European Journal of Clinical Nutrition (2002) 56, 264–270
 0954–3007/02 $25.00
www.nature.com/ejcn

ORIGINAL COMMUNICATION

Lipoprotein responses to weight loss and weight maintenance in high-risk obese subjects

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Objective: To examine changes in plasma lipids and lipoproteins after 51 months of reduced energy intake and sustained weight loss.
Methods: One-hundred patients were randomized to one of two dietary interventions for 3 months (weight loss period). Groups A and B received an energy-restricted diet plan of 5.2–6.3 MJ/day but group B was further instructed to replace two of three meals with a nutrient-fortified liquid meal replacement (MR). Upon completion of the weight loss period, all patients were given the same instructions regarding energy intake and were advised to use one MR daily. Body weight and 7 day food diaries were measured monthly or bimonthly and blood lipids at baseline, 3, 9 and 51 months.
Results: Of the original 100 patients 75 had completed 4 y. Of those 75, 73 had complete lipid records. Baseline body weights of Groups A and B were 90.7 ± 14.0 and 91.6 ± 9.8 kg, respectively. The percentage change in total cholesterol (%ΔTC) decreased in a linear fashion with increasing weight loss, when all data was combined, but did not approach statistical significance ($P \leq 0.26$, $r = 0.02$). Further regression analysis found a significant negative linear relationship ($P \leq 0.0001$, $r = 0.69$) between initial total cholesterol (TC) concentrations and %ΔTC. Hence, data from 27 of the 73 completers who exhibited an elevated serum total cholesterol (≥ 6.2 mmol/l) were isolated and analyzed further. Baseline TC was 6.75 ± 0.64, 5.85 ± 0.63 at 9 months ($P < 0.05$) and 5.76 ± 0.52 mmol/l at 51 months ($P < 0.05$). Similar values for VLDL-cholesterol were 1.33 ± 0.80, 0.74 ± 0.24 and 0.66 ± 0.21 mmol/l by 51 months ($P < 0.05$). Weight decreased by 5.2 ± 5.1, 7.6 ± 4.9 and 6.7 ± 4.6% at 3, 9 and 51 months, respectively.
Conclusion: Continuous energy restriction associated with a clinically meaningful weight loss significantly improved the lipid profile of high-risk patients. Similar weight and diet changes occurring in patients with normal plasma cholesterol were either increased or without affect.
European Journal of Clinical Nutrition (2002) **56,** 264–270. DOI: 10.1038/sj/ejcn/1601375

Keywords: obesity; weight loss; weight maintenance; lipids

Introduction

The association of excess weight with dyslipidemia and increased risk of cardiovascular disease (CVD) as well as the importance of diet to reduce the risk of CVD has been well established (Eckel, 1999; Pi-Sunyer, 1993; National Heart, Lung and Blood Institute, NIH, 1998; Van Gaal *et al*, 1997) In 1993, the second report of the National Cholesterol Education Program (NCEP) re-emphasized the need to reduce the dietary intake of fat, saturated fat and cholesterol to decrease high blood cholesterol (NCEP, 1993). The report also addressed the need for improving weight control and physical activity. This new emphasis on weight control is partially credited to the growing body of information demonstrating a causal relationship between reduced body weight and improved serum lipids (National Heart, Lung and Blood Institute, NIH, 1998; Denke *et al*, 1993).

Most studies that have shown a relationship between modest weight loss and improvement in lipid parameters is of relatively short duration (Flynn *et al*, 1999; Lichtenstein *et al*, 1994). In fact, long-term studies, such as those by Wadden *et al*, (1999) and Weinser *et al* (1992) suggest that the lipid-lowering effect of weight loss is not sustainable. Indeed, a recent editorial on the subject indicated that

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Received 29 June 2001; revised 30 October 2001; accepted 31 October 2001

weight loss during hypo-energetic feeding resulted in decreased triglyceride (TG), total cholesterol (TC), and cholesterol in the high- (HDL-C) and low-density lipoprotein (LDL-C) fraction. However, during weight maintenance and normalization in caloric intake these lipid and lipoproteins are likely to increase toward baseline (Eckel, 1999).

A recent study of 4 y duration evaluated the long-term effects of sustained weight loss in obese individuals referred to a University Obesity Center (Flechtner-Mors *et al*, 2000). The report indicated that there was a lack of significant improvement in plasma TC and LDL-C despite sustained weight loss. This finding supports the previous assumptions, that weight loss does not sustain a long-term improvement in plasma cholesterol. However, this lack of improvement might have resulted from the inclusion of patients with normal initial lipid values when calculating the overall mean change.

Using the raw data from the previous report (Flechtner-Mors *et al*, 2000), we evaluated the relationship between diet, weight loss and changes in serum lipids, focusing primarily on those patients at high risk for CVD. We hypothesized that patients at higher risk would respond more favorably to caloric restriction and sustained weight loss. Patients were categorized according to their plasma cholesterol concentration prior to weight loss, and according to the guidelines established by the NCEP of low risk (< 5.2 mmol/l), moderate risk (5.2 – 6.1 mmol/l) and high risk (≥ 6.2 mmol/l; NCEP, 1993).

Materials and methods

Subjects

Physicians referred patients with previous poor performance using caloric restriction, to the University of Ulm Obesity Center for this study. Patients were men and women aged > 18 y whose body mass index (BMI) was > 25 and ≤ 40 kg/m^2. The study followed the principles of the Helsinki Declaration and was approved by the Freiburg Ethics Committee International (Freiburg, Germany) and the Ulm University Investigational Review Board. Individuals with a medical history of significant disease, alcohol or drug abuse or clinically significant abnormal laboratory test results were excluded. Women who were pregnant, lactating or who wished to become pregnant were also excluded. Average age and BMI of the 21 male and 79 female patients was 45.2 ± 10.1 y and 33.6 ± 3.6 kg/m^2, respectively.

Study design and dietary intervention

The study design has been previously reported (Flechtner-Mors *et al*, 2000). Briefly, the study consisted of two phases, a 3-month active weight loss phase (phase I) and a 48-month weight maintenance phase (phase II). Patients were randomized to group A (control) or group B (meal replacements). During phase I, all patients were prescribed an individualized reduced-energy diet containing 5.02 – 6.28 MJ/day (energy supplied as 19 – 21% protein, 48 – 54% carbohydrate and 25 – 34% fat). Group A patients restricted their intake of conventional foods for all meals and snacks. Patients in group B used the same diet selection strategy but were instructed to replace two of the meals with meal-replacement shakes, soups or hot chocolate and two of the snacks with nutrient-fortified snack bars (Slim Fast®; Slim Fast Foods Company, West Palm Beach, FL, USA). During phase II (months 4 – 51), patients in both groups continued the reduced-energy regimen with instructions to replace one daily meal with a meal-replacement and one snack with a nutrient-fortified snack bar.

During each phase of the study a staff nutritionist provided monthly, personalized counseling with the aid of food exchange lists and food diaries to equalize the prescribed energy intakes for each patient. All patients were instructed to maintain their respective body weights during the maintenance period and their energy intakes were adjusted to accomplish that.

Dietary records

Patients were instructed on food selection, portion control, and accurate recording of daily dietary intakes. Seven-day food diaries were maintained during the 2 weeks prior to each visit for the first 27 months of the study. A nutritionist reviewed the food diaries with each patient and analyzed the intakes monthly using the German Food Code BLS and the NUTRILOG program (GiV, Göttingen, Germany).

Laboratory analyses

Blood samples were obtained by veni-puncture after an 8 – 14 h overnight fast and centrifuged at 4°C for 15 min at 2000 *g*. Biochemical measurements were performed in the Department of Clinical Chemistry at the University Hospital. Triglycerides were measured enzymatically and cholesterol was measured colorimetrically. Cholesterol in HDL was measured after isolation of HDL using phosphotungstic acid and magnesium ions. Cholesterol in VLDL was measured after isolation of VLDL by ultra-centrifugation at 100 000 rpm for 4 h at 4°C. Low-density lipoproteins and VLDL-C were calculated using the formula of Friedewald *et al* (1972). Plasma insulin was measured by an enzyme immunoassay and glucose was measured enzymatically. Blood measurements were taken at baseline, 3, 9 and 51 months along with reports of side effects.

Statistical Analysis

Weight loss over time was evaluated using the Generalized Estimating Equation (Elashoff *et al*, 1999). This method allows for the analysis of longitudinal data that do not rely on strong distributional assumptions; specification of the first two moments is all that is required. A first-order autoregressive working correlation structure was assumed for

percentage weight change and a compound symmetric structure for the risk factors. Additionally, the relationship between the initial plasma total cholesterol and the changes in lipids and lipoproteins were calculated using a least square linear regression model (Snedecor & Cochran, 1967) that is specified by the equation:

$$Y = \alpha + \beta X + \epsilon$$

where ε is a variable drawn from $N(0, \sigma_{y.x})$.

Weight measurements were analyzed monthly or bimonthly. Student's paired *t*-test was used to make group comparisons of these measurements at each of the major time points. To adjust for multiple comparisons for weight differences a test was considered significant if its *P* was less than 0.01 rather than the traditional 0.05. A significance level of 0.05 was used for all other measures.

Results

Sixty-three of the original 100 patients completed the first 24 months of phase II; by the 36th month, a total of 58 patients continued their monthly appointments. Thirty-two of the 42 patients who had not kept regular clinic appointments were contacted, and 22 of these patients agreed to re-enter the study at month 39 of phase II. Seventy-five patients completed the 51 month study, and 73 (15 males and 58 females) had repeat blood lipid measurements at month 51. Baseline body weights for the three NCEP cholesterol classifications of <5.2, $5.2-6.1$ and ≥ 6.2 mol/l were 89.5 ± 12.8, 93.0 ± 14.6 and 90.7 ± 8.5 kg, respectively. Gender distribution for the above cholesterol classifications were three males and 17 females, four and 22 and eight and 19, respectively.

Dietary intake

Energy intakes for phase I in Group A decreased from 7.52 ± 0.85 to 6.96 ± 0.36 MJ/day ($P \leq 0.05$) and in group B from 7.59 ± 0.35 to 6.17 ± 0.18 MJ/day ($P < 0.05$). Similar values for fat energy were 2.83 ± 0.33 to 2.29 ± 0.34 MJ/day ($P \leq 0.05$) and 2.74 ± 0.23 to 1.63 ± 0.18 MJ/day ($P \leq 0.05$). Fat intake as a percentage of total dietary energy decreased from 37.6 to 32.9% in group A and from 36.1 to 26.4% in group B. Dietary cholesterol intake, during this same period, decreased from 422 ± 57 to 244 ± 30 mg/day ($P \leq 0.05$) in group A and from 378 ± 43 to 154 ± 14 mg/day ($P \leq 0.05$) in group B. Energy, fat and cholesterol intake continued to decline through the 15th month for group A and was 6.55 ± 0.39 MJ/day, 1.92 ± 0.25 MJ/day and 187 ± 24 mg respectively, with no further decrease through month 27. Dietary changes for group B remained constant beyond the first 3 months of active weight loss. There were no significant differences between the two groups from months 4 to 27. Dietary protein intake was unchanged during both phases of the study and was not different between study groups.

Weight and lipid changes

A summary of the weight loss for the 100 original patients after the active weight loss phase of 3 months, showed that although both groups lost significant weight, group A lost less than group B, 1.5 ± 2.6 *vs* $7.8 \pm 3.7\%$ ($P \leq 0.01$), respectively. At 51 months, group A ($n = 37$) had lost $3.2 \pm 4.9\%$ and group B ($n = 38$) $8.4 \pm 5.0\%$ ($P \leq 0.01$) of initial body weight. Combining the two groups a $5.9 \pm 5.6\%$ weight loss was achieved for all 75 patients. Plasma triglycerides and total cholesterol decreased over time in both groups but did not reach significance, with the exception of triglycerides for group B at 3, 27 and 51 months.

Changes in body mass index (BMI) also reflected the magnitude of body weight loss. The baseline, 3 month (weight loss) and 51 month (weight maintenance) BMI (kg/m^2) for group A was 33.6 ± 3.2, 33.2 ± 3.5, and

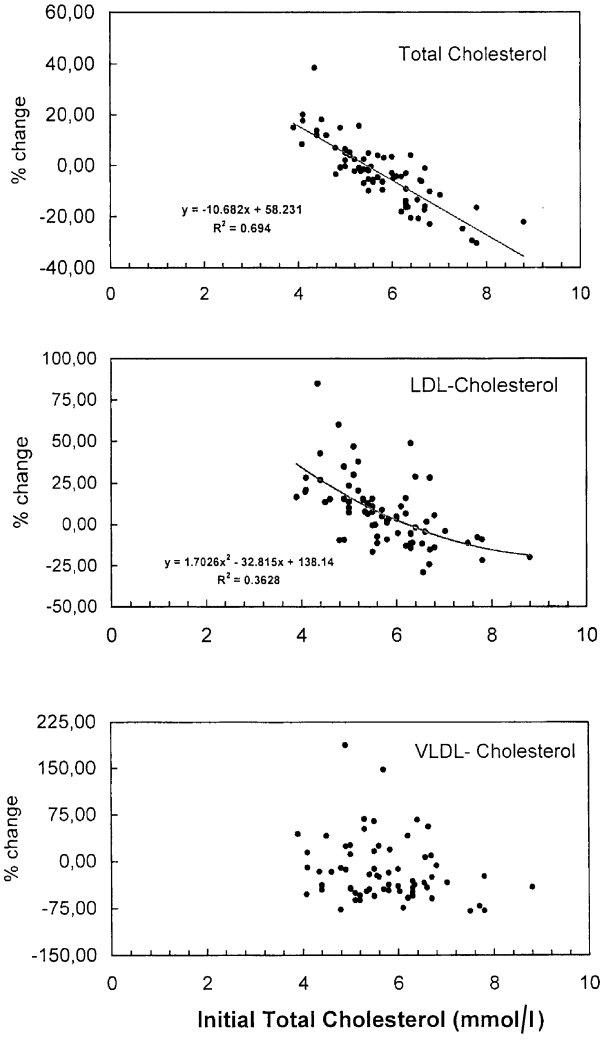

Figure 1 Percentage change from baseline from total cholesterol, LDL-cholesterol and VLDL-cholesterol regressed from initial total cholesterol.

Table 1 Plasma changes in obese patients with different baseline cholesterol values

	Baseline	*3 months*	*9 months*	*51 months*
Cholesterol ≥ 6.2 mmol/l				
Number (*n*)	27	27	26	27
Weight change (%)	—	− 5.2 ± 5.1‡	− 7.6 ± 4.9‡	− 6.7 ± 4.6‡
Cholesterol mmol/l				
Total	6.75 ± 0.64	6.56 ± 0.64[a]	5.85 ± 0.63*[a]	5.76 ± 0.52*
LDL	4.18 ± 0.90	4.21 ± 0.82	3.92 ± 0.58	3.90 ± 0.53
VLDL	1.33 ± 0.80	1.16 ± 0.82[a]	0.74 ± 0.24*[a]	0.66 ± 0.21*
HDL	1.24 ± 0.43	1.18 ± 0.35	1.19 ± 0.16	1.20 ± 0.12
Total-C/HDL-C	5.99 ± 1.77	5.93 ± 1.56[a]	5.00 ± 0.86*[a]	4.82 ± 0.60*
Triacylglycerol (mmol/l)	2.90 ± 1.76	2.53 ± 1.79[a]	1.61 ± 0.52*[a]	1.44 ± 0.45*
Glucose (mg/dl)	95.2 ± 19.0	89.7 ± 17.2*	85.8 ± 7.4*	79.3 ± 6.1*
Insulin (μU/ml)	20.4 ± 7.9	17.1 ± 8.2	15.2 ± 3.0*	12.4 ± 2.8*
Cholesterol 5.2 – 6.1 mmol/l				
Number (*n*)	26	26	25	26
Weight change (%)	—	− 3.3 ± 5.0‡	− 4.8 ± 7.6‡	− 4.2 ± 7.0‡
Cholesterol mmol/l				
Total	5.60 ± 0.26	5.44 ± 0.74[a]	5.65 ± 0.39[a]	5.48 ± 0.34
LDL	3.41 ± 0.55	3.29 ± 0.81	3.70 ± 0.40*	3.61 ± 0.44*
VLDL	0.89 ± 0.47	0.88 ± 0.64	0.75 ± 0.24[a]	0.62 ± 0.17*
HDL	1.30 ± 0.46	1.28 ± 0.36	1.19 ± 0.15	1.25 ± 0.19
Total-C/HDL-C	4.90 ± 2.02	4.62 ± 1.50	4.80 ± 0.66	4.48 ± 0.77
Triacylglycerol (mmol/l)	1.94 ± 1.02	1.92 ± 1.39	1.64 ± 0.51[a]	1.35 ± 0.36*[a]
Glucose (mg/dl)	89.5 ± 12.7	87.6 ± 11.6	86.2 ± 7.8	78.3 ± 6.0*
Insulin (μU/ml)	17.6 ± 6.0	15.3 ± 8.0[a]	15.2 ± 6.3[a]	12.6 ± 2.8*
Cholesterol < 5.2 mmol/l				
Number (*n*)	20	20	19	20
Weight change (%)	—	− 5.6 ± 3.7‡[a]	− 8.6 ± 4.8‡[a]	− 6.5 ± 4.6‡[a]
Cholesterol mmol/l				
Total	4.64 ± 0.39	5.11 ± 0.81*[a]	5.59 ± 0.57*[a]	5.07 ± 0.38*[a]
LDL	2.53 ± 0.45	3.12 ± 0.83*[a]	3.56 ± 0.54*	3.23 ± 0.41*
VLDL	0.83 ± 0.45	0.64 ± 0.25*	0.79 ± 0.24[a]	0.59 ± 0.13*
HDL	1.28 ± 0.26	1.34 ± 0.36	1.25 ± 0.2	1.25 ± 0.07
Total-C/HDL-C	3.76 ± 0.79	4.05 ± 1.16	4.60 ± 0.85*[a]	4.07 ± 0.43[a]
Triacylglycerol (mmol/l)	1.82 ± 0.97	1.41 ± 0.55*	1.71 ± 0.51[a]	1.29 ± 0.28*
Glucose (mg/dl)	85.2 ± 11.3	81.8 ± 13.2[a]	81.2 ± 7.1	79.2 ± 5.9*
Insulin (μU/ml)	18.0 ± 6.1	13.7 ± 6.4*[a]	13.0 ± 2.7*	11.4 ± 2.9*

*$P \leq 0.05$ compared to baseline; ‡$P \leq 0.01$ compared to baseline.
[a]Significant treatment differences between time points, $P \leq 0.05$.

32.5 ± 3.5, respectively. Similar values for group B were 33.0 ± 3.9, 30.4 ± 3.9 and 29.7 ± 3.6 and were significantly lower at 3 and 51 months ($P \leq 0.01$).

Figure 1 shows the linear expression for the percentage change in total cholesterol as a function of initial plasma cholesterol. There was a significant negative linear relationship between baseline blood values and terminal values ($P \leq 0.0001$, $r = 0.69$), suggesting that high-risk patients experienced a greater benefit from weight loss and dietary change. Correlations were strongest for initial plasma cholesterol and percentage decrease in total cholesterol but were also significant for LDL-C. Patients were categorized by risk based on initial cholesterol values and analyzed further.

Table 1 summarizes the change in body weight, lipids, lipoproteins, glucose and insulin for patients with initial cholesterol classified according to the NCEP guidelines (total cholesterol values ≥ 6.2; 5.2 – 6.1; and < 5.2 mmol/l). After 3 months the high-risk patients (total cholesterol greater than 6.2 mmol/l) had a 5.2% body weight loss and no change in plasma lipids and lipoproteins. By 9 months, these same patients had a cumulative weight loss of 7.6% and a significant decrease ($P \leq 0.05$) in total cholesterol of 0.90 mmol/l (35 mg/dl) as well as significant reductions in triglycerides and VLDL-C ($P \leq 0.05$) when compared to baseline. Triglycerides and VLDL-C continued to decline through the end of the study, whereas total cholesterol stabilized. High-density lipoproteins (HDL-C) and LDL-C remained unchanged for all time periods. The risk factor ratio of total cholesterol to HDL-C decreased significantly over time, starting at a baseline value of 5.99 ± 1.77 mmol/l and ending with a value at 51 months of 4.82 ± 0.60 mmol/l ($P \leq 0.05$).

Table 1 also compares the plasma lipid changes, over time, in those patients with initial cholesterol levels less than 6.2 mmol/l. The patients in these two categories, < 5.2 and 5.2 – 6.1 mmol/l, maintained an average weight loss of 4.2 and 6.5% of initial body weight, respectively. However, in most instances the plasma lipids and lipoproteins either

Table 2 Plasma changes in obese patients having a baseline total cholesterol ≥ 6.2 mmol/l and treated with energy restricted diets[a]

	Baseline	*3 months*	*9 months*	*51 months*
Patient numbers (n)				
Group A	17	17	17	17
Group B	10	10	9	10
Weight change (%)				
Group A	—	-2.2 ± 2.9	$-5.6\pm3.5^{\ddagger}$	$-5.2\pm3.5^{\ddagger}$
Group B	—	$-10.4\pm3.3^{\ddagger}$	$-11.3\pm5.3^{\ddagger}$	$-9.4\pm5.3^{\ddagger}$
Cholesterol (mmol/l)				
Total				
Group A	6.58 ± 0.37	6.57 ± 0.61	6.00 ± 0.55*	5.76 ± 0.54*
Group B	7.02 ± 0.90	6.53 ± 0.72*	5.56 ± 0.71*	5.77 ± 0.49*
LDL				
Group A	4.11 ± 0.79	4.10 ± 0.84	4.04 ± 0.54	3.83 ± 0.52
Group B	4.29 ± 1.11	4.39 ± 0.78	3.69 ± 0.60*	4.00 ± 0.56
VLDL				
Group A	1.25 ± 0.88	1.26 ± 0.99	0.75 ± 0.25*	0.78 ± 0.22*
Group B	1.46 ± 0.68	0.98 ± 0.38*	0.72 ± 0.22*	0.58 ± 0.17*
HDL				
Group A	1.22 ± 0.36	1.20 ± 0.36	1.21 ± 0.18	1.21 ± 0.13
Group B	1.26 ± 0.54	1.15 ± 0.34	1.14 ± 0.12	1.19 ± 0.10
Triacylglycerol (mmol/l)				
Group A	2.72 ± 1.91	2.75 ± 2.16	1.63 ± 0.54*	1.54 ± 0.47*
Group B	3.20 ± 1.49	2.14 ± 0.82*	1.57 ± 0.49*	1.26 ± 0.38*
Glucose (mg/dl)				
Group A	94.5 ± 15.3	91.9 ± 14.5	84.4 ± 6.4*	80.3 ± 6.3*
Group B	96.5 ± 24.9	85.9 ± 21.4*	88.3 ± 8.9	77.6 ± 5.7*
Insulin (μU/ml)				
Group A	20.5 ± 7.6	20.0 ± 8.6	16.0 ± 3.1*	13.3 ± 2.2*
Group B	20.2 ± 8.6	12.5 ± 4.8*	13.6 ± 2.0	10.9 ± 3.3*

[a]Both groups A and B used, on average, one meal replacement each day for the 48 month maintenance period. This followed a 3 month weight loss period on a conventional reduced energy diet of 5.2 – 6.3 MJ/day (group A) or the same weight loss diet with two meal replacement exchanges each day (group B).
*$P \leq 0.005$; $^{\ddagger}P \leq 0.01$; significantly different compared to baseline.

remained unchanged or increased. For example, patients with an initial cholesterol of < 5.2 mmol/l showed a significant increase in both total and LDL-C ($P \leq 0.05$) by the end of the 4 y. However this increase was not clinically relevant as none of the patients in this category had a concentration above 5.1 mmol/l.

In contrast to the above, we evaluated the changes in the high-risk (≥ 6.2 mmol/l) group separating out the patients into their original randomized treatment groups, ie group A and group B, Table 2. After 3 months, and 10% body weight loss, group B ($n = 10$) had significant reductions in plasma total cholesterol, LDL-C and VLDL-C concentrations relative to their baseline values ($P \leq 0.05$). There was no further decline in weight for the next 48 months of study. On the other hand, total cholesterol continued to decline an additional 0.76 mmol/l for a total cholesterol reduction of -1.25 mmol/l. Group A ($n = 17$) with a mean weight loss of 2% at 3 months showed no change in lipids or lipoproteins. However, by 9 months these patients averaged a 5% body weight loss and a decrease in plasma cholesterol of 0.58 mmol/l. Significant reductions in LDL-C and VLDL-C ($P \leq 0.05$) were also apparent. By the end of the study, Group A experienced a further decrease in total cholesterol of 0.24 mmol/l, without additional weight loss.

Discussion

The effect of a meal replacement strategy to aid patients in maintaining long-term control of energy intake and weight loss was evaluated for 4 y. Periodic measurements of several key risk factors associated with obesity were also made to determine the contribution of initial weight loss and subsequent weight maintenance. Initially, patients in this study were randomly assigned to one of two treatment groups for active weight loss (3 months) but treated similarly for the ensuing 48 months of weight maintenance. By the fourth month of the study, group A had lost 5% of initial body weight and group B 10%. The reduced body weight at 4 months was stable for the following 48 months.

Patients at high risk for CVD (total cholesterol >6.2 mmol/l), regardless of initial treatment designation, showed significant improvements in cholesterol with maintenance of a 7% weight loss. The reduction in total cholesterol, observed with weight loss, was followed by a further decrease during weight stabilization. To our knowledge this finding has not been reported previously. Typically, with weight stabilization triglycerides remain decreased and total and LDL-C revert toward baseline (Eckel, 1999). Wadden *et al* (1999), evaluated individuals with clinically significant elevations in total cholesterol (>5.17 mmol/l) and categorized them based on their percentage body weight loss over a 2 y period. These investigators found that despite an initial reduction in cholesterol and body weight the percentage change in total and LDL cholesterol tended to increase towards baseline values over time. Weinsier *et al* (1992) also suggested that the initial decrease in lipids and lipoproteins caused by short-term energy restriction is likely to be reversed once a caloric surfeit is imposed. Wadden *et al* (1999) suggested that studies examining the benefits of modest weight loss should consist of patients exhibiting elevated risk. This was corroborated in this study. Our findings demonstrate the relationship between greater initial CVD risk (ie initial total cholesterol ≥ 6.2 mmol/l) and significantly greater decreases in cholesterol and cardiovascular risk with sustained weight loss.

This study selected a subset of patients exhibiting an elevated serum cholesterol, hence the numbers of patients analyzed for an association with initial cholesterol are small ($n=27$). These small numbers may not contain sufficient power to draw a definitive conclusion; however, it is of value to mention two key studies that examined this relationship using a meta-analytic approach (Dattilo & Kris-Etherton, 1992; Yu-Poth *et al*, 1999). In (Dattilo & Kris-Etherton, 1992) a strong and consistent pattern was found, ie 'the greater the initial TC the greater decrease occurred with weight loss'. This observation corroborates the findings in the present study as well as Wadden *et al*'s (1999) recommendation. Yu-Poth *et al* (1999), on the other hand, found no such relationship. The discrepancy in these two studies may be explained by the magnitude of the average weight loss. The weight loss in (Dattilo and Kris-Etherton, 1992) the summarized studies was 16.6 ± 12.6 kg whereas in Yu-Poth *et al* (1999) it was 3.4 ± 2.6 kg. Hence, it could be suggested that the lack of a relationship found in this second study might be related to the small weight loss observed. The weight loss of the high risk patients in the present study was 6.1 ± 4.3 kg and, although it did not approach the findings of Datillo and Kris-Etherton (1992), it was approximately double that found in the later meta-analysis.

The recently reported lipid changes in the SOS study (Sjöström *et al*, 1999) found that patients who lost 33% body weight on average exhibited a less than dramatic decrease in serum cholesterol. These patients, for the most part, had normal serum cholesterol and it would not be expected that large decreases would occur with significant weight loss. In the present study patients exhibiting normal cholesterol values (<6.2 mmol/l) with comparable weight losses, as in the high-risk patients, exhibited cholesterol values that were unchanged or significantly increased.

Because either weight loss or reduction in dietary fat and cholesterol are expected to promote individual improvements in blood lipid values (Blackburn, 1995), the relative contributions of the two combined interventions have not been characterized during the active weight loss or weight maintenance period. The present study provided the opportunity to separate the effects of initial weight loss as compared to long-term weight maintenance and reduction in dietary fat and cholesterol. During the maintenance period, group B patients with total cholesterol values ≥ 6.2 mmol/l had a stable body weight yet experienced a further reduction in cholesterol of 0.76 mmol/l. This would suggest that any subsequent lipid reduction would most likely be due to the reduction in the dietary intake of fat and cholesterol. In contrast, group A patients had no decrease in plasma lipids despite a modest weight loss and reduction in dietary energy. Changes in total plasma cholesterol in group A were not apparent until the introduction of the meal replacement regime, which caused a further reduction in energy, fat and cholesterol intake above that of the reduced calorie regimen. Hence, during the first four months of the meal replacement therapy, group A decreased body weight from -2.2 to -5.6% and total cholesterol decreased 0.57 mmol/l.

High serum lipids commonly accompany the obese state (Eckel, 1999; National Heart, Lung and Blood Institute, NIH, 1998; Denke *et al*, 1993). The NCEP recommends a step-wise dietary therapy with emphasis on reducing dietary saturated fat and cholesterol with weight loss, if patients are overweight (NCEP, 1993). Without energy restriction and weight loss, a low-fat, high-carbohydrate diet may elevate serum triglycerides and reduce HDL-C. Both changes can increase risk for CVD. Flynn *et al* (1999), in short-term studies, demonstrated maximum improvement in the lipid responses to the NCEP Step II diet with the inclusion of energy restriction and weight loss.

The changes observed in the lipid parameters relative to body weight change provided the opportunity to evaluate Blackburn's (1995) original thesis, ie that a weight loss of 5% can improve biomarkers associated with disease. In our recent report, a 5–10% weight loss significantly improved serum triglycerides, glucose and insulin whereas total cholesterol did not change after 4 y (Flechtner-Mors *et al*, 2000). This observation is consistent with other studies of shorter duration that showed minimal sustained reductions in cholesterol with weight loss (Lichtenstein *et al*, 1994; Weinsier *et al*, 1992; Pi-Sunyer, 1996). In contrast to the average change in the overall population, Wadden *et al* (1999) made a clear distinction between the population average and those patients at a high risk as measured by serum total cholesterol. By categorizing patients according to initial cholesterol values, clinically significant improvements in serum cholesterol can be demonstrated in high risk obese individuals who

lose weight and are able to maintain the loss. The health implication for the practitioner confronted with an obese individual exhibiting elevations in total cholesterol is clear, ie that a modest sustained weight loss can play a significant role in lowering the risk for heart disease.

Acknowledgements

We thank Katja Huber (research laboratory of the Department of Medicine, University of Ulm, Ulm, Germany) for her technical assistance. We thank Richard Deckelbaum, MD, PhD (Columbia University, College of Physicians and Surgeons, New York, NY, USA) for assistance with the data analysis and fruitful discussions. We thank the Slim-Fast Foods Company (West Palm Beach, FL, USA) for providing the diet shakes and nutrition bars for use in this study.

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