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Comparison of time-restricted eating and a six-meal diet: Effects on body composition and biochemical parameters

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Running title: Time restricted vs six meals diet: which wins?

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ABSTRACT

Background and Objectives: Obesity and obesity-related diseases is increasing worldwide. The widely accepted approach in the dietary treatment of obesity is the calorie-restricted six meal diet; however, alternative approaches are needed. This study aimed to compare time-restricted eating (TRE), a method that can be easily conveyed and applied in over-coming obesity, to six meals diet. **Methods and Study Design:** A total of 174 participants aged 18-65, BMI>25 kg/m² were included, with 88 participants in the time-restricted eating group and 86 participants in the six-meal group. Diet lists with similar calorie, macro counts suitable for their respective groups were prepared. Anthropometric measurements, blood pressure, blood tests were analyzed before the study and at the end of the 8-week. **Results:** More weight loss [MD: 1.17 kg, (95% CI: 0.23-2.06), Cohen's d=0.42], higher decrease in BMI [MD: 0.41 kg/m² (95% CI: -0.77 to -0.06), Cohen's d=0.39], decrease in waist-to-hip ratio [MD: 0.008 (95% CI: -0.016-0.000), Cohen's d=0.35], decrease in obesity degree [MD: 2.35 (95% CI: -3.99 to -0.70), Cohen's d=0.50] were observed in the time-restricted eating group ($p<0.05$). In the six meals group, decrease in LDL values was higher compared to the time-restricted eating group [$p<0.05$, MD:0.23 mmol/L (95% CI:0.41-15.79), Cohen's d=0.36]. More participants preferred to continue TRE ($p<0.001$). **Conclusions:** TRE resulted in greater weight loss, body fat reduction, and improved metabolic parameters, proving more effective for weight management. The six-meal diet was superior for LDL reduction. Both approaches yielded positive outcomes, with TRE emerging as an alternative weight loss strategy.

Key Words: obesity, nutrition therapy, time-restricted eating, weight loss, intermittent fasting

INTRODUCTION

Obesity is a global public health problem. The prevalence of obesity has been on the rise as a result of increasing sedentary lifestyles in parallel with industrialization, and the increase in the consumption of foods providing high-energy intake.¹ There is also a positive correlation between its prevalence and the strain obesity and related diseases put on the costs of healthcare services. This strain can be relieved if the number of obese and overweight individuals is decreased.² In the etiology of obesity, genetic factors are classified as primary causes; and factors related to one's lifestyle, use of drugs, and psychological and neuroendocrine factors are classified as secondary causes.³ The principal method in weight loss treatment of obese and overweight patients is changing the patient's diet and lifestyle.

Although daily calorie intake restriction is the primary dietary regime recommended and used today, a considerable number of patients find hard to follow it.⁴ Therefore, studying alternative approaches in dietary plans other than calorie restriction and submitting the findings to the literature are important.⁵

Intermittent fasting and its variants have recently gained popularity as alternative methods for weight loss treatment. Such regimes might be easier to follow for some compared to the energy-restricted three-meal plans.⁶ There are different types of fasting, such as whole-day fasting, alternate-day fasting, time-restricted eating, Ramadan fasting, and other religious fasts.⁷ The eating window in time-restricted eating, a highly preferred intermittent fasting method, shouldn't exceed 12 hours.⁸ Reviewing twenty-seven studies on intermittent fasting showed that the range of weight loss is 0.8% to 13%. Waist circumference decreased by 3–8 cm in studies that continued longer than 4 weeks.⁹ The decrease in systolic blood pressure was statistically significant at its end of the twelve-week research period in obese adults who applied 16:8 time-restricted eating.¹⁰ A meta-analysis of twenty articles with 1,288 participants proved that time-restricted eating significantly decreased body fat percentage and mass, weight, body mass index (BMI), and waist circumference, although increasing low density lipoprotein (LDL) levels. It was indicated that while it may elevate LDL levels, it does not provide a safety concern and is a good dietary strategy for lowering body fat.¹¹ The aim of this study is to present intermittent fasting as an alternative method in the nutritional treatment in the pandemic of obesity by comparing the effects of two dietary regimes on body composition and biochemical parameters during an 8-week observation period. Several studies in the literature support our hypothesis about intermittent fasting.^{6,12,13,14}

MATERIALS AND METHODS

Place and period of the study, and sample size calculation

Our study was conducted with participants, aged between 18 and 65 years and with a BMI >25 kg/m², who consulted a family medicine clinic in Istanbul, accepted the terms and conditions of the study and signed the volunteer consent form. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Bezmîâlem Vakıf University Interventional Research Ethics Committee; E-54022451-050.05.04-30677. Sample analysis was performed by T.M. with G Power 3.1.9.7 (Franz Faul, Germany), using data from Sundfør et al.'s study.¹⁵ The effect size was assumed to be Cohen's d: 0.382 for the purposes of calculation, where Cohen's d represents the standardized mean difference. After the

calculation made with the aforementioned effect size, with 80% power and 10% margin of error, it was concluded that a cohort of at least 126 samples, of which 63 would be in the patient group and 63 would be in the control group, should be used in this study.

Study design, and the dietary regimes applied

People with a history of bariatric surgery, eating disorders, alcohol and drug addiction, anti-obesity medication use, a diagnosis of diabetes and hypothyroidism, active cancer and symptoms of infectious diseases were excluded from the study. This study were designed to evaluate the effects of two different dietary models with equivalent daily energy intake on weight loss and metabolic markers. This approach was chosen to isolate the effects of time-restricted eating while minimizing the influence of differences in total energy intake on the outcomes. At the beginning of the study, groups were decided by the participants' preferences and 88 people were included in the 16:8 time-restricted intermittent fasting (time-restricted eating) group, with an eating plan of 25% daily energy restriction and with similar macronutrient content (50% carbohydrates, 25% fat and 25% protein); and 86 people were included in the energy-restricted six-meal group with an eating plan of %25 daily energy restriction and with similar macronutrient content (50% carbohydrates, 25% fat and 25% protein). Diet lists suitable for each group were prepared, and food substitution lists were handed out to the participants. Given that long-term compliance is a critical factor in the effectiveness of dietary interventions, allowing participants to choose their preferred diet was intended to improve adherence and reduce dropout rates. Both groups were matched in terms of baseline characteristics, including age, sex, BMI, and metabolic parameters, to ensure comparability. Control measurements were performed after the 4th week.

In order to keep the participants' motivation high throughout the study, an online chat group with the participation of a physician and dietitian, was set up. The study was concluded with 137 patients. During the two-month follow-up period, 37 participants dropped out the study. Nineteen participants were enrolled in the time-restricted feeding group, whereas 18 people were in the six-meal-per-day group. The principal reasons for dropout were associated with the participants' failure to comply with the dietary guidelines and their unwillingness to keep going with the study. Factors such as time constraints, challenges in maintaining the prescribed eating patterns, and personal preferences likely contributed to their decisions. The study was concluded with 69 participants on a time-restricted eating diet, and 68 people who were on a six-meals-a-day diet.

Total daily energy expenditures were calculated using the Harris-Benedict formula.¹⁶ Participants in the time-restricted eating group were allowed to drink calorie-free soda, unsweetened tea, herbal tea and coffee during their 16-hour fast.¹⁰ Subjects in both groups were not advised to exercise and were asked to carry out similar activities.

Data collection and evaluation of biochemical parameters

Anthropometric measurements [weight, BMI, waist circumference (the smallest diameter between the last costa and the highest point of the iliac crest), hip circumference, waist-to-height ratio (WHtR)], blood pressure measurements, as well as fasting blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lipid panel and glycated hemoglobin (HbA1c) values in blood samples were checked at the start and the end of the study. Both measurements were taken by the same researcher. Blood pressure measurements were made on the upper arm with an Omron brand M6 Comfort HEM-7360-E model device. Body composition, metabolic age and obesity degree was measured with the bioelectric impedance method with a Tanita Compacto CS 601. The bioelectrical impedance method is prone to error because of fluctuations in body water content. However, it is accepted as a valid method for assessing changes in weight loss studies when duly accompanied by X-ray absorptiometry and reference methods suitable for evaluating multi-compartment body composition under standard conditions.¹⁷ Metabolic age is estimated by comparing an individual's Basal Metabolic Rate (BMR) to the average BMR of their chronological age group, referencing normative BMR data to determine whether an individual's metabolism aligns with or deviates from their actual age. This metric is considered better to chronological age and waist-height ratio for predicting cardiological risk.^{18, 19} The degree of obesity is the percentage difference from an individual's optimal weight.²⁰ The device categorizes individuals into different obesity levels by integrating body fat percentage with BMI, providing an assessment of obesity severity beyond conventional BMI measurements. This approach allows for a more comprehensive evaluation of body composition and metabolic health. Waist circumference, waist-to-hip ratio and waist-to-height ratio (WHtR), which is recently being recommended, correlate better than BMI in assessing the obesity-related health burden, including total mortality rate, type 2 diabetes, and cardiovascular disease (CVD) risk.²¹ The Complete Blood Count (CBC) tests were performed with a Mindrat BC-6800 device, using the SF Cube technology; biochemical tests were performed with a Roche Cobas C702 device that works with photometry; and HbA1c tests were performed with an Arkray

HA-8180V device that performs measurements based on the High Performance Liquid Chromatography (HPLC) technique.

Statistical analysis

All the statistical analyses were performed with the help of SPSS v. 25.0. The conformity of variables to the normal distribution pattern were checked with histogram graphics and Kolmogorov-Smirnov test. Average, standard deviation, median, IQR, min.-max. values were used while presenting defining analyses. Categorical variables were compared with Pearson Chi Square Test. Mann Whitney U Test was used in examining the nonparametric variants between groups. The Wilcoxon Test was used for assessing the change in the monitored values within a group, and Repeated Measures Analysis was used for the same purpose when the comparison was being made between the groups. An intention-to-treat (ITT) analysis was not utilized in this study because the primary objective was to compare the effects of two different dietary interventions on weight loss and metabolic parameters. While ITT analysis accounts for all randomized participants regardless of adherence, a per-protocol approach was chosen to better assess the actual physiological effects of each dietary regimen among those who followed the prescribed protocols. Given that dietary interventions rely heavily on adherence, including non-compliant participants could have introduced significant variability, potentially diluting the true effects of the interventions. Despite participant dropouts, the required sample size was achieved. Based on the effect size calculation, with 80% power and a 10% margin of error, it was determined that a minimum of 126 participants (63 in each group) was necessary for the study. The final sample consisted of 137 participants, ensuring sufficient statistical power to analyze the study outcomes. The primary outcome of this study was the effect of time-restricted eating and six-meal-per-day dietary interventions on weight loss. Secondary outcomes included changes in body composition, BMI, waist-to-height ratio (WHtR), waist circumference, blood pressure, lipid profile, fasting blood glucose, and HbA1c levels. Cases where the p value was under 0.05 were taken as statistically significant results. The study also provides the Cohen's d value. Effect sizes are categorized by Cohen as small ($d = 0.2$), medium ($d = 0.5$), and large ($d \geq 0.8$).²²

RESULTS

Sample description

137 people in total, of which 21 were men (15.33%) and 116 were women (84.67%), participated in the study. As can be seen in the chart about sociodemographic data (Table 1),

the study was concluded with 69 participants on a time-restricted eating diet, and 68 people who were on a six-meals-a-day diet. There were 38 smokers (27.74%), and 25 alcohol drinkers (18.25%). 51 people had junior high education or less (37.23%), 47 people had high school education (34.31%), and 39 people had college-level or higher education (28.47%). The rate of those with college-level education or higher in the time-restricted eating group was higher compared to the six-meals-a-day group (37.68% vs. 19.12%, $p<0.05$). When asked about their willingness to continue the same nutritional regimen, 98 people responded that they were keen (72.06%). The rate of those who wish to keep following the same diet is higher in the time-restricted eating group than the six-meals-a-day group (88.41% vs. 55.22%, $p<0.05$). (Table 1).

Age, exercise levels, weight, height, BMI, BMR, total daily energy expenditure (TDEE). There was a balanced distribution with regard to age, height, weight, BMI, weekly exercise time.

Time-restricted eating group

While weight, BMI, waist circumference, hip circumference, waist-to-height ratio (WHtR), systolic blood pressure values, HbA1c, high density lipoprotein (HDL), ALT, AST, body fat ratio, obesity degree and metabolic age decreased before and after the two-month diet in the time-restricted eating group; there was an increase in body muscle ratio and body fluid ratio.

Calorie-restricted three meals-three snacks eating group

Meanwhile, when the values before and after the two-month diet were compared for the six-meal group, a decrease in weight, BMI, waist circumference, hip circumference, waist-to-height ratio (WHtR), systolic blood pressure values, diastolic blood pressure measurements, HbA1c, HDL, LDL, total cholesterol, ALT, body fat ratio, obesity degree and metabolic age was observed; whereas body muscle ratio and body fluid ratio increased.

Comparison of the two groups

When the two groups were compared at the end of the study, the decrease in weight [mean-MD: 1.17 kg, (95% confidence interval (CI) 0.23 to 2.06), $p<0.05$, Cohen's $d=0.42$], BMI [MD: 0.41 kg/m² (95% CI: -0.77 to -0.06), $p<0.05$, Cohen's $d=0.39$], waist-to-height ratio (WHtR) [MD: 0.008 (95% CI: -0.016 to 0.000), $p<0.05$, Cohen's $d=0.35$], and obesity degree [MD: 2.35 (95% CI: -3.99 to -0.70), $p<0.05$, Cohen's $d=0.50$] in the time-restricted eating group was statistically significantly higher than that in the six-meal group. Nevertheless,

although there was a greater decrease in waist circumference, hip circumference, body fat percentage, metabolic age and increase in muscle mass in the time-restricted feeding group, this difference was not found to be significant ($p>0.05$). (Table 2)

The decrease in LDL values in the six-meal group is statistically significantly higher than in the time-restricted eating group [MD:0.23 mmol/L (95% CI:0.41 to 15.79), $p<0.05$, Cohen's $d=0.36$]. However, there were no significant differences between groups for changes in fasting blood glucose, HbA1c, systolic blood pressure, diastolic blood pressure or HDL and triglyceride (TG) cholesterol levels ($p>0.05$). (Table 3)

There were no significant differences in the effect of the dietary interventions on weight loss between males and females ($p>0.05$).

DISCUSSION

There is a balanced distribution between the two groups in our study in terms of sociodemographic profile and initial weight, height, and BMI. However, as for the education level, the proportion of those who have received college-level education or above in the time-restricted eating group is statistically significantly higher. It might be because people in the active workforce find having multiple meals challenging when it comes to dietary plans, and have difficulty adapting thereto.

This finding is supported by the fact that the willingness to continue the same diet is higher in the time-restricted eating group. In a study by Tinsley et al. in which participants' feedback was taken about time-restricted eating, people who had a time-restricted eating diet were found to be more willing to continue their diet.²³

It goes without saying that both dietary approaches have positive outcomes, as evidenced by the similar decreasing trends in both laboratory and physical parameters as a result of both diets. In studies where other studies on intermittent fasting were systematically reviewed, it was inferred that intermittent fasting could be proposed as an alternative option to and an equivalent of traditional calorie-restricted diets in helping weight loss.^{14,9} In our study, in congruence with the literature on the subject, a decrease in weight, BMI, waist-to-height ratio and degree of obesity was achieved in the time-restricted eating group.²⁴⁻²⁶ A decrease in LDL value was observed in the six-meal diet group.^{27, 28}

When the two groups were compared at the end of the two-month follow-up period, there was a greater decrease in weight, BMI, waist-to-height ratio and degree of obesity in the time-restricted eating group. The beneficial effects of intermittent fasting involve metabolic switching, increased autophagy, improved mitochondrial function, and cellular stress

resistance, which facilitate weight loss.²⁹ Statistically significant weight loss was achieved in 73% of reviews on intermittent fasting. There are studies showing that the food consumption is reduced, weight control and weight loss are assured, and fat deposition and waist circumference decrease when the eating window is shortened.^{5,7,9,17,30} In a study by Byrne et al. comparing intermittent and continuous energy restriction for 16 weeks, in parallel to our study, there was greater weight loss (12.6%) in the intermittent energy restriction group.³¹ In the systematic literature review by Seimon et al., 12 out of 13 studies examining the effect of intermittent fasting on waist circumference found reduction in waist circumference. Moreover, in 3 studies examining its effect on hip circumference, it was observed that intermittent fasting reduced hip circumference.¹⁴

In terms of its effects on body composition, it was found that the muscle ratio increased, the fat ratio decreased, the fluid ratio increased, the degree of obesity decreased and the metabolic age became lower in both dietary regimes; however, no statistically significant difference was detected between the groups. In a former study by Trepanowski et al. where two diet methods were compared for 24 weeks, no difference was found between the groups in terms of the effects on body composition.³² There are studies in the literature showing that intermittent fasting helps reduce fat mass.^{33, 34} To give an example, an article that systematically reviews the literature on intermittent fasting concludes by saying that it can be an alternative and equivalent to traditional diets by contributing to weight loss.¹⁴

A notable limitation of our study is that participants were not randomly allocated into groups. This lack of randomization may introduce selection bias, potentially affecting the comparability of the groups and the generalizability of our findings. Future studies should aim to include randomization to strengthen the validity of the results. The lack of difference in terms of its effects on body composition may be caused by the fact that our study is based only on two-month results. Longer-term and randomized controlled studies are needed for further results. The limitation another of our study is that the patients' compliance with the diet was not monitored with a method such as a diet diary, and that the macro and micro nutrient intake of the patients was not monitored because the meals were not provided by us. These factors may have influenced the outcomes and should be addressed in future research.

Conclusions

In a world where the threat of obesity is snowballing; the main recommended treatment method is diet and lifestyle changes. As calorie-restricted diets have problems in terms of long-term compliance and sustainability, different dietary approaches are the subject of

medical research. This study was carried out to compare time-restricted eating, a type of intermittent fasting, with a calorie-restricted diet and to present the effects of time-restricted eating as an alternative nutritional treatment to the literature on the subject. From this perspective, a time-restricted diet, with an eight-hour eating window, appears to be a good alternative in light of the findings of our study. It was found to be superior for weight loss.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Demographic and baseline characteristics of participants

Characteristic	Time-restricted eating (n=69)	Six meals (n=68)	p-value
Age (Years, Mean±SD)	41.62±10.55	41.44±10.32	0.760
Gender (Male/Female)	12/57	9/59	0.500
Education level (College and above, %)	37.68%	19.12%	0.012
Smoking rate (%)	23.19%	32.35%	0.219
BMI (kg,m ² , Mean±SD)	32.52±4.37	32.98±4.61	0.511
Wish to follow the same dietary plan (%)	88.41%	55.22%	<0.001

Chi-square test, Mann Whitney U Test.

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Table 2. The characteristics of participants

	Time-restricted		Six meals		Cohen's d	p-value
	Absolute difference (Mean \pm SD)	Relative difference (%)	Absolute difference (Mean \pm SD)	Relative difference (%)		
Weight (kg)	-4.31 \pm 3.05	5.01%	-3.14 \pm 2.31	3.67%	0.42	0.013
BMI (kg/m ²)	-1.65 \pm 1.19	5.07%	-1.24 \pm 0.90	3.76%	0.39	0.024
Waist circumference (cm)	-4.36 \pm 4.74	4.16%	-3.06 \pm 2.98	2.93%	0.33	0.058
Hip circumference (cm)	-5.78 \pm 3.69	4.90%	-4.88 \pm 3.77	4.13%	0.24	0.160
Waist-to-hip ratio (WHtR)	-0.02 \pm 0.03	3.13%	-0.02 \pm 0.02	3.07%	0.35	0.042
Body fat percentage (%)	-1.61 \pm 2.59	4.07%	-1.02 \pm 1.73	2.55%	0.26	0.124
Muscle mass percentage (%)	1.65 \pm 2.46	2.87%	1.02 \pm 1.64	1.79%	0.30	0.082
Degree of obesity	-7.15 \pm 5.18	19.11%	-4.80 \pm 4.23	12.46%	0.50	0.004
Metabolic age	-0.94 \pm 1.61	1.94%	-0.58 \pm 1.01	1.18%	0.26	0.128

Repeated measurements analysis.

Table 3. Blood pressure and biochemical parameters changes between the study groups

	Time-restricted		Six meals		Cohen's d	p-value
	Absolute difference (Mean \pm SD)	Relative difference (%)	Absolute difference (Mean \pm SD)	Relative difference (%)		
Systolic blood pressure (mmHg)	-4.04 \pm 13.94	3.14%	-5.64 \pm 11.96	4.50%	0.12	0.471
Diastolic blood pressure (mmHg)	-1.16 \pm 9.95	1.32%	-2.29 \pm 9.76	2.61%	0.11	0.502
Fasting blood glucose (mg/dL)	0.27 \pm 7.95	0.29%	-0.75 \pm 10.62	0.79%	0.10	0.523
HbA1c (%)	-0.13 \pm 0.27	2.29%	-0.13 \pm 0.36	2.30%	0.00	0.990
LDL (mmol/L)	-0.03 \pm 0.59	0.96%	-0.26 \pm 0.57	8.15%	0.36	0.039
HDL (mmol/L)	-0.06 \pm 0.17	4.65%	-0.04 \pm 0.14	3.15%	0.09	0.583
TG (mmol/L)	-0.21 \pm 0.94	12.80%	-0.08 \pm 0.60	5.26%	0.16	0.349

Repeated measurements analysis.