 ± 0.13
Group B	0.86 ± 0.15	0.84 ± 0.13	0.95 ± 0.09	0.93 ± 0.11
SBP (mm Hg)				
Group A	141 ± 16	142 ± 16	136 ± 15	134 ± 14
Group B	139 ± 18	130 ± 14[2,3]	142 ± 15	132 ± 10[2]
DBP (mm Hg)				
Group A	84 ± 8	82 ± 6	82 ± 8	80 ± 4
Group B	82 ± 8	80 ± 5	83 ± 7	82 ± 3
Triacylglycerol (mmol/L)				
Group A	1.96 ± 1.10	1.93 ± 1.10	2.92 ± 2.03	3.16 ± 2.50
Group B	2.00 ± 1.07	1.57 ± 0.74[2]	2.94 ± 1.48	2.29 ± 1.70[2]
Cholesterol (mmol/L)				
Group A	5.97 ± 1.00	5.78 ± 1.01[2]	6.17 ± 0.61	6.12 ± 0.97
Group B	5.75 ± 1.02	5.70 ± 0.94	6.07± 0.97	6.09 ± 0.66
HDL cholesterol (mmol/L)				
Group A	1.33 ± 0.34	1.30 ± 0.30	1.02 ± 0.15	0.96 ± 0.16
Group B	1.40 ± 0.41	1.34 ± 0.46	1.04 ± 0.28	1.15 ± 0.33
Blood glucose (mmol/L)				
Group A	5.05 ± 0.78	5.08 ± 0.77	5.01 ± 1.05	5.06 ± 0.88
Group B	4.96 ± 0.28	4.55 ± 0.69[2,3]	5.11 ± 1.02	4.74 ± 0.99[2]
Insulin (pmol/L)				
Group A	129.5 ± 45.8	128.6 ± 59.7	172.3 ± 60.3	171.6 ± 65.9
Group B	128.5 ± 51.7	78.9 ± 23.4[2,3]	143.5 ± 53.6	100.8 ± 34.9[2,3]

[1] $\bar{x}$ ± SD. Group A: n = 41 F, 9 M; group B: n = 38 F, 12 M. Group A received the energy-restricted diet only; group B received the energy-restricted diet with 2 meals and 2 snacks replaced by energy-controlled, nutrient-dense meal-replacement products. SBP, systolic blood pressure; DBP, diastolic blood pressure.
[2] Significantly different from baseline, $P < 0.001$ (paired t test).
[3] Significantly different from group A, $P < 0.001$ (two-sample t test).

Food diaries

Energy intakes in group A were 7.15 ± 0.48 MJ/d at 3 mo, 6.50 ± 0.42 MJ/d at 15 mo, and 6.72 ± 0.35 MJ/d at 27 mo. Energy intakes in group B also changed little during this period: 5.96 ± 0.27 MJ/d at 3 mo, 6.28 ± 0.36 MJ/d at 15 mo, and 6.60 ± 0.29 MJ/d at 27 mo.

Biomarkers for disease risk

Changes in important biomarkers for disease risk as they related to changes in body weight during phase 2 are shown in Table 3. The results are reported for baseline and 3, 15, and 27 mo. With use of GEEs (13, 14), further decreases in systolic and diastolic blood pressure were noted during phase 2 in both groups; group B had significantly lower blood pressure than did group A at baseline ($P < 0.001$).

Serum triacylglycerol concentrations decreased significantly over time in both groups ($P < 0.01$). Values in group A fell from 2.13 ± 1.34 mmol/L at baseline to 1.77 ± 0.62 mmol/L at 27 mo. Values in group B were 2.23 ± 1.24 and 1.40 ± 0.49 mmol/L at the same time points. Significant group effects were apparent and may have been related to the degree of weight loss. Total serum cholesterol decreased similarly over time in both groups. There were no significant changes in concentrations of HDL cholesterol.

In group B, insulin concentrations did not change significantly after the initial weight-loss phase, whereas in group A, insulin concentrations decreased at 12 mo and remained unchanged for the balance of the study. By 27 mo, GEEs showed that blood glucose concentrations in groups A and B had decreased by an average of 0.56 and 0.59 mmol/L ($P < 0.001$).

Phase 1 and phase 2 percentage weight changes

Weight-loss data were analyzed as a percentage of initial body weight on an available case basis (**Figure 1**). Expressed in this manner, there were no differences by sex. After 3 mo, there was a 1.5 ± 2.6% decrease in group A and a 7.8 ± 3.7% decrease in group B; this difference between groups was highly significant ($P < 0.001$, Figure 1, months 0–3). At 15 mo (12 mo of phase 2), group A had lost 3.9 ± 5.5% of their original weight and group B had lost 9.5 ± 5.6%. The total percentage loss by the end of the study (phases 1 and 2) was 5.9 ± 5.0% for group A and 11.3 ± 6.8% for group B. According to the percentage of total weight lost, 7 of 50 patients (14%) in group A and 21 of 50 patients (42%) in group B had reduced their body weight by >10% of their initial weight.

DISCUSSION

In this study, we compared energy-controlled meal and snack replacements with a standard weight-loss diet for 3 mo (Table 2). During the subsequent 24 mo, daily meal replacements were

TABLE 3
Anthropometric and biochemical measurements for phase 1 and phase 2 of treatment with an energy-restricted diet (5.2–6.3 MJ)[1]

	Phase 1		Phase 2	
	Baseline (n = 100)	3 mo (n = 100)	15 mo (n = 78)	27 mo (n = 63)
Body weight (kg)[2,3]				
Group A	92.7 ± 10.8	91.4 ± 11.6	87.5 ± 12.1	85.0 ± 11.8
Group B	92.6 ± 13.7	85.5 ± 13.4	84.3 ± 13.8	82.2 ± 13.4
Waist-to-hip ratio				
Group A	0.90 ± 0.10	0.86 ± 0.21	0.85 ± 0.24	0.84 ± 0.18
Group B	0.89 ± 0.12	0.86 ± 0.18	0.85 ± 0.20	0.85 ± 0.19
SBP (mm Hg)[2,3]				
Group A	140 ± 14	141 ± 16	135 ± 12	138 ± 13
Group B	139 ± 15	130 ± 13	123 ± 11	124 ± 12
DBP (mm Hg)[4]				
Group A	83 ± 6	82 ± 5	78 ± 5	80 ± 6
Group B	82 ± 6	80 ± 5	76 ± 5	78 ± 5
Triacylglycerol (mmol/L)[2,3]				
Group A	2.13 ± 1.34	2.15 ± 1.50	1.65 ± 0.53	1.77 ± 0.62
Group B	2.23 ± 1.24	1.75 ± 1.09	1.58 ± 0.41	1.40 ± 0.49
Cholesterol (mmol/L)[3,5]				
Group A	6.01 ± 0.94	5.84 ± 1.00	5.45 ± 0.93	5.69 ± 0.60
Group B	5.83 ± 1.01	5.79 ± 0.89	5.51 ± 0.53	5.35 ± 0.95
HDL cholesterol (mmol/L)				
Group A	1.27 ± 0.33	1.24 ± 0.31	1.24 ± 0.26	1.18 ± 0.17
Group B	1.31 ± 0.41	1.30 ± 0.44	1.24 ± 0.30	1.39 ± 0.77
Glucose (mmol/L)[2,3]				
Group A	5.05 ± 0.85	5.07 ± 0.79	4.55 ± 0.40	4.52 ± 0.42
Group B	4.97 ± 0.87	4.58 ± 0.74	4.75 ± 0.63	4.40 ± 0.39
Insulin (pmol/L)[3,5,6]				
Group A	134.6 ± 50.4	139.1 ± 63.2	93.1 ± 28.4	98.8 ± 30.0
Group B	132.0 ± 53.1	84.9 ± 30.4	96.2 ± 48.0	81.8 ± 30.2

[1] $\bar{x}$ ± SD. SBP, systolic blood pressure; DBP, diastolic blood pressure. During phase 1, group A received the energy-restricted diet only and group B received the energy-restricted diet with 2 meals and 2 snacks replaced by energy-controlled, nutrient-dense meal-replacement products; during phase 2, both groups received the energy-restricted diet and 1 meal and 1 snack were replaced by energy-controlled, nutrient-dense meal-replacement products.
[2] Significant treatment effect based on the generalized estimating equation, $P < 0.01$.
[3] Significant time effect based on the generalized estimating equation, $P < 0.01$.
[4] Significant sex-by-group interaction, $P < 0.01$.
[5] Significant group-by-time interaction, $P < 0.01$.
[6] Significant sex-by-time interaction, $P < 0.01$.

evaluated in all patients for maintenance of weight loss (Figure 1). Changes in weight and biomarkers of disease risk were measured throughout the 27-mo study (Table 3).

The first 3 mo (phase 1) was a prospective, randomized, parallel intervention study in which patients in both the control group (group A) and meal-replacement group (group B) lost weight. Although the same energy intake was prescribed in both groups, group B lost significantly more weight. There were no dropouts during phase 1, an unusual finding in most weight-loss studies. Weekly visits to the clinic and excellent support from the clinical staff may have played a contributory role in this zero dropout rate. Heber et al (10), in a study using minimal intervention with the same meal replacements and diet strategy as in the present study, found a high approval rating for appetite satisfaction (≥78%) and taste (≥96%). These factors may have played a similar role in the present study.

During phase 2, all patients were prescribed the same diet of one meal replacement and one nutrition bar as a snack; the original randomization was maintained for reporting the results. In both groups, the average weight lost was maintained, with additional losses over the next 2 y (Figure 1). Although weight loss in group B was greater than in group A during phase 1, the rate of weight loss between the groups was not significantly different during phase 2. Once the meal-replacement therapy was initiated, group A patients experienced an average weight loss of 3.8 ± 5.0% of their initial body weight after 15 mo and 4.7 ± 5.5% by the end of the study (Figure 1). Percentage weight losses at comparable time points for group B were 8.5 ± 6.1% and 9.4 ± 7.1%. Because both patient groups were provided the same meal-replacement therapy and dietary guidelines during phase 2, the lack of significant difference in the rate of weight loss was expected.

Seven-day food diaries showed a decline in energy intake from baseline, with the greatest decline observed in group B during phase 1. However, when the diary data were compared with change in body weight, it appeared that patients reported less than they consumed. Furthermore, they became less compliant in accurate reporting of food consumption as the study progressed. This tendency to underreport food intake has been documented by other investigators involved in dietary intervention studies (15, 16). For this reason, body weight loss and the link between this and changes in biomarkers was emphasized rather than the report of dietary intake.

Several biomarkers of disease risk were monitored throughout the 27-mo study and links were observed between weight loss and

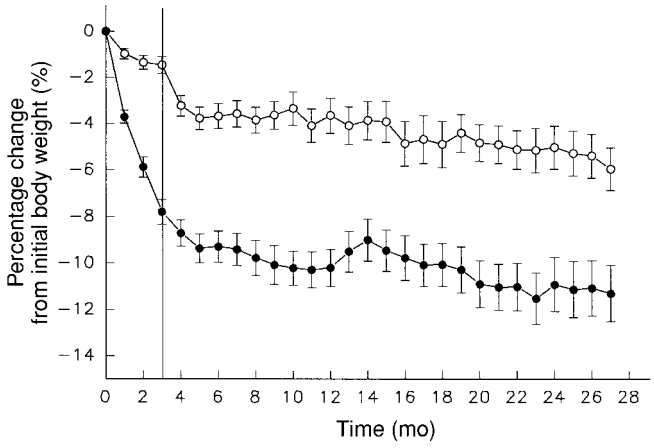

FIGURE 1. Mean (±SEM) percentage change from initial body weight in obese patients during 27 mo of treatment with an energy-restricted diet containing 5.2–6.3 MJ/d. Data were analyzed on an available case basis. During the first 3 mo (phase 1), patients were randomly assigned to receive the energy-restricted diet only (group A, ○) or to receive the energy-restricted diet with 2 meals and 2 snacks replaced by energy-controlled, nutrient-dense meal-replacement products (group B, ●). During the next 24 mo (phase 2), all patients received the energy-restricted diet and 1 meal and 1 snack were replaced by energy-controlled, nutrient-dense meal-replacement products.

improvement in biomarker values. During phase 1, patients in group A showed no significant improvement in the measured biomarkers, but did show subsequent improvement with further weight loss (Tables 2 and 3). Group B sustained improvements in biomarkers throughout the 27-mo study period. In a similar study, patients lost an average of 7.5 kg in 12 wk without experiencing significant changes in their lipid profiles (10). However, these patients weighed less at the start of the intervention and had plasma lipid concentrations within the normal range. The lack of elevated plasma lipids might explain the difference in responses between the study by Heber et al (10) and the present one.

In longitudinal clinical trials, dropouts are cause for concern because they may bias the interpretation of study results. To reduce the likelihood of bias while maximizing the data available, we analyzed weight changes at 3 mo and showed that there was no significant difference in body weight losses or percentage weight-loss data between the patients who dropped out and those who completed the full 2-y study. Hence, the phase 2 data were analyzed on an available case basis. Because the test of dropouts versus those who completed the study was performed with the 3-mo data, it is possible that the patients who dropped out of the study during the following 2 y might be informative. This is highly unlikely, however, because the reasons for patients dropping out of the study did not appear to be related to poor weight control performance.

The most relevant finding was the significant improvement in biomarkers of disease risk with the sustained reduction in body weight over a 27-mo period. This study supports previous findings (17–23) that a modest, sustained weight loss can have long-term health benefits as measured by improvements in biomarkers of disease risk. This dietary intervention, which lasted 2 y, gave results comparable with drug treatment (24–26) but without the adverse events and with only minimal, transient gastrointestinal side effects. In addition, the 8% weight-loss standard, recently established for dietary management of obesity with low-energy diets (27), was attained in the group receiving the meal replacements for the full 27 mo of this study.

It is often difficult to select and prepare energy-restricted diets for long-term weight control that include all of the required nutrients at recommended intakes. The use of meal replacements coupled with a variety of low-fat foods for a sensible food plan may have helped our patients adhere to the energy-reduced diet. This strategy not only promotes versatility but also supports the continuation of healthy eating patterns, which is necessary for permanent lifestyle changes. Other benefits of the meal replacements cited by Heber et al (10) include convenience, low cost, and the relatively minimal time needed for professional intervention. In conclusion, long-term dietary interventions in obese patients that include the use of nutrient-dense meal-replacement products were effective in improving long-term weight control in addition to blood pressure and metabolic biomarkers of comorbid disease.

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