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The Mediterranean diet pattern with intermittent semi-fasting may facilitate weight loss: randomised controlled trial

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Abstract.
BACKGROUND: Alterante-day fasting regimens have been suggested as a possible approach for calorie restriction and weight loss. The aim was to compare the effect of a 6-week weight loss regimen based on the Mediterranean diet versus the Mediterranean diet with 5-day semi-fast, in achieving weight loss in overweight or obese people.
METHOD: Randomized, controlled, prospective, semi-clinical trial of 44 participantes, aged 30 to 65 years, with overweight type II (BMI >27) or obesity (BMI >30). Subjects were distributed by randomization in group 1 (Mediterranean diet + semi-fast) and group 2 (standard hypocaloric Mediterranean diet). Anthropometric measurements were taken and eating habits of the participants were recorded.
RESULTS: No statistically significant differences were found when comparing anthropometric measurements between groups. Similar changes were observed between the two groups. However, when analysing anthropometric measurements inter-group, statistically significant differences (p<0.05) were obtained within each group.
CONCLUSION: The low calorie Mediterranean diet and the low calorie Mediterranean diet + semi-fast diet used in this study appear to be equally as effective in decreasing body weight, fat mass, visceral fat mass and waist circumference. However, semi-fast regimens may be superior to daily restriction regimens in facilitating weight loss. These findings add to the growing body of evidence showing that altenate-day fasting regimens may be implemented as another viable option for weight loss in overweight and obese populations.

Keywords: Fasting, Mediterranean diet, fat mass, body mass index, obesity.

1. Introduction

Overweight and obesity are major global health concerns owing to the predominance of sedentary lifestyles and the abundance of energy-dense foods (1). The worldwide prevalence of obesity more than doubled between 1980 and 2014. In 2014, more than 1.9 billion (39%) adults aged 18 years and older (38% of men and 40% of women) were overweight. Of these over 600 million (13%) adults (11% of men and 15% of women) were obese (2).

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A common health consequence of overweight and obesity, derived from raised BMI, is a major risk factor for noncommunicable diseases such as cardiovascular diseases, diabetes, musculoskeletal disorders and some cancers (2). As the prevalence of overweight and obesity increases, so does the prevalence of obesity-related disorders (1).

Overweight and obesity, as well as their related noncommunicable diseases, are largely preventable. Supportive environments and communities are fundamental in shaping people's choices, by making the choice of healthier foods and regular physical activity the easiest choice (3).

Reducing body weight by decreasing energy intake has been shown to improve biomarkers for disease risk such as plasma lipid concentrations (4), blood pressure (5), C-reactive protein (6) and insulin and glucose levels (7).

With the increasing obesity epidemic comes the search for effective dietary approaches for calorie restriction and weight loss (3). The major form of dietary restriction currently implemented is daily calorie restriction (decreasing energy intake by 15–60% of baseline needs every day) (1). Intermittent energy restriction has been suggested as a possible alternative approach. Alterante-day fasting regimens consist of a "feed day" (ad libitum food intake for 24 h) alternated with a "fast day" (complete fast for 24 h). Modified alterante-day fasting regimens that allow for the consumption of 20–25% of energy needs on the fast day, as is our study case, have also been implemented (8). Intermittent fasting may be easier to follow, as restriction is only required *every other day*, rather than *every day* as with calorie restriction (8), and potentially has greater positive metabolic effects, as it includes repeated spells of more profound energy restriction than achieved with dietary control, albeit for shorter periods (3).

A short-term risk linked to the weight loss therapy per se may be outweighed by the longer-term health benefits of the weight loss (3). Therefore, fasting should be considered in the modern day context of the range of therapies now available for weight loss. The risks of obesity and obesity-related conditions are now better documented, and thus treatments with known but low risks may need to be re-evaluated.

The aim of this study was to compare the possible effect of a 6-week regimen based on the Mediterranean diet, including 5 days of semi-fast, versus the Mediterranean diet itself, to achieve weight loss in persons with overweight type II (BMI >27) or obesity (BMI >30).

2. Methodology

2.1. Study type

Randomized, controlled, prospective, semi-clinical trial.

2.2. Study population:

A sample of 50 participants, of both sexes, aged 30 to 65 years, was selected from the Community of Madrid in 2017.

Inclusion criteria were as follows: subjects aged 30 to 65 years, of both sexes, with no severe diseases (cronic, autoimmune or neurological diseases, eating disorder, cancer, hepatitis, chronic obstructive pulmonary disease or disabilities) and no bariatric surgery, with overweight type II (BMI >27-30) or obesity (BMI >30-40), who agreed to participate voluntarily, following the diet, and filled in the informed consent. Participants who did not meet inclusion criteria (n=2), who did not complete all questionnaires (n=3), who did not follow the diet as stated (n=3), who were under medication or were absent on the control visit were excluded. Hence a total of 42 participants (23.8% men and 76.2% women) were finally included.

We followed the Declaration of Helsinki principles and respected the rights of all participants. They all signed an informed consent to participate in the study.

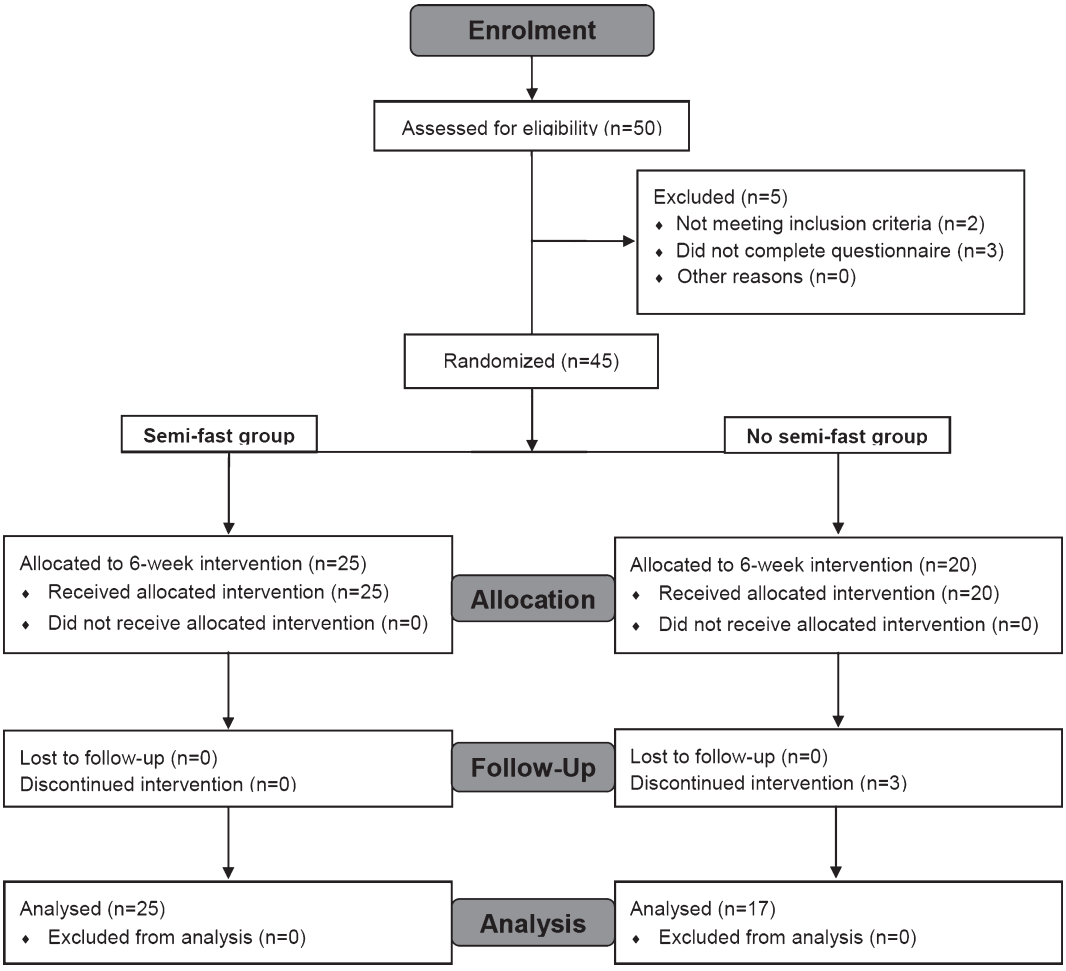

Fig. 1. Flow diagram of study design and methodology.

This research project was approved by the Ethical Committee of Clinical Research of Hospital Universitario Severo Ochoa, Madrid (Spain), in December 2016.

2.3. Study design:

The study population consisted of 42 subjects (n = 25 in group 1 [G1] and n = 17 in group 2 [G2]), who were distributed by randomization (Figure 1). G1 was the study group (semi-fast) and G2 was the control group (standard hypocaloric Mediterranean diet).

The sample size was calculated by comparison of means: $n = 2 * (1.645 + 1.282)^2 * 2.29^2 / 2^2 = 22.46$ subjects per group. The dropout rate was estimated at 10%, so 50 subjects were recruited in total (25 subjects per group). A 95% confidence interval and a statistical power of 90% were used.

A deviation of ±2.29 kg for a habitual weight loss in the Spanish obese population in a slimming program with a hypocaloric Mediterranean diet (500 kcal restriction), with a mean loss of 2–4 kg/month, were taken into account. A loss of 3 kg of loss was estimated in the Mediterranean diet group and 5 kg in the semi-fast group, assuming a difference of 2 kg extra in the study group.

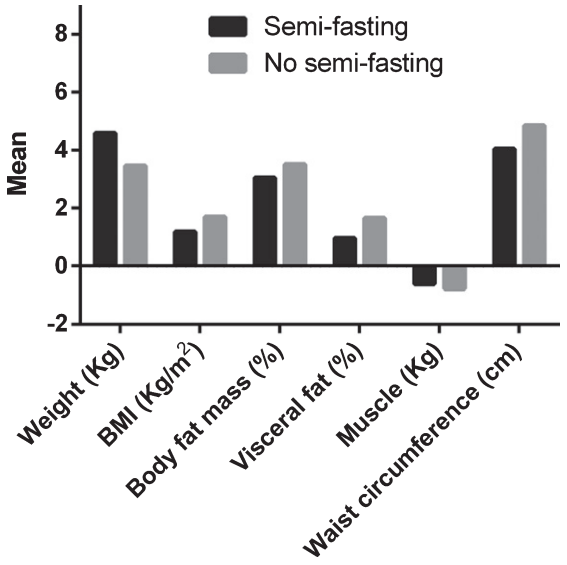

Fig. 2. Mean's comparison of anthropometry measurements between groups.

2.4. Study factors:

Participants' anthropometric measurements were taken. Participants' eating habits were also assessed and analysed for the adjustment of dietary guidelines at baseline (results not shown), with the PREDIMED questionnaire (9) and NHANES Food Frecuency Questionnaire (10).

Anthropometric measurements: The anthropometric measurements were taken first thing in the morning and included: height, weight, BMI, fat mass, visceral fat, muscle mass and waist circumference. Height was measured with the subjects standing barefoot, according to the WHO (11) protocol, with a SECA mobile stadiometer with a 1 mm accuracy. Weight was measured with a digital bioimpedance analyser TANITA model BP-601, ranging from 0.1 to 150 kg. The bioimpedance was also used to measure body fat mass, visceral fat and muscle mass. Quetelet index, based on weight and height, was used to calculate BMI (12). BMI >27-30 was considered overweight type II and BMI >30-40 was considered obese. Waist circumference was measured around the midpoint between the lowest rib and the iliac crest, with non-extensible tape measures (range 0-150 cm).

Dietary assessment: G1 (study group) followed the standard hypocaloric Mediterranean Diet for 6 weeks including 5 days of semi-fast. G2 (control group) followed the same standard hypocaloric Mediterranean Diet with no period of caloric restriction.

Basal and total metabolic expenditure were calculated for every subject, and their diet was adjusted to a caloric restriction of 500 kcal, deducted from the estimated individual resting energy expenditure. Diets were established by trained dieticians. There was an adjustment of guidelines during two previous weeks, so that all participants acquired similar habits from baseline.

The general guidelines for implementing the Mediterranean diet include the following recommendations: a) the abundant use of olive oil for cooking and dressing dishes; b) consumption of 2 servings of vegetables per day (at least one of them as fresh vegetables in a salad), not counting garnishes; c) 2-3 servings per day of fresh fruit (except natural juices); d) 3 weekly servings of legums; e) 3 servings per week of fish or shellfish (at least a portion of oily fish); f) 1 weekly portion of nuts or seeds; g) select white meat (poultry without skin or rabbit) instead of red meat or processed meats (hamburgers, sausages); h) cook regularly (at least twice a week) with tomato, garlic and onion, adding or not other aromatic herbs; pasta, rice and other dishes with tomato, garlic and onion adding or not herbs. There are also recommendations for eliminating or limiting

consumption of cream, butter, margarine, sausage, pate, duck, sugar and / or carbonated beverages, pastries, industrial bakery products (such as cakes, bagels, or cookies), industrial desserts (flans, custards), chips, and pre-cooked cakes and pastries. Dietitians insist that two main meals should be eaten per day (sitting at a table for more than 20 minutes). For regular drinkers, the advice is to use wine as the main source of alcohol (maximum 300 ml, 1-3 glasses of wine a day). If wine intake was customary, it is recommended to take one glass of wine a day (larger for men, 150 ml, than for women, 100 ml) during meals. Consumption Ad libitum is allowed for the following foods: nuts (raw and unsalted), eggs, fish (daily intake recommended), seafood, low fat cheese, chocolate (only dark chocolate, with more than 50% cocoa), and whole grain cereals. Limited consumption (1 portion per week) of ham, red meat (after removing all visible fat), and cured cheeses are recommended.

Semi-fast consisted in a 5 day-diet of 600-700 kcal, distributed in 5 crushed or liquid doses: 700 ml of juice to be distributed throughout breakfast, mid-morning and afternoon snack, 400 ml of puree and 500 ml of gazpacho to distribute between lunch and dinner. Water could be added to dilute juices, puree and gazpacho and increase the dose.

Organic fruits and vegetables, zucchini, leek, aubergine, carrot, pineapple, papaya, orange and packaged gazpacho, were delivered by BioSabor in boxes specially prepared for the study and with the corresponding instructions. The main recommendations were to ingest only the food supplied made puree and juice and add spices to taste, moderate salt and olive oil.

Two previous days of adaptation and two days of exit from the semi-fast were included in the schedule. The two previous days of adaptation consisted in: a) 1 whole-yogurt with chopped fruit and oat for breakfast, b) 300 ml of multifruit juice for mid-morning, c) salad with white fish and gazpacho for lunch, d) 300 ml of multifruit juice and 5 nuts for afternoon snack and e) meat or fish with boiled vegetables for dinner. The two days of exit from the semi-fast contained: a) 1 yogurt and 4 plums or any other fuit for breakfast, b) multifruit juice and yogurt or cooked ham for mid-morning, c) steamed vegetables with white fish and gazpacho for lunch, d) multifruit juice or chopped fruit for afternoon snack, and e) 1 avocado with chopped tomato dressed with olive oil, garlic, salt and lemon, and a French omelette for dinner (day 1); steamed vegetables with white fish (day 2).

Work schedule: all participants signed informed consent, filled in food habit questionnaires, and anthropometric measures taken at the first visit. Participants were supervised at 3 weeks (diet control and adherence to treatment survey). At this point, G1 participants were indicated how to follow the semi-fast diet during week 3 and 4. The final visit, after 6 weeks of intervention, served to take the final anthropometric measures.

2.5. Statistical analysis

The statistical analysis entailed descriptive analyses, presenting the results in means, standard deviation and percentages. We used parametric statistical tests such as Student's t-test to analyse the differences between the means in two groups of quantitative variables and a Chi-square test for non-parametric qualitative variables. A value of $p<0.05$ was considered a significant difference. Analysis of the data collected was processed with system SPSS® (version 20).

3. Results

We evaluated 42 participants aged 30 to 65 years, 10 (23.8%) of the male gender and 32 (76.2%) of the feminine. The baseline characteristics of participants are summarized in Table 1.

In the population studied, BMI showed that 71.4% (n=30) were obese and 28.6% (n=12) were overweight type II.

Changes between baseline and final anthropometric measures were observed (Figure 2), although they were not statistically significant different between both groups (MD and MD with 5-day semi-fast) (Table 2). This is especially relevant from the point of view of the meaning obtained.

Table 1
Demographic data of the sample.

		Semi-fast group (n=25)		No semi-fast group (n=17)		p-value
Sex (%)	Men	28.0		17.6		0.452
	Women	72.0		82.4		
Physical exercise (%)	No	20.0		47.1		0.065
	Yes	80.0		52.9		
		Mean	SD	Mean	SD	
Age (years)		46.32	8.03	47.88	7.67	0.532
Height (m)		1.67	0.09	1.66	0.08	0.674
Weight (kg)		92.21	13.82	97.99	18.05	0.247
BMI (kg/m^2)		32.83	3.73	35.92	5.32	0.035
Body fat mass (%)		40.76	6.61	44.51	6.40	0.075
Visceral fat (%)		11.96	3.77	13.12	4.00	0.346
Muscle (kg)		51.81	10.02	51.47	11.16	0.919
Waist circumference (cm)		106.24	11.89	110.49	14.17	0.299
Exercise (h/week)		4.54	3.33	4.13	3.39	0.785

Note. SD: standard deviation.

For example subjects had lost 13.1 kg and 13.8 kg, respectively, in 6 weeks, there would not have been significant differences between groups, not because it is not a big change, but because the change between the two groups is very similar. However, when analyzing each group separately, we observed statistically significant differences in anthropometric values (Table 2).

4. Discussion

Six human studies (8,13–17) to date have examined the effect of intermittent calorie restriction on weight reduction. Findings from these trials reveal that intermittent calorie restriction is able to produce significant declines in body weight after very short trial durations. More specifically, after only 2 and 3 weeks of diet, overweight men and women lost 3% and 4%, respectively, of their initial body weight (14,15). In our study, subjects lost in average 4.8% in G1 and 3.5% in G2 of their baseline body weight. Our results were in harmony with those in the literature, although our intervention period doubled that in previous trials.

Body composition changes were only assessed in three of the intermittent calorie restriction trials included in this review (8,15,17). Short-term trials (4 to 12 weeks) of intermittent calorie restriction decreased fat mass by 11–16%, and fat free mass by 1–4% from baseline (8,17). Our sample also showed a decreased of their initial body fat mass, 7.3% in G1 and 8.5% in G2, even though the loss was less pronounced than in trials mencioned above. This could be due to the semi-fast intervention instead of a complete fast for 24 h. To date, there are no moderate-term trials (13 to 24 weeks) of intermittent calorie restriction, so no comparisons between diets could be made for longer intervention periods.

Two trials (8,17) to date have examined the effects of intermittent calorie restriction on regional fat distribution. After 8 to 12 weeks of treatment, visceral fat mass was reduced by 4–10% from baseline. These decreases in visceral fat were positively associated with body weight loss. For instance, the most potent reduction in visceral fat mass (10%) was attained in the trial that achieved the greatest amount of weight loss (8%) (17), whereas the smallest reduction in visceral fat (4%) was noted for the study with the least amount of weight loss (6%) (8). In our case, the average loss of visceral fat mass was 11.7%, with similar decrease in both groups. On the contrary

Table 2
Differences between groups in baseline and final anthropometry measurements

	Semi-fast group (n = 25)							No semi-fast group (n=17)							p-value
	Baseline		Final		Difference		p-value	Baseline		Final		Difference		p-value	
	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	Mean	SD		
Weight (kg)	94.81	16.30	90.37	15.68	4.59	2.38	<0.001	97.99	18.05	94.79	18.15	3.46	2.21	<0.001	0.130
BMI (kg/m^2)	33.91	5.30	32.31	5.12	1.29	0.71	<0.001	35.92	5.32	34.76	5.24	1.69	0.96	<0.001	0.138
Body fat mass (%)	41.82	7.41	38.27	8.07	3.05	1.48	<0.001	44.51	6.40	41.74	7.18	3.79	1.57	<0.001	0.140
Visceral fat (%)	12.37	3.91	11.00	3.90	1.42	0.83	<0.001	13.12	4.00	12.12	3.85	1.56	1.09	<0.001	0.634
Muscle (kg)	52.00	9.71	52.81	9.88	-0.62	1.31	0.021	51.47	11.16	51.96	11.85	-0.79	1.17	0.016	0.669
Waist circumference (cm)	107.67	12.70	102.62	13.07	4.2	1.75	<0.001	110.49	14.17	106.94	14.32	4.84	2.49	<0.001	0.341

Note. BMI: body mass index; SD: standard deviation.

to the evidence above, this decrease was not positively associated with body weight loss, as G2 diminished a higher visceral fat procentage (11.9%) than G1 (11.5%) while having a lower amount of weight loss.

In viewof these similar effects on body weight, body and visceral fat mass, semi-fast diets may be considered a suitable alternative to calorie restriction to help overweight and obese individuals lose weight.

It should be noted that of the 67 subjects initially recruited to partake in the study, some individuals dropped out due to inability to comply with the fast day diet protocol. Thus, on the basis of these findings, it is possible that this dietary restriction protocol may not be well tolerated by everyone of the obese population.

It is also worth noting that at the conclusion of the study, when food directives are no longer provided, the individual generally returns to their baseline food intake pattern (18). It would be ideal if dietary counseling is provided to the participant at the end of the study to aid the subject in maintaining his or her newly acquired healthy eating regimen, and being able to achieve a stable, healthy rate of weight loss even during periods of self-implementation.

It must also be noted, however, that the degree of weight loss achieved by alternate day fasting may not be sustainable long term. Whether or not obese individuals are able to adhere to alternate day fasting over the long term and experience sustained weight loss will be an important focus of future research.

5. Conclusion

Dietary restriction is an effective strategy for weight loss in obese individuals, although it remains unknown whether intermittent fasting produces superior changes in body weight and body composition when compared to daily calorie restriction.

Fasting is assumed to be a relative 'quick fix' to achieve a substantial weight loss over a period of a few weeks, and therefore may be a useful tool for weight loss.

It is necessary to further investigate solutions and new protocols that help the scientific and medical community to change the numbers of overweight and obesity.

Limitations: The major limitation of this study was the sample size, which limited us from being able to extrapolate the results to the Spanish population. Due to the higher costs of a more sophisticated analysis and a bigger cohort, we opted for a smaller, humble research. In addition, the use of the bioimpedance by TANITA device does not represent a gold standard for the definition of fat mass. Satiety levels of the participants during the study were not assessed. Additional future research is necessary to further elucidate all aspects.

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Transparency Declaration: The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with CONSORT guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned (Ethical Committee of Clinical Research of Hospital Universitario Severo Ochoa, Madrid (Spain)) have been explained.

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