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Applied nutritional investigation

Acute effects of time-restricted feeding in low-income women with obesity placed on hypoenergetic diets: Randomized trial

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ABSTRACT

Objective: The aim of this study was to evaluate the acute effects of time-restricted feeding in obese women living in social vulnerability who were placed on diets with the same energy deficit.
Methods: Fifty-eight obese women (19–44 y of age) were randomized to a group with a hypoenergetic diet and 12 h of fasting daily or to a group with only a hypoenergetic diet for 21 d, with body weight and waist circumference monitoring up to 81 d of intervention. The determination of the individual's energy content of the diets was based on their resting metabolic rate (by indirect calorimetry) and physical activity level (by triaxial accelerometers). Body composition, temperature, blood pressure, appetite, adhesion difficulty, thyroid axis hormones, leptin, glucose concentration, and insulin were measured before and after 21 d of intervention. A mixed analysis of variance test was performed.
Results: The women had a mean age of 31 y and mean body mass index of 33 kg/m^2. Significant interaction between group × time was observed only in axillary temperature (0.44°C; 95% confidence interval [CI], 0.17–0.74°C; $P < 0.01$), which increased in the experimental group and in body fat (−0.75%; 95% CI, −1.43% to −0.07%; $P = 0.02$) decreased in the experimental group. Also, there was a significant decrease in waist circumference in the time-restricted feeding group after 81 d. There were no differences in hormonal profile, resting metabolic rate, reported appetite, or adherence difficulty.
Conclusion: Time-restricted feeding may be considered an alternative strategy for treating obesity in socially vulnerable women.

Introduction

Obesity is a global public health problem, and by estimates, most of the world's population lives in places where obesity-related causes kill more frequently than malnutrition [1]. In Brazil, the population with the highest prevalence of obesity in the country are women with low levels of schooling. Their obesity prevalence is 27.8%, which is considerably high when compared with the global obesity prevalence; it is only 14.4% in women in the highest stratum of schooling [2,3].

It is a consensus that negative energy balance is an adequate strategy to promote weight loss [4]. However, the most significant limitation of the success of any dietary intervention involves adherence to treatment by the patient, which drives the development of efficient and straightforward dietary strategies [5]. This development is even more necessary in low-income individuals who commonly present a monotonous food consumption pattern, with high intake of foods with a high glycemic index and lipid content, as they

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are usually the lowest-cost foods and consequently more accessible to this population [6]. Thus, interventions that require the acquisition of foodstuffs different from those commonly obtained by this population, implying higher costs, may constitute a limiting factor for adherence to the dietary treatment [7].

One strategy that has gained considerable scientific and popular appeal is intermittent fasting (IF), which can assume many forms, including the one that promotes daily fasting periods longer than the regular overnight fasting, starting from a 12-h fasting period per day, referred to as the time-restricted feeding (TRF) [8,9]. Restricting the period of food intake to a few hours without an explicit attempt to decrease energy intake triggers the fasting physiology [9], adaptive mechanism of the human body developed in the face of periods of food shortage and prolonged fasting and is determinant for species survival [8].

This mechanism would be driven by the metabolic changes required to meet energy demands, in which hepatic glycogen stores are depleted after 10 h of fasting, promoting β-oxidation of fatty acids in adipocytes and production of acetyl-coenzyme A and ketones in hepatocytes for adenosine triphosphate production [8]. The levels of adiponectin and 5-AMP-activated protein kinase, which is inhibited by feedback, regulates this process [10]. In humans, the effects result in resistance to stress, lipolysis, and autophagy stimulation [8]. If performed frequently, daily or alternate periodic fasting may exert pleiotropic effects and become an effective treatment strategy for chronic diseases as well [9].

It is believed that the effects of IF depend not only on weight loss but also on the period of food consumption [11]. However, there are not enough studies involving TRF, and clinical trials usually do not present a control group with identical energy restriction to that of the experimental group, which does not allow to affirm if the effects observed are due to the differences in energy intake or to the fasting itself. Additionally, the results are even scarcer in obese individuals, probably because of the idea that the hunger sensation, common in different types of IF, would be a limitation for using such intervention in these individuals [12]. Considering the studies investigating the effects of TRF [11,13–19], few assessed thyroid hormones [19] and energy expenditure [17–19] on humans, factors that may be mediators of the supposed beneficial effects of IF.

Thus, the present study aims to evaluate the acute effects of a TRF regimen in obese women in social vulnerability submitted to diets with the same energy deficit.

Methods

The protocol of this study was previously published in the Brazilian Registry of Clinical Trials. There was no financial compensation to participate in the study. This paper is reported following the Consolidated Standards of Reporting Trials (CONSORT) [20]. This study was approved by the Ethics in Research Committee of the Federal University of Alagoas and was therefore conducted in accordance with the ethical standards set out in the 1964 Helsinki Declaration and subsequent amendments. All participants provided written informed consent before their inclusion.

Study design and participants

This was a 21-d randomized, parallel, controlled trial with two research groups. Owing to the nature of the intervention, it was neither double-blind nor placebo-controlled.

The research was carried out at the obesity outpatient clinic of the Centro de Recuperação e Educação Nutricional (CREN), linked to the Universidade Federal de Alagoas. CREN is a center for the treatment of undernourished children in a day-hospital system. It is in the seventh administrative region of the municipality of Maceió-AL, a region of high social vulnerability.

Sampling was conducted in a non-probabilistic way, by convenience, and recruitment was done through announcements in the community, direct invitations to women attending CREN activities, or directly to those women who went to CREN on the days of screening for nutritional care.

Women (19–44 y of age) living in social vulnerability, classified as economic class "C" or "D–E," as determined by the Brazilian Economic Classification Criterion (CCEB) [21], were included. The CCEB is an instrument consisting of questions about assets, household employees, housing data, head of household instruction, and access to piped water and paved streets. Each item yields a different score. According to the achieved score, individuals are placed into one of six classes that vary from "A," the highest one, to "D–E," the lowest.

Obesity was defined by the presence of two of the following three criteria:

1. Body mass index (BMI) $\geq$30 and <45 kg/m^2
2. Waist circumference (WC) $\geq$88 cm
3. Body fat percentage $\geq$35% [22] determined by bioimpedance.

Only women who wished to lose weight but who reported to be weight stable for $\geq$1 mo were included. Exclusions included women with chronic use of medicines (e.g., antidiabetic, antihypertensive, antiretroviral, immunosuppressive, antidepressants, thyroid hormones, and diet pills); menopausal, pregnant, or nursing women; those engaged in shift work; or women who have already undergone a surgical intervention for weight loss. Participants who became pregnant during follow-up, those who needed to perform any surgical procedure, or those who requested a decline in the study were excluded.

Intervention

Two interventions were compared: one composed of a hypoenergetic diet (HD) with TRF (HD + TRF) and another composed of a diet with the same energy restriction but without TRF. In the TRF diet, women were instructed to eat only during a 12-h period and fasted during the other 12 h, from the time of the last meal, determined by the participant. The determination of the energy content of the diets was individualized; that is, each woman had her estimated energy requirements based on her total energy expenditure (TEE). Resting metabolic rate (RMR) was estimated by indirect calorimetry through a gas analyzer (Quark, Cosmed, Rome, Italy), and the physical activity level (PAL) was estimated by triaxial accelerometers (ActivPAL, Glasgow, UK), which yield an estimated metabolic equivalent of task (MET) for each participant. To determine the TEE, the factorial approach (i.e., TEE = RMR × PAL) [23] was used, and 500 to 1000 kcal were subtracted to determine the energy content of the proposed HD plan for each woman. This deficit is proposed by the Brazilian obesity guideline [24] and it is aimed at ensuring a proportional decrease in the total energy value of the diet according to the participant's measured energy expenditure. For all participants, dietary total energy values could not be below their RMR. As well, the macronutrient distribution was distributed as 45% to 55% carbohydrates, 25% to 30% lipids, and 15% to 25% proteins [24]. Additionally, for the construction of the proposed meal plan, information on food consumption was collected through three 24-h dietary recalls, two for weekdays and one for a weekend day, to promote qualitative and quantitative dietary changes, but without implying higher costs with the acquisition of foodstuffs that did not correspond to the dietary pattern of this population, which could lead to non-adherence. Thus, the only difference between the investigated groups was the restriction or not of the feeding period. The women had individual weekly consultations, and during the consultations, a dietitian made the necessary adjustments in the diet to maintain weight loss during the 21-d period and fortnightly until day 81.

Outcomes

Outcomes were measured before and after 21 d of intervention, with the exception of body weight and WC, which were measured up to 81 d. For all measurements women fasted for 10 h, with preparation by the participants that included abstinence from alcoholic beverages and physical activity in the previous 24 h and emptying of the bladder 30 min before the procedures.

Vital signs

Axillary temperature was measured by a clinical digital thermometer (Techline, São Paulo, Brazil). Systolic blood pressure, diastolic blood pressure, and heart rate were measured using a tensiometer (HEM-4030, Omron, Japan), before performing indirect calorimetry and electrical bioimpedance tests.

Body composition

BMI was calculated and classified according to the World Health Organization [25]. WC was measured using an inelastic tape measure, in the largest perimeter between the last rib and the iliac crest [24]. Body fat was estimated from four-electrode electrical bioimpedance Sanny BI 1010 (Sanny, São Paulo, SP), with participants in a supine position, wearing light clothing, barefoot, and without metallic props, in the right hemicorp of the evaluated ones and four electrodes were fixed as proposed by Kyle et al. [26]. The data of resistance and reactance, obtained in the evaluation, were interpreted in the software Bio Tectronic Sanny version 1.2.2, defining the percentage of body fat.

Resting metabolic rate

A gas analyzer was used to estimate the RMR. Participants were taken by car to the place, and the collection took place in the morning (between 0700 and 0900), in a quiet environment, with low light and temperature between 22 and 26°C. Before each test session, the equipment was calibrated with gases at a concentration of 20.9% oxygen and 5% carbon dioxide, and a 3-L syringe with a secondary manometer adjustable between 40 and 60 psi. Before starting the test, axillary temperature, blood pressure levels, and heart rate were measured to avoid calorimetric measurements in individuals with signs of hyperthermia (>37.5 C) or tachycardia (>100 bpm). Participants were asked to wear the equipment's silicone mask so that inspired oxygen and expired carbon dioxide volumes were counted for 15 min. The first 5 min of measurement were discarded to avoid discrepancies owing to the location and use of the silicone mask, and data were collected every 60 s [27]. Oxygen and carbon dioxide volumes collected in L/min were used to estimate the RMR in the Weir equation.

Hunger

Hunger was measured using a visual analog scale [28] where 0 meant *I am not hungry* and 10 meant *I am starving*; the participants were instructed to mark at the point where their sense of hunger approached the referred extremity.

Adherence difficulty

The evaluation of the degree of difficulty in adhering to the proposed dietary plan was evaluated by a visual analog scale of 0 to 10 to predict difficulty, where 0 was classified as *very easy* and 10 as *very difficult*.

Biochemical tests

The blood levels of glucose, insulin, leptin, and thyroid hormones (thyroid-stimulating hormone [TSH], free T3, and free T4) were measured from blood samples collected by peripheral venous puncture in the left or right cubital fossa, withdrawing 20 mL of blood on average, and transferred for separator gel tube; the procedure was performed by qualified local laboratory accredited contracted as provider of such services. The GOD-trinder technique (Glucose-PP Analisa kit) was used for serum glucose levels, the immunoassay method enzyme-linked immunosorbent assay (Linco Research, St. Charles, MI, USA) was used for leptin, and the chemiluminescence method (Unissel Dxl 800 from Beckman Coulter) was used for insulin, TSH, free T3, and free T4 hormones. From the plasma levels of insulin and fasting glucose, the sensitivity to insulin was quantified by calculating the homeostatic model of insulin resistance (HOMA-IR) by the equation developed by Matthews et al. [29].

Complementary data

A triaxial accelerometer was used to measure the level of physical activity. The device was fixed in the frontal thigh of the participants, at the midpoint between the inguinal line and the upper edge of the patella. Two transparent and hypoallergenic dressings (VitaMedical, Minas Gerais, Brazil) were used to avoid the contact of the device with the participant's skin, keeping the device isolated. The women used the accelerometers for 3 d consecutively and were told not to remove it for any activity. Data captured by the device was transferred to ActivPAL3 version 7.2.32 software, which provides the intensity and duration of each activity performed by the individual. The system computes the periods in which the individual spent lying/sitting, standing, walking and running every 10th of a second, for the entire period in which the device was used, based on the acceleration of three-body axis: anteroposterior, lateral, and vertical. It provides the MET value for the entire period that individuals used the device by multiplying the MET value for each activity by the duration of the activity, based on default values for sitting/lying (1.25 MET), standing (1.40 MET), and stepping at 120 steps per minute (4 MET). For cadences that differ from 120 steps per minute, the following equation is used to calculate the MET estimate:

$$\text{MET.h} = (1.4 \times d) + (4 - -1.4) \times (c/120) \times d$$

where c is the cadence (steps per minute), and d is the duration of the activity (in hours) [30]. The MET value expresses the energy expenditure of physical activity as a multiple of RMR, regardless of the individuals' characteristics and type of activity. According to what is recommended by the Food and Agriculture Organization joint report (2001) [31], the total MET value is divided by the total amount of hours that the individual used the accelerometer, yielding the estimated MET.h, which is a proxy of the individual's PAL.

Sample size

Assuming a 5% α and 80% statistical power and that the difference in weight loss between interventions would be 1.5 ± 2 kg, 28 individuals per group were needed.

Randomization

Based on a random sequence of numbers generated using the RUNIF command of the software R v 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) [32], women were allocated to the group receiving the HD + TRF intervention or to the group receiving HD intervention. The random sequence was guarded by a researcher who had no initial contact with the participants to ensure the allocation concealment.

Statistical method

The normality assumption was verified by the Lilliefors' test and by the values of asymmetry and kurtosis. Variables that did not meet normality assumptions were log-transformed for analysis. For presentation, the geometric means of the log-transformed variables were back-transformed and shown in the tables. Data is presented as mean and 95% confidence interval (CI) for continuous variables and relative and absolute frequencies for categorical variables. A mixed analysis of variance (ANOVA) was conducted to verify if treatment effect existed over the intervention period, where the independent factor was the designated group (HD versus HD + TRF), and the dependent factor was the moment of measurement (before and after the intervention). Additionally, mixed analysis of covariance was performed to evaluate the intrasubject variation of the RMR adjusted by the body weight variation. A *t* test was performed for independent samples for the data collected only before or after the intervention. An α value of 5% was adopted. Intention-to-treat analyses were performed using the last observation carried forward method to minimize the risk for bias from follow-up losses. All analyses were conducted using the R software v 3.6.1 [32], with the "Rcmdr" [33] and "RcmdrPlugin.aRnova" [34] packages.

Results

Participants were recruited between July 2018 and January 2019. The mean age of participants was 31.03 y (95% CI, 28.20–33.87) and 31.80 y (95% CI, 29.25–34.36) in the HD and HD + TRF groups, respectively. The sample composition and dropouts are shown in Figure 1. The baseline characteristics of the participants are described in Table 1. The assigned dietary energy reduction was 651.85 kcal on average (95% CI, 583.88–719.81 kcal) for the HD group and 637.16 kcal (95% CI, 578.33–696.00 kcal) for the HD + TRF group, without difference between groups ($P = 0.73$). After 21 d of intervention, there were no significant changes in weight loss, hormonal profile, and RMR between groups, even in the analysis of covariance adjusting RMR by bodyweight variation ($P = 0.14$). Significant changes were observed only in axillary temperature (0.44°C; 95% CI, 0.17–0.74°C; $P < 0.01$), which increased in the experimental group and in the percentage of body fat (−0.75%; 95% CI, −1.43 to −0.07%; $P = 0.02$) which lowered in the experimental group compared with the control group, as presented in Table 2. For the 81-d analysis, the mean percentage weight loss was −0.97% (95% CI, −0.72% to −1.23%) in the HD group and −1.52% (95% CI, −1.25% to −1.80%) in the HD + TRF group, without significant interaction between group and time ($P = 0.14$; Fig. 2) and the mean WC change was −0.49% (95% CI, −0.01% to −0.98%) in the HD group and −2.2% (95% CI, −1.64% to −2.75%) in the HD + TRF group, with significant interaction between group and time ($P < 0.01$; Fig. 3).

Discussion

In the present study, at 21 d of follow-up, there was an increase in axillary temperature and a decrease in the percentage of body fat in women submitted to the HD + TRF intervention compared with those submitted only to HD. However, no significant change was observed in weight loss, thyroid hormone levels, insulin sensitivity, leptin, and RMR between groups after 21 d of TRF. In the analysis of follow-up data performed for 81 d after the

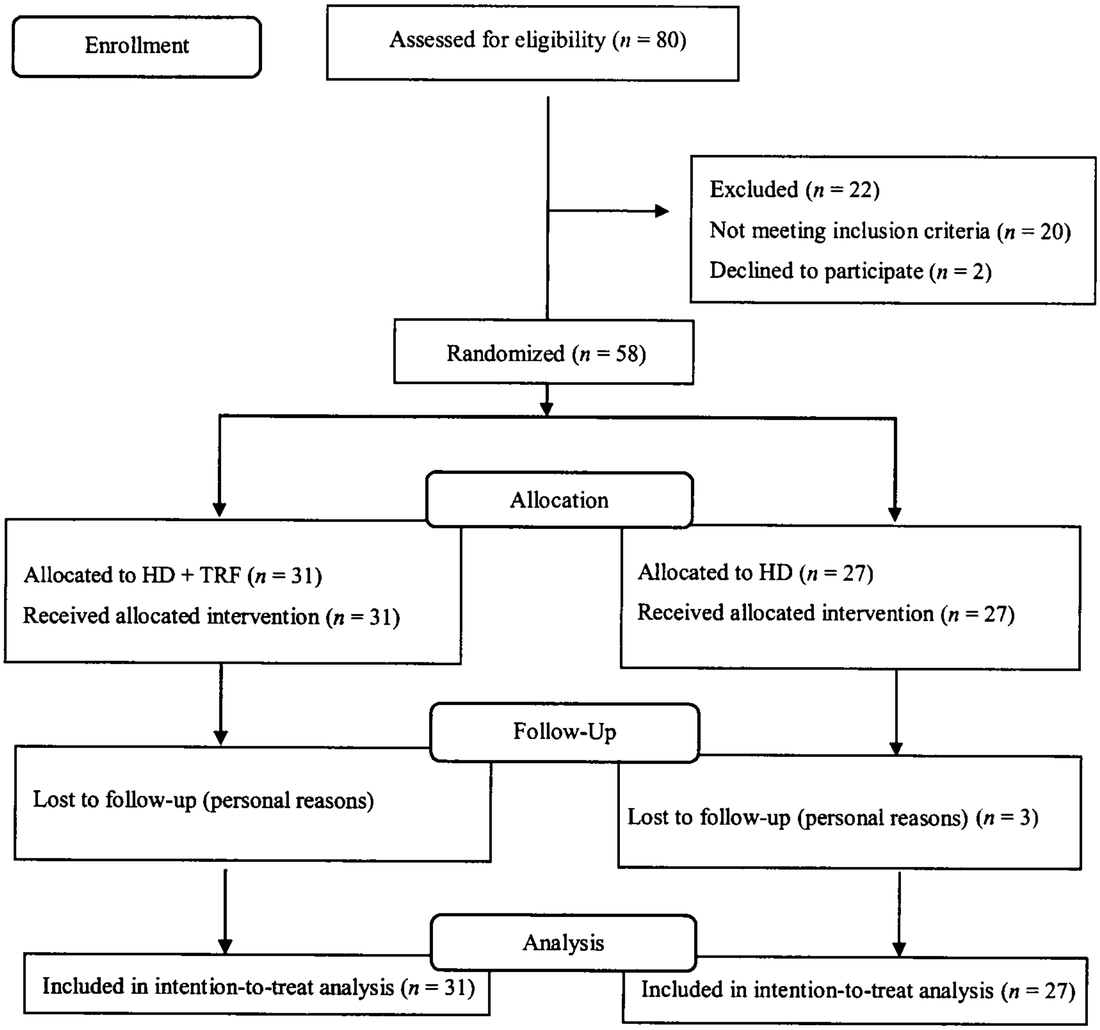

Fig. 1. Participant recruitment and study flow diagram. CI, confidence interval; HD, hypoenergetic eiet; TRF, time-restricted feeding; HD+TRF, hypoenergetic diet + time-restricted feeding.

intervention, we observed interactions between group and time for WC changes but not for weight loss.

Different from our findings, a greater weight loss in TRF intervention compared with control interventions had already been documented in several other studies involving individuals performing resistance training and overweight individuals". [13,14,19]. The small decrease in body weight observed in both groups, as well as the absence of weight loss difference between groups, may be due to the short intervention period and because no important changes in RMR were observed. However, the results of the present study are consistent with a trial involving 10-h TRF with overweight men and women, where no change was found in the percentage of weight loss either in the short-term (after 16 wk of intervention) or long-term (after 1 y of intervention) [14]. Additionally, the percentage of weight loss observed in the present study showed similar results to other studies with TRF ranging from 16 to 20 h during 8 wk, which resulted in a decrease of 1% to 3% of body weight [13,19] with trained men. Rynders et al. [36], in their narrative review, suggested that intermittent energy restriction paradigms, including TRF, produce equivalent weight loss when compared with continuous energy restriction, showing no differences between groups in weight or body fat loss [36].

Regarding the interaction between group × time for WC observed during 81 d of follow-up, our findings agree only with a German pilot study involving TRF as an intervention [37]. This study involved adult, primary care, male and female, eutrophic and overweight individuals, whose primary endpoint was the proportion of days participants attained the proposed fasting goal (≥15 h) of the total number of days recorded by each participant. The authors reported a significant reduction in mean WC of 5.26 cm, 3 mo after TRF intervention, although they also found differences in body weight, which differs from the present findings.

To our knowledge, only one study involving TRF reported body fat reduction; however, it consisted of a sample of resistance-trained men followed for 8 wk with 16-h dietary restriction [19]. In other investigations with individuals in TRF, no significant changes in body composition were found, and in those studies, the intervention group was not submitted to energy restriction in addition to TRF [13–15]. The purpose of nutritional interventions for weight loss is to promote the reduction of adipose tissue and, as far as possible, preserve fat-free mass to maintain functional capacity and to mitigate the decline of RMR, thus contributing to avoiding weight regain [38], although a recent study conducted with 54 obese adults undergoing a very low-energy diet, observed that changes in RMR do not predict long-term weight recovery

Table 1
Characteristics of the participants at the beginning of the intervention (n = 58)

Variables	HD (n = 27)		HD+TRF (n = 31)	
Sociodemographic	n	%	n	%
Has a biological child				
No	5	18.50	6	19.40
Yes	22	81.50	25	80.60
Uses alcohol				
Yes	10	37.00	14	45.20
No	17	63.00	17	54.80
Smokes				
Yes	2	7.40	4	12.90
No	25	92.60	27	87.10
	Mean	95% CI	Mean	95% CI
Anthropometric				
Weight (kg)	80.25	76.53–83.98	81.25	76.47–87.01
Height (m)	1.55	1.55–1.58	1.55	1.53–1.57
BMI (kg/m²)	33.12	31.68–34.56	33.53	32.00–35.50
WC (cm)	98.86	95.06–102.66	102.79	98.58–107.00
Vital signs				
Temperature (°C)	36.06	35.90–36.22	35.88	35.69–36.07
SBP (mm Hg)	124.03	119.57–128.50	127.10	121.18–133.02
DBP (mm Hg)	86.51	82.53–90.50	86.20	81.08–91.32
HR (bpm)	71.85	68.09–75.60	76.27	72.94–79.61
Body composition				
% body fat	43.55	41.69–45.41	44.41	42.33–46.49
Biochemical tests				
Glucose concentration (mg/dL)	78.37	74.75–81.98	79.74	75.43–83.04
Insulin (μUI/mL)*	13.11	10.43–16.48	12.73	10.85–14.94
HOMA-IR*	2.46	1.96–3.23	2.44	2.07–2.97
Leptin (ng/mL)*	37.58	30.61–55.32	32.08	27.00–43.37
TSH (μUI/mL)*	1.58	1.25–2.10	1.57	1.27–2.03
Free T3 (pg/mL)	2.74	2.53–2.95	2.93	2.74–3.12
Free T4 (ng/dL)	0.93	0.88–0.98	0.92	0.86–0.98
Indirect calorimetry				
RMR (kcal)	1 598.11	1478.94–1717.27	1 504.08	1399.99–1608.18
RQ	0.84	0.82–0.86	0.84	0.82–0.86
MET.h (24 h multiple of RMR)	1.45	1.42–1.47	1.43	1.41 –1.45
Hunger (Likert scale score)	4.48	3.36–5.59	5.00	3.94–5.78
Energy intake (kcal)	1 587.56	1322.27–1 852.84	1783.45	1529.30–2037.61
Carbohydrates (%)	53.07	50.13–56.00	52.18	49.12–55.24
Lipids (%)	27.37	24.84–29.89	27.21	25.10–29.32
Protein (%)	19.79	17.47– 22.10	20.87	18.54–23.20
TEE (kcal)	2326.46	2134.88–2518.04	2137.21	1990.41–2284.02

BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; HD, hypoenergetic diet; HR, heart rate; RMR, resting metabolic rate; RQ, respiratory quotient; SBP, systolic blood pressure; TEE, total expenditure energy; TRF, time-restricted feeding; TSH, thyroid stimulating hormone; WC, waist circumference
*Back-transformed (geometric means).

[39]. Although only the control group showed decreases in RMR and RMR adjusted by body weight values, no statistical differences were observed between groups, which is similar to that found in a randomized, crossover, isocaloric, controlled feeding trial, with overweight U.S. individuals undergoing TRF for 4 d [18].

Important decreases in RMR during weight loss, regardless of the type of dietary intervention, were observed in studies with >6 wk of intervention period and not in studies with shorter follow-up [40]. On the other hand, persistent deviations of energy balance, even small ones, would be to attribute to alter energy expenditure and energy misalignment, resulting in changes in body energy stocks and consequent changes in body weight over time [41]. Although it is not clear whether RMR is related to weight loss success, a lower RMR may be a predisposing risk factor for the development of obesity because with a low RMR an energy imbalance is expected to lead to excessive fat accumulation and eventually to obesity as it equates to lower basic maintenance costs in conditions of higher energy consumption and lower energy expenditure with physical activity [42]. We believe that the lack of statistically or clinically significant changes in RMR contributed to the absence of significant weight change between groups in our study.

To our knowledge, none of the studies involving TRF found in the literature analyzed body temperature as an outcome [11,13–19]. In the present study, increase in axillary temperature in the TRF group was observed, with no detectable increase in the levels of TSH, free T3, free T4, and the RMR values. However, fat depletion alone is also considered a determinant factor for adaptive thermogenesis [43]. Thus, this increase in body temperature may likely be associated with fasting lipolysis, which promotes intense stimulation of uncoupling proteins (UCPs) in brown adipose tissue through interaction with peroxisome proliferator-activated receptors, by the action of adiponectin. UCPs play an essential role in cell energy homeostasis by decoupling proton transport into mitochondria by generating heat rather than adenosine triphosphate [44,45]. Energy restriction (or adequate feeding/fasting cycles) will likely promote bioenergetic adaptation, which could explain some of the beneficial effects associated with the energy restriction during fasting [45]. This fact can be evidenced by the higher body fat percentage decrease in the TRF group in the present study. The glycemic and hormone levels collected remained unchanged after the intervention, which has also been observed in other trials with similar intervention, in which no

Table 2

Final values and changes (final values - initial) of the anthropometric variables, vital signs, body composition, biochemical tests, calorimetry, appetite and difficulty of adherence to the protocol of both groups after 21 days of intervention

Outcomes	HD (n = 27)		ΔHD	HD+TRF (n= 31)		ΔHD+TRF	Effect size		p*
	MEAN	CI95%	MEAN	MEAN	CI95%	MEAN	MEAN	CI 95%	
Anthropometric									
Weight loss (%)	–	–	−1.11	–	–	−1.67	−0.56	−1.32 to 0.19	0.14
BMI (Kg/m^2)	32.78	32.25–34.30	−0.34	32.97	31.42–34.90	−0.56	−0.22	−0.46 to 0.29	0.08
WC (cm)	97.73	93.82 – 101.65	−1.12	100.21	96.04 – 104.37	−2.30	−1.18	−2.93 to 0.57	0.18
Vital signs									
Temperature (°C)	35.67	35.48–35.86	−0.38	35.93	35.79–36.07	0.06	0.44	0.17 to 0.74	< 0.01
SBP (mmHg)	117.9	114.09–121.83	−6.07	122.2	115.89–128.38	−4.64	1.43	−2.85 to 5.71	0.50
DBP (mmHg)	80.55	76.12–84.98	−5.96	82.80	77.90–87.60	−3.22	2.74	−1.32 to 6.80	0.18
HR (bpm)	70.66	66.32–75.01	−1.18	73.61	70.54–76.68	−2.09	−0.91	−5.11 to 3.29	0.66
Body Composition									
% Body fat	43.87	41.99–45.75	0.31	43.59	41.56–45.63	−0.44	−0.75	−1.43 to −0.07	0.02
Biochemical tests									
Glucose concentration (mg/dL)	79.8	75.92–82.44	0.8	80.3	76.16–82.66	−2.0	−2.8	−9.3 to 3.7	0.39
Insulin (μUI/mL)†	11.24	9.4–15.4	0.92	11.66	10.4–13.9	0.94	0.02	−0.15 to 0.20	0.41
HOMA-IR†	2.29	1.83–3.00	0.93	2.33	2.02–2.75	0.92	0.01	−0.16 to 0.20	0.84
Leptin (ng/mL)†	32.41	27.27–42.06	0.14	26.03	22.00–39.19	0.85	0.71	−0.33 to 0.24	0.77
TSH (μUI/mL)†	1.49	1.24–1.86	0.93	1.62	1.29–2.18	1.04	0.11	−0.14 to 0.36	0.39
Free T3 (pg/mL)	2.81	2.63–2.99	0.07	2.91	2.76–3.07	0.02	-0.05	−0.29 to 0.20	0.73
Free T4 (ng/dL)	0.90	0.85–0.96	−0.02	0.94	0.89–0.99	0.02	0.04	−0.01 to 0.09	0.10
Indirect calorimetry									
RMR (kcal)	1 529.22	1 399.49–1 658.94	−68.89	1 494.33	1 388.95–1 599.72	7.69	76.58	−38.50 to 191.67	0.18
RQ	0.84	0.82–0.86	−0.01	0.84	0.82–0.86	−0.02	−0.01	−0.05 to 0.03	0.60
Hunger (likert scale score)	3.96	2.86–5.06	−0.51	4.00	2.63–5.36	−1.25	−0.74	−2.62 to 1.14	0.43
Difficulty of adhesion (likert scale score)	6.11	4.94–7.27	–	5.41	4.43–6.40	–	−0.70	−2.17 to 0.79	0.35

Δ, difference between final and initial measures; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; HD, hypoenergetic diet; HD+TRF, hypoenergetic diet + time-restricted feeding; HR, heart rate; RMR, resting metabolic rate; RQ, respiratory quotient; SBP, systolic blood pressure; TRF, time-restricted feeding; WC, waist circumference; TSH, thyroid stimulating hormone.

*P values for interaction between group (DH x DH + TRF) × moment (beginning and end) using Mixed ANOVA. Except for the variables "weight loss (%)" and "difficulty of adhesion" because they do not present initial data, only final data, and were compared using an independent sample t-test.

†Back-transformed (geometric means).

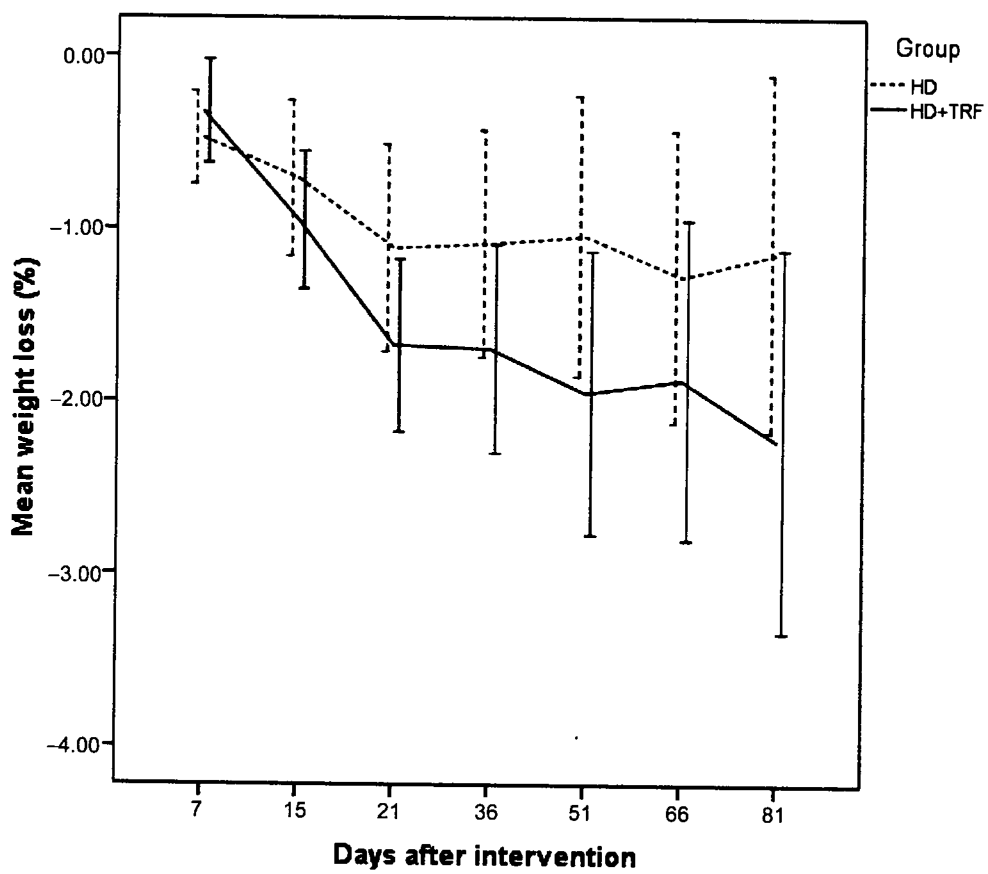

Fig. 2. Mean weight loss (%) for 81 d after the intervention separated by groups. Error bar, 95% CI. CI, confidence interval; HD, hypoenergetic diet; HD+TRF, hypoenergetic diet + time-restricted feeding.

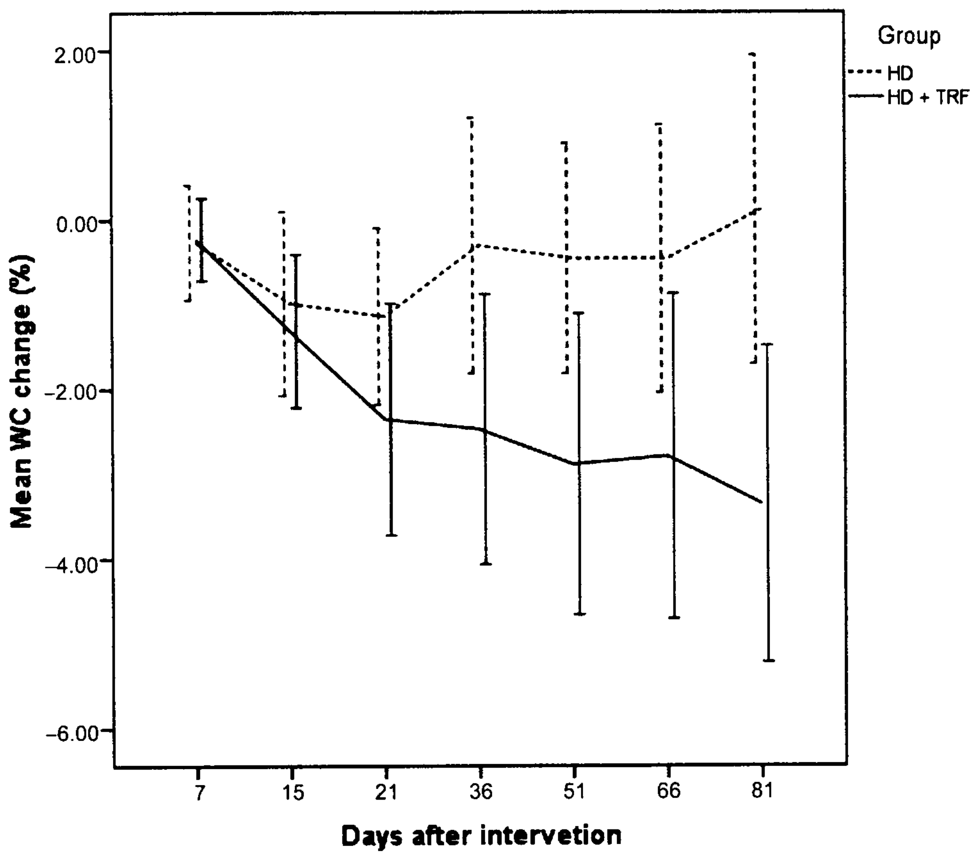

Fig. 3. Mean waist circumference change (%) for 81 d after the intervention separated by groups. Error bar: 95% CI. HD, hypoenergetic diet; HD+TRF, hypoenergetic diet + time-restricted feeding; WC, waist circumference.

significant changes in glucose levels [11,15,19], insulin [15–17], HOMA-IR [11,15,19], leptin [11], and T3 [19] were found.

Additionally, TRF did not promote changes in hunger between the groups in the present study, which is a different result than that found in a study with obese individuals submitted to fasting on alternate days, who reported a greater sensation of hunger compared with the continuous energy restriction group, after 3, 6, and 12 mo, when follow-up concluded [46]. On the other hand, Ravussin et al. [18] reported that participants undergoing early TRF (eating from 0800 to 1400) had a lower sense of hunger compared with the control group (eating from 0800 to 2000). Similar to the present findings, Hutchinson et al. [17] reported no differences in subjective appetite classifications, including hunger, when assessing the effects of an early or delayed TRF, on glucose tolerance in men at risk for type 2 diabetes, a result also found by Coutinho et al. [47] in individuals with obesity but undergoing alternate-day modified fasting.

At the end of the intervention, no statistical difference was observed in the adherence difficulty to the protocol, on average, the participants reported being adherent to both protocols as moderately challenging. These results resemble those of a cross-controlled clinical trial involving overweight and prediabetic men undergoing 18-h fasting for 5 wk. These participants, using a visual analog scale, reported that adhering to the protocol was not challenging or was only moderately challenging [11]. Such findings can be attributed to the fact that the participants were able to choose when it was appropriate to begin the fasting period each day, as long as the period of targeted dietary restriction of 12 h was respected, in a similar way to the present study, which may have facilitated adherence.

Limitations

The present study had some limitations. The findings of axillary temperature increase and body fat percentage were not our primary outcome; hence, these may be seen only as hypothesis-generating findings. Also, we were not able to determine if the women effectively followed the proposed dietary energy deficit as the study was not conducted in a strictly controlled environment; however, participants had weekly consultations with a dietitian to adjust the dietary consumption and maintain weight loss throughout the study. Also, the dietary prescription was based on the three 24-h recalls, which shows that the women already reported the proportions of dietary macronutrients within the range proposed by the Brazilian obesity guideline [24], which was the range proposed in the present study, despite the probable underreporting, usual in this population [35]. Hence, it may be considered that all women would be able to follow the proposed dietary plan, as it did not present major deviations from what the women already reported to eat. Furthermore, one may consider that the fasting period proposed in the present study would not be long enough to induce the metabolic changes associated with TRF regimens. Nevertheless, it is acknowledged that 12 h is the minimum period required for an intervention to be considered as TRF [9]. Also, considering that the present sample was composed of women with low levels of education and high levels of non-adherence to weight loss regimens [48], we believed that the 12 h regimen would be a feasible approach in this population and, possibly, more extreme regimens would importantly decrease the adherence of the participants and the external validity of the study. At last, despite the short follow-up period, the 21-d period is relatively longer compared with other studies [17,18, 49, 50] and should be enough to witness acute changes, especially in the hormonal profile and RMR.

Strengths

The present study also had some strengths: the use of a homogenous sample of obese adult women living in social vulnerability, a population with high levels of obesity worldwide; the fact that the individuals were free-living, which enhances the external validity of the study; and the dietary energy restriction that was applied to both groups, which may isolate the effects of the TRF itself.

Conclusions

TRF associated with HD did not induce significantly different weight loss in 21 d of intervention compared with HD alone, but did induce a decrease in the percentage of body fat and increased the body temperature, whereas the HD group showed a decrease in body temperature. There were no differences in RMR, thyroid hormone levels, insulin, or leptin between the two groups. After 81 d, a significant decrease in WC was found in the TRF group compared with the HD group. The findings indicate that the TRF can be considered an alternative strategy in the treatment of obesity in socially vulnerable women. Effects of TRF in body temperature deserves further investigation.

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