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Effect of Meal Replacement on Metabolic Risk Factors in Overweight and Obese Subjects

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Key Words
Metabolic syndrome · Weight reduction · Soy protein · Physical exercise · Leptin

Abstract
Aim: Our objective was to assess alterations in metabolic risk factors, body weight, fat mass and hormonal parameters following 6 weeks of lifestyle intervention with increased physical activity and either a meal-replacement regimen or a low calorie diet. ***Research Methods and Procedures:*** 90 overweight or obese subjects (age 47 ± 7.5 years, weight 90.6 ± 11.3 kg, BMI 31.5 ± 2.3) were included in this randomized controlled clinical trial. Subjects in the fat-restricted low-calorie-diet group (LCD-G; n = 30) received 2 dietary counseling sessions and instructions on how to increase physical activity. Subjects in the meal-replacement-diet group (MRD-G; n = 60) received the same lifestyle education and were instructed to replace 2 daily meals by a low-calorie high soy-protein drink. ***Results:*** Subjects in the MRD-G lost significantly more weight (6.4 vs. 3.1 kg, $p < 0.01$) and fat mass (5.1 vs. 2.8 kg, $p < 0.01$) than the LCD-G. Most metabolic risk parameters were reduced in both the MRD-G and the LCD-G; however, subjects in the MRD-G showed a higher reduction in waist circumference (6.1 vs. 1.8 cm, $p < 0.01$) and a larger decrease in triglycerides (–19.6 vs. +12.5 mg/dl, $p < 0.01$). The prevalence of the metabolic syndrome was reduced in subjects in the MRD-G only (–12%, $p < 0.05$) compared to an unchanged risk score in the LCD-G. The reductions in leptin (18.2 vs. 6.97 ng/ml) and insulin (4.92 vs. 0.58 μU/ml) were only significant in the MRD-G ($p < 0.01$). ***Discussion:*** Our data suggest that even over a short period of time, a meal-replacement diet is more effective in reducing metabolic risk factors, insulin, and leptin, and in improving anthropometric measures than a fat-restricted low-calorie diet.

Introduction

The results of NHANES III have shown that approximately 44% of the US population over 50 years of age meet the National Cholesterol Education Program (NCEP) criteria for the metabolic syndrome [1]. Visceral obesity is part of the definition, but also a major risk factor for this metabolic disorder which includes insulin resistance, alterations in glucose and lipid metabolism, and increased blood pressure. In the presence of the metabolic syndrome, the prevalence of cardiovascular disease has been shown to be markedly increased.

Therefore, successful strategies for reducing overweight and improving metabolic risk factors are of utmost importance. There is widespread consensus that long-term therapeutic lifestyle changes, such as improving in dietary habits and increasing daily physical activity, are the cornerstones in the prevention and therapy of obesity and the metabolic syndrome.

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Recent studies have shown that meal-replacement regimens are safe and are associated with greater weight loss than individualized diet plans [2, 3]. Although there are conflicting results [4], it has been suggested that diets containing soy protein may further accelerate weight loss [5, 6]. In addition, it has been reported that isoflavones in soy protein could favorably influence metabolic risk factors and blood lipids [7–9].

In the present investigation, the effect of a very-low-calorie meal-replacement diet (MRD), using soy protein drinks, on changes in metabolic risk factors, body weight, fat mass and hormonal parameters was investigated during a 6-week intervention period. The effects of the MRD were compared against a conventional fat-restricted low calorie diet (LCD). The focus of interest was whether the 2 diets would bring about different results with respect to an improvement in the components of the metabolic syndrome and a subsequent reduction in the prevalence of the metabolic syndrome in a short period of time.

Methods

90 pre-obese and obese men and women (age 47 ± 7.5 years, weight 90.6 ± 11.3 kg, BMI 31.5 ± 2.3) were included in the study. All subjects completed a comprehensive medical examination and routine blood tests. Subjects with type 2 diabetes, clinical illnesses or those who took lipid-lowering drugs or medications that affect body weight were excluded. Written informed consent was provided by all subjects, and the study protocol was approved by the ethical committee of the University of Freiburg. Subjects were randomized into 3 equal groups as described previously [10]. Two groups were designated to receive the same lifestyle education and MRD and were therefore pooled for analysis (MRD-G, n = 60). This was feasible, since the guided exercise program that was intended for 1 of the dietary intervention groups was not started before the end of the 6-week period. The LCD-G (n = 30) received lifestyle education only.

Both groups were instructed in 2 counseling sessions and by educational pamphlets on how to improve dietary behavior and increase physical activity. The sessions were led by experienced physicians and experts in nutritional counseling.

The LCD was a fat-reduced diet with approximately 60% of calories coming from carbohydrates, 25% from fat, and 15% from protein (1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men). The subjects assigned to the MRD were instructed to replace 2 daily meals by a commercially available soy-yoghurt-honey preparation (Almased®), known to have a low glycemic index [11] and a high content of bioactive genisteins [12]. This diet contained about 1,000 kcal/day for women and 1,200 kcal/day for men. Data collected at enrolment and after 6 weeks were body weight, fat mass, waist circumference, blood pressure, and serum levels of total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, glucose, insulin and leptin. For the measurement of body composition, air displacement plethysmography was used (Bod Pod®).

Table 1. Characteristics of subjects

Variable	Baseline	6 weeks' follow-up
LCD-G	30	29
Weight, kg	91.4 ± 11.5	88.4 ± 11[a, c]
BMI	32.1 ± 2.3	31 ± 2.4[b, c]
Waist circumference, cm	104.4 ± 9.3	102.7 ± 8.4[a, c]
Fat mass, kg	37.1 ± 6.1	34.3 ± 6.6[c]
Systolic blood pressure, mm Hg	148 ± 18.3	138 ± 14.9[c]
Diastolic blood pressure, mm Hg	91.7 ± 11.5	86.7 ± 8.89[d]
MRD-G	60	59
Weight, kg	90.3 ± 11.3	83.9 ± 10.5[a, c]
BMI	31.6 ± 2.5	29.2 ± 2.4[b,c]
Waist circumference, cm	104.2 ± 9.4	98.1 ± 8.9[a, c]
Fat mass, kg	36.2 ± 6.4	31.1 ± 6.9[c]
Systolic blood pressure, mm Hg	143 ± 16.8	137 ± 14.1[c]
Diastolic blood pressure, mm Hg	90.7 ± 9.54	85.5 ± 8.54[c]

All values expressed as mean ± SD.

[a] $p < 0.05$, [b] $p < 0.01$ between groups; [c] $p < 0.01$, [d] $p < 0.05$ within groups.

Normality of all variables was tested before statistical analyses using the Kolmogorov-Smirnov test procedure. Testing for changes between examination at baseline and examination after 6 weeks was done by paired-sample t tests. Unpaired-sample t tests were used to establish significant differences between the 2 groups at both examinations. In addition, the change from baseline to 6 weeks was calculated in each subject and compared between the 2 groups using unpaired-sample t test analysis. All p values were two-sided and $p < 0.05$ was considered to indicate statistical significance. Analyses were conducted with SPSS software (version 13.0).

Results

A total of 88 subjects completed 6 weeks of study (29 subjects in the LCD-G and 59 subjects in the MRD-G). The reasons why 2 subjects discontinued the study were associated with personal motivation and unrelated to side effects or adverse events. Table 1 shows the anthropometric data and blood pressures at baseline and after 6 weeks. In both groups, the parameters improved significantly; however, the reductions in weight, waist circumference and fat mass were significantly higher ($p < 0.01$) in the MRD-G (fig. 1). The reduction in waist circumference per kilogram weight loss was 0.57 cm/kg in the LCD-G and 0.96 cm/kg in the MRD-G.

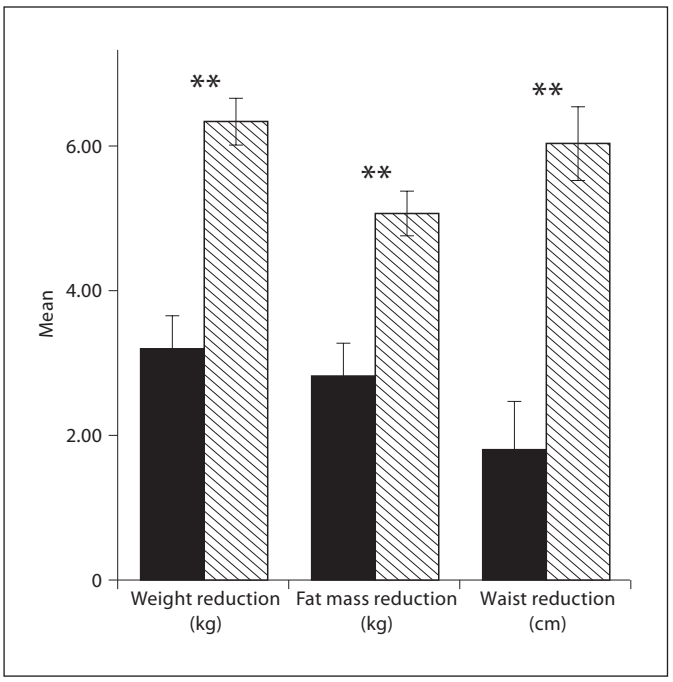

Fig. 1. Changes in weight, fat mass and waist reduction from baseline to 6 weeks. ■ = LCD-G (n = 30); ▨ = MRD-G (n = 60); **$p < 0.01$.

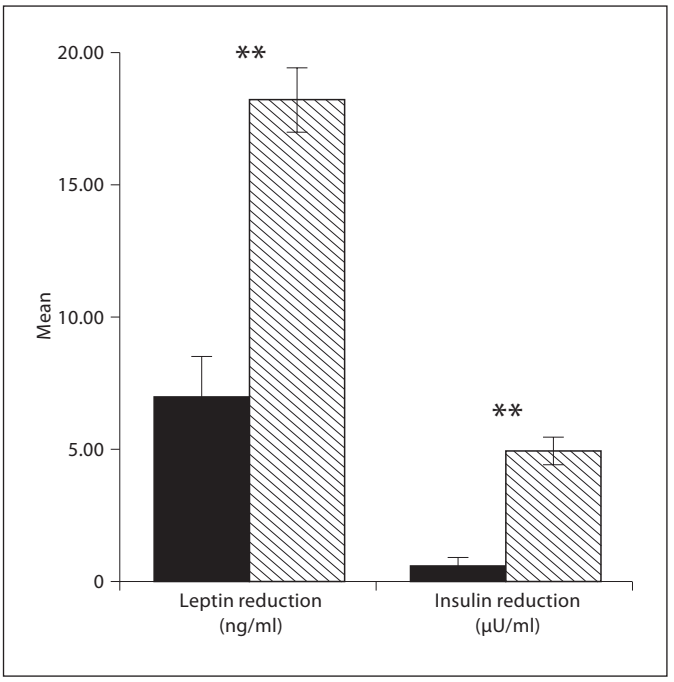

Fig. 2. Changes in leptin and insulin from baseline to 6 weeks. ■ = LCD-G; ▨ = MRD-G; **$p < 0.01$.

Table 2. Blood lipids, glucose, insulin and leptin

Variable	Baseline	6 weeks' follow-up
LCD-G	30	29
Total cholesterol, mg/dl	222 ± 27.3	206 ± 26.1[c]
Triglycerides, mg/dl	127 ± 68.3	139 ± 74
HDL-cholesterol, mg/dl	58.1 ± 19.3	51.1 ± 16.1[d]
LDL-cholesterol, mg/dl	129 ± 25.7	120 ± 22.9[c]
Glucose, mg/dl	95 ± 14.1	91.2 ± 10.9[d]
Insulin, μU/ml	8.81 ± 3.92	8.23 ± 4.15
Leptin, ng/ml	36.5 ± 29.2	29.5 ± 22.7[a]
MRD-G	60	59
Total cholesterol, mg/dl	223 ± 32.2	194 ± 29.9[c]
Triglycerides, mg/dl	142 ± 65.1	123 ± 54.7[c]
HDL-cholesterol, mg/dl	59.4 ± 14	51.9 ± 13.6[c]
LDL-cholesterol, mg/dl	128 ± 26.9	112 ± 23.7[c]
Glucose, mg/dl	95 ± 12.2	91 ± 11.5[c]
Insulin, μU/ml	12.7 ± 10.1	7.75 ± 5.37[c]
Leptin, ng/ml	36.5 ± 25.4	18.3 ± 11.8[a, c]

All values expressed as mean ± SD.
[a] $p < 0.05$ between groups; [c] $p < 0.01$, [d] $p < 0.05$ within groups.

LDL- and HDL-cholesterol decreased significantly in both groups (table 2). Triglycerides increased in the LCD-G and decreased significantly in the MRD-G.

Glucose, insulin and leptin were reduced in both groups (table 2) and once again the changes were far more pronounced In the MRD-G (fig. 2). The reductions in insulin and leptin/fat mass loss were 0.21 μU/mg in the LCD-G vs. 0.97 μU/mg in the MRD-G for insulin ($p < 0.01$) and 2.5 ng/ml versus 3.57 ng/ml for leptin ($p < 0.01$).

The prevalence of the metabolic syndrome (calculated according to the NCEP definition [13]) at baseline was 27% in the LCD-G (n = 8) and 36% in the MRD-G (n = 22). After 6 weeks, there was no change in the LCD-G. In the MRD-G the prevalence of the metabolic syndrome was reduced by 12% (n = 7, $p < 0.05$).

Discussion

The main result of the present study was that when following the MRD, subjects showed a stronger improvement in metabolic risk factors and thus a 12% reduction in the prevalence of the metabolic syndrome. In addition, the changes in weight and body composition were mark-

edly higher than those found in the LCD-G following an energy-restricted diet.

These findings are in keeping with the results of a recent meta-analysis of weight-loss trials, showing that soy-based very-low-calorie diets promote rapid weight loss in a short period of time [6].

Though the LCD-G had a mean daily caloric intake 1.5 times that of the MRD-G, the weight reduction in the MRD-G was 1.8 times higher. This may be due to more effective compliance to the dietary restrictions using meal-replacement strategies or a specific effect of the chosen dietary regimen.

Within metabolic risk factors, the reductions in waist circumference and triglycerides in particular were far more pronounced in the MRD-G than in the LCD-G. Most likely, the decrease in the prevalence of the metabolic syndrome after 6 weeks can be largely attributed to the improvements in waist circumference and triglyceride concentration. The finding that HDL-cholesterol levels decreased in both groups was expected. The reduction of HDL-cholesterol in the initial phase of fat-reduced energy-restricted diets is well known [14]. Improvements in HDL-cholesterol have commonly been observed in studies lasting more than 12 weeks [8].

In a recent study, Ross et al. [15] showed that a reduction in waist circumference by 1 cm is equivalent to a loss in abdominal fat of 0.33 kg. If applied to our study, the subjects in the MRD-G would have lost 1.8 kg of abdominal fat vs. 0.5 kg in the LCD-G. Given the importance of abdominal fat in the pathogenesis of the metabolic syndrome [16], it could be speculated that the observed reduction in abdominal fat is an important factor in explaining the reduced prevalence of the metabolic syndrome, even in this relatively short time period.

Therefore, the difference in fat mass and metabolic risk factors may simply be explained by the different energy content of the diets investigated. However, although the effects were relatively small, a recent meta-analysis on the effects of soy protein on the lipid profile concluded that soy protein significantly improves blood lipid levels [8]. It has been suggested that this beneficial effect is mediated by the high content of isoflavones in intact soy protein. These isoflavones may alter lipoprotein metabolism by their biological similarities to estrogen and estrogen-receptor-dependent gene expression [17]. In addition, soy isoflavones have been shown to be involved in the regulation of enzymes and proteins important in lipid metabolism [18, 19]. The effect of soy protein on gene expression or the regulation of nuclear transcription factors might also, at least in part, be accounted for by the alterations in insulin and leptin. The reduction in insulin and leptin per kilogram fat mass loss was significantly higher in the MRD-G than in the LCD-G. However, the study design was not suitable for detecting a possible soy-specific effect since the 2 diets were not comparable in their energy content.

Nevertheless, our data suggest that even in a short period of time, a MRD is more effective in reducing metabolic risk factors, insulin and leptin than a fat-restricted LCD. If these results are confirmed by forthcoming studies, a meal-replacement regimen may be of particular benefit for overweight or obese subjects with a need to reduce metabolic risk factors. In particular, future investigations should address the question of whether an MRD could avoid the initiation of drug therapy according to the ATP III treatment guidelines or reduce the use of specific medications as shown in the study by Li et al. [20].

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