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Efficacy of High Carbohydrate versus High Protein Meal Replacements on Weight Reduction - A Randomized Controlled Trial

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Abstract

Background: While formula diets as meal replacements are evident for weight loss, the macronutrient composition is still in the focus of interest. This study was designed to determine effects of a carbohydrate-riched meal replacement on weight loss and waist circumferences (WC) in comparison with a protein-riched meal replacement.

Methods: Two groups (high carbohydrate formula diet (HC) and high protein formula diet (HP)) of 80 matched subjects each underwent a randomized parallel intervention trial for eight weeks followed by a 12-week follow-up. The intervention consisted of three phases: (1) week 1 and 2: total replacement of three meals, (2) week 3 and 4: replacement of two meals and (3) week 5 to 8: replacement of one meal. Measurements were taken at week 0, 2, 8, and 20.

Results: After two weeks of total meal replacement, there was a significant ($p<0.001$) weight loss in both groups (HC: -4.0 ± 4.7 kg vs. HP: -4.3 ± 1.8 kg). After eight weeks, 66.2% of all subjects achieved a weight loss of 5% and more (HC: -8.5 ± 2.5%, $p<0.001$ vs. HP: -8.8 ± 2.8%, $p<0.001$), and 18.2% of the participants lost more than 10% of their initial body weight. Waist circumferences decreased from 105.9 ± 9.7 cm to 97.4 ± 8.4 cm ($p<0.001$) after eight weeks. During the follow up, further weight loss was observed in both groups. There were no significant differences between the HC and HP-group regarding changes in weight and WC.

Conclusion: Both dietary intervention strategies had a similar effect on weight loss and WC reduction. In this short-term study macronutrient compositions of meal replacements are not crucial for the efficacy of formula diets.

Trial registration: German Clinical Trials Register DRKS00005481.

Keywords: Meal replacement; Formula diet; Weight loss; High carbohydrate; High protein

Introduction

Obesity and related diseases have become a worldwide problem of public health. Currently, an estimated 39% of the adult population is categorized as overweight and 13% as obese [1]. Given the prevalence of obesity, effective strategies are necessary for the prevention and treatment of obesity [2]. Energy reduction and low caloric diets have consistently been proven to encourage weight loss and to have beneficial health effects in obese subjects [3].

Therefore, formula diets as meal replacements have already been accepted as useful therapeutic strategies for weight loss in the evidence-based guidelines [4]. Meal replacement strategies cause weight reduction by creating greater energy deficit than is usual with a conventional diet [5] and are widely used to attain initial weight loss [4,6]. Due to the micronutrient composition laid down in European directives, formula diets ensure adequate intake of minerals, trace elements and vitamins [7]. Several studies have demonstrated that weight loss and weight maintenance was greater in the meal replacement groups compared to the conventional energy restricted diets while the calorie goal for the groups was equivalent [8-10]. Meal replacements coupled with low-calorie diet considerably increase the number of responders [11,12] and provide an effective option for weight reduction in overweight and obese subjects [13,14].

A further recommended strategy for achieving a reduction in energy balance is modifying macronutrient composition. There is still interest in whether the sources of energy in the diet might be the most beneficial for weight loss and weight maintenance [15]. Several randomized controlled trials observed favorable short-term effects of a high protein diet on body weight [16,17]. A high protein (HP) diet might increase the amount of weight loss by a reduction in appetite and increased thermogenesis [18]. On the other side, successful effects of high carbohydrate (HC) diets for weight loss have also been proven [19-22].

However, reduced energy intake for weight loss and maintenance by modification of macronutrient distribution is difficult to maintain by conventional dietary approaches, mostly due to the increase levels of hunger [23]. The individuals may have some difficulties in selecting or cooking the complicated low-calorie menus, in which various factors such as energy, carbohydrates, proteins or fat are involved. Hence, deficiency of macro- and micronutrients can occur [24,25].

Therefore, we aimed to determine the effect on weight loss using a HC meal replacement compared to a HP meal replacement. A novel aspect of this study was the use of two low-fat meal replacements either high in carbohydrates or high in proteins as a method for providing a diet with recommended daily intake that is feasible to sustain.

Materials and Methods

Study design and population

This trial was designed as an 8-week, single center, randomized, double-blind and parallel group intervention study, including a follow-up of twelve weeks. The study protocol was approved by the Ethical Committee of the Medical Chamber of Lower Saxony (Ärztekammer Niedersachsen) on 21th November 2013. Written informed consent was obtained from all subjects according to the guidelines for Good Clinical Practice. The clinical investigation was registered in the German Clinical Trials Register with the identification number DRKS00005481.

The study was carried out at the Institute of Food Science, Leibniz University Hannover, Germany. Subjects were recruited through advertisements in daily newspapers and pre-screened via structured telephone interviews. The criteria for participation were: (1) age 30-65 years, (2) body mass index (BMI between 27.9 and 35.1 kg/m^2). Exclusion criteria were defined as major chronic diseases (e. g. cancer diseases, manifest cardiovascular disease (CVD), insulin-dependent type 1 or 2 diabetes, severe renal or liver diseases, endocrine and autoimmune diseases), gastrointestinal disorders (e. g. ulcers, chronic inflammatory bowel diseases, coeliac disease, pancreatitis), prior gastrointestinal surgical procedures (e.g. gastrectomy, short bowel syndrome, gastric bypass, gastric banding, stomach balloon), lactose intolerance, pregnancy, breastfeeding, and alcohol or drug addiction. Additionally, subjects were excluded if currently following a diet or taking any supplements that could interfere with the given preparations. The existence of inclusion and exclusion criteria was audited using a structured questionnaire sent by post. After returning the completed admission questionnaire, subjects meeting the inclusion criteria without the presence of any exclusion criteria were included and invited to the first examination (t_0). Subjects (stratified according to their gender and BMI) were assigned to their respective intervention groups by means of block randomization appropriate to the sample size. The chief investigator, investigators, study staff, and participants were all blinded to the treatment allocation. One hundred and sixty overweight (12%) and obese (88%) subjects (n=94 females, n=66 males) were enrolled in the trial in February 2014.

The participants consumed either a HC formula diet or a HP formula diet. Study products were provided by Certmedica International GmbH (Aschaffenburg, Germany). They were administered daily as a drink meal replacement. Shakes were prepared by combining 30 g of powdered HC formula diet and 34 g of powdered HP formula diet with 300 ml milk (low fat) and 5 g vegetable oil. The macronutrient composition of the HC formula diet was approximately 24% protein, 49% carbohydrate, 25% fat, and 2% fiber relating to the recommended preparation. The macronutrient composition of the HP formula diet was approximately 38% protein, 34% carbohydrate and 28% fat. The nutritional composition of the two preparations is presented in Table 1.

	High-carbohydrate formula diet*		**High-protein formula diet****	
	Preparation per 100 g	Preparation per serving	Preparation per 100 g	Preparation per serving
Energy (kJ)	1560 (371 kcal)	1319 (313 kcal)	1548 (364 kcal)	1311 (311 kcal)
Protein (g)	22.5	16.9	56.4	29.2
Carbohydrate (g)	65.6	34.1	34.0	26.0
Fat (g)	0.03	7.8	0.2	9.8
Fiber (g)	7.41	2.2	0	0
Vitamin A (µg)	614.5	226.4	1001	379
Vitamin D (µg)	5.2	1.6	4.4	1.6
Vitamin E (mg)	11.1	5.3	19.8	6.8
Vitamin C (mg)	34.9	15.6	73.5	30.1
Vitamin B1 (mg)	0.9	0.4	1.7	0.7
Vitamin B2 (mg)	0.00	0.5	4.3	2.0
Niacin (mg)	11.1	5.4	22.1	7.8
Vitamin B6 (mg)	1.2	0.5	2.5	1.0
Folate (µg)	299.3	113.8	362.4	136.7
Vitamin B12 (µg)	0.00	1.2	6.1	3.4
Biotin (mg)	0.00	12.0	90.6	0.04

Pantothenic acid (mg)	0.00	1.1	7.9	3.7
Calcium (mg)	11.7	357.5	676	584.0
Phosphor (mg)	218.9	338.7	348	391.0
Potassium (mg)	169.4	515.9	197	532
Iron (mg)	18.7	7.9	15.3	5.3
Zinc (mg)	6.0	4.7	8.7	4.1
Copper (mg)	1.6	0.6	1.3	0.5
Iodine (µg)	13.1	50.0	119.1	50.3
Sodium (mg)	105.1	172.6	426.0	286.0
Magnesium (mg)	29.9	45.0	164	92.0
Manganese (mg)	1.0	0.3	0.9	0.3
Selenium (µg)	54.9	16.5	58.7	20.0
*Recommended preparation: 300 ml milk (low fat)+30 g carbohydrate-rich powder+5 g vegetable oil **Recommended preparation: 300 ml milk (low fat)+34 g protein-rich powder+5 g vegetable oil				

Table 1: Nutrient and energy content of the formula diets with recommended preparation.

Within the first two weeks of intervention, subjects were advised to replace three meals a day. The received low-calorie diet provided 800 kcal/3347 kJ per day. Subjects could add the daily intake with a hand-full of vegetables. Therefore, the low calorie diet provided a total of 800 to 1000 kcal (3347 to 4184 kJ) per day. In week 3 and 4, the subjects consumed two meal replacements for both, lunch and dinner. During the last intervention period (week 5 to 8), participants were encouraged to replace either lunch or dinner (depending on the daily routine). During the follow-up, the formula diets were taken ad libitum.

All participants received preparation instructions as well as recipe suggestions for the meal replacement drinks to avoid monotony and to offer variation in the preparation. Week 2 to 8, breakfast and either lunch or dinner were prepared according to the principles of a balanced whole food diet and based on national recommendations (German Nutrition Society). A recipe book was given to all participants to encourage healthy eating habits. The required amount of investigational products in neutral packaging was provided to the participants prior to the trial commencement and after two weeks. At the end of the study, the remaining formula powders were weighed to check compliance.

After 4, 7 and 19 weeks, all participants filled in a three daynutrition protocol which was typically kept for two weekdays and one weekend day, respectively. Thus, three nutrition protocols were available from each subject. Nutrition calculations were carried out using PRODI® (Nutri-Science GmbH, Freiburg, Germany).

Questionnaires, anthropometric measurements

Anthropometric measurements were taken at baseline, after 2, 8, and 20 weeks (t_0, t_2, t_8, t_{20}). The height was measured once at the beginning of the study in an upright position without shoes with a stadia rod (SECA, Model 217, seca gmbh & co kg, Germany). Body weight was recorded dressed in light clothes and without shoes. Waist circumference (WC) was measured at the midpoint between the lower border of the rib cage and the top of the iliac crest. Hip circumference (HipC) was defined as being the widest circumference over the buttocks. The measurements of the WC and HipC were taken with the subjects standing relaxed, breathing normally, with the measuring tape placed horizontally. The waist-to-hip ratio (WHR) was calculated. Blood pressure was measured under standardized conditions after 10 min. resting period. The examinations were performed in the morning after an overnight fasting period of at least 12 h.

Statistical analysis

Statistical comparison between the HC and HP group were performed using the nonparametric Mann-Whitney U test for unpaired data. The changes in the parameters in comparison with baseline were analyzed using the Wilcoxon test. The chi-square test was used to compare the difference between the frequencies of the two groups. Differences were considered significant at $p<0.05$. The results were shown as the mean value ± standard deviation (s.d.).

A modified intention-to-treat (mITT) population was evaluated comprising subjects with a baseline value (t_0) and at least one further measurement value. For all subjects the missing values were constantly updated with the last observation carried forward after the prior measurements. The statistical data analysis was carried out by using the Statistical Package for Social Sciences SPSS 21.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Baseline characteristics

A total of 280 individuals were pre-screened for this study. 85 subjects did not fulfill the inclusion criteria and were excluded during screening. Subjects from the waiting list moved up if others did not

fulfill the BMI criteria at the baseline visit. 80 participants were randomized either to the HC or to the HP group. Six participants (3.9%) dropped out before week 2 (t_2) because of intolerance to the study formula diet, acute illness or other reasons. Consequently, 154 participants were included in the mITT analysis: 78 of them received HC formula diet (n=45 female, n=33 male) and 76 the HP formula diet (n=45 female, n=31 male). After completion of the follow-up in week 20, 103 participants remained in the study (60 in the HC group and 43 in the HP group). A flowchart is illustrated in Figure 1. At baseline, no differences were observed between both groups regarding to the parameters listed in Table 2. Preobestiy (27.0-29.9 kg/m^2) applied to 14 subjects (9%), 131 subjects (85%) had obesity stage I (30.0-34.9 kg/m^2) and 9 subjects (6%) could be allocated to obesity stage II (35.0-39.9 kg/m^2).

	Total group	HC group	HP group	p*
Number of participants (n)	154	78	76	
Sex distribution (m/w)	64/90	33/45	31/45	0.848**
Age (years)	50.4 ± 8.2	50.6 ± 8.3	50.3 ± 8.2	0.755
Initial weight (kg)	97.9 ± 12.6	98.2 ± 12.9	97.6 ± 12.4	0.811
Height (cm)	173.3 ± 10.0	173.7 ± 9.8	172.8 ± 10.1	0.52
BMI (kg/m^2)	32.5 ± 1.7	32.4 ± 1.8	32.5 ± 1.6	0.712
Number of participants (n) with a				
BMI 27.0–29.9 kg/m^2	14 (9%)	8 (10%)	6 (8%)	0.857**
BMI 30.0–34.9 kg/m^2	131 (85%)	65 (83%)	66 (87%)	0.816**
BMI 35.1-39.9 kg/m^2	9 (6%)	5 (6%)	4 (5%)	0.317**
WC (cm)	105.9 ± 9.7	105.9 ± 9.8	105.8 ± 9.6	0.918
WC m (cm)	112.2 ± 5.9	113.6 ± 5.7	110.8 ± 5.7	0.053
WC w (cm)	101.4 ± 9.3	100.3 ± 5.7	102.4 ± 10.3	0.334
HipC (cm)	115.1 ± 6.4	115.4 ± 6.5	114.9 ± 6.4	0.366
SBP (mmHg)	140.9 ± 16.9	139.4 ± 15.3	142.4 ± 18.4	0.245
DBP (mmHg)	84.9 ± 10.6	84.5 ± 10.2	85.3 ± 11.1	0.57

mean ± SD; *Mann-Whitney-U test; **Chi-square test; BMI: Body Mass Index; DBP: Diastolic Blood Pressure; HipC: Hip Circumference; HC group: High Carbohydrate; HP group: High Protein; m: Men; w: Women; SBP: Systolic Blood Pressure; WC: Waist Circumference

Table 2: Baseline participant´s characteristics (n=154).

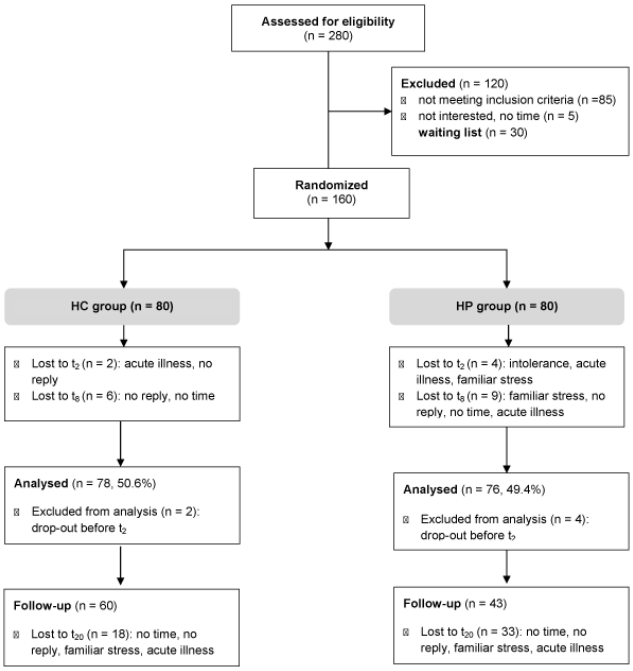

Figure 1: Flowchart. HC group: High Carbohydrate; HP group: High Protein.

Energy intake and macronutrient intake

At baseline, the dietary intakes of energy (kJ/day), carbohydrates, protein and fat were similar in both groups (Table 3). During the two weeks of total meal replacement, energy intake was reduced by 65.2% from baseline in the HC group ($p<0.001$) and by 60.1% in the HP group ($p<0.001$). At week 4 and 7, energy intake continual increased, but reduced energy intake was still maintained throughout the study in both groups. At week 2 and 4, absolute carbohydrate intakes and percent of energy from carbohydrates in the HC group increased compared to baseline ($p<0.001$ each). Percent energy intake from carbohydrates in the HC group were greater than in the HP group at week 2, 4 ($p<0.001$ each) and 7 ($p<0.05$). Percent energy derived from protein increased in both groups at week 2, 4 and 7 compared to baseline ($p<0.001$ each). However, the increase was significantly lower in the HC group. Absolute intake of fat decreased in the HC group ($p<0.001$) and in the HP group ($p<0.001$), as well as percentage from fat in both groups ($p<0.001$ each). There was no significant difference in fat intake between the groups. Nevertheless, at week 2 absolute intake of fat and percentage intake from fat was modestly higher in the HP group than in the HC group ($p<0.05$). Comparison of the groups showed a slightly higher fiber intake for the HC group ($p<0.05$). In both groups, fiber intake compared to baseline decreased at 2, 4 and 7 weeks ($p<0.001$ each) and was greater in the HC group than in the HP group ($p<0.001$ each).

	Baseline	Week 2a	Week 4b	Week 7c	Week 19d
Diaries analysed (number of diaries (HC group/HP group))	(74/73)	(78/76)	(68/62)	(65/61)	(48/32)

Total Energy intake (kJ/day)					
HC	10275.8 ± 3198.8	3516**	5344.5 ± 1780.4**	6385.4 ± 2084.3**	7498.2 ± 2363.9**
HP	9929.8 ± 3418.8	3969**,#	5598.4 ± 2207.3**	6527.4 ± 1857.2**	7424.7 ± 2586.8**
Total Energy intake (kcal/day)					
HC	2454.0 ± 764.1	853.4**	1285.7 ± 424.8**	1530.5 ± 497.9**	1789.5 ± 564.1**
HP	2371.2 ± 916.4	946.5**,#	1335.6 ± 526.7**	1558,7 ± 443,4**	1772.1 ± 615.9**
Protein (g)					
HC	93.2 ± 25.0	50.7**	63.8 ± 16.9**	75.2 ± 22.3**	76.1 ± 23.3**
HP	95.3 ± 30.8	87.6**,##	91.1 ± 24.1**,##	87.3 ± 19.7**,##	87.5 ± 25.6
Carbohydrate (g)					
HC	251.3 ± 91.7	102.3**	154.4 ± 47.8**	164.7 ± 53.2**	197.8 ± 65.4**
HP	245.6 ± 108.2	78.0**,##	133.3 ± 46.4**,#	160.9 ± 55.2**	182.5 ± 68.4**
Fat (g)					
HC	103.6 ± 41.2	23.4**	40.8 ± 21.3**	60.6 ± 30.3**	66.5 ± 30.4**
HP	103.8 ± 40.3	29.4**,#	44.0 ± 23.3**	57.1 ± 20.2**	67.6 ± 29.0**
Fiber (g)					
HC	22.7 ± 7.9	6.6**	14.7 ± 12.8**	16.9 ± 5.9**	18.4 ± 5.7*
HP	20.6 ± 7.2#	0**,#	8.8 ± 4.1**,##	13.8 ± 4.1**,##	15.6 ± 5.9*
Protein (%)					
HC	16.1 ± 3.6	24.4**	20.8 ± 3.0**	20.7 ± 4.2**	17.7 ± 3.3*
HP	16.9 ± 3.6	37.9**,##	29.1 ± 4.9**,##	23.7 ± 3.9**,##	20.9 ± 4.7**,#
Carbohydrate (%)					
HC	42.4 ± 9.2	49.1**	49.6 ± 5.4**	44.8 ± 7.7	45,5 ± 7.3
HP	42.1 ± 8.0	33.8**,##	41.3 ± 5.5##	42.1 ± 7.1#	42.3 ± 6.7
Fat (%)					
HC	36.7 ± 5.8	25.1**	27.2 ± 5.5**	34.1 ± 10.7**	32.3 ± 6.6*
HP	38.3 ± 6.7	28.3**,#	28.3 ± 4.8**	32.1 ± 5.4**	33.4 ± 7.0*
Total fiber (%)					
HC	2.0 ± 0.7	1.6**	2.4 ± 1.1**	2.4 ± 0.9**	2.4 ± 0.7*
HP	1.9 ± 0.5	0**,##	1.4 ± 0.5**,##	1.9 ± 0.6##	2.0 ± 0.7#

mean ± SD; a calculated from the intake of 3 formula diets per day; b including intake of 2 formula diets per day; cincluding 1 formula diet per day; including formula diets as reported at 3-day food record; %, percentage of total Energy; *p<0.005, **<0.001; Wilcoxon-test compared to baseline; #p<0.005, ##p<0.001 Mann-Whitney-U-test compared two groups

Table 3: Energy and macronutrient intake of available dietary diaries during the study in both groups at baseline and during the 8-week intervention.

Changes in anthropometric data

A significant weight loss of 4.0 ± 1.7 kg (4.1%) in the HC group and 4.3 ± 1.8 kg (4.5%) in the HP group after two weeks and of 6.5 ± 3.5 kg (6.6%) in the HC group and 6.8 ± 3.6 (7.0%) in the HP group after 8 weeks was observed. In the HP group, weight loss was 0.27 kg higher than in the HC group. Although difference between the two groups was statistically not significant (Table 4). Furthermore, the number of subjects who lost 0 - ≤ 5%, >5 - ≤ 10% and >10% of initial body weight

after eight weeks of intervention was analyzed. A total of 29.6% individuals in the HC group (n=38) lost between 5 and 10% of initial body weight. Whereas 27.4% (n=36) in the HP group lost >5-10% of their initial body weight (Figure 2). In Detail, 46 subjects (n=19 HC group, n=27 HP group) lost >5% of their initial body weight in the first two weeks.

n (HC group/HP group)		Baseline (78/76)	2 weeks (78/76)	8 weeks (78/76)	20 weeks (60/43)
Weight (kg)	HC	98.2 ± 12.9	94.2 ± 12.4**	91.7 ± 12.3**	90.2 ± 11.4**
	HP	97.6 ± 12.4	93.2 ± 11.9**	90.8 ± 12.1**	89.1 ± 11.0**
Relative weight (%)	HC	100 ± 0	96.1 ± 1.5**	93.4 ± 3.4**	92.6 ± 5.5**
	HP	100 ± 0	95.6 ± 1.8**	93.0 ± 3.5**	91.9 ± 3.4**
BMI (kg/m²)	HC	32.4 ± 1.8	31.1 ± 1.9**	30.3 ± 2.2**	30.1 ± 1.6**
	HP	32.6 ± 1.6	31.1 ± 1.8**	30.3 ± 2.0**	29.8 ± 2.4**
WC (cm)	HC	105.9 ± 9.8	101.1 ± 9.5**	97.4 ± 8.6**	98.9 ± 10.1**
	HP	105.8 ± 9.6	100.6 ± 8.5**	97.5 ± 7.3**	98.0 ± 8.3**
WC m (cm)	HC	113.6 ± 5.7	108.0 ± 6.7**	103.3 ± 6.7**	103.0 ± 9.1**
	HP	110.8 ± 5.7	105.5 ± 6.5**	102.5 ± 6.9**	99.6 ± 7.7**
WC w (cm)	HC	100.3 ± 8.2	96.1 ± 8.1**	93.0 ± 7.2**	95.7 ± 9.8**
	HP	102.2 ± 10.3	97.2 ± 8.1**	94.0 ± 7.4**	96.8 ± 8.7**
HipC (cm)	HC	115.4 ± 6.5	112.4 ± 5.8**	109.5 ± 6.3**	107.9 ± 7.7**
	HP	114.9 ± 6.4	111.8 ± 5.8**	109.2 ± 5.8**	108.8 ± 6.8**
WHR (WC/HC)	HC	0.92 ± 0.1	0.90 ± 0.01*	0.89 ± 0.09**	0.9 ± 0.09
	HP	0.92 ± 0.1	0.90 ± 0.08*	0.89 ± 0.08**	0.9 ± 0.07*

mean ± SD; *p<0.05; **<0.001; Wilcoxon-test compared to baseline; # p<0.05 Mann-Whitney-U-test compared two groups; BMI: Body Mass Index; HipC: Hip Circumference; HC: High Carbohydrate formula diet; HP: High Protein formula diet; WC: Waist Circumference; WHR: Waist-To-Hip-Ratio

Table 4: Changes of anthropometric data in study population after two and eight weeks of intervention and 12-week follow-up phase (n=154).

Figure 3 shows weight loss as percentage of initial body weight in subjects who lost ≤5% or >5% of initial body weight in the first two weeks, with regard to the diet intervention groups. Subjects who lost >5% of initial body weight in the first two weeks had a higher weight loss after eight weeks than participants who lost ≤5% of initial body weight (p<0.001). Both groups maintained significant weight loss (from baseline to week 20) with a mean net loss of 7.1 ± 5.1% (p<0.001) in the weight loss group ≤5% of initial body weight and 9.2 ± 5.6% (p<0.001) in the weight loss group >5% of initial body weight. There was a significantly difference between groups (p<0.05). During the follow up, HC group gained weight compared to week 8 of intervention, however this weight gain was not significant different to the HP group. After the 8-week intervention, there was also a significant reduction in the mean BMI from obesity stage I to preobesity in both groups (Table 4). At week 8, WC decreased by a mean of 8.6 cm (8.0%) in the HC group and 8.3 cm (7.8%) in the HP group (p<0.001). Correspondingly, waist-to-hip ratio (WHR) significantly decreased to a similar extent.

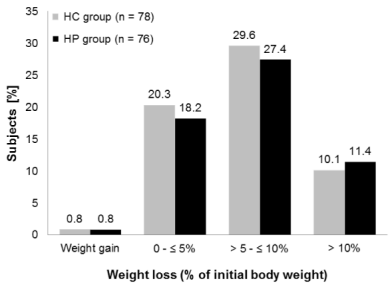

Figure 2: Percentage of subjects in the carbohydrate-rich and the protein-rich groups classified according to percentage weight loss of initial body weight after 8 weeks of the study. There were no statistical differences between the groups. HC group: High Carbohydrate; HP group: High Protein.

Adverse events and side effects

Incidences of all kind of adverse events (e.g. common cold) were comparatively similar in both treatment groups. At visit t_2, there were statistically significant differences between the HC and the HP group

in the proportion of subjects with flatulence and diarrhea. While flatulence occurred significantly more frequent in the HC group (n=13 vs. n=4; p<0.05, chi-square test), complaints of diarrhea (n=8) only occurred in the HC group (p<0.005), (multiple answers were possible). Also at week 8, diarrhea (n=8) only occurred in the HC group (p<0.05; chi-square test). Effects such as nausea, eructation or bloating were rarely mentioned.

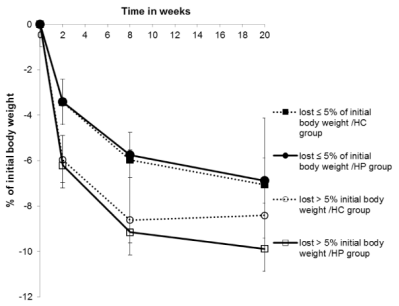

Figure 3: Subjects who lost more than 5% of initial body weight in the first two weeks (open symbols) showed also a higher weight reduction than subjects who lost at least 5% or less than 5% of initial body weight in the first two weeks (filled symbols) at week 8 and 20 (p<0.001). Weight loss as percentage of initial body weight is not significantly different in subjects in HC group (dotted lines) and HP group (solid lines). **p<0.001 compared to baseline; ap<0.05, aap < 0.001 Mann-Whitney-U-test compared weight loss groups which lost ≤ 5% or >5 % of initial body weight. HC group: high carbohydrate; HP group: high protein.

Discussion

Our results indicate that both weight loss strategies are effective treatment options for overweight and obese women and men. In the first two weeks, we chose three formula diets per day to take account of a total meal replacement diet plan on weight loss. In accordance to studies which used low calorie diets (800-1000 kcal/day) for weight loss [26,27], the results of this intervention can deliver weight loss rates of 2 kg per week. We further chose formula diets with partial meal replacement for week 5 to week 8 of intervention, because of being more flexible than total meal replacement plans [8]. In both groups, the average weight loss was maintained with additional losses within the last six weeks. Weight loss effects were more pronounced in total meal replacement plan than in partial meal replacement plan. This was expected. The difference is most likely due to the fact that restricted energy intake in the first two weeks. Our results are consistent with those reported by Hemmingsson et al. Overweight and obese subjects achieved significant more weight loss after being prescribed with a liquid-based formula diet (providing approximately 500 kcal/day) compared to a 1200-1500 kcal diet, consisting of two meal replacements and a reduced-calorie dinner meal [28].

After eight weeks of intervention, mean weight loss in both groups (6.5 ± 3.5 kg in HC group and 6.8 ± 3.6 kg in HP group) were similar to other studies done previously (5.9-7.4 kg) which lasted twelve weeks [10,12,29]. A modest weight loss up to 5% has been shown to reduce the risk of developing obesity associated diseases [30]. Weight loss of 5% and more (equivalent to 4.9 kg of mean initial body weight of the total study group) was exceeded by at least 1.6 kg in the HC group and by 1.9 kg in the HP group, reflecting a decreasing risk in both groups. Moreover, it has been shown that weight loss of around 5 kg, as achieved by 66.2% of subjects, is associated with a reduction in all-cause mortality [31].

In order to determine the energy and macronutrient intake, all participants were instructed to keep 3-day food records at baseline, week 4 and 7 during the trial, as well as week 19 of the follow-up. It is useful to consider that self-reported food diaries may not provide highly accurate information. But well-kept food records delivered data were used to assess macronutrient intake and also to compare the results with those from other dietary trials. In the present study, weight reduction was not significantly different in the HP group compared to the HC group. These results disagree with trials which had shown that increased protein as a percentage of total calories can enhance weight loss [16,32] and that HP diets lead to more weight loss than HC diets [33]. At week 2, the protein intake was about 0.5 g/kg body weight in the HC group and 1.1 g/kg body weight in the HP group. Protein intake increased to 0.7 g/kg body weight in the HC group and declined to 0.9 g/kg body weight in the HP group during the partial meal replacement plan. In two studies lasted three months, protein intake of 1.2 or 0.9 g protein/kg body weight was more effective on weight loss than 0.8 or 0.6 g protein/kg body weight [34,35]. Analysis of food records also showed significant reduction in percentage of fat intake in both groups from baseline. Recent research indicates that substitution of carbohydrates or proteins for fat is associated with weight loss [21]. Furthermore, diets high in protein with low glycemic index are associated with an increase satiating and decreased energy intake, which achieved weight loss [18,33,36]. However, in both groups, food records showed that the energy intake was decreased to the same extent throughout the intervention. Sacks et al. (2009) have demonstrated that the most important factor influencing weight loss over term is creating a state of negative energy balance [37]. Therefore, the mechanism responsible for the weight loss caused by HC formula diet and HP formula diet can be attributed to a reduced energy intake. Overall weight reduction was probably not caused by an increase in physical activity determined in the questionnaires. The levels of physical activity reported were similar in both groups.

In addition, this randomized trial in overweight and obese people had useful effects on abdominal fat reduction. The role of body fat distribution phenotype has been shown to be even more essential than body weight [38]. Visceral fat is attended by a higher cardio metabolic risk compared to high proportions of subcutaneous risk. Therefore, reduction in WC is regarded to be more important than weight loss exclusively [39]. At week 8, the significant decrease in WC by 9.3 ± 5.4 cm in males and 7.9 ± 7.0 cm in females indicates that the body fat distribution phenotype has changed. This could be of major clinical interest, because even a 3 cm reduction of WC results in a significant improvement of cardio metabolic risk factors [40]. A general cutoff of 102 cm in men and 88 cm in women has been shown for WC [41]. However, these values were not achieved in women at any time of the study. On the contrary, after the follow up men with higher protein intake obtained values below the general cutoff. There are two possible reasons for the observed gender differences. Firstly, males entered the study with higher body mass index and lost essentially more weight. Secondly, low calorie diets mean more restriction in energy intake for males than for females [42].

One argument against the use of formula diets is the rapid weight gain afterwards [43]. In the present study, subjects who lost more than

5% of body weight in the first two weeks, maintained greater weight reduction during the intervention and follow-up. This result is in accordance with Purcell and colleagues who reported that initial rate of weight loss did not affect the amount of weight regain [44]. Furthermore, Christensen et al. (2013) demonstrated that partial use of formula diets showed statistically significant better weight maintenance than the control group [45]. Studies looking at weight maintenance over 24 to 26 weeks after weight loss reported that a diet with high protein intake [46] and reduction in glycemic index [27] led to an improvement in maintenance of weight loss. In the present study, subjects with higher protein intake during the follow-up demonstrate no differences in weight maintenance compared to HC group.

Limitations

First, the remaining powder of the formula diets was weighted to control compliance. It had been shown that the measuring spoon supplied in both groups did not enter the predefined quantity of formula diet. Therefore, there was great variability. Second, although physical activity has been monitored during the study, the actual influence cannot be quantified. Third, this study may represent only a short-term effect over eight weeks. The short duration of intervention could have led to an underestimation of the full potential of HC and HP diet plan. With a view to lasting weight maintenance, long-term effects are required.

Conclusion

In conclusion, both formula diets were safe and had similar effects in weight and abdominal fat reduction. Based on these findings, individuals who have preferences to consume favorable proteins for weight reduction, a HC meal replacement diet offers an alternative for those, who choose not to increase protein intake.

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References

1. World Health Organisation 2015.
2. Astrup A (2008) Dietary management of obesity. J Parenter Enteral Nutr 32: 575-577.
3. Abete I, Astrup A, Martínez JA, Thorsdottir I, Zulet MA (2010) Obesity and the metabolic syndrome: role of different dietary macronutrient distribution patterns and specific nutritional components on weight loss and maintenance. Nutr Rev 68:214-231.
4. Keogh JB, Clifton PM (2005) The role of meal replacements in obesity treatment. Obes rev 6: 229-234.
5. Leeds AR (2014) Formula food-reducing diets: A new evidence-based addition to the weight management tool box. Nutr Bull 39: 238-246.
6. Davis LM, Coleman C, Kiel J, Rampolla J, Hutchisen T, et al. (2010) Efficacy of a meal replacement diet plan compared to a food-based diet plan after a period of weight loss and weight maintenance: a randomized controlled trial. Nutr J 9: 1-10.
7. Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods, OJ L 404
8. Heymsfield SB, van Mierlo CAJ, van der Knaap HCM, Heo M, Frier HI (2003) Weight management using a meal replacement strategy: Meta and pooling analysis from six studies. Int J Obesity 27: 537-549.
9. Vázquez C, Montagna C, Alcaraz F, Balsa JA, Zamarrón I, et al. (2009) Meal replacement with a low-calorie diet formula in weight loss maintenance after weight loss induction with diet alone. Eur J Clin Nutr 63: 1226-1232.
10. Flechtner-Mors M, Boehm BO, Wittmann R, Thoma U, Ditschuneit HH (2010) Enhanced weight loss with protein-enriched meal replacements in subjects with the metabolic syndrome. Diabetes Metab Res Rev 26: 393-405.
11. Cheskin LJ, Mitchell AM, Jhaveri AD, Mitola AH, Davis LM, et al. (2008) Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: A controlled clinical trial. Diabetes Educ 34: 118-127.
12. Metzner CE, Folberth-Vögele A, Bitterlich N, Lemperle M, Schäfer S, et al. (2011) Effect of a conventional energy-restricted modified diet with or without meal replacement on weight loss and cardiometabolic risk profile in overweight women. Nutr Metab 8: 1-9.
13. Flechtner-Mors M, Ditschuneit HH, Johnson TD, Suchard MA, Adler G (2000) Metabolic and weight loss effects of long term dietary intervention in obese patients: Four year results. Obes Res 8: 399-402.
14. Koohkan S, Schaffner D, Milliron BJ, Frey I, König D, et al. (2014) The impact of a weight reduction program with and without meal-replacement on health related quality of life in middle-aged obese females. BMC Womens Health 14: 1-7.
15. Claessens M, van Baak MA, Monsheimer S, Saris WHM (2009) The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight loss maintenance and metabolic risk factors. Int J Obesity 33: 296-304.
16. Noakes M, Keogh JB, Foster PR, Clifton PM (2005) Effect of an energy-restricted, high-protein, low-fat diet relative to a conventional high-carbohydrate, low-fat diet on weight loss, body composition, nutritional status, and markers of cardiovascular health in obese women. Am J Clin Nutr 81: 1298-1306.
17. Layman DK, Evans EM, Erickson D, Seyler J, Weber J, et al. (2009) A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. J Nutr 139: 514-521.
18. Weigle DS, Breen PA, Matthys CC, Callahan HS, Meeuws KE, et al. (2005) A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. Am J Clin Nutr 82: 41-48.
19. Bradley U, Spence M, Courtney CH, McKinley MC, Ennis CN, et al. (2009) Low-fat versus low-carbohydrate weight reduction diets. Diabetes 58: 2741-2748.
20. Hernandez TL, Sutherland JP, Wolfe P, Allian-Sauer M, Capell WH, et al. (2010) Lack of suppression of circulating free fatty acids and hypercholesterolemia during weight loss on a high-fat, low-carbohydrate diet. Am J Clin Nutr 91: 578-585.
21. Champagne CM, Broyles ST, Moran LD, Cash KC, Levy EJ, et al. (2011) Dietary intakes associated with successful weight loss and maintenance during the weight loss maintenance trial. J Am Diet Assoc 111: 1826-1835.
22. Wycherley TP, Brinkworth GD, Clifton PM, Noakes M (2012) Comparison of the effects of 52 weeks weight loss with either a high-protein or high-carbohydrate diet on body composition and cardiometabolic risk factors in overweight and obese males. Nutr Diabetes 2: 1-8.

23. Anton SD, Han H, York E, Martin CK, Ravussin E, et al. (2009) Effect of calorie restriction on subjective ratings of appetite. J Hum Nutr Diet 22: 141-147.
24. Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G (1999) Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. Am J Clin Nutr 69: 198-204.
25. Ashley JM, Herzog H, Clodfelter S, Bovee V, Schrage J, et al. (2007) Nutrient adequacy during weight loss interventions: a randomized study in women comparing the dietary intake in a meal replacement group with a traditional food group. Nutr J 6: 1-9.
26. Due A, Larsen TM, Mu H, Hermansen K, Stender S, et al. (2008) Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. Am J Clin Nutr 88: 1232-1241.
27. Larsen TM, Dalskov SM, van Baak M, Jebb SA, Papadaki A, et al. (2010) Diets with high or low protein content and glycemic index for weight-loss maintenance. New Engl J Med 363: 2102-2113.
28. Hemmingsson E, Johansson K, Eriksson J, Sundstrom J, Neovius M, et al. (2012) Weight loss and dropout during a commercial weight-loss program including a very-low-calorie diet, a low-calorie diet, or restricted normal food: observational cohort study. Am J Clin Nutr 96: 953-961.
29. König D, Deibert P, Frey I, Landmann U, Berg A (2008) Effect of meal replacement on metabolic risk factors in overweight and obese subjects. Ann Nutr Metab 52: 74-78.
30. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM (2003) Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension 42: 878-884.
31. Shea MK, Houston DK, Nicklas BJ, Messier SP, Davis CC, et al. (2010) The effect of randomization to weight loss on total mortality in older overweight and obese adults: The ADAPT study. J Gerontol A Biol Sci Med Sci 65A: 519-525.
32. Meckling KA, Sherfey R (2007) A randomized trial of a hypocaloric high-protein diet, with and without exercise, on weight loss, fitness, and markers of the Metabolic Syndrome in overweight and obese women. Appl Physiol Nutr Metab 32:743-752.
33. Skov AR, Toubro S, Ronn B, Holm L, Astrup A (1999) Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. Int J Obes 1999: 528-536.
34. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA (2003) A Randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab 88: 1617-1623.
35. Volek JS, Phinney SD, Forsythe CE, Quann EE, Wood RJ, et al. (2009) Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. Lipids 44:297-309.
36. Thomas D, Elliott EJ, Baur L (2007) Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database Syst Rev 3: 1-40.
37. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, et al. (2009) Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med 360: 859-873.
38. Després J, Lemieux I (2006) Abdominal obesity and metabolic syndrome. Nature 444:881-887.
39. Shen W, Punyanitya M, Chen J, Gallagher D, Albu JA, et al. (2006) Waist circumference correlates with metabolic syndrome indicators better than percentage fat. Obesity 14:7 27-736.
40. Balkau B, Picard P, Vol S, Fezeu L, Eschwege E (2007) Consequences of change in waist circumference on cardiometabolic risk factors over 9 years: Data from an epidemiological study on the insulin resistance syndrome (DESIR). Diabetes Care 30: 1901-1903.
41. Report of a WHO Expert Consultation (2008) Waist circumference and waist-hip ratio.
42. Tsai AG and Wadden TA (2006) The evolution of very-low-calorie diets: An update and meta-analysis. Obesity 14: 1283-1293.
43. Franz MJ, van Wormer JJ, Crain AL, Boucher JL, Histon T, et al. (2007) Weight-loss outcomes: A systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. J Am Diet Assoc 107: 1755-1767.
44. Purcell K, Sumithran P, Prendergast LA, Bouniu CJ, Delbridge E, et al. (2014) The effect of rate of weight loss on long-term weight management: a randomised controlled trial. Lancet Diabetes Endocrinol 2: 954-962.
45. Christensen P, Frederiksen R, Bliddal H, Riecke BF, Bartels EM, et al. (2013) Comparison of three weight maintenance programs on cardiovascular risk, bone and vitamins in sedentary older adults. Obesity 21: 1982-1990.
46. Lejeune MP, Kovacs, EM, Westerterp-Plantenga MS (2005) Additional protein intake limits weight regain after weight loss in humans. Br J Nutr 93: 281-289.