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The Influence of a Meal Replacement Formula on Leptin Regulation in Obese Adults

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Abstract

Background and Purpose: The increasing prevalence of overweight and obese adults warrants improved dietary strategies for weight management and metabolic control. Hence, the objective of this study was to investigate the effects of a high-protein diet on leptin regulation.

Methods: This study was a secondary analysis of data collected from a randomized controlled trial, conducted in 90 overweight adults (age: 47.5 ± 7.5 yrs.; BMI: 31.5 ± 2.3 kg/m^2) who were followed over a 24-week control period. Changes in leptin levels were quantified to determine the influence of age, gender, leptin baseline levels, weight loss and intervention type. Participants were randomized into 3 interventions groups: 1) therapeutic lifestyle changes, (LS); 2) standardized meal replacement (Almased®) (MR); and 3) standardized meal replacement accompanied by supervised physical training (MRPT). For the analyses, both diet groups (MR, MRPT) were pooled into one common group and compared to the LS group in a parallel two-group study design with endpoint assessment after 24 weeks of intervention.

Results: In total, 83 participants completed the 24-week study. Significant improvements in body composition and metabolic regulation occurred in all intervention participants regardless of their group assignment (LS; MR, MRPT). Participants' consumption of the meal replacement (MR; MRPT) had an independent, significant effect on serum leptin levels (-15.5 ± 7.5 and -12.5 ± 7.8 vs. -8.7 ± 6.1 ng/ml). Greater body weight reductions were also observed in the diet groups (-8.9 ± 3.9 kg) compared to the LS group (-6.2 ± 4.2 kg). Conclusions
our findings suggest that meal replacement can safely and effectively produce significant weight loss, which may be in part due to a reduction in plasma leptin levels. ClinicalTrials.gov Identifier: NCT00356785

Keywords: Leptin; Meal Replacement; Energy Metabolism; High Protein Diet; Weight Regulation;

Abbreviations

Yrs: Years; BMI: Body Mass Index; kg/m2: Kilogram/Meter2; LS: Lifestyle group; MR: Standardized meal replacement group; MRPT: Standardized meal replacement accompanied by supervised physical training; ng/ml: Nanogram/millilitre; kg: Kilogram; h-CRP: High-sensitivity C-reactive protein; IL6: Human Interleukin 6; SD: standard deviations; SPSS: Analytical Software; BW: Body Weight; G: Gramm

Introduction

Obesity levels have dramatically increased in the United States (US) and in the majority of European countries during the past few decades [1-3]. A study in 2001 [4] revealed increases in obesity among US adults for both sexes and across all ages, ethnic backgrounds, educational levels and smoking levels. A chronic imbalance between energy intake and energy expenditure appears to play a role in the development of obesity [5, 6].

Serum leptin levels may have a potential role in the prediction of weight loss and weight-loss maintenance [7]. Serum leptin levels may influence weight loss and weight-loss maintenance through lifestyle changes in overweight adults [8, 9]. Leptin, as a circulating adipokine, is a regulatory factor for food intake, energy expenditure and body fat distribution. Leptin also participates in a signalling system regulating the amount of adipose energy stored in the brain [5]. In addition, leptin resistance may be responsible, in part, for the development of obesity among the aging population [10].

Appropriate intervention strategies to reverse body weight gain and elevated body fat, respectively, are still a matter of debate because additional metabolic and endocrine effects may influence the course and outcomes of the weight loss process [11]. According to several studies, a high-protein, low-glycaemic

diet may influence leptin regulation and weight management [11-13]. For this reason, a subgroup analysis was performed on the data collected from an intervention study to examine the effects of a protein-rich meal replacement on the body composition and metabolic conditions of overweight adults.

Materials and Methods

For the secondary data analyses, we used data collected from a randomized controlled three-arm study including 90 men and women. All volunteers were overweight middle-aged adults (31.5 ± 2.3 kg/m^2; 47.5 ± 7.5 yrs.); non-smokers; free from known food allergies, metabolic diseases; and none regularly used any medications.

For the main trial, participants were randomized into 3 intervention groups: 1) therapeutic lifestyle changes: LS; 2) standardized meal replacement (Almased ®), MR; and 3) standardized meal replacement accompanied with supervised exercise/physical training (MRPT). All participants completed a comprehensive medical examination before and after the intervention, including body composition analysis by air displacement plethysmography (Bod Pod®) [14] and laboratory investigations, i.e., blood glucose, insulin, plasma lipids, inflammatory markers (h-CRP, IL6) and leptin [11].

For this investigation, we analysed leptin and insulin changes to determine the effects of age, gender, baseline level, weight loss, and intervention type. In this analysis, the effects of the therapeutic lifestyle vs. diet with and without supervised exercise interventions on the selected laboratory criteria were evaluated. We also evaluated the change from baseline to the end of intervention at the 24-week visit.

All volunteers were interviewed and screened before participating in this study at the Department of Sports Medicine of the Freiburg University hospital. The study was conducted in accordance with the Declaration of Helsinki guidelines. All procedures involving human subjects were approved by the Ethics Commission of Freiburg University (EK-Freiburg No. 230/01) and registered as a controlled clinical trial (ClinicalTrials.gov Identifier: NCT00356785). All participants provided written informed consent. The clinical trial was designed and performed according to an approved, published protocol [11].

Statistical Analysis

For the secondary data analysis, both meal replacement groups were merged into a single group (MR/MRPT) due to the similarity of their outcomes (Table 1). The meal replacement groups were compared to the lifestyle group (LS) in a parallel two-group evaluation. The endpoint assessment occurred 24 weeks after the interventions.

The results are expressed as the means ± Standard Deviations [SD] for all parameters. Descriptive, multivariable analyses were performed to evaluate the changes from baseline using the exact Mann-Whitney test and the ANOVA test. For each participant, complete data sets were available in Microsoft® Excel XP spreadsheets. Significance was defined as $p < 0.05$ (Two-Way). All analyses were performed using SPSS version 18.02.

Results

The data from the first analysis in the original study [11, 12] indicated that there were no significant differences between MR and MRPT ($p > 0.1$) (Table 1).

Therefore, for this secondary data analysis, both meal replacement groups using the meal replacement formula were merged into a single group (MR/MRPT) and compared to the lifestyle group (LS) with endpoint assessment after 24 weeks of intervention (Table 2). At baseline, all demographic, clinical and laboratory variables were not different between groups. Independent of the intervention (LS vs. MR/MRPT), the 83 patients who completed the study had significant improvements in body composition and metabolic regulation (Table 2). The MR and MRPT groups experienced changes in body weight (BW -8.9 ± 3.9 kg) (independent of training) and had significantly greater weight reductions compared to the LS group (-6.2 ± 4.2 kg).

We also detected significant differences from baseline in fat mass, serum leptin levels, and insulin between the interventions (Table 2). Even after adjusting for weight loss differences, participants in the MR/MRPT group showed significantly larger reductions in serum leptin levels (-13.9 ng/ml) compared with participants in the LS group (-9.8 ng/ml) post-intervention. This effect was not observed for insulin.

Discussion

In this study, we compared the effects of different weight-management interventions, including therapeutic lifestyle changes and the use of a meal replacement product with or without supervised exercise training. Overall weight and fat loss were significantly greater in the meal replacement group. This group also demonstrated greater improvements in blood markers of metabolic health.

In 2003, for the first time, a team at Freiburg University published their findings regarding the positive effects of a soy-yoghurt-honey-based meal replacement product (Almased®) on weight reduction and the regulation of insulin and leptin [11]. According to this randomized controlled trial, insulin and leptin levels decreased more in participants using the meal replacement compared to participants receiving lifestyle group counselling. In the current study, we conducted a secondary analysis of the first 24-weeks of intervention by merging the data of the MR and MRPT groups. The main trial findings were published in 2003 and indicated the beneficial effects of the meal replacement formula on reductions in leptin and insulin levels. These results were confirmed by our secondary analyses.

When the leptin results were adjusted for age, gender, baseline leptin level, body weight change, and intervention type (LS vs. MR/MRPT), the meal replacement approach clearly had an independent effect on plasma leptin levels and improved the effects on leptin reduction caused by weight loss. Therefore, the results suggest a relationship between protein intake and leptin regulation in the overweight adults examined. Several studies have demonstrated that an increase in the

Table: 1

Biochemical parameter	Before	MR groupn=28 After	p -value[a]	Before	MRPT groupn=27 After	p -value[a]	p -value[b]
Total cholesterol (mg/dl)	225 ±30.4	196±23.1	0.000	221±34.8	198±32.6	0.000	0.396
HDL-cholesterol (mg/dl)	59±14.1	52±10.4	0.003	59±14.0	54±15.6	0.002	0.763
LDL-cholesterol (mg/dl)	128±25.6	114±15.2	0.003	127±29.2	112±26.3	0.000	0.897
Apo B (mg/dl)	119±20.9	101±16.2	0.000	115±27.4	92.5±25.5	0.000	0.085
Leptin (ng/dl)	37.9±26.7	22.5±13.9	0.000	33.9±24.2	21.3±16.3	0.000	0.226
Insulin (μU/ml)	11.7±8.92	6.3±3.97	0.003	13.8±11.35	7.8±5.90	0.001	0.139
Glucose (mg/dl)	92±9.4	90.0±9.1	0.226	98±14.4	91.0±10.5	0.000	0.260

Data comparison between the MR and MRPT groups [11].
[a]For changes before–after
[b]For differences in changes between the groups

Table 2: Results for body composition, metabolic and inflammatory status (mean ± SD) in the subgroups before and after intervention. p-values for pre-post intra-group paired differences were p<0.05 (a), p<0.01(b), p<0.005 (c). p-values for the pre-post inter-group unpaired differences were p<0.05 (x), p<0.01(y), - n.s.

	LS (n=28) Pre RCT	MR/MRPT(n=55) Pre RCT	LS (n=28) Post RCT	MR/MRPT (n=55) Post RCT
Body Weight (kg)	91.2±11.6	90.2±11.3	84.9±10.8 c / y	81.8±11.7 c / y
Fat Mass (kg)	36.9±6.27	36.2±6.38	30.4±7.60 c / x	26.8±7.80 c / x
Triglyceride (mg/dl)	127±68.4	143±66.0	137±55.2 -	133±71.9 -
Apolipoprotein B (mg/dl)	115±20.3	117±23.9	105±20.9 - /c	97±21.6 c / x
Fasting Blood Sugar (mg/dl)	95±14.1	95±12.2	90±9.9 a / -	90±9.8 c / -
Insulin (μU/ml)	8.8±3.92	12.7±10.1	7.4±3.98 - / y	7.1±5.02 c / y
HOMA- Index (U)	2.2±1.26	3.1±2.65	1.7±1.00 - / y	1.6±1.17 c / y
Leptin (ng/ml)	37±29.2	36±25.4	28±20.7 b / y	22±15.0 c / y
Interleukin-6 (pg/ml)	1.8±1.25	2.2±2.05	1.8±2.30 -	1.7±1.29 A
hs-CRP (mg/dl)	0.27±0.22	0.30±0.28	0.23±0.16 -	0.19±0.17 C

proportion of dietary protein from 15% to 30% of energy intake with a constant level of carbohydrate intake produces a sustained decrease in ad libitum energy intake, which may be mediated by increased central nervous system leptin sensitivity resulting in significant weight loss, while sparing muscle protein loss and enhancing glycaemic control [7, 11-12, 15-16]. Participants consuming a diet high in protein with a low glycaemic index continue to lose weight after the initial weight loss [13]. In fact, higher dietary protein intake was achieved by reducing carbohydrate intake, which adds further support to the concept that reducing glycaemic load (defined as dietary carbohydrate content (g) multiplied by glycaemic index) is important for controlling body weight in obese patients [17-19]. The satiating effect of protein and specific peptides (such as those found in soy protein isolates) may also contribute to the weight loss produced by low-carbohydrate diets [7, 20]. Moreover, weight loss interventions using meal replacement approaches together with dietary counselling and increased physical activity lead to substantial, favourable changes in both anthropometric and metabolic risk factors, while preserving lean muscle mass [12, 21]. Recent studies have shown that meal replacement regimens are safe and associated with greater weight loss than individualized diet plans [22, 23]. A meal replacement regimen high in soy protein may be more effective at improving body weight and body composition and reducing associated cardio-metabolic risk factors, such as insulin, leptin, endothelial function and anthropometric measures compared to lifestyle interventions (e.g., fat restricting low calorie diets and increased physical activity) [11, 24, 25]. When the meal replacement formula was consumed, significant changes occurred in metabolic and inflammatory markers (compared to baseline). As a soy and milk protein-based product, the meal replacement used in this study had an energy-sparing effect and may also have potential additional health benefits [26]. Soy proteins have been noted to improve receptor-mediated transport of insulin and leptin through the blood brain barrier

and are responsible for an increased effect of these hormones in the hypothalamus. This effect not only impacts appetite regulation but may also impact peripheral insulin and leptin resistance in obese participants [27-30]. These effects may be mediated by isoflavones and attributable peptides, which exhibit a variety of biological and molecular activities [20,25]. Soy isoflavones are involved in the regulation of enzymes and proteins important for lipid metabolism [31, 32]. The effects of soy protein on gene expression or the regulation of nuclear transcription factors might also, at least in part, be able to account for the alterations observed in insulin and leptin [33, 34]. Therefore, isoflavones and biologically active peptides in this meal replacement product [20] may account for some of the beneficial effects identified in this study. Specifically, we observed a reduction in body fat mass and hepatic fat accumulation, in addition to improved fatty acid metabolism, which led to lower plasma lipid levels and inflammatory markers and decreased insulin resistance [33].

Conclusions

In summary, the meal replacement strategy utilized for weight reduction in this trial may provide therapeutic benefits for obesity-associated metabolic dysregulation, including impaired glucose tolerance and leptin resistance. These findings support the hypothesis that dietary components influence energy balance, body composition and the metabolic milieus that are responsible for weight stabilization. Moreover, the meal replacement product can safely and effectively produce significant, sustainable weight loss through a reduction in serum leptin.

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Competing interests

This research was funded by Almased Wellness GmbH, Bienenbüttel, Germany. A. Berg has written "The Almased Wellness Concept" outlining the effects of a soy-enriched diet in ealth and disease.

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