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SENPE

Estudio del mundo real de 24 semanas para evaluar el efecto de un programa de sustitución parcial de comidas sobre el síndrome metabólico y sus componentes en pacientes adultos con obesidad

Real-world study of 24 weeks to assess the effect of a partial meal replacement program on metabolic syndrome and its components in adult patients with obesity

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ABSTRACT

Background: meal replacement (MR) diets consist of replacing one or more meals. The objective was to evaluate the effect of a MR diet on weight reduction and metabolic syndrome (MS).

Methods: a real-world study was designed with a MR diet. The first phase consisted of the replacement of one meal (12 weeks); and the second phase the reintroduction of foods following a low-calorie diet (-300 to -500 calories per day) (12 weeks). Anthropometric and biochemical measurements were performed at initiation of the study; 12 and 24 weeks.

Results: the mean age was 45.6 ± 3.5 years (n = 364). There were 100 males (27.5 %) and 264 females (72.5 %) enrolled. We observed significant improvements at 12 weeks and 24 weeks in body weight, BMI, fat mass, waist circumference, serum triglycerides, LDL cholesterol, glucose, insulin, HOMA-IR, and frequencies of (MS, central obesity, hypertriglyceridemia, hypertension, and hyperglycaemia). The odds ratio of MS after phase 2 (24 weeks) was 0.66 (95 % CI = 0.49-0.90; p = 0.03). The number needed to treat was 10.17 patients for the resolution of one MS (95 % CI 6.15-41.2; p = 0.02).

Conclusions: in patients with obesity, those MR diet decreased in weight and fat mass with a secondary improvement in metabolic parameters.

Keywords: Obesity. Meal-replacement diet. Metabolic syndrome. Real world study.

RESUMEN

Antecedentes: las dietas de reemplazo de comidas (MR) consisten en reemplazar una o más comidas. El objetivo fue evaluar el efecto de una dieta MR en la reducción de peso y el síndrome metabólico (SM).

Métodos: se diseñó un estudio en el mundo real con una dieta MR. La primera fase consistió en el reemplazo de una comida (12 semanas); y la segunda fase en la reintroducción de alimentos luego de una dieta baja en calorías (-300 a -500 calorías por día) (12 semanas). Se realizaron mediciones antropométricas y bioquímicas al inicio del estudio; 12 y 24 semanas.

Resultados: la edad media fue de 45,6 ± 3,5 años ($n = 364$). Se inscribieron 100 hombres (27,5 %) y 264 mujeres (72,5 %). Observamos mejoras significativas a las 12 y 24 semanas en peso corporal, IMC, masa grasa, circunferencia de cintura, triglicéridos séricos, colesterol LDL, glucosa, insulina, HOMA-IR y frecuencias de (SM, obesidad central, hipertrigliceridemia, hipertensión e hiperglucemia). La razón de probabilidades de SM después de la fase 2 (24 semanas) fue de 0,66 (IC del 95 % = 0,49-0,90; $p = 0,03$). El número necesario a tratar fue de 10,17 pacientes para la resolución de un SM (IC del 95 % 6,15-41,2; $p = 0,02$).

Conclusiones: en pacientes con obesidad, aquellos con dieta MR disminuyeron en peso y masa grasa con una mejora secundaria en los parámetros metabólicos.

Palabras clave: Obesidad. Dieta sustitutiva de comidas. Síndrome metabólico. Estudio del mundo real.

INTRODUCTION

Obesity is a chronic condition, and it is the most prevalent metabolic disease in the developed world. Obesity increases the risk of several diseases including type 2 diabetes (DM2), some types of cancer, cardiovascular disease, psychological disorders, and metabolic syndrome (MS) (1). MS is a constellation of risk entities related to being overweight or obese. This includes glucose intolerance or diabetes *mellitus;* abdominal obesity; hyperlipidaemia; and high blood pressure (2). MS is a multifactorial, polygenic disorder which results from the interaction of numerous genes with environmental factors, and in which adipose tissue plays an important role (3). MS is also related to the risk of cardiovascular events and development of DM2 (4). A weight reduction of 5 % improves metabolic syndrome features such as hypertension, dyslipidaemia, and DM2, thereby reducing cardiovascular risk (5).

The main treatment of obesity involves the two fundamental pillars of diet and physical exercise. Losing and maintaining body weight reduction are the goals of any obesity treatment, although it is necessary to ensure that the interventions avoid the loss of muscle (6). Full and partial meal replacements (MR) have been proposed as effective treatments to assist patients to lose weight and gain metabolic advantages while maintaining protein intake (7,8). This strategy has been demonstrated to be cost-effective (9). However, there are no data examining the effectiveness of MR on MS as an overall entity. There is a need to evaluate real-world weight management programs incorporating MR and later restoring a diet with conventional low-calorie foods.

MR diets consist of replacing one or several meals with an artificial supplement. They are based on the artificial control of caloric and

nutrient intake while maintaining protein intake. The increase of involuntary intake made with normal foods in conventional hypocaloric diets is avoided with this replacement strategy. In a meta-analysis comparing conventional diets with MR diets substituting one or two meals, it was observed that at 12 weeks the weight loss was greater in the MR diet group than in the usual diet group. Of patients taking the replacement diet, 72 % achieved > 5 % weight loss, compared to 34 % of those taking conventional diets (10). However, another meta-analysis comparing different types of diets reported a weight loss similar to that of other diet types that included intensification of follow-up (11). There are other recent randomised clinical trials that corroborate the data referred to in both previous meta-analysis (12), but there are also studies that have not found a difference compared to conventional diets (13).

Given the difficulty of carrying out this type of MR diet and the lack of specific data on the effect of this intervention on MS, it is necessary to evaluate the effect of this type of diets on MS and its components. Furthermore, most of the above-mentioned studies use substitute two meals rather than one (8-11). This strategy is more difficult to implement over time and replacing only one meal may be a more successful strategy in the real-world setting.

The objective of this study was to evaluate the effect of a MR diet on weight reduction, metabolic parameters, and MS in patients with obesity. The diet involves substitution of one meal per day for 24 weeks with an initial intervention phase and a second phase of a conventional hypocaloric diet.

METHODS

A real-world study was conducted at a Public Hospital in Spain from January 2019 to December 2022. The patients were sent to the Nutrition Unit for weight control. The dietary intervention was divided into two phases as follows: phase 1 involved the replacement of one meal per day for 12 weeks; and phase 2 the reintroduction of foods,

and following a low-calorie diet with a moderate limitation of caloric intake over basal needs (-300 to -500 calories per day) for a further 12 weeks. We prescribed these subjects an MR diet with one daily normocaloric-hyperproteic supplement.

We recruited 364 subjects with obesity using a consecutive method of sampling in our Health Area. The inclusion criteria for the study protocol were body mass index (BMI) ≥ 30 kg/m^2 and age between 20 and 70 years. Patients with un-controlled thyroid disease, previous cardiovascular events (heart attack or stroke), hepatic dysfunction, active alcoholism, malignant tumour, active medications known to influence lipid or glucose levels, severe psychiatric pathology, severe or terminal renal impairment (Stage IV or higher [Creatinine clearance < 30 ml/min]), refusal to participate in the study, and/or non-compliance with informed consent were excluded. All participants provided written informed consent to the protocol approved by the local ethical review of the Hospital Clínico Universitario de Valladolid (HCUVA) Ethics Committee, approval number 14-151. This study was registered in the clinical trial registry of the HCUVA and Universidad de Valladolid with the code FUNGE 061/140242. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Program description

After the recruitment of patients with obesity in the study, they received nutritional instructions for a hypocaloric MR diet. This MR diet was distributed into six meals: breakfast, morning snack, lunch, afternoon snack, dinner, and after dinner snack. Either lunch or dinner was substituted during the 12 weeks of phase 1 by one normocaloric-hyperproteic nutritional supplement (VEGESTART Complete®) (Vegenat Healthcare SL, Badajoz, Spain), whose composition is reported in table I. The remaining meals consisted of natural foods.

The composition of the nutritional supplements used are regulated by the European Commission Directive 98/6/CD, which is included in Spanish Legal System by the “Real Law 1430/1997”. Following this MR phase (phase 1), the lunch or dinner supplement was replaced with natural foods for 2 weeks, maintaining the supplement every other day. From then onwards the patient continued a diet with moderate calorie restriction, with a deficit of 300 calories/day in females and 500 calories/day in males. A dietitian provided reinforcement by phone call twice per week to improve adherence to diet and supplement intake and all subjects reported their dietary intakes for 72 hours in order to estimate their daily intakes of calories and macronutrients, before and after 12 and 24 weeks of dietary intervention. The dietary registrations were evaluated with professional software (Dietsource®, Nestlé, Geneve, Switzerland). Aerobic physical activities were encouraged at least 3 times per week (60 minutes per session) and the proposed exercises were walking, running, cycling, and swimming. Physical activity was self-reported through a questionnaire by each subject.

Anthropometric and metabolic data

Anthropometric data were collected at baseline and after dietary intervention, both at the end phase 1 (MR phase, at 12 weeks) and phase 2 (food reintroduction phase, at 24 weeks). This included body weight, height, BMI, systolic and diastolic blood pressure, waist circumference and, using electrical impedance, fat mass, fat free mass, and skeletal muscle mass. At all three measurement points, fasting blood samples were collected using EDTA collection tubes for analysis of basal fasting (8 hours) glucose, insulin, insulin resistance calculated (homeostasis model assessment) (HOMA-IR), total cholesterol, LDL cholesterol, HDL cholesterol, and plasma triglycerides. The Adult Treatment Panel III (ATPIII) criteria (14) were used to diagnose the presence of MS. These consist of: elevated fasting glucose or treatment for diabetes *mellitus;* elevated

triglycerides (> 150 mg/dl); low HDL cholesterol < 40 mg/dl (males) or < 50 mg/dl (females); elevated systolic or diastolic blood pressure (> 130/85 mmHg); and increased waist circumference (> 88 cm in females and > 102 cm in males). Patients who met at least three of these criteria were diagnosed with MS.

Anthropometric parameters and blood pressure

The data were obtained according to standardised techniques. The height was estimated with the patient in an upright position using a stadiometer (Omrom, LA, Ca, USA). Body weight was measured without clothing with an accuracy of 10 grams, using a manual scale (Omrom, LA, Ca, USA). The BMI was calculated using the above-mentioned parameters with the following equation:

$$\text{Weight (kg)} / (\text{Height} \times \text{Height } [m^2])$$

A bioelectrical impedance analysis (BIA) was also conducted using an alternating current of 0.8 mA at 50 kHz produced by a calibrated signal generator (EFG, Akern, Firenze, Italy) The equation of this device was used $(0.756\ \text{Height}^2/\text{Resistance}) + (0.110 \times \text{Body mass}) + (0.107 \times \text{Reactance}) - 5.463$. The parameters analysed using BIA were total fat mass (kg), fat free mass (kg) and skeletal muscle mass (SMM) (15). The skeletal muscle mass index (SMMI) (kg/m^2) was calculated using the formula SMM (kg)/(height x height) (m^2).

Waist circumference was taken as the narrowest circumference between the xiphoid process and the iliac crest, measured using an extendable tape measure with the patient standing (Omrom, LA, Ca, USA). Arterial blood pressure was taken as the mean over three measurements taken after a 10 minute rest period using a random zero mercury sphygmomanometer (Omrom, LA,CA, USA).

Biochemical parameters:

Serum glucose, insulin, total cholesterol, HDL cholesterol, and triglyceride levels were measured using the COBAS INTEGRA 400 analyser (Roche Diagnostic, Basel, Switzerland). LDL cholesterol was determined using the Friedewald formula (LDL cholesterol = total cholesterol - HDL cholesterol - triglycerides/5) (16). Based on these parameters, the homeostasis model assessment for insulin resistance (HOMA-IR) was calculated using these values (glucose x insulin/22.5) (17).

Statistical analysis

Statistical analysis was performed using SPSS version 23.0 (Chicago, IL. USA). Sample size was calculated to detect differences of over 9 kg with 90 % power and 5 % significance (n = 350). All parameters were examined for normality with the Kolmogorov-Smirnov test. The results were reported as mean ± standard deviation. In within-groups, the paired Student's t-test was used to compare biochemical parameters at baseline, at 12 weeks and at 24 weeks. The Mann-Whitney U test was used for non-parametric variables. Categorical and qualitative variables were evaluated with Chi-Square test, with Yates correction as required. Fisher's exact test was used for qualitative variables when the conditions required it.

RESULTS

We recruited 364 patients with obesity into the study. All patients completed phase 1 (the 12-week MR phase) and phase 2 (the 24-week food reintroduction phase). No dropouts and no adverse effects secondary to the dietary intervention were reported. The average age was 45.6 ±3.5 years (range: 32-56 years). There were 100 males (27.5 %) and 264 females (72.5 %) in the study.

Subjects demonstrated a statistically significant decrease in daily intakes of energy, carbohydrate, fat, and protein in phases 1 and 2 (Table II). Only dietary fibre remained unchanged during the two

phases of dietary intervention. Physical exercise time was similar at baseline and after the intervention (Table II). During the MR phase, 95 % of all the prescribed VEGESTAR complete® bricks were taken.

As shown in table III, there were statistically significant improvements in body weight, BMI, fat mass, and waist circumference at 12 and 24 weeks compared to baseline. The differences between the values at 12 weeks (phase 1) and the values at week 24 (phase 2) were also significantly different. No significant differences were found throughout the study in phase angle or skeletal muscle mass.

Table IV shows all biochemical parameters and blood pressure. Systolic blood pressure improved at 12 weeks and 24 weeks compared to the baseline value; there was no significant differences between the values at 12 and 24 weeks. Diastolic pressure remained unchanged throughout the study. Triglycerides, total cholesterol, LDL cholesterol, glucose, insulin, and HOMA-IR improved with weight reduction in weeks 12 and 24. However, there were no differences between the values achieved in weeks 12 and 24. The values of HDL cholesterol remained unchanged throughout the study.

Table V shows MS and the percentage of subjects who meet criteria for each component. The percentages of MS, central obesity, hypertriglyceridemia, hypertension, and hyperglycaemia improved significantly at 12 and 24 weeks compared to baseline. There were no differences in the percentages between 12 and 24 weeks. The percentage of patients with low HDL cholesterol levels remained unchanged during both phases of the dietary intervention. The odds ratio (OR) of improved percentage of patient with MS after phase 1 (12 weeks) was 0.68 (95 % CI 0.51-0.92; $p = 0.03$). The number needed to treat (NNT) with MR diet was 11.38 for the resolution of one case of MS (95 % CI 6.36-53.8; $p = 0.03$). After the completion of phase 2 (reintroduction of foods) the NNT for the resolution of one case of MS was 10.17 (95 % CI 6.15-41.2; $p = 0.02$). The OR for improved percentage of MS after phase 2 (24 weeks) was 0.66 (95 % CI 0.49-0.90; $p = 0.03$).

DISCUSSION

This study demonstrates that a meal replacement diet strategy with two phases in Caucasian adults with obesity leads to body weight reduction, with a relative decrease in the adiposity component and an improvement in cardiovascular risk factors, including decreased risk of having metabolic syndrome (MS).

The main outcomes of interest in this study were changes in body weight and body mass index (BMI). The first phase involved replacement of one meal for 12 weeks (phase 1) in patients with obesity, and a second 12-week phase involving the reintroduction of foods for 14 days, and subsequently following a low-calorie diet with a moderate limitation of caloric intake over basal needs (-300 to -500 calories/day) (phase 2). A significant decrease in weight and BMI was observed over both phases. The effectiveness of meal replacement diets has been studied several times. Here we compare the effect of these short-term diets (12 weeks) and they resulted in similar weight losses. For example, in a previous meta-analysis (10), six randomised controlled studies were evaluated in which it was observed that there was an average weight reduction of 6.19-6.50 kg (7 % of total weight) compared to the control group, where a reduction of 3.23-3.99 kg (4 % of the initial weight) was observed. Another recent meta-analysis showed that an MR diet has an adequate effect on weight loss both in the short and long term (7,8). Most of the studies have been carried out over short time periods (12 weeks) and the withdrawal of the supplement and reintroduction of foods has not been evaluated. In the literature, there are studies in patients with obesity and osteoarthritis before orthopaedic surgery (18,19), in patients with osteoarthritis without surgery (20), and in patients with metabolic fatty liver disease (21). All of these studies confirm the positive findings of body weight reduction in line with those obtained in our study. Our findings of weight reduction and improvements in MS compared to baseline show that this dietary intervention with two

phases is useful for Caucasian patients with obesity. Each MR contained 200 kcal compared to the 500 kcal that is consumed in a typical meal. In contrast to other studies (22,23), after cessation of the MR intervention, our subjects did not regain weight at 24 weeks. In our study, skeletal muscle mass was maintained, and only fat mass decreased. This data shows that, despite the caloric restriction, the maintenance of an adequate protein intake can help prevent an excess of muscle loss and subsequent weight gain. The predominant decrease in fat mass with maintenance of muscle mass has been observed in different studies with hyperproteic diets replacing one or more meals (24) and in studies comparing MR and a usual diet (25).

Waist circumference (WC) also decreased significantly following the intervention. When comparing meal replacement diets with hypocaloric diets, a greater decrease in WC has been observed in the replacement diet group (26). WC is a strong predictor of DM2 and cardiovascular events. A previous study reported that every 1 cm increase in WC was associated with a 2 % increase in cardiovascular risk (27). In our intervention we report a WC decrease of 11 cm with the potential beneficial metabolic effects that it is associated with. Glycaemic control (glucose) and insulin sensitivity (insulin levels and HOMA-IR) were significantly improved at 24 weeks. This could be explained by the weight reduction, and lower energy and carbohydrate consumption during the intervention. The ingestion of high protein/low glycaemic index MR promoted greater fat oxidation and thus improved insulin resistance (28). Our results also support the effectiveness of MR in reducing systolic blood pressure and improving the lipid profile. All of these metabolic benefits, together with the decrease in the percentage of patients with metabolic syndrome, show that MR strategies to be interesting therapeutic tools in obese patients with high cardiovascular risk, as recently demonstrated by Halle et al. (29) in an RCT of 463 patients with obesity. The improvements were higher in the MR branch than in the lifestyle intervention branch (12). This has also been demonstrated in

a 52-week study, which demonstrated a reduced 10-year risk of a cardiovascular event (29).

An important feature of note contributing to the excellent weight loss and metabolic improvements is the intervention from a Nutrition Unit. For example, in a pharmacy-delivered weight loss program with two MRs daily, an average weight reduction of 5 kg was reported over 12 weeks (30). Another study found weight reduction to be slightly lower in a self-selected sample of participants who had to purchase their MR and monitoring via the internet and received limited personal contact (31). The level of patient retention of our study is 100 %, which is higher than in the 50-75 % reported in the above studies (30,31). This is also likely secondary to the in-person care in our protocol.

The main limitation of this study is that it was designed to evaluate short-term changes. Furthermore, the study of cardiovascular risk factors was carried out using surrogate parameters and not actual cardiovascular events. It would be more appropriate to evaluate the rate of vascular events, but this requires a study of very long duration and the maintenance of the interventions for longer. In the other hand, these patients are probably more motivated to perform a nutritional intervention when attending a Unit of nutrition to weight loss. Finally, the self-reported dietary intake and physical exercise may include bias due to under- or over-reporting.

However, there are several strengths of this study. First, the MR strategy used was in a real-world setting. Second, this intervention is less expensive than intensive lifestyle interventions. Third, we demonstrated that after cessation of the MR phase, there was no weight regain in medium term follow-up until 24 weeks.

The main conclusion of this study was that in patients with obesity, the strategy of one meal-replacement resulted in a significant decrease in weight and fat mass with a secondary improvement in metabolic parameters. A significant decrease in the percentage of patients with MS was observed, with a low number needed to treat.

Therefore, an MR intervention strategy with physical contact with the patient and subsequent reintroduction of foods in the context of a hypocaloric diet is an easy intervention to carry out in real clinical practice with excellent metabolic and weight loss results. Further designs are necessary in which the longer-term outcome of these patients and the recurrence rates of these patients are evaluated.

Table I. Distribution of macronutrients in the meal replacement diet (five intakes as natural food and one intake as artificial formula)

Composition	**Oral diet + formula in females**	**Oral diet + formula in males**	**Normocaloric hyperproteic formula (200 ml per brick)**
Calories (kcal)	1035	1192	200
Protein (%TCV) (g)	64.4 (25 %)	71.9 (24 %)	15.4 (31 %)
Fat (%TCV) (g)	19.1 (17 %)	19.9 (15 %)	5.2 (23 %)
Carbohydrate (%TCV) (g)	151.6 (59 %)	181.5 (61 %)	21 (42 %)
Dietary fiber (g)	15.9	17.4	4.2

Normocaloric hyperproteic formula is VEGESTART COMPLETE® %TCV = % total caloric value).

Table II. Average daily intakes and physical activity at baseline and after dietary interventions (mean [SD])

Parameters	**Baseline**	**12 weeks**		**P1**	**24 weeks**		**P2**	**P3**
Calorie intake (kcal/day)	1629.9 (121.8)	1017.9 (29.1)	612.9 (5.6)	0.01	1258.4 (32.1)	390.9 (15.6)	0.02	0.32
Carbohydrate intake (g/day) (PTC %)	169.9 (51.9) 39.6 %	130.8 (41.1) 63.4 %	39.5 (3.1)	0.02	150.1 (39.1) 63.2 %	19.5 (3.1)	0.02	0.04
Fat intake (g/day) (PTC %)	58.4 (20.2) 37.0 %	26.0 (12.1) 22.6 %	32.4 (6.3)	0.01	36.1 (8.3) 22.7 %	22.8 (9.2)	0.01	0.03
Protein intake (g/day) (PTC %)	75.0 (14.2) 23.4 %	54.1 (12.3) 23.0 %	21.8 (9.8)	0.02	60.2 (12.9) 23.3 %	15.2 (9.4)	0.03	0.04
Fibre intake (g/day)	16.3 (6.1)	17.1 (4.8)	0.9 (0.8)	0.23	16.9 (4.2)	0.6 (0.4)	0.43	0.27
Physical activity (minutes/week)	123.1 (12.2)	128.9 (12.1)	4. 7 (4.6)	0.22	131.9 (13.2)	3.5 (4.1)	0.49	0.28

PTC: percentage of total calorie; differences between baseline vs 12 weeks and baseline vs 24 weeks. *p* values: P1 = statistical differences between baseline and 12 weeks; P2 = statistical differences between baseline and 24 weeks; P3 = statistical differences between 12 and 24 weeks.

Table III. Changes in anthropometric and bioimpedance parameters before and after dietary intervention (mean [SD])

Parameters	**Baseline**	**12 weeks**		**P1**	**24 weeks**		**P2**	**P3**
Weight (kg)	102.9 ± 6.7	93.4 (5.1)	8.5 (3.1)	0.02	90.5 (3.2)	12.6 (3.6)	0.01	0.01
BMI (kg/m^2)	39. 2 (3.2)	36.6 (2.1)	2.6 (3.1)	0.03	35.5 (2.1)	1.1 (3.0)	0.03	0.01
Waist (cm)	120.5 (4.5)	112.6 (3.1)	8.7 (2.2)	0.01	109.2 (3.1)	3.1 (2.2)	0.02	0.01
Fat mass (kg)	46.9 (4.1)	39.4 (2.1)	7.1 (2.3)	0.01	37.1 (2.1)	1.1 (1.6)	0.02	0.01
Phase angle (º)	5.8 (1.1)	5.7 (0.9)	0.03 (0.7)	0.52	5.8 (1.1)	0.01 (0.9)	0.61	0.34
SMM (kg)	36.9 (4.4)	35.5 (4. 2)	1.4 (1. 5)	0.21	33.9 (4.1)	1.6 (1.4)	0.28	0.11
iSMM (kg/m^2)	14.4 (2.8)	13.8 (2. 5)	0.6 (0.8)	0.33	13.2 (2. 6)	0. 9 (0.4)	0.21	0.11

BMI: body mass index; SMM: skeletal muscle mass; iSMM: index skeletal muscle mass. = differences between baseline vs 12 weeks and baseline vs 24 weeks. *p* values: P1 = statistical differences between baseline and 12 weeks; P2 = statistical differences between baseline and 24 weeks; P3 = statistical differences between 12 and 24 weeks.

Table IV. Changes in biochemical parameters and blood pressure before and after dietary intervention (mean [SD])

Parameters	Baseline	12 weeks		P1	24 weeks		P2	P3
SBP (mmHg)	131.9 (7.1)	123.2 (6.5)	9.6 (6.1)	0.01	123.7 (9.1)	9.5 (5.9)	0.01	0.34
DBP (mmHg)	79.6 (6.3)	78.6 (6.6)	0.9 (0.5)	0.39	78.1 (6.9)	0.4 (1.0)	0.37	0.38
Triglycerides (mg/dl)	145.5 (21.7)	123. 8 (19. 3)	22.6 (6.3)	0.02	117.1 (13. 3)	28.7 (6.1)	0.03	0.32
Total cholesterol (mg/dl)	193.9 (21.9)	179.4 (19.5)	14.5 (7.2)	0.03	179.1 (21.1)	14.6 (4.5)	0.03	0.45
HDL (mg/dl)	50.4 (8.6)	51.6 (7.2)	0.8 (2.1)	0.41	51.05 (7.8)	0.6 (2.1)	0.39	0.53
LDL (mg/dl)	124.6 (11.8)	110. 5 (9.1)	14.3 (8.4)	0.02	109.8 (11.9)	15.9 (9.6)	0.01	0.46
Glucose (mg/dl)	106.4 (4.8)	98.5 (3.7)	8.8 (5.05)	0.02	97.1 (4.1)	9.8 (2.6)	0.01	0.42
Insulin (U/ml)	20.2 (6.2)	14.6 (5.1)	5.6 (4.1)	0.01	14.3 (5.2)	5.9 (4.3)	0.01	0.51
HOMA-IR	5.3 (1.2)	3.6 (1.0)	1.7 (1.1)	0.03	3.5 (1.1)	1.8 (1.2)	0.03	0.31

SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high density lipoprotein; LDL: low density lipoprotein. differences between baseline vs 12 weeks and baseline vs 24 weeks. *p* values: P1 = statistical differences between baseline and 12 weeks; P2 = statistical differences between baseline and 24 weeks; P3 = statistical differences between 12 and 24 weeks.

Table V. Percentage of patient's metabolic syndrome and components of metabolic syndrome before and after dietary intervention

Parameters	Baseline	12 weeks	P1	24 weeks	P2	P3
Percentage of MS	40.1 %	33.3 %	0.03	30.8 %	0.01	0.22
Percentage of central obesity	44.5 %	37.9 %	0.03	33.3 %	0.01	0.23
Percentage of hypertriglyceridemia	31.3 %	21.4 %	0.02	20.3 %	0.02	0.42
Low HDL cholesterol	38.7 %	36.7 %	0.43	36.4 %	0.54	0.56
Percentage of hypertension	75.1 %	39.3 %	0.001	35.9 %	0.001	0.32
Percentage of hyperglycaemia	23.4 %	15.9 %	0.02	13.2 %	0.01	0.21

The cut off points for central obesity are waist circumference > 88 cm in females and > 102 cm in males; for hypertension, systolic blood pressure > 130 mmHg or diastolic blood pressure > 85 mmHg or specific treatment; for hypertriglyceridemia, triglycerides > 150 mg/dl or specific treatment; for hyperglycaemia, fasting plasma glucose >110 mg/dl; for low HDL cholesterol, < 40 mg/dl (males) or <50 mg/dl (females). *p* values: P1 = statistical differences between baseline and 12 weeks; P2 = statistical differences between baseline and 24 weeks; P3 = statistical differences between 12 and 24 weeks.

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