A new dietary strategy for long-term dietary treatment of metabolic syndrome is compared to the AHA guidelines: the RESMENA project.

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Key words: obesity, energy restriction, fibre, macronutrient distribution.

Summary

The long-term effects of dietary strategies designed to combat metabolic syndrome (MetS) remain unknown. This study evaluated the effectiveness of a new dietary strategy based on macronutrient distribution, antioxidant capacity and meal frequency (RESMENA diet) for the MetS treatment as compared to the AHA guidelines, used as Control. Subjects with MetS (52men/41women, 49±1years, BMI 36·11±0·5kg/m^2), were randomly assigned to each diet. After a 2-month nutritional-learning intervention where participants received nutritional assessment every fifteen days, a 4-month- self-control period began. No significant differences between groups were found concerning anthropometry, but the RESMENA group significantly lost body weight (-1·7%; p = 0·018), body mass index (-1·7%; p = 0·019), waist circumference (-1·8%; p = 0·021), waist-to-hip ratio (-1·4%; p = 0·035), and android fat mass (-6·9%; p = 0·008). RESMENA group significantly reduced ALT and AST levels (-26·8%; p = 0·008 and -14·0%; p = 0·018, respectively), while glucose concentrations (7·9%; p = 0·011), AST (11·3%; p = 0·045) and uric acid (9·0%; p < 0·001) significantly increased in the Control group. LDL-c values rose (34·4%; p < 0·001 and 33·8%; p < 0·001 Control and RESMENA, respectively), but interestingly also the LDL-c/Apo B ratio (28·7%; p < 0·001, 17·1%; p = 0·009, respectively) and the HDL-c (21·1%; p < 0·001, 8·7; p = 0·001, respectively). Fibre was the dietary component that most contributed to the improvement of anthropometry, while body weight loss explained some biochemical markers's changes. In conclusion, the RESMENA diet is a good long-term dietary treatment for MetS. www.clinicaltrials.gov; NCT01087086.

Introduction

The metabolic syndrome (MetS) is a clinical entity of substantial heterogeneity, represented by the combination of obesity (especially central obesity), insulin resistance and impaired glucose tolerance, atherogenic dyslipidemia (high levels of triglycerides and low levels of high density lipoprotein cholesterol) and hypertension [(1)]. This cluster of factors co-occurs to a greater degree than expected by chance alone, affecting approximately 10-25% of adults worldwide. The International Diabetes Federation (IDF) states that this syndrome is driving the twin global epidemics of type 2 diabetes and cardiovascular disease (CVD) [(2)]. People with the MetS have three times more risk of suffering a heart attack or stroke – and twice the risk of dying from such an event – compared with people without the syndrome [(2)].

The dietary treatment of MetS should address the different cornerstones presented in this process [(3)]. Therefore, since most individuals with the MetS are overweight, dietary treatment should be primarily focused on weight reduction. Moreover, the Mediterranean diet [(4)], the ω-3 fatty acids (FA) [(5, 6)], the total antioxidant capacity (TAC) [(7, 8)] or the meal frequency increment [(9)] are dietary patterns that have shown positive effects on MetS. Furthermore, the type and percentage of carbohydrates (CHO), the glycemic index (GI) or the glycemic load (GL), and the dietary fibre content are some of the most relevant aspects related to insulin resistance and impaired glucose tolerance [(10-12)], which are important comorbidities of the MetS.

Many subjects can follow a prescribed diet during a few months, but most people have difficulty in maintaining the acquired habits over the long term [(13)]. In this context, although many studies have separately examined the impact of different dietary factors and mainly during nutritional interventions, none of them have apparently considered all integrated within a unique dietetic plan to ameliorate MetS comorbidities during an autonomous period after a nutritional learning period. Therefore, the RESMENA-S (MEtabolic Syndrome REduction in NAvarra-Spain) study (www.clinicaltrials.gov; NCT010-7086) [(3)] aimed to evaluate the effect of a novel dietary strategy involving together all those dietary elements and to compare it with the American Heart Association (AHA) guidelines, which is considered a dietary strategy of reference, in order to improve MetS features and maintain them over the long term [(14)].

Methods

Subjects

Ninety three Caucasian adults (52 men/41 women) with a body mass index (BMI) of 36·11±0·5 kg/m^2 aged 49±1 years, diagnosed of MetS according to the IDF criteria [(15)] started the intervention

trial. Exclusion criteria were: the presence of psychiatric or psychological disorders, the difficulty for changing dietary habits, eating disorders, body weight changes during the last 3 months, chronic diseases related to the energy or nutrients metabolism, the special diets pursuit or food allergies or intolerances, as described elsewhere [3]. During the 6-month-study, 26 volunteers dropped out, 9 during the first intervention period and 17 during the autonomous period. Therefore, 67 individuals completed the study and were included in the final statistical analysis (Figure 1).

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee of the University of Navarra (065/2009). Written informed consent to participate in the intervention trial (www.clinicaltrials.gov; NCT01087086) was obtained from all subjects.

Study protocol

The study was designed as a randomized, controlled trial to compare the effects of two dietary strategies on improving MetS comorbidities during 4 months of autonomy, after 2 months of nutritional advice. Participants were randomly assigned to the control or the experimental diet (Control and RESMENA groups, respectively). The study lasted a total of six months divided in two sequential periods: a previous 8 week- nutritional learning intervention period during which the participants received nutritional assessment every fifteen days [16], and a following 4-month- self-control period in which they followed the previously acquired nutritional habits. This article focuses on the self-control period information.

The CONSORT 2010 guidelines [17] were followed by taking into account the design of the present study as two-groups longitudinal intervention, except for blinding. Participants were asked to maintain their normal physical activity during the study, which was checked by a 24-h physical activity questionnaire [18] at the beginning and at the end of both intervention and autonomous periods.

During the 2-month- nutritional-learning intervention period, volunteers visited the Metabolic Unit at the University of Navarra every two weeks for anthropometrical measurements and bioimpedance's body composition analysis by trained nutritionists following validated protocols [3]. Moreover, nutritionists asked the volunteers about the feelings and sensations they were experiencing with the new diet to determine their well-being. Finally, different advice was given to the participants in each situation as well as recipes, general information about food and the importance of dietary adherence. Before and after the 4-month- long self-control period, body composition by Dual-energy X-ray Absorptiometry (DXA) was measured and fasting blood and 24h urine samples were collected in addition to the anthropometric and bioimpedance assessments.

Diets

Two energy-restricted diets (-30% energy of the studied requirements) were prescribed and compared. The Control diet was based on the AHA guidelines [14], including 3-5 meals per day, a macronutrient distribution of 55% Total Caloric Value (TCV) from CHO, 15% proteins and 30% lipids, a healthy FA profile and a cholesterol consumption lower than 300 mg/day. The RESMENA diet was characterized by a higher meal frequency, consisting of seven meals per day (including breakfast, lunch, dinner and two snacks in the morning and two snacks in the afternoon), and by a different macronutrient distribution, 40% TCV from CHO, 30% proteins and 30% lipids [3]. Furthermore, this pattern tried to reinforce the high ω-3 polyunsaturated FAs (ω-3 PUFAs) and high natural antioxidants foods consumption and promoted low GL carbohydrates intake. It also maintained a healthy FA profile and a cholesterol content of less than 300 mg/day as the Control diet.

RESMENA participants were prescribed a 7-day menu plan, while in the Control group, a previously described [19] food exchange system plan, was provided to participants. A 48-hour weighed food record was collected at the beginning and at the end of both, the nutritional-learning and the autonomous periods, in order to assess the volunteer's adherence to the prescribed nutritional patterns. The designed diets composition, as well as the different dietary records, were analyzed by the DIAL (Alce Ingenieria, Madrid, Spain) software [20].

The sum of eicosapentaenoic and docosahexaenoic fatty acid (EPA+DHA) obtained by the DIAL program [20] was used to estimate ω-3 PUFAs consumption. To calculate the Healthy Eating Index (HEI) score, the DIAL program gives different values between 0 and 100 considering the daily servings of cereals, vegetables, fruits, dairy products and meat and taking into account the percentage of energy provided by total and saturated fats, the amount of cholesterol and sodium per day and the variety of the diet expressed by the number of different foods consumed each of the three days. The final score is classified in 5 categories: > 80 points indicates "excellent diet", 71-80 points express "very good diet", 61-70 points is considered a "good diet", 51-60 "acceptable diet" and a final score between 0 and 50 points indicate an "inadequate diet" [20]. TAC was calculated using the Carlsen et al. 2010 data, considering raw or cooked preparations [21, 22]. Finally, the GL was obtained from the international updated website database based in the Human Nutrition Unit, School of Molecular Biosciences from the University of Sydney 2012 [23].

Clinical and biochemical assessments

Anthropometric measurements were performed in fasting conditions as previously described [24]. Body weight was assessed to the nearest 0·1 kg by using a bioimpedance (TANITA SC-330, Tanita Corporation, Tokyo, Japan) equipment. Body mass index (BMI) was calculated as the body weight divided by the squared height (kg/m²). Waist and hip circumferences were measured with a commercial measure tap following validated protocols as previously described [3]. Total body fat mass, android fat mass, lean mass and fat-free mass were evaluated by DXA (Lunar iDXA™, software version 6·0, Madison, Wisconsin, USA). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed using a digital monitor (Medisana, MTC) following World Health Organization (WHO) criteria.

Total cholesterol, HDL-cholesterol (HDL-c), triglycerides (TG), non-esterified fatty acids (NEFA), glucose, homocysteine (HCIS), uric acid, total proteins, creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) serum concentrations were measured in an autoanalyser Pentra C-200 (HORIBA ABX, Madrid, Spain) with specific kits. Insulin concentrations were determined by an enzyme-linked immunosorbent assay (ELISA) kit (Mercodia, Uppsala, Sweden) in a Triturus autoanalyzer (Grifols SA, Barcelona, Spain). Insulin resistance was estimated by the Homeostasis Model Assessment Index (HOMA-IR), which was calculated as stated in the following formula: HOMA-IR = [glucose (mmol/L) × insulin (μU/ml)]/22·5 as described elsewhere [25]. LDL-cholesterol (LDL-c) levels were calculated following the Friedewald formula: LDL-c = Total cholesterol - HDL-c - TG/5 [26]. Apo B values were measured with a specific kit (Tina-quant Apolipoprotein B ver.2, Mannheim, Germany) using a Roche/Hitachi autoanalyzer (Mod.904 Modular, Tokio, Japan).

Statistical analyses

Based upon previous studies [27, 28], the sample size (40 per group) was calculated to detect a difference of 4·3 cm with a variation of ± 6·8 cm between groups in the reduction of the waist circumference with a $p < 0·05$ and a power of 80%. The estimated dropout rate was 25% and the initial number of recruited subjects was 109. However, 12 did not present MetS according to the IDF criteria when the study began and another four volunteers decided not to start the dietary treatment after signing the written informed consent. Therefore, 93 subjects presenting MetS started the intervention trial (n = 45 Control group, n = 48 RESMENA group).

Mean values and standard errors were reported for the measured variables. Differences between the beginning and the end of the autonomous period were analyzed by a paired t-test. Differences

between both groups (RESMENA vs. Control) were assessed through a multivariate analyses of variance (MANOVA) adjusted for gender and age.

A linear regression analysis was applied to assess the potential relationships and associations, among the different components of the diet and anthropometrical and biochemical parameters variation. The comparison between the median body weight loss and median dietary fibre intake categories were performed using MANOVA adjusted for gender and age. Analyses were carried out using SPSS 15·1 software for Windows (SPSS Inc, Chicago, USA). Values of $p < 0{\cdot}05$ were considered as statistically significant.

Results

Dietary records

As expected, the dietary records after the self-control period revealed that the RESMENA individuals had a higher protein ($p = 0{\cdot}001$), PUFAs ($p = 0{\cdot}017$), TAC ($p = 0{\cdot}043$) and meal frequency intake ($p < 0{\cdot}001$) than the Control group, but both consumed the same amount of energy. However, no significant differences were found regarding fibre, GL and EPA+DHA intake. Furthermore, the quality score based on the HEI values evidenced no differences between dietary groups (Table 1).

Anthropometrical and biochemical parameters

After the 4 months of autonomy, both Control and RESMENA groups, significantly diminished total fat mass (-3·3 % $p = 0{\cdot}044$ and -4·4% $p = 0{\cdot}004$, respectively). However, only the RESMENA group individuals presented a significant decrease in body weight ($p = 0{\cdot}018$), BMI ($p = 0{\cdot}019$), waist circumference ($p = 0{\cdot}021$), WHR ($p = 0{\cdot}035$) and android fat mass ($p = 0{\cdot}008$). No significant differences were found in either of the experimental groups concerning lean mass, fat-free mass and blood pressure (Table 2).

At the end of the study, both Control and RESMENA groups had significantly increased the total cholesterol ($p < 0{\cdot}001$ and $p = 0{\cdot}020$, respectively), LDL-c ($p < 0{\cdot}001$), LDL-c/Apo B ratio ($p < 0{\cdot}001$ and $p = 0{\cdot}009$, respectively) and HDL-c ($p < 0{\cdot}001$ and $p = 0{\cdot}001$, respectively) concentrations (Table 3), as well as the total proteins levels ($p < 0{\cdot}001$ and $p = 0{\cdot}005$). Interestingly, only the Control group volunteers showed a significant increase in glucose ($p = 0{\cdot}011$), AST ($p = 0{\cdot}045$) and uric acid ($p < 0{\cdot}001$) concentrations. However, the RESMENA individuals had significantly decreased both transaminases, ALT ($p = 0{\cdot}008$) and AST ($p = 0{\cdot}018$). Significant

differences between groups were found concerning changes on uric acid, ALT and AST ($p = 0{\cdot}047$, $p = 0{\cdot}024$ and $p = 0{\cdot}002$, respectively). Finally, creatinine concentrations increased in the Control group and decreased in the RESMENA group, resulting in significant differences between them ($p = 0{\cdot}041$).

A linear regression was modeled to evaluate individual nutritional factors potentially involved in the variations of anthropometric and biochemical parameters (Table 4). The TAC values seemed to influence the AST concentrations ($p = 0{\cdot}037$), the EPA+DHA showed a role on creatinine depletion ($p = 0{\cdot}017$) and sex appeared to influence body weight ($p = 0{\cdot}032$) and creatinine ($p = 0{\cdot}002$) changes. However, the main influential dietary factor was the dietary fibre, showing a positive potential role on the body composition parameters, by reducing body weight ($p = 0{\cdot}001$), BMI ($p = 0{\cdot}003$), waist circumference ($p = 0{\cdot}043$), total fat mass ($p = 0{\cdot}001$) and android fat mass ($p = 0{\cdot}030$). This resulted in a model p value significant for body weight ($p < 0{\cdot}001$), BMI ($p = 0{\cdot}003$), and total fat mass ($p = 0{\cdot}002$), independently of the dietary group. In this context, the population was categorized, considering the median value fibre consumption ($\leq 18{\cdot}3$g and $> 18{\cdot}3$g), and the body composition parameters changes were compared between groups (Table 5). Individuals consuming $> 18{\cdot}3$g fibre showed a significant decrease on body weight ($p = 0{\cdot}001$), BMI ($p = 0{\cdot}006$), waist circumference ($p = 0{\cdot}010$), total fat mass ($p = 0{\cdot}002$) and android fat mass ($p = 0{\cdot}001$) and showed a trend towards significance to reduce the WHR ($p = 0{\cdot}057$). Significant differences between groups were found concerning weight ($p = 0{\cdot}008$), BMI ($p = 0{\cdot}035$) and android fat mass ($p = 0{\cdot}008$).

As no nutritional factors potentially involved in blood biochemical variations were found, the body weight reduction influence on them was separately analyzed. Therefore, the population was categorized by the body weight loss median, $\leq 0{\cdot}400$ kg (non responders to weight loss: NR) and $> 0{\cdot}400$ kg (responders to weight loss: R), as cut-offs and biochemical parameters were compared between groups (Table 6). Both experimental sets significantly increased total cholesterol ($p = 0{\cdot}012$ and $p < 0{\cdot}001$, NR and R respectively), LDL-c ($p < 0{\cdot}001$), HDL-c ($p < 0{\cdot}001$ and $p = 0{\cdot}001$, NR and R respectively), LDL-c/ Apo B ratio ($p = 0{\cdot}005$ and $p < 0{\cdot}001$, NR and R respectively) and total proteins ($p = 0{\cdot}001$ and $p < 0{\cdot}001$) without significant differences between groups. However, individuals that had lost $> 0{\cdot}400$ kg presented, as expected, a higher decrease of glucose ($p = 0{\cdot}005$), insulin ($p = 0{\cdot}001$), HOMA-IR ($p < 0{\cdot}001$), ALT ($p = 0{\cdot}037$) and AST ($p = 0{\cdot}024$) levels compared with individuals that had lost $\leq 0{\cdot}400$ kg of body weight regardless of the dietary group. However, no significant differences were found between both experimental sets concerning the remaining biochemical measurements.

Discussion

As MetS prevalence is reaching epidemic rates, and since maintenance of acquired healthy dietary habits is still a pending subject for clinical nutrition research, this study provides a new dietary strategy to combat MetS comorbidities during a self-control period after a nutritional learning intervention period.

Under the same caloric restriction (-30% TCV), this new dietary strategy (RESMENA group) showed more effectiveness continuing to maintain/improve some anthropometrical measurements than the diet based on the AHA guidelines (Control group), although statistical significance between dietary groups was not reached. These results are consistent with other studies concerning moderately high protein content diets [29]. These RESMENA diet positive effects were shown specifically in losing body weight at the expense of android fat mass, and reducing the waist circumference, the WHR and BMI. Since it has been demonstrated that central obesity is associated with increased risks of diabetes mellitus, hypertension, CVD [30, 31] and MetS manifestations in general [31], the RESMENA dietary strategy effects presented here should be considered in future nutritional intervention research.

Unexpectedly, regarding biochemical values independently of the dietary treatment or absolute weight loss, individuals increased total cholesterol and LDL-c, even when diets were based on a healthy FA profile, especially the RESMENA diet, where ω-3 fatty acids intake was also reinforced. These results agree with different systematic reviews that do not show clear effects of hypocaloric diets on LDL-c depletion [32, 33] and with studies which state that in some cases LDL-c values may rise despite weight loss [34]. Moreover, LDL/Apo B ratio that predicts the LDL-c particle size [35] significantly rose in all participants irrespectively of the diet or weight loss reduction, which indicates an increase in LDL-particle size and lower risk of ischemic cardiac events [36]. HDL-c concentrations, increased in both dietary groups, but the increment was higher in the Control group than in the RESMENA group. This outcome seems logical since the Control diet is specifically based on the AHA guidelines, which are mainly focused on CVD care and, therefore, on lipid profile management.

Since insulin resistance has been proposed to be related to the MetS development [37], one of the main aims in the MetS treatment regarding diet is to improve related parameters such as serum glucose concentrations and HOMA-IR. In this study, individuals following the Control diet worsened these values while RESMENA group individuals barely changed them. This could be explained by the fact that central obesity usually precedes insulin resistance, being a risk factor for the development of type 2 diabetes [37, 38] and RESMENA individuals were the only dietary group

that significantly lowered android fat mass. Furthermore, these results are in accordance with other investigations that have shown a positive role of low-CHO diets in insulin resistance syndromes [39].

Although uric acid was proposed to be able to function as an antioxidant [40], some studies associate the rise of this purine-end-product levels with gout and uric acid kidney stones [41] and, more importantly, with adverse effects in obesity [42], diabetes [43] hypertension [44], CVD [45], fatty liver [46] and with the MetS prevalence in general [47]. According to the results of the present study, the RESMENA diet might be better to follow for patients with high uric acid concentrations than the diet based on the AHA guidelines, as uric acid levels significantly increased in the Control group, while remained almost unchanged in the RESMENA group.

High serum creatinine levels are well known as an index of renal function [48] and are associated with obesity [49]. In this study it was found that these serum creatine-end-product levels increased in the Control group and lowered in the RESMENA group individuals, despite a higher protein intake.

Transaminases, mainly ALT, are markers of hepatocyte injury that have shown a correlation with insulin resistance and later development of diabetes, liver lipid content and histological features of non-alcoholic fatty liver disease (NAFLD), which is increasingly regarded as the main hepatic manifestation of the MetS [50, 51]. ALT transaminase has also been correlated with C-reactive protein levels, a marker of the low-grade inflammation associated with the MetS [52]. Dietary weight loss has been associated with a depletion of these liver enzymes [53], but irrespective of the type of diet [54]. However, in this study, the RESMENA diet showed better benefits in the treatment of MetS volunteers regarding these markers, as both ALT and AST transaminase levels significantly diminished on RESMENA volunteers, while AST concentrations significantly increased on the Control group.

Several health benefits of dietary fibre have been described including the prevention and mitigation of type 2 diabetes mellitus, CVD and colon cancer by reducing the risk of hyperlipidemia, hypercholesterolemia and hyperglycemia [55]. Moreover, diverse clinical studies have examined the role of this dietary component in body weight reduction, and a strong relationship has been established [56, 57]. Different mechanisms by which dietary fibre intake can influence body weight have been proposed. Recently, the role of the dietary fibre in gut microbiota in the development of obesity and its associated co-morbidities has come to the forefront [58]. Data suggest that fibre can reduce the risk of obesity by promoting satiety and reducing energy intake [59, 60] and numerous studies have been carried out to clarify the effects of dietary fibre on satiety [61-63]. Many different mechanisms have been suggested, such as a lower metabolisable energy content of fibre than that of other nutrients [64], a relatively constant meal intake volume [65], a decreased total energy intake by

consuming foods rich in fibre; and the increased chewing activity or oral exposure time to foods after a high dietary fibre intake, which may result in earlier satiation [66]. Furthermore, fibre can slow down gastric emptying and consequently increase stomach distension, which also leads to satiation [67]. In the present study, when the impact of this dietary component was studied on anthropometrical and body composition measurements, the results obtained agreed with the studies mentioned above, as the fibre consumption showed positive effects on the improvement of these measurements in individuals affected by MetS.

As most individuals with MetS are overweight, the dietary treatment of this syndrome might be primarily focused on body weight and abdominal fat reduction. Moreover, obesity is considered the main cause of insulin resistance and type 2 diabetes, important comorbidities of the MetS [38]. Therefore, body weight reduction should also be a main target for improving related parameters such as glucose and HOMA-IR. Serum TG levels, correlated with insulin sensitivity [68] have also been associated with MetS [69] as the IDF uses them for the diagnosis of MetS [1]. Furthermore, since high levels of ALT and AST concentrations are correlated with NAFLD and as obesity is frequently associated with NAFLD, it is clear that body weight loss can involve a reduction in transaminase levels. In this study, when volunteers were categorized by the weight loss median as a cut-off, it could be noted that volunteers that had lost more body weight presented significantly higher decreases of TG, glucose, insulin, HOMA-IR, ALT and AST levels compared with individuals that had lost less body weight. Only RESMENA individuals significantly lost body weight and obtained the best results regarding glucose, HOMA-IR, ALT and AST. Any nutritional factors potentially involved in blood biochemical variations were found. Therefore it can be hypothesized that body weight loss as well as waist circumference reduction were the main factors contributing to the improvement of those biochemical parameters on RESMENA group individuals.

The dietary records after the self-control period showed the expected differences between the designed dietary patterns composition, except for the fibre, GL and EPA+DHA intake. This could be explained by the fact that, although the RESMENA diet was specially enriched in high fibre food, the Control group consumed 15% TCV from CHO more than the RESMENA group did. Moreover, the dietary records analyzed in this study were collected at the endpoint. Therefore, volunteers may not complete them with the same thoroughness as they completed the former dietary records, which were provided before and after the nutritional learning period. In addition, as both diets were designed following a healthy pattern, it is logical that the quality score based on the HEI evidenced similar values between dietary groups.

Conclusion

In summary, this study suggests a new dietary treatment, the so called RESMENA pattern, to combat MetS during an autonomous period. This programme showed more beneficial effects than a diet based on the AHA guidelines concerning body composition, especially central obesity, and regarding several biochemical parameters, by reducing transaminase levels and maintaining uric acid and serum glucose concentrations. Therefore, the prescription of the RESMENA diet might be a good option as a long-term dietary treatment of MetS comorbidities.

Acknowledgements

The authors thank the volunteers for taking part in this study and the physician Blanca E. Martínez de Morentín, the nurse Salomé Pérez, and the technician Verónica Ciaurriz for excellent technical assistance at the Metabolic Unit of the University of Navarra.

Financial support

The present work was supported by the Health Department of the Government of Navarra (48/2009) and the Línea Especial about Nutrition, Obesity and Health (University of Navarra LE/97). The support from CIBERobn and RETICS schemes is gratefully accredited. Carlos III Health Institute provided a predoctoral grant to RI (nº FI10/00587). None of the funding Institutions and frameworks had a role in the design, analysis or writing of the article.

Conflicts of interest

None of the authors have conflicts of interest to declare.

Authorship

The authors contributions were as follows: RI contributed to the design and the fieldwork, data collection, analysis and writing of the manuscript. PLL and IA were involved in the design and the fieldwork. IBP contributed to the sample collection, interpretation and critical reading of the last version. SNC and LF were involved in the recruitment and volunteers' selection. MAZ was responsible for the general coordination, follow-up, design and financial management. JAM, project

coleader, was responsible of the follow-up, design, financial management and editing of the manuscript. All the authors actively participated in the manuscript preparation, as well as read and approved the final manuscript.

Figure legends

Figure 1. Flow diagram of participants during the study.

Abbreviations: MetS, metabolic syndrome

Tables

Table 1. Comparison of Control and RESMENA dietary records after the self-control period.

	Control		RESMENA		P
	Mean	SE	Mean	SE	
Energy (kJ)	6389	207	6505	284	0·737
Meal Frequency	4·4	0·1	5·8	0·2	< 0·001
Proteins (% TCV)	17·2	0·5	20·5	0·8	0·001
CHO (% TCV)	37·1	1·3	36·4	1·1	0·679
Lipids (% TCV)	40·7	1·3	37·9	0·9	0·087
PUFAs (% TCV)	5·2	0·2	6·2	0·4	0·017
EPA+DHA (g)	0·28	0·07	0·35	0·15	0·624
Fibre (g)	18·7	1·6	18·9	1·1	0·903
Fibre (% TCV)	2·7	0·3	2·7	0·2	0·957
GL	74·1	5·4	68·0	4·9	0·420
TAC (mmol)	6·4	0·6	8·4	0·8	0·043
HEI	68·1	2·3	68·8	1·9	0·823

Abbreviations: TCV, total caloric value; CHO, carbohydrates; PUFAs; polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; GL, glycemic load; TAC, total antioxidant capacity; HEI, healthy eating index.

Table 2. Changes in anthropometric, body composition and blood pressure parameters in both experimental groups (Control and RESMENA) after a 4 months self-control period.

	Control Group						RESMENA Group						Difference
	Before self-control period		After self-control period		%Δ	P	Before self-control period		After self-control period		%Δ	P	P†
	Mean	SE	Mean	SE			Mean	SE	Mean	SE			
Weight (kg)	93·2	2·8	92·4	3·0	-0·9	0·211	96·2	2·8	94·6	2·9	-1·7	0·018	0·378
BMI (kg/m^2)	33·2	0·7	33·0	0·8	-0·5	0·495	33·8	0·8	33·2	0·8	-1·7	0·019	0·235
Waist circumference (cm)	105·6	2·0	104·9	2·2	-0·6	0·366	106·5	1·9	104·6	2·0	-1·8	0·021	0·297
WHR	0·96	0·01	0·96	0·02	-0·4	0·497	0·95	0·02	0·93	0·02	-1·4	0·035	0·369
Total fat Mass (kg)	36·1	1·4	35·0	1·6	-3·3	0·044	38·4	1·7	36·7	1·6	-4·4	0·004	0·527
Android Fat Mass (kg)	4·0	0·2	4·0	0·3	2·0	0·785	4·1	0·2	3·8	0·2	-6·9	0·008	0·195
Lean mass (kg)	53·9	2·0	54·3	2·1	0·7	0·268	54·3	1·8	54·6	1·9	0·5	0·420	0·961
Fat-free mass (kg)	56·8	2·0	57·2	2·2	0·7	0·273	57·5	2·0	57·9	2·0	0·7	0·279	0·895
SBP (mmHg)	139·5	2·8	138·1	2·3	-1·0	0·664	138·1	3·2	135·7	2·8	-1·7	0·533	0·972
DBP (mmHg)	77·9	1·8	78·5	1·7	0·8	0·766	77·6	1·9	78·8	1·8	1·6	0·574	0·699

Abbreviations: BMI, body mass index; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; %Δ, percentage of change; P†, comparison between dietary groups.

Table 3. Changes in biochemical parameters in both experimental groups (Control and RESMENA) after a 4 months self-control period.

	Control Group						RESMENA Group						Difference
	Before self-control period		After self-control period		%Δ	P	Before self-control period		After self-control period		%Δ	P	P†
	Mean	SE	Mean	SE			Mean	SE	Mean	SE			
Total Cholesterol (mmol/L)	5·14	0·18	5·78	0·19	12·3	< 0·001	5·06	0·19	5·51	0·18	8·9	0·020	0·555
HDL-c (mmol/L)	1·07	0·04	1·29	0·05	21·1	< 0·001	1·07	0·04	1·16	0·04	8·7	0·001	0·006
LDL-c (mmol/L)	3·34	0·15	4·48	0·17	34·4	< 0·001	3·25	0·16	4·35	0·17	33·8	< 0·001	0·987
LDL-c/Apo B	1·48	0·04	1·91	0·04	28·7	< 0·001	1·63	0·11	1·91	0·03	17·1	0·009	0·204
TG (mmol/L)	1·60	0·14	1·64	0·18	2·1	0·794	1·61	0·14	1·72	0·17	6·6	0·387	0·480
NEFA (mmol/L)	0·51	0·03	0·46	0·03	-9·8	0·145	0·51	0·05	0·49	0·04	-3·6	0·707	0·450
Glucose (mmol/L)	6·05	0·13	6·53	0·25	7·9	0·011	6·23	0·27	6·28	0·30	0·8	0·884	0·471
Insulin (µU/mL)	9·02	1·26	9·32	1·45	3·4	0·697	9·59	1·06	8·70	1·06	-9·3	0·226	0·261
HOMA-IR	2·55	0·42	2·95	0·55	15·6	0·179	2·85	0·38	2·53	0·33	-11·0	0·304	0·135
HCIS (µmol/L)	16·35	0·70	16·16	0·76	-1·1	0·803	15·24	0·66	17·05	1·29	11·9	0·175	0·139
Uric Acid (mg/dL)	5·59	0·18	6·09	0·23	9·0	< 0·001	6·09	0·18	6·02	0·22	-1·2	0·724	0·047
Total Proteins (mg/dL)	71·99	0·84	76·23	1·11	5·9	< 0·001	70·23	0·71	73·17	0·91	4·2	0·005	0·173
Creatinine (mg/dL)	0·97	0·02	1·01	0·03	4·4	0·067	0·99	0·04	0·96	0·04	-3·6	0·260	0·041
ALT (U/L)	27·04	1·78	26·37	1·47	-2·5	0·645	31·57	2·50	23·09	1·53	-26·8	0·008	0·024
AST (U/L)	20·34	1·10	22·64	1·03	11·3	0·045	23·68	1·07	20·36	0·88	-14·0	0·018	0·002

Abbreviations: HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; TG, triacilglycerides; NEFA, non-esterified fatty acids; HOMA-IR, homeostasis model assessment of insulin resistance; HCIS, homocysteine; ALT, alanine aminotranferase; AST, aspartate aminotransferase; %Δ, percentage of change P†, comparison between dietary groups.

Table 4. Regression analyses, considering the change in anthropometric and biochemical parameters as the dependent variable and different dietary components evaluated as the independent ones.

	Sex		Meal Frequency		Fibre (g)		Proteins (%)		TAC (mmol)		EPA+DHA (g)		P Model	Corrected r^2
	B	P	B	P	B	P	B	P	B	P	B	P		
Weight (kg)	1·924	0·032	0·147	0·710	-0·193	0·001	-0·072	0·522	-0·109	0·345	-0·922	0·203	< 0·001	0·292
BMI (kg/m²)	0·590	0·098	0·087	0·582	-0·068	0·003	-0·022	0·631	-0·061	0·186	-0·291	0·317	0·003	0·229
Waist circumference (cm)	1·637	0·155	-0·122	0·811	-0·146	0·043	-0·040	0·784	-0·039	0·794	-1·751	0·065	0·065	0·105
Total fat mass (kg)	1·318	0·100	0·161	0·650	-0·166	0·001	-0·093	0·361	-0·085	0·413	-0·611	0·348	0·002	0·245
Android fat mass (kg)	-0·176	0·645	0·097	0·569	0·052	0·030	0·010	0·843	0·051	0·307	0·131	0·677	0·128	0·072
Total cholesterol (mmol/L)	0·105	0·695	0·070	0·560	-0·018	0·277	-0·024	0·496	-0·006	0·856	0·063	0·784	0·826	-0·060
HDL-c (mmol/L)	-0·048	0·425	0·005	0·859	-0·001	0·771	-0·009	0·286	-0·003	0·726	0·067	0·199	0·797	-0·055
LDL-c (mmol/L)	-0·254	0·314	-0·039	0·726	0·021	0·176	-0·003	0·921	-0·017	0·605	0·208	0·336	0·554	-0·019
TG (mmol/L)	0·084	0·674	0·018	0·840	-0·022	0·078	0·019	0·472	0·004	0·864	-0·042	0·808	0·591	-0·024
Glucose (mmol/L)	0·317	0·428	0·008	0·966	-0·019	0·440	-0·043	0·408	-0·033	0·529	0·039	0·909	0·729	-0·045
Uric acid (mg/dL)	0·270	0·309	0·080	0·497	0·005	0·777	-0·042	0·232	-0·030	0·389	-0·383	0·096	0·330	0·019
Creatinine (mg/dL)	0·134	0·002	-0·015	0·438	0·001	0·567	1E-04	0·986	-0·006	0·303	-0·090	0·017	0·022	0·161
ALT (U/L)	4·454	0·091	-1·792	0·128	0·125	0·437	-0·158	0·643	-0·460	0·181	-1·676	0·454	0·138	0·071
AST (U/L)	-0·732	0·719	-1·182	0·198	0·034	0·786	-0·214	0·423	-0·568	0·037	1·537	0·381	0·093	0·091

Abbreviations: BMI, body mass index; HDL-c, high density lipoprotein-cholesterol; LDL-c, low density lipoprotein-cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 5. Fibre consumption effects on anthropometric and body composition parameters.

Abbreviations: BMI, body mass index; WHR, waist to hip ratio; P†, comparison between dietary groups

	Fibre ≤ 18·3g (n=30)					Fibre > 18·3g (n=29)					Difference
	Before self-control period		After self-control period		P	Before self-control period		After self-control period		P	P†
	Mean	SE	Mean	SE		Mean	SE	Mean	SE		
Weight (kg)	94·6	2·9	94·8	3·0	0·820	95·2	3·3	92·5	3·6	0·001	0·008
BMI (kg/m^2)	33·2	0·8	33·2	0·8	0·828	33·2	0·8	32·3	0·9	0·006	0·035
Waist circumference (cm)	105·3	2·1	104·9	2·1	0·531	107·7	2·2	105·5	2·6	0·010	0·080
WHR	0·95	0·02	0·95	0·02	0·577	0·97	0·02	0·96	0·02	0·057	0·194
Fat Mass (kg)	36·8	1·7	36·2	1·7	0·111	36·9	1·7	34·5	1·9	0·002	0·092
Android Fat Mass (kg)	3·9	0·2	4·2	0·3	0·455	4·2	0·2	3·8	0·2	0·001	0·008

Table 6. Body weight reduction effects on biochemical parameters.

Abbreviations: HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; TG, triacilglycerides; NEFA; non-esterified fatty acids;

	Weight loss ≤ 400g (n=33)					Weight loss > 400g (n=32)					Difference
	Before self-control period		After self-control period		P	Before self-control period		After self-control period		P	P†
	Mean	SE	Mean	SE		Mean	SE	Mean	SE		
Total Cholesterol (mmol/L)	5·26	0·20	5·70	0·18	0·012	4·94	0·17	5·59	0·19	< 0·001	0·293
HDL-c (mmol/L)	1·05	0·04	1·22	0·04	< 0·001	1·09	0·04	1·24	0·05	0·001	0·698
LDL-c (mmol/L)	3·39	0·17	4·48	0·17	< 0·001	3·19	0·14	4·35	0·17	< 0·001	0·468
LDL-c/Apo B	1·61	0·10	1·92	0·03	0·005	1·50	0·04	1·90	0·03	< 0·001	0·092
TG (mmol/L)	1·77	0·16	2·01	0·21	0·125	1·44	0·11	1·33	0·10	0·150	0·055
NEFA (mmol/L)	0·50	0·03	0·48	0·03	0·629	0·52	0·05	0·47	0·04	0·247	0·783
Glucose (mmol/L)	6·39	0·19	7·12	0·33	0·012	5·88	0·21	5·67	0·12	0·392	0·005
Insulin (μU/mL)	10·45	1·37	11·72	1·47	0·121	8·02	0·82	6·06	0·67	0·002	0·001
HOMA-IR	3·11	0·46	3·84	0·54	0·027	2·23	0·30	1·56	0·18	0·004	< 0·001
HCIS (μmol/L)	15·12	0·59	16·96	1·14	0·128	16·51	0·76	16·23	0·94	0·757	0·144
Uric Acid (mg/dL)	5·83	0·16	6·14	0·23	0·047	5·84	0·21	5·96	0·22	0·549	0·657
Total Proteins (mg/dL)	71·84	0·87	74·91	1·02	0·001	70·38	0·68	74·53	1·09	< 0·001	0·299
Creatinine (mg/dL)	0·97	0·03	0·99	0·04	0·260	0·99	0·03	0·98	0·03	0·697	0·676
ALT (U/L)	28·22	1·45	27·73	1·52	0·777	30·35	2·77	21·69	1·33	0·004	0·037
AST (U/L)	21·00	1·05	22·61	0·90	0·169	23·00	1·17	20·39	1·02	0·067	0·024

HOMA-IR, homeostasis model assessment of insulin resistance; HCIS, homocysteine; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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