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RAPID COMMUNICATION

Safety of 8-h time restricted feeding in adults with obesity

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Abstract

This study examines the safety of time restricted feeding (TRF; 8-h feeding window/16-h fasting window daily) in obese adults. Twenty-three subjects participated in an 8-h TRF intervention for 12 weeks. Self-reported adverse events, body image perception, complete blood count and disordered eating patterns did not change from baseline to week 12. These findings suggest that consuming food within an 8-h window can safely facilitate weight loss in subjects with obesity.

Key Words: Intermittent fasting, time restricted feeding, weight-loss, safety, adverse events, obese adults

Introduction

Intermittent fasting regimens involve periods fasting followed by periods of eating freely. The most common forms of intermittent fasting are alternate day fasting (500 calorie fast days alternated with ad libitum feast days) and the 5:2 diet (two 500 calorie fast days and 5 ad libitum feast days per week). Time restricted feeding (TRF) is a newer form of intermittent fasting and involves shortening the eating window to 4-10 h/d. The most common form of TRF is 16:8 during which subjects consume all food within 8 hours and water fast during the remaining 16 hours. Accumulating evidence suggests that TRF is an effective means of decreasing body weight while maintaining lean mass in normal weight and overweight subjects (Gill and Panda 2015; Moro et al. 2016; Tinsley et al. 2017). More recently, it's been shown that TRF may also be effective for weight loss in adults with obesity (Gabel K 2017). Although TRF appears to have beneficial effects on body weight, the safety of this diet has been questioned. For instance, increased frequency of constipation, irritability and fatigue are common safety concerns with all forms intermittent fasting (unpublished observations). Additionally, consistent dietary restriction has been postulated to increase disordered eating behaviors (Conceicao et al. 2013; Elran-Barak et al. 2015; Yanovski and Sebring 1994). Accordingly, this study was undertaken to determine the effects of TRF on certain safety parameters, including: eating disorder symptoms, body image perception, complete blood count, and frequency of adverse events, in adults with obesity. We hypothesized that TRF would not negatively impact any of these parameters during the 12-week trial.

Methods

Subject selection

This 12-week study is a secondary analysis of a larger study (Gabel K 2017). The UIC Office for the Protection of Research Subjects approved the experimental protocol, and all participants gave informed consent (IRB #2016-0119). Subjects were recruited from Chicago via advertisements. A total of 40 subjects were assessed for eligibility, 11 subjects were excluded because they did not meet one or more inclusion criteria, and 6 subjects declined to participate after qualifying. Twenty-three subjects began the study. Key inclusion criteria were: BMI between 30 and 45 kg/m^2; age between 25 and 65 y; sedentary to moderately active (<7500 steps/d); weight stable for 3 months prior to the beginning of the study (< 4 kg weight loss or weight gain); non-diabetic; non-smoker; not a shift worker.

Study design and time restricted feeding protocol

The study consisted of a 2-week baseline period followed by a 12-week TRF intervention period. During baseline, subjects continued with their usual diets and kept their weight stable. During the TRF intervention, subjects were instructed to eat ad libitum within an 8-h window (10:00 to 18:00 h daily), and fast from 18:00 to 10:00 h daily. During the 8-h feeding window, subjects were not required to monitor caloric intake. During the fasting period, subjects drank water and calorie-free beverages only.

Body weight, resting metabolic rate, activity and food intake

Body weight was assessed at the beginning of every week to the nearest 0.25 kg using a balance beam scale (HealthOMeter, Boca Raton, FL) at the research center. Resting metabolic rate (RMR) was measured by a handheld open circuit indirect calorimeter in between the 6:00 and 9:00 h (MedGem Indirect Calorimeter, Microlife, USA) at the research center. Subjects were instructed to abstain from food, drink, and exercise for 12 h prior to the visit. Timing since the last meal (12 h) was standardized for each subject prior to the RMR measurement. Subjects first rested in a dark room in the supine position for 15 min, then a mouthpiece and nose clip were placed on the subject, and oxygen consumption was measured until it reached a stable flow (approx. 10 min). Subjects were instructed to maintain their activity level throughout the trial. Step counts were measured over 7-d during the baseline period and at week 12 by a pedometer (Yamax Digi-walker SW-200, San Antonio, TX). Intake of energy, macronutrients and timing of food consumption was assessed by a 7-d food record at baseline and week 12.

Adverse event, eating disorder, body image, and eating behavior questionnaires

Gastrointestinal and neurological issues were assessed by an adverse events questionnaire. Eating disorder symptoms were measured using the Multidimensional Assessment of Eating-Disorder Symptoms (MEADS) (Anderson et al. 1999). Body image was assessed by the Body Shape Questionnaire (BSQ) (Dowson and Henderson 2001). Dietary restraint, uncontrolled eating, and emotional eating were assessed by the validated three-factor eating questionnaire (TFEQ) (Stunkard and Messick 1985).

Complete blood count and ketones

Twelve-h fasting blood samples were collected between 5:00 and 9:00 h at baseline, week 1, and week 12. Complete blood counts were performed using a BC-5500 automatic blood cell analyzer, and the ketone, β-hydroxybuterate, was measured by the biosensor method (Medisense, Abbott, Bedford, MA).

Statistical analyses

All data are presented as mean ± standard error of the mean (SEM). Statistical analyses were performed using SPSS 24.0 (SPSS Inc., Chicago, IL). ANOVA was used to assess changes in continuous variables over time. McNemar's test was used to assess changes in categorical variables over time. Data were included for the 23 participants who began the study, and means were estimated using an intention-to-treat analysis using last observation carried forward. $P < 0.05$ was considered statistically significant.

Results

Body weight, resting metabolic rate, activity, and food intake

Body weight significantly ($P < 0.001$) decreased by 2.6 ± 0.5% after 12 weeks of TRF. Resting metabolic rate did not change over time (baseline: 1431 ± 62 kcal/d; week 1: 1393 ± 82 kcal/d; week 12: 1318 ± 61 kcal/d). Activity level did not change from baseline (6896 ± 723 steps/d) to week 12 (7443 ± 880 steps/d). Before starting the TRF intervention, subjects typically started eating at 8:30 ± 0:30 h:min and finished eating by 19:30 ± 0:30 h:min. Energy intake decreased ($P < 0.05$) from baseline (1676 ± 114 kcal/d) to week 12 (1335 ± 162 kcal/d). There were no changes in percent energy intake from protein (baseline: 16 ± 1%; week 12: 17 ± 1%), carbohydrates (baseline: 47 ± 2%; week 12: 46 ± 2%) or fat (baseline: 37 ± 1%; week 12: 37 ± 2%).

Adverse events, eating disorder symptoms, body image, and eating behaviors

Self-reported adverse events (gastrointestinal or neurological) did not change over time (**Table 1**). Eating disorder symptoms including depression, binge eating, purgative behavior, fear of fatness, restrictive eating, and avoidance of forbidden foods, did not change from baseline to week 12 (**Table 2**). Concerns about body size and shape remained unchanged (**Table 2**). Cognitive restraint, uncontrolled eating and emotional eating did not change over time (**Table 2**).

Complete blood count and ketones

There were no significant changes in any of the complete blood count parameters over time (**Table 3**). Beta-hydroxybuterate also remained unchanged over the course of the study (baseline: 1.0 ± 1.1 mmol/L; week 1: 0.9 ± 0.4 mmol/L; week 12: 1.2 ± 1.2 mmol/L).

Discussion

This study is the first to show that TRF is a safe diet therapy for weight loss as it does not negatively impact eating disorder symptoms, eating behaviors, or measures of overall health, such as complete blood count. Moreover, no gastrointestinal or neurological adverse events were reported with 12 weeks of TRF.

It has been speculated that fasting or calorie restriction may increase eating disorder symptoms. However, recent findings suggest that this is not the case. For instance, in a previous trial (Williamson et al. 2008), daily calorie restriction did not increase eating disorder symptoms and had no harmful psychological effects. Likewise, alternate day fasting has been shown to have no negative impact on eating disorder symptoms in adults with obesity (Hoddy et al. 2015). Indeed, alternate day fasting may have beneficial effects by increasing dietary restraint and improving body image perception (Hoddy et al. 2015; Bhutani S 2013).

In the present trial, no significant increase in adverse events was reported with 12 weeks of TRF. These results are in line with what has been shown with alternate day fasting. For instance, 8-weeks alternate day fasting did not increase the frequency of gastrointestinal events (constipation, diarrhea, water retention or bad breath) in adults with obesity (Hoddy et al. 2015). Rates of dizziness, general weakness, or sleep disturbances also did not increase with alternate day fasting (Hoddy et al. 2015). The present trial also demonstrates no change in complete blood count with TRF. Similarly, in a previous trial (Stote et al. 2007), complete blood count did not change when normal weight adult subjects were required to consume all of their

152 food within a 4-h period each day. Taken together, these findings suggest that TRF regimens are
153 well tolerated by normal weight and obese adults.
154
155 There are several limitations to our study. First, we had a small sample size (n = 23) which limits
156 our ability to detect a significant difference from pre- to post-treatment for many variables,
157 most notably RMR (effect size = 0.25). Second, we did not utilize a control group. Third, our
158 adverse events questionnaire is not very comprehensive. A more elaborate list of adverse
159 events should be developed to more accurately examine the safety TRF. Fourth, using the
160 MedGem to assess RMR is a limitation as this tool has been shown to overestimate RMR when
161 compared to a traditional indirect calorimeter (Anderson et al. 2014). The MedGem is also
162 limited in that it does not provide measures of respiratory ratio. Fifth, our study was short (12
163 weeks). Longer-term studies will be needed to examine how these measures of safety change
164 over time.
165
166 In summary, these pilot findings suggest that TRF is a safe diet therapy for weight loss. TRF did
167 not have any negative impact on eating disorder symptoms, body image perception, or eating
168 behaviors. No adverse events were reported during the study, and blood chemistry remained
169 unaffected. These findings offer promise for the use of TRF as a safe lifestyle intervention for
170 weight loss in adults with obesity.

171 **Conflict of interest:**

172 The authors declare no conflict of interest.

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Table 1.

Self-reported adverse events after 12 weeks of time restricted feeding

Adverse events	Baseline	Week 1	Week 12	P-Value
Gastrointestinal				
Nausea	0%	0%	6%	1.00
Vomiting	0%	0%	0%	1.00
Diarrhea	0%	0%	12%	1.00
Constipation	17%	29%	24%	1.00
Bad Breath	18%	14%	12%	0.50
Dry Mouth	32%	14%	12%	0.13
Neurological				
Dizziness	9%	0%	18%	1.00
Weakness	14%	0%	6%	0.50
Headache	32%	24%	24%	0.50
Fatigue	14%	10%	12%	1.00
Irritability	23%	19%	6%	0.25
Unhappiness	14%	14%	0%	1.00

Values reported as mean % occurrences at each time point (baseline n = 23; week 1 n = 23; week 12 n = 17).
Baseline values were measured 2 weeks before the start of the intervention (week 1).
P-value: McNemar's test.

Table 2.

Eating disorder symptoms, body shape perception, and eating behaviors after 12 weeks of time restricted feeding

	Baseline	Week 1	Week 12	P-Value
Eating disorder symptoms				
Depression	32 ± 1	32 ± 1	32 ± 1	0.90
Binge Eating	28 ± 2	27 ± 1	27 ± 1	0.79
Purgative behavior	13 ± 1	11 ± 1	12 ± 1	0.23
Fear of fatness	41 ± 2	39 ± 2	41 ± 2	0.89
Restrictive eating	28 ± 2	27 ± 2	29 ± 2	0.68
Avoidance of forbidden foods	37 ± 2	38 ± 2	38 ± 2	0.93
Body image perception				
Concerns about body size/ shape	47 ± 3	46 ± 3	47 ± 3	0.96
Eating behaviors				
Dietary restraint	17 ± 1	16 ± 1	17 ± 1	0.51
Uncontrolled eating	18 ± 1	18 ± 1	18 ± 1	0.89
Emotional eating	7 ± 1	7 ± 1	6 ± 1	0.96

Values reported as mean ± SEM (baseline n = 23; week 1 n = 23; week 12 n = 17).
Baseline values were measured 2 weeks before the start of the intervention (week 1).
P-value: ANOVA.

Table 3.

Complete blood count after 12 weeks of time restricted feeding

	Normal range	Baseline	Week 1	Week 12	P-value
White cell count (K/UL)	5-10	5.7 ± 0.7	5.1 ± 0.5	5.1 ± 0.4	0.70
Red cell count (M/UL)	4.2-6.1	4.3 ± 0.2	4.4 ± 0.1	4.4 ± 0.1	0.91
Hemoglobin (g/dL)	12-18	12.5 ± 0.2	12.6 ± 0.2	12.6 ± 0.3	0.95
Hematocrit (%)	37-52	38.1 ± 1.3	38.0 ± 0.7	38.5 ± 0.9	0.99
Mean corpuscular volume (FL)	80-100	89.3 ± 5.1	88.0 ± 2.4	87.8 ± 1.9	0.87
Mean corpuscular hemoglobin (pg)	27-32	29.4 ± 1.6	29.2 ± 0.9	29.1 ± 0.7	0.93
Mean corpuscular hemoglobin concentration (%)	32-36	32.9 ± 0.6	33.1 ± 0.3	33.1 ± 0.2	0.95
Red blood cell distribution (%)	11-15	14.4 ± 0.5	13.8 ± 0.3	13.9 ± 0.3	0.69
Platelet count (K/UL)	150-450	202.7 ± 12.8	218.8 ± 8.8	212.1 ± 9.9	0.61
Neutrophil (%)	35-80	56.3 ± 5.6	49.8 ± 3.0	51.9 ± 4.9	0.45
Lymphocyte (%)	18-44	32.3 ± 4.7	38.5 ± 4.2	35.8 ± 3.1	0.47
Monocyte (%)	4.7-12.5	7.2 ± 1.5	7.5 ± 0.6	7.5 ± 0.7	0.96
Eosinophil (%)	0-4	3.7 ± 1.2	3.6 ± 0.6	3.5 ± 0.6	0.99
Basophil (%)	0-1.2	0.8 ± 0.2	0.7 ± 0.2	1.1 ± 0.2	0.27
Neutrophil count (K/UL)	1.8-7.7	3.3 ± 0.6	2.7 ± 0.4	2.8 ± 0.3	0.59
Lymphocyte count (K/UL)	0.8-4.8	1.7 ± 0.3	1.9 ± 0.2	1.8 ± 0.2	0.67
Monocyte count (K/UL)	0.2-0.9	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.94
Eosinophil count (K/UL)	0.0-0.8	0.2 ± 0.1	0.2 ± 0.0	0.2 ± 0.0	0.68
Basophil count (K/UL)	0-0.1	0.1 ± 0.0	0.0 ± 0.0	0.1 ± 0.0	0.39

Values reported as mean ± SEM (baseline n = 23; week 1 n = 23; week 12 n = 17).
Baseline values were measured 2 weeks before the start of the intervention (week 1).
P-value: ANOVA.