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Original article

Weight loss and body composition change among workers undergoing a meal replacement dietary program: feasibility and efficacy

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Summary. *Introduction.* Partial meal replacements supplementing low calorie diets may be convenient for working people in time-constrained occupational settings. However, we have limited data from non-obese, healthy subjects, and very few real-life clinical studies corroborating findings from clinical experiments. *Methods.* We evaluated weight loss, glycemic control and body composition change among volunteer workers undergoing a 4-week low calorie diet followed by a 4-week maintenance regimen both supplemented with meal replacements products. *Results.* Forty-two employees took part in the study and completed the 4-week intervention, whereas 36 completed the maintenance phase. Thirty-one patients (73.7%) experienced a weight loss greater than 3% of initial body mass. There was a reduction in serum glucose (Δ_{28d}= -6.9 mg/dL, p<0.01), insulin resistance (Δ_{28d}= -0.40, p<0.01), insulin (Δ_{28d}= -1.54 pmoll^{-1}, p<0.05), and fatty mass (Δ_{28d}= -2.2%, p<0.01) after adjustment for potential confounders. The reduction in lean body mass (Δ_{28d}=-0.3%, Δ_{60d}=-0.2%; p for trend =0.54) and basal metabolic rate was negligible (Δ_{28d}=-8.0, Δ_{60d}=-6.0; p for trend =0.44). *Conclusions.* We observed significant weight loss during a 2-month intervention period. The dietary strategy, irrespective of age, dietary regimen and sex was well accepted. We also observed an improvement in glycemic control, both among overweight and normal weight volunteers.

Key words: weight loss, dietary intervention, energy intake, meal replacement, workers, occupational, health promotion

Introduction

With the current worldwide epidemics of overweight and metabolic syndrome in adults, medically assisted dietary programs are becoming a key aspect of healthcare for an increasing share of the population (1). Guidelines based on recent evidence suggest that weight losses however small (5 to 10% of initial body weight) can improve obesity-related health complications (2). Moreover, achieving and maintaining a desirable weight, is a valued health outcome for patients. For such reasons there is an increasing interest in evaluating the efficacy, safety and feasibility of different types of weight controlling diets. Energy reduced diets are the cornerstone of modern weight control interventions. Despite very low calorie diets (i.e. <800

Kcal/day) be effectively and safely used when a fast weight reduction is medically necessary (4), they are not suitable for overweight or normal weight people who desire losing only a small amount of body weight.

Incorporating meal replacements (1–2 per day) into a low calorie diet (i.e. 800-1600 Kcal/day) has been shown to be effective and safe in treating overweight or obese patients (3). Such substitutes may be particularly convenient for working patients since they simplify meal preparation and are more suitable in occupational context where short breaks are allowed for lunch (5-8).

However, we have limited data from non-obese, healthy subjects and very few real-life clinical studies corroborating findings from RCTs and a recent meta-analysis.

In this longitudinal, single arm, intervention study we sought to evaluate the feasibility and the efficacy of a short-term, low calorie weight reduction diet supplemented with meal replacements products offered to employees as part of an Occupational Health Promotion program.

Methods

Design, study conduct and intervention

Study flowchart is represented in Figure 1. This is a single arm, open label, longitudinal intervention study, evaluating weight loss and body composition change among volunteers. They underwent a 4-week low calorie diet followed by a 4-week maintenance regimen; the whole 8-week period was supplemented with Pesoforma® meal replacements products. The meal replacements have been recognized as useful products in weight loss by EFSA (European Food Safety Authority) (9). Their composition in macro and micronutrient and calorie intake is established by Ministerial Decree D. n ° 519/98 of the Ministry of Health. Indications on the label and instructions for use are defined by European Directive 96/8 /CE on foods for low-calorie diets.

All patients underwent a medical examination before intervention onset. All subjects meeting the inclusion/exclusion criteria and willing to participate underwent a thorough dietary assessment. Three regimens (1100, 1300, 1500 Kcal) were devised based on patients' sex and Body Mass Index (BMI) (Tabs. 1-3). Men were prescribed the dietary regimen with the highest energy intake while women with BMI<25 were prescribed the lowest energy intake. The dietary regimens were structured to provide 1,2 -1,0 g protein/kg of body weight, 25-30% of daily energy intake from proteins, 40-45% from carbohydrates, and 27-30% from lipids. The suggested fiber intake was 22-26 g daily, whereas cholesterol dietary intake was < 200 mg/day. During the low calorie phase, workers received two substitutive meals. All subjects willing to continue with the dietary program after the low calorie phase, were advised on maintenance strategies. During such intervention stage, workers were advised to eat 1 substitutive meal (i.e. breakfast or lunch) and the dietary regimen was modified to allow an increased energy intake of 200 Kcal/day. All Pesoforma® meal replacements products have been offered free to participants by Nutrition et Santè Italia.

We evaluated change in anthropometric measures at 10, 28 and 60 days. We also repeated the Bioelectrical Impedance Analysis evaluation and laboratory tests at 28 days.

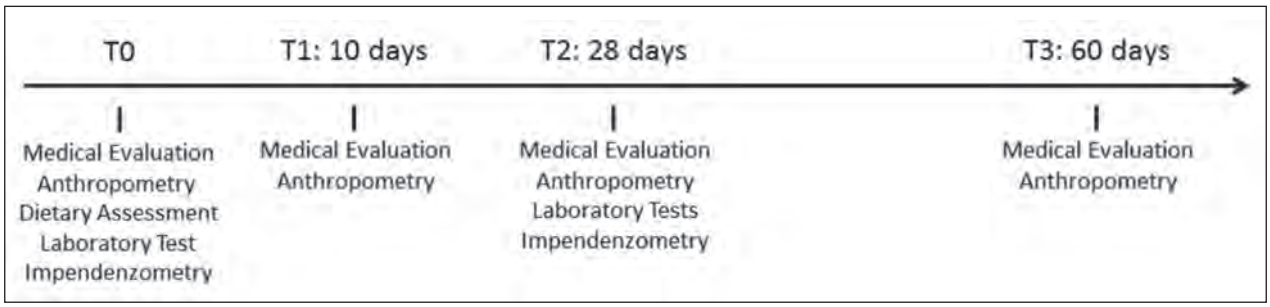

Figure 1. Study flowchart. Timing of clinical assessments in the course of the study.

Table 1. 1100 kcal meal replacement weekly diet protocol to be repeated four weeks in women with BMI < 25 kg/m².

Diet Protocol	1100 Kcal	(the weights are considered at raw and without waste)					
	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
BREAKFAST	1 bottle Pesoforma chocolate,1 cup of: coffee or tea or barley coffee without sugar	1 cup of Pesoforma chocolate, 1 cup of: coffee or 1 barley tea or coffee without sugar	Soy milk (200 ml), 1 snack Pesoforma coffee and 1 cup of: tea or coffee or barley coffee without sugar	1 bottle Pesoforma chocolate,1 cup of: coffee or tea or barley coffee without sugar	1 cup caramel Pesoforma and 1 cup of: coffee or tea or barley coffee without sugar	3 whole wheat rusks, low-fat milk 200 ml, 1 orange juice, jam without sugar 15 g, 1 coffee or 1 tea or 1 barley coffee without sugar	3 whole wheat biscuits, 1 cup of tea or barley coffee or coffee without sugar, 1 low-fat yogurt
BREAK	1 apple	1 pear	1 pear	1 pear	Kiwi (150 g); 1 square of dark chocolate (5 g)	1 snack Pesoforma flavour almond / apricot	1 pear 5 hazelnuts
LUNCH	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	3 cannelloni with ricotta and spinach and raw vegetables with vinaigrette, lemon sorbet
BREAK	Wholemeal bread (30 g) and lean cured meat (30g)	Whole wheat bread (30g) and ham (30 g)	1 snack pizza Pesoforma	Whole wheat bread (30 g) and cottage cheese or ricotta (30 g)	1 pocket of Pesoforma chips (25 g)	Wholemeal bread (30 g) and lean cured meat (30g)	1 orange juice
DINNER	Veal chops(about 120 g) with lemon juice, zucchini (about 200 g) and boiled brown rice (about 50 g), extra virgin olive oil (10 g)	Grilled tuna (about 120 g) cherry tomatoes with celery salad, and boiled pearl spelt (about 50 g), extra virgin olive oil (10 g)	Baked code (about 150 g) with oven peppers (200 g) and boiled brown rice (about 50 g), extra virgin olive oil (10 g)	Turkey breast (about 120 g) with mushrooms and boiled pearl barley (about 50 g), extra virgin olive oil (10 g)	Trout fillets (about 130 g) curried tomatoes and asparagus and wholemeal bread (50 g), extra virgin olive oil (10 g)	Shirataki with vegetables; 2 eggs with spinach and grilled vegetables (zucchini, eggplant and peppers), 50 g wholemeal bread and 10 g extra virgin olive oil	Grilled chicken breast (about 120 g), green beans (about 150 g) and boiled potatoes (100 g) with 10 g of extra virgin olive oil

Vegetarians can substitute milk vaccine with vegetable drinks at breakfast. For breaks they can add to the bread some vegetable origin cheeses or tofu. For dinner replace meat or fish with tofu or tempeh or seitan or mopur.

Table 2. 1300 kcal meal replacement weekly diet protocol to be repeated four weeks in women with BMI > 25 kg/m².

Diet Protocol	1300 Kcal	(the weights are considered at raw and without waste)					
	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
BREAKFAST	1 bottle Pesoforma chocolate; 1 cup of: coffee or tea or barley coffee without sugar	1 cup of Pesoforma chocolate; 1 cup of: coffee or tea or barley coffee without sugar	Soy milk (200 ml), 2 snacks Pesoforma coffee; 1 cup of tea or coffee or barley coffee without sugar	1 bottle Pesoforma chocolate; 1 cup of: coffee or tea or barley coffee without sugar	1 cup caramel Pesoforma, 3 wholemeal biscuits and 1 cup of: coffee or tea or coffee without sugar	3 whole wheat rusks, low-fat milk 200 ml, 1 orange juice, jam without sugar 20 g, 1 cup of coffee or tea or barley coffee without sugar	4 Whole wheat biscuits, 1 cup of: coffee or barley coffee or tea without sugar, 1 low-fat yogurt
BREAK	1 apple and 4-5 almonds	1 pear and 2 nuts	1 pear and 2-3 walnuts	1 pear, 3 nuts	Kiwi (150 g); 2 squares dark chocolate (10 g), 1 low fat yogurt	1 snack Pesoforma flavour almond / apricot	1 pear 5 hazelnuts
LUNCH	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	3 cannelloni with ricotta and spinach and raw vegetables with vinaigrette, lemon sorbet
BREAK	Whole wheat bread (30 g) and lean cured meat (30 g)	Whole wheat bread (40g) and ham (30 g)	1 snack pizza Pesoforma	Whole wheat bread (30 g) and cottage cheese or ricotta (30 g)	1 pocket of Pesoforma chips (25 g)	Wholemeal bread (30 g) and lean cured meat (30g)	1 orange juice
DINNER	Veal chops (about 140 g) with lemon juice, zucchini (about 200 g) and boiled brown rice (about 50 g), extra virgin olive oil (10 g)	Grilled tuna (about 140 g) cherry tomatoes with celery salad, and boiled pearl spelt (about 50 g),extra virgin olive oil (10 g)	Baked code (about 160 g) oven peppers (200 g); boiled brown rice (about 50 g), extra virgin olive oil (10 g)	Turkey breast (about 140 g) with mushrooms and boiled pearl barley (about 50 g), extra virgin olive oil (10 g)	Trout fillets (about 180 g) curried tomatoes and asparagus and wholemeal bread (60 g), extra virgin olive oil (10 g)	Shirataki with vegetables and 2 eggs with spinach and grilled vegetables (zucchini, eggplants and peppers), 50 g wholemeal bread and 10 g extra virgin olive oil	Grilled chicken breast (about 150 g), green beans (about 150 g) and boiled potatoes (100 g) with 10 g of extra virgin olive oil

Vegetarians can substitute milk vaccine with vegetable drinks at breakfast. For breaks they can add to the bread some vegetable origin cheeses or tofu. For dinner replace meat or fish with tofu or tempeh or seitan or mopur.

Subjects and setting

We enrolled 42 volunteers among employees and medical students of a large hospital in Milan, Italy. Volunteers have been recruited with flyers advertising the study posted on dedicated boards in the Hospital building. All prospective participants have been screened for eligibility at the Obesity and Work Center of the same hospital. All healthy subjects willing to lose weight and with BMI greater than 23 Kg/m²,

Table 3. 1500 kcal meal replacement weekly diet protocol to be repeated four weeks in men

Diet Protocol **1500 Kcal** (the weights are considered at raw and without waste)

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
BREAKFAST	1 bottle Pesoforma chocolate, 3 wholemeal biscuits, 1 coffee or tea or barley coffee without sugar	1 cup of Pesoforma chocolate, 3 wholemeal biscuits, 1 coffee or 1 barley tea or coffee without sugar	Soy milk (200 ml), 2 snacks Pesoforma coffee; 1 cup of: tea or coffee or barley coffee without sugar	1 bottle Pesoforma chocolate, 3 wholemeal biscuits, 1 coffee or tea or barley coffee without sugar	1 cup caramel Pesoforma 1 cup of: coffee or barley tea or coffee without sugar	4 wholemeal rusks, low-fat milk 250 ml, 1 orange juice, jam without sugar 15 g, 1 cup of: coffee or tea or barley coffee without sugar	5 Wholemeal biscuits, 1 cup of: tea or barley coffee or tea without sugar, 1 low-fat yogurt
BREAK	1 apple and 4-5 almonds, 1 low-fat yogurt	1 pear and 2 nuts, 1 low-fat yogurt	1 pear and 2-3 walnuts, 20 g parmesan cheese	1 pear, 3 nuts, 1 low-fat yogurt	Kiwi (150 g); 2 squares dark chocolate (10 g)	1 snack Pesoforma flavour almond / apricot	1 pear 5 hazelnuts
LUNCH	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	Pesoforma meal replacement: (2 bars) choosing among bars or biscuits or salty meal; 1 portion of fruit (about 150 g)	4 cannelloni with ricotta and spinach and raw vegetables with vinaigrette. lemon sorbet
BREAK	Whole wheat bread (30 g) and lean cured meat (30 g)	Whole wheat bread (30g) and ham (30 g)	1 snack pizza Pesoforma	Whole wheat bread (30 g) and cottage cheese or ricotta (30 g)	1 pocket of Pesoforma chips (25 g)	Wholemeal bread (30 g) and lean cured meat (30g)	1 orange juice
DINNER	Veal chops(about 150 g) with lemon juice, zucchini (about 200 g) and boiled brown rice (about 50 g), extra virgin olive oil (10 g)	Grilled tuna with (about 150 g) cherry tomatoes with celery salad, and tomatoes and boiled pearl spelt (about 50 g),extra virgin olive oil (10 g)	Baked code (about 180 g) with oven peppers (200 g) and boiled brown rice (about 70 g), extra virgin olive oil (10 g)	Turkey breast (about 150 g) with mushrooms and boiled pearl barley (about 60 g), extra virgin olive oil (10 g)	Trout fillets (about 180 g) curried tomatoes and asparagus and wholemeal bread 60 g, extra virgin olive oil (10 g)	Shirataki with 100 g salmon and 1 egg with spinach and grilled vegetables (zucchini, eggplants and peppers), 50 g of wholemeal bread and 10 g extra virgin olive oil	Grilled chicken breast (about 150 g), green beans (about 150 g) and boiled potatoes (100 g) with 10 g of extra virgin olive oil

Vegetarians can substitute milk vaccine with vegetable drinks at breakfast. For breaks they can add to the bread some vegetable origin cheeses or tofu. For dinner replace meat or fish with tofu or tempeh or seitan or mopur.

have been invited to participate and sign an informed consent. Patients with chronic conditions or those on pharmacological treatment for chronic conditions have been excluded from the study. Patients reporting symptoms suggestive of any acute disease potentially interacting with the dietary program such as infectious or inflammatory disease or injuries, have been excluded as well. The study has been communicated to ethical committee of the hospital and by internal stakeholders (i.e. workers' Unions, hospital management, occupational health service).

Measures

A trained dietician evaluated anthropometric measures including height, weight, waist, hip and thigh circumferences and assessed body composition with an impedenzometer. Bioelectrical Impedance Analysis have been conducted with the subject in upright position with the arms comfortably abducted from the body and the legs comfortably separated. We recorded body fatty mass, lean mass, muscular mass and we calculated the resting metabolic rate based on manufacturer equations (InBody 230®, Wunder). Laboratory tests including blood count, serum uric acid, fasting glucose, triglycerides, cholesterol, insulin were also conducted on blood samples obtained during the screening visit. We also calculated insulin resistance with the HOMA score (10). Insulin resistance was defined by HOMA score greater than 2.8 (11). Renal function (eGFR) was estimated adopting the 4 variable MDRD equation for patients with BMI<30 (12) and the Cockcroft-Gault equation corrected for adjusted body weight for obese patients (13, 14). Based on eGFR we classified CKD stage according to KIDOQI categories (15). Finally, patients answered a very brief satisfaction questionnaire comprising 3 items rated over a 5 point Likert scale: 1. Do you think that meal substitute products were practical and easy to use? 2. Do you think that meal substitute products tasted good? 3. Everything considered, how would you rate your satisfaction for the program?

Statistical analysis

We calculated mean and standard deviation or relative and absolute frequencies for continuous or discrete variables respectively. To account for the longitudinal design of the study, the change of anthropometric measures, laboratory test results, insulin-resistance score, and basal metabolic rate along the follow up have been assessed with generalized estimating equations. Inter-

correlation of observations within patients along time have been accounted for with robust standard error estimates. Contrary to more common statistical techniques adopted for the analysis of longitudinal designs such as ordinary least square regression, paired t-test, ANCOVA or repeated measure ANOVA, generalized estimating equations yield unbiased estimates of patients trajectory, making full use of data available and explicitly accounting for the inter-correlation of repeated observations within subjects (16). We adjusted all models for age, gender, basal metabolic rate, basal BMI, calorie intake. We also inspected whether age, sex, baseline resting metabolic rate, baseline BMI, calorie intake were associated with different trajectories of study outcomes over time. Thus, we estimated the interactions of follow up time (T0, T1, T2, T3) and each of these variables in the fully adjusted model. Statistically significant interactions suggest that the rate of change in the outcome variable would be different across levels of the examined variable (e.g. men and women would have had different responses to the dietary program). When an interaction is not significant, there is no evidence that the rate of change is different across levels of the examined variable (e.g. men and women would have had similar responses to the dietary program). For this reason, we stratified the analysis only when an interaction between an explanatory variable and time was observed. We considered a $p<0.05$ statistically significant for main effects and a $p<0.10$ statistically significant for interactions. All analysis have been conducted with SAS 9.4 ™.

Results

Study sample

Forty-two patients took part in the workplace dietary intervention (Tab. 4). Among them, 32 were women (76%). Thirty-one % of patients were overweight, 13 were normal weight (31%) and 16 were obese (38%). No subject was severely obese (BMI>40). Men had larger waists (97.9 vs 85.4 cm, $p<0.01$) resulting in greater waist-to-hip ratios (0.92 vs .80, $p<0.01$). Such difference was robust to adjustment for age and basal BMI ($p<0.01$). Among men, there was a trend indicating that waist-to-hip ratio was moderately correlated with glycaemia (r=0.32), and low-density lipoprotein cholesterol (r= 0.47) but not with HOMA score (r=-0.02). On the contrary such associations were very weak among women (r range=0.03-0.13). Insulin resistance was observed in 8 subjects (22.9%), prediabetes, according to fasting serum glucose levels, was observed in 2 subjects, 8 patients had hyperuricemia and none had hyperlipemia. All participants completed the low calorie diet intervention and 85% completed the following maintenance phase; 75% considered meal substitutes easy to use and convenient; 88% reported that meal substitutes had a moderate/good/excellent palatability and 81% were satisfied or very satisfied by dietary program.

Table 4. Sample characteristics.

Characteristics	**N (%) or mean (STD)**
Age	42.9 (13.3)
Women	32 (76.2)
Regimen	
1100 Kcal	11 (26.8)
1300 Kcal	21 (51.2)
1500 Kcal	10 (21.0)
BMI (Kg/m^2)	28.5 (4.6)
Weight (Kg)	78 (15.3)
Waist (cm)	89.3 (12.3)
Hip (cm)	107.9 (8.8)
Tighs (cm)	61.1 (5.5)
Waist-To-Hip Ratio	0.8 (0.1)
Basal Metabolic Rate (Kcal/day)	1455.7 (210.0)
Fatty Mass (%)	27.7 (9.5)
Muscolar Mass (%)	27.8 (5.9)
Lean body mass (%)	50.3 (9.7)
Total H_2O (%)	36.8 (7.1)
eGFR ($mL/min/1.73m^2$)	96,1 (18,5)
Glucose (mg/dL)	81,4 (10,4)
Insulin (μIU/ml)	9,1 (4,1)
HOMA_IR	1,9 (0,9)
Triglicerydes (mg/dL)	96,5 (44,9)
Cholesterol	
LDL (mg/dL)	114,6 (23,2)
HDL (mg/dL)	54,1 (15)
Uric Acid (mg/dL)	4,8 (1,3)
Hemoglobine (g/dL)	13.3 (0.21)

Body Mass Trajectory

During the low calorie diet phase, one patient did not lose weight, 4 were not willing to continue the study in the maintenance phase, 1 did not appear at the follow-up visit and 36 lost weight. Among the last group, 8 had a weight loss greater than 5% of initial body mass, while 23 (64%) lost more than 3% of initial body mass. There was a moderate correlation between weight loss and initial body weight (r=0.42, p<0.01) and a weak, non-significant correlation between percent weight loss and initial body weight (r=0.16, p=0.35). During the maintenance phase, most subject experienced a small yet significant reduction in body weight. The fully adjusted trajectory of weight loss along the follow up is represented in figure 2. There was no statistically significant difference in weight loss rate across alternative dietary regimens (i.e. calorie intake), sex, basal BMI and age groups, suggesting that groups defined by these variables experienced similar weight losses during the follow up. However, we observed that patients with higher basal metabolic rate at T0 had slightly greater weight loss during the follow up compared to patients with low basal metabolic rate (p of interaction<0.06) (figure 2).

Figure 2. Adjusted body weight trajectory along the follow up. Adjusted for age, sex, basal BMI, calorie intake, and basal metabolic rate. Adjusted patients weight at each time point are estimated with generalized estimating equation. Robust standard errors have been used to account for the longitudinal design of the study. The cross-interaction between basal metabolic rate and follow-up time was marginally significant (p=0.06) indicating that patients with high metabolic rate at T0 had a slightly greater weight loss at the end of the study compared patients with low basal metabolic rate.

Anthropometric measures

The average reduction at 28 days in waist, hip and thigh circumferences was 4.3%, 2.7% and 3.3% of initial measures, respectively. The majority of patients

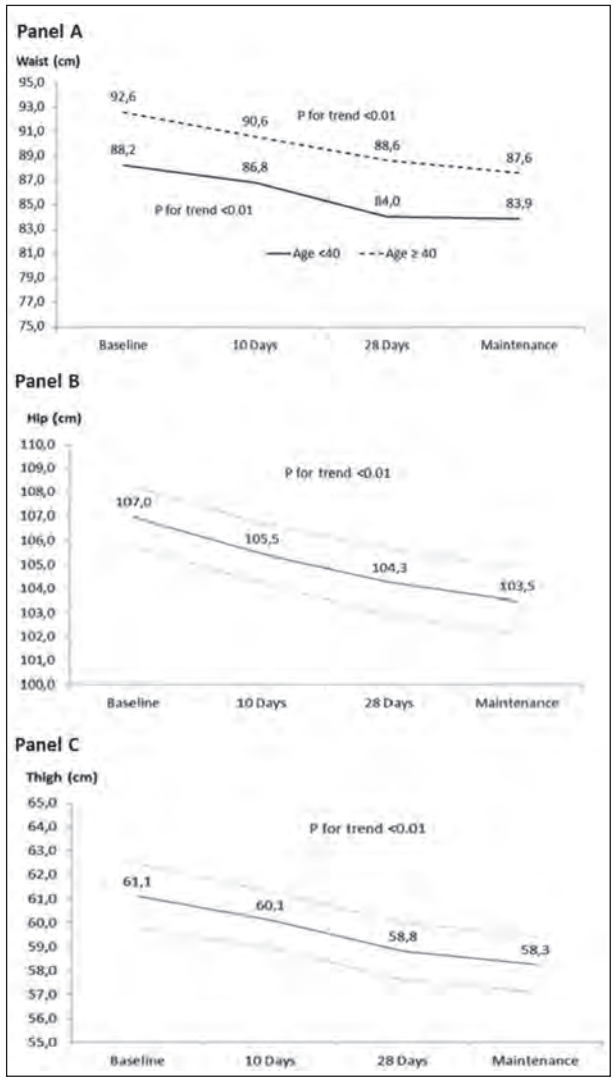

Figure 3. Trajectory of Waist, Hip and Thigh circumference reduction during the study and the maintenance period. Adjusted for age, sex, basal BMI, calorie intake, and basal metabolic rate. Adjusted patients circumferences (cm) at each time point are estimated with generalized estimating equation. Robust standard errors have been used to account for the longitudinal design of the study. The cross-interaction between age and follow-up time was marginally significant (p=0.06) in the model of waist circumference change along time, indicating that young patients had a slightly greater reduction in waist circumference loss at the end of the study compared to older patients.

had at least some reduction in body size (83.3%, 88.1% and 88.1% for waist, hip and thigh, respectively); however only 35.7%, 14.3% and 21.4% had circumference reduction greater than 5% of initial measures. Such decrements were robust to adjustment for potentially important confounders and persisted after the maintenance phase of the study (figure 3). We observed a trend indicating greater reductions in waist circumference among younger patients compared to older patients (p for interaction=0.06). No further statistically significant difference in body circumferences reduction rate was observed across alternative dietary regimens (i.e. calorie intake), sex, and basal BMI.

Laboratory test

We detected a statistically significant reduction in serum glucose (Δ_{28d}=6.9 mg/dL, p<0.01) at 28 days after adjustment for basal metabolic rate, basal BMI, age, sex, dietary regimen and variations in lean body mass, H_2O content, fatty mass and weight. Such reduction was coupled with a reduction in insulin resistance score (Δ_{28d}=0.40, p<0.01) and insulin levels (Δ_{28d}=1.54 pmoll^{-1}, p<0.05). Conversely no variation in cholesterol, triglycerides, and uric acid levels was observed at 28 days.

Bioelectric Impedance Analysis

The analysis of body mass composition revealed that reduction in fatty mass was the main driver of weight loss among program completers. After adjustment for age, sex, basal BMI, dietary regimen, basal metabolic rate, we observed a statistically significant reduction in the share of fatty mass at 28 days (Δ_{28d}=-2.2%, p<0.01). Such reduction persisted after the maintenance phase (Δ_{60d}=-2.9%, p<0.01). On the contrary we observed no reduction in lean body mass (Δ_{28d}=-0.3%, Δ_{60d}=-0.2%; p for trend =0.54) and basal metabolic rate (Δ_{28d}=-8.0, Δ_{60d}=-6.0; p for trend =0.44) during the study period. The reduction in fatty mass fully explained the weight loss trajectory, after adjustment for basal metabolic rate, basal BMI, age, sex, dietary regimen and variations in lean body mass, H_2O content, uric acid, serum glucose, cholesterol, triglycerides over time (Fatty mass, β= 1.05, p<0.01).

Discussion

In this single arm, prospective study, we have found a moderate, clinically important reduction in body weight during a 2-month intervention based on partial meal replacement dietary program. Previous meta-analyses demonstrated that partial meal substitution strategies are effective in inducing weight loss in adult overweight (BMI>25) patients (3). Our study demonstrated that such positive effect also extends to normal weight subjects and that the reduction achieved is similar in all initial body weights. The effect size observed in our study was comparable to that reported in previous randomized controlled trials, thus corroborating the validity of our results (3).

Of note weight loss trajectory was not different in men and women after adjustment for basal metabolic rate at baseline, suggesting that the dietary program was equally acceptable for both sex groups. Such hypothesis is confirmed by subjects' self-report of adherence and satisfaction and by the very low dropout rate observed in this study in both sexes. Given that men are usually less adherent to any behavioral change intervention (17, 18), the partial low calorie meal substitution dietary program devised for this study seems to be a promising approach for this group of workers. Of note, only 3 men had a basal metabolic rate much greater (i.e. BMR>1800 Kcal) than the calorie intake provided by the dietary program, a condition possibly enhancing adherence. Additionally, despite patients were required only minimal reductions in daily energy intake, the weight loss was substantial even in our short follow-up period, a condition which may boost adherence as subjects had the chance to observe quickly and clinically important achievements. Previous RCTs on dietary interventions have long follow up, since long-term benefits can be achieved only through persistent weight control and educated dietary behavior (19). However closer monitoring and shorter treatment horizons might be less discouraging for healthy individuals looking for moderate weight loss. It should also be mentioned that behavioral interventions delivered in the workplace usually achieves better participation (20). Several group factors facilitate participation and compliance including peer support, convenient and time-saving dispensing of products, timely access to health-care providers and program managers, financial

incentives (including coverage of products costs) (20). Whether such encouraging results could be replicated in non-occupational settings is a matter of further research.

However weak, there was a trend indicating that basal metabolic rate was a moderator of weight loss trajectory during the follow up. Given the absence of a reference group receiving no behavioral intervention, we cannot discount the possibility that natural weight loss trend have occurred. However, even in the low basal metabolic rate tertile, the weight loss trend was substantial and hardly attributable to fluctuations in body weight. Additionally, contrary to intensive low calorie weight loss programs which may cause a reduction in basal metabolic rate in response to excessive reduction in calorie intake, subjects enrolled in our study maintained stable energy consumption rates during the entire follow up. Altogether, our findings suggest that patients with low basal metabolic rate might need (and tolerate) a greater calorie restriction to achieve the same weight loss results of their more "consuming" counterparts.

Such excellent results concerning subjects' metabolic rate are confirmed by evaluating of body composition change during the study. An important finding of our study was that the weight loss observed was entirely driven by loss of fatty mass whereas no loss in lean/muscular mass occurred, a circumstance which explains the observed stability of basal metabolic rate. Such changes were coupled with substantial reductions in waist, hip, and thigh circumferences and by the observed reduction in insulin resistance score, serum insulin and serum glucose concentrations.

Our single-arm design cannot prove causality, but the effectiveness of structured, dietary programs incorporating meal replacements (1–2 per day) into a low calorie diet has been nonetheless proven (3). The usefulness of such interventions rests on their acceptability and suitability in real life settings, where every day activities might interfere with adherence and persistence behaviors. Overall, our results suggest that the partial low calorie meal substitution dietary program devised for our study was suitable and well-accepted among participants in occupational health promotion programs with little interference on working activity; they might even enhance glycaemic control parallel to weight loss achievements. Our results are particularly important because few studies have evaluated such endpoint for meal substitution strategies.

In conclusion, we have found that volunteers undertaking this workplace meal substitution program achieved significant weight loss during a 2-month intervention period and that the dietary strategy was well-accepted by the majority of subjects, irrespective of age, dietary regimen and sex. Such achievements were coupled with reduction in waist, hip, thigh circumferences and a sizeable improvement in glycemic control, both for overweight and normal weight patients. Such encouraging results should be confirmed in randomized controlled trial. Finally, further studies should evaluate whether this meal substitution strategy is equally effective in non-occupational clinical settings, where peer-empowering factors are not in place.

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