

Effect of Short-Term Modified Alternate-Day Fasting on the Lipid Metabolism in Obese Women

Samira Eshghinia ^{*1}, Michael Gadjevich Gapparov ²

1. Biochemistry and Metabolic Disorder Research Center, Cardiovascular Research Center, Golestan University of Medical Sciences, Gorgan, Iran
2. Nutrition Department, Russian Postgraduate Medical Academy

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ABSTRACT

OBJECTIVE: Obesity is a worldwide health problem, with increasing prevalence associated with an increased risk of chronic diseases. Decrease in energy intake has been shown to lower the risk of coronary artery disease (CAD) in obese. The common form of dietary restriction is daily calorie restriction (CR). Another form is alternate-day fasting (ADF). The ability of modified ADF to facilitate weight loss and lower cardiovascular risk factors has not been tested. This study examined the effects of combination CR and ADF in obese adults.

MATERIALS AND METHODS: 26 female obese inpatients completed a 4 week trial of controlled food intake during modified ADF period. All subjects consumed very low calorie diet on the fast day and then consumed diet including 1600 - 1700 Kcal in every other day. Body weight (BW) and blood pressure (BP) were measured daily. Fasting blood samples were collected at the first and 29th day of trial for biochemical analysis.

RESULTS: During the course of the trial (4 wk), BW of the subjects decreased ($P < 0.0001$) from 96.87 ± 21.34 kg to 92.16 ± 19.85 kg. Mean BMI of the subjects at baseline was 37.38 ± 7.35 kg/m², at the end of course decreased ($P < 0.0001$) to 35.56 ± 6.78 kg/m². Systolic BP decreased ($P < 0.0001$) from 142 ± 13 to 122 ± 12 mm Hg. Total cholesterol decreased ($P < 0.0001$) from 6.12 ± 1.1 to 5.42 ± 1 mmol/L, LDL ($P < 0.0001$) from 3.99 ± 0.96 to 3.34 ± 0.87 mmol/L, fasting blood sugar ($P < 0.0001$) from 5.87 ± 1 to 5.23 ± 0.9 mmol/L, whereas change in triacylglycerol concentrations was not significant, HDL decreased ($P < 0.005$) from 1.43 ± 0.38 to 1.3 ± 0.31 mmol/L.

CONCLUSION: These findings suggest that short time CR plus ADF is a viable dietary option to help obese individuals lose weight and decrease systemic blood pressure and some CAD risk factors. More and longer-term studies in human subjects are needed to support this important result.

KEY WORDS: Alternate-day Fasting, Weight Loss, Cardiovascular Risk Factors.

INTRODUCTION

Obesity has become an important worldwide health problem, with a rapidly increasing prevalence. World Health Organization has

estimated that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million obese (1). Obesity is associated with an increased risk of diabetes,

*Correspondence: Samira Eshghinia, Biochemistry and Metabolic Disorder Research Center, Cardiovascular Research Center, Golestan University of Medical Sciences, Gorgan, Iran. **Tel:** (+98) 171 4421651. **Email:** eshghinia@goums.ac.ir

cardiovascular events, stroke and cancer. Achieving a healthy weight and preventing weight gain are integral components of optimal diabetes management (2). Moreover, a decrease in energy intake has been shown to lower the risk of coronary artery disease (CAD) in obese populations (3). The most common form of dietary restriction implemented is daily calorie restriction (CR), which requires individuals to decrease their energy intake by 15 to 40% of baseline, needs each day. Another form of dietary restriction used, although far less commonly, is alternate-day fasting (ADF) (4). In long term, CR results in metabolic and behavioral adaptation with decreased physical activity levels (5). The ability of modified alternate-day fasting (ADF; i.e., consuming 25% to 40 % of energy needs on the fast day and ad libitum food intake on the following day) to facilitate weight loss and lower vascular disease risk in obese individuals remains unknown. The relation between alternate-day fasting (ADF) and cardio protection remains uncertain.

MATERIALS AND METHODS

Objective: This study examined the effects of both diet ADF (3 days fasting: Monday, Wednesday and Friday) and moderate CR (4 days weekly), administered under controlled condition, on body weight, BMI, waist circumference and cardiovascular risk factors such as systolic and diastolic BP, FBS, serum TG, LDL, HDL and total cholesterol in obese women.

Design: In clinic of nutrition therapy (The Russian Institute of Nutrition, Russian Academy of Medical Sciences – Moscow) 26 inpatient obese (BMI ≥ 30 kg/m²) women voluntarily completed a 4-wk trial, which consisted of controlled food intake during modified ADF period. Inclusion criteria were BMI ≥ 30 kg/m², no weight changes more and less than 10% for 3 months before the beginning of study, nondiabetics and usual activity. All subjects consumed very low calorie diet (25 to 40% energy needs) on the fast day (3 days a week) and then consumed

antiatherogenic diet (low fat – low Na – high fiber) including 1600 - 1700 Kcal/d in every other day (4 days a week). All foods were prepared in the food preparation unit of clinic and served in dining room in 3 meals (breakfast, lunch, dinner) 8 a.m to 8 p.m. liquid intake such as water, tea and other drink without sugar was free. Nutrient composition of feed day and fast day is shown in Table 1 and Table 2. The subjects had similar level of physical activity. Body weight, blood pressure and pulse rate were measured every day. Blood pressure was measured with the Omron upper arm blood pressure monitor in a seated position after a five-minute rest. Body weight was measured with a mechanical column scale to the nearest 0.1 kg in the fasted state (before breakfast), without shoes, and in light clothing. BMI was assessed as the weight in kilograms divided by the square of the height in meters. Fasting blood samples were collected (at 8.00 – 9.00 am) at the first day and 4 weeks (day 29) for biochemical analysis.

Statistical Analysis: Data were analyzed using SPSS software (version 16). Results are presented as means \pm SD. Comparison between results before and after the trial was assessed by paired T-test.

Table 1- Nutrient composition of fast days

Nutrients	Fast day 1	Fast day 2	Fast day 3
	(Apple)	(Milk or Kefir)	(Fish & Vegetable)
Energy (kcal)	460	826 – 800	600
Total fat (g)	4	45	21
Protein (g)	4	40	83
Carbohydrate (g)	102	66 – 59	21

Table 2- Nutrient composition of feed days

Nutrients	Feed days	Nutrients	Feed days
Energy (kcal)	1650	Trans Fat (g)	0
Total fat (g)	70	Cholesterol (mg)	<300
Vegetable source	30	Protein (g)	75
Saturated fatty acids (g)	28.5	Carbohydrate (g)	190
Monounsaturated fatty acids (g)	24	Simple	15
Polyunsaturated fatty acids (g)	17.5		

RESULTS

During the course of the trial (4 wk), body weight of the subjects decreased ($P < 0.0001$) from mean 96.87 ± 21.34 kg to 92.16 ± 19.85 kg. Mean BMI of the subjects at baseline was 37.38 ± 7.35 kg/m². At the end of the modified ADF course, BMI decreased ($P < 0.0001$) to 35.56 ± 6.78 kg/m², and waist circumference from 105.25 ± 13.43 cm to 101.63 ± 12.89 cm.

Systolic blood pressure decreased ($P < 0.0001$) from 142 ± 13 mmHg to 122 ± 12 mmHg and diastolic BP ($P < 0.05$) from 93 ± 10 mmHg to 80 ± 8 mmHg. Mean blood lipid concentrations over the 4-week trial are presented in Table 3. Total cholesterol decreased ($P < 0.0001$) from 6.12 ± 1.1 to 5.42 ± 1 mmol/L, LDL cholesterol ($P < 0.0001$) from 3.99 ± 0.96 to 3.34 ± 0.87 mmol/L, fasting blood sugar ($P < 0.0001$) from 5.87 ± 1 to 5.23 ± 0.9 mmol/L whereas change in triacylglycerol concentrations was not significant after 4 weeks of modified ADF, HDL cholesterol decreased ($P < 0.005$) from 1.43 ± 0.38 to 1.3 ± 0.31 mmol/L.

DISCUSSION

This study shows that modified ADF is an effective, short term dietary intervention to help obese individuals lose weight and lower CAD risk. Specifically, we show here that an ADF regimen combined with mild CR diet (-15% of baseline needs), resulted in a mean 4.7% weight loss of subjects from baseline after 4 wk of treatment. Decreases in several key biomarkers of CAD risk such as total cholesterol, LDL cholesterol, systolic and diastolic blood pressure and heart rate, were also observed. Although CR is often used to

facilitate weight loss (6,7), many obese patients find it difficult to continue because food intake must be limited every day (8,9). The ADF is a new strategy that is capable for subject of self-selecting foods to continue their individual fast day energy goals with the help of a dietitian for long time (4).

Our weight loss findings after 4 wk (4.7 ± 2.5 kg) are comparable to those of Johnson et al. (10) 4 kg weight loss after 4 wk of ADF in overweight individuals and Varady et al. findings (4), 5.6 ± 1 kg weight loss after 8 wk diets.

According to these effects on body weight, ADF may be considered a suitable alternative to CR to help obese individuals lose weight in short period. However, the degree of weight loss achieved by ADF may not be sustainable in long term.

The effects of 4 wk diet on blood pressure were also assessed. Systolic and diastolic BP were lowered ($P < 0.0001$) by 12.6% and 13.6%, respectively. Results from another human studies indicated that after 3 wk of intervention, neither systolic nor diastolic BP changed in subjects (11). Varady et al. (4) reported 5.1% reduce in systolic BP after 8 wk intervention, whereas diastolic BP did not change. This difference may be due to that these studies included only normotensive persons, our subjects had mild to moderate hypertension and consumed hyponatremic diet in all period of trial.

We also found that alternate-day fasting significantly reduces glucose from baseline after 4 wk. This is in contrast with results in Heilbronn et al. (11) study, in which glucose and insulin concentrations did not significantly change from baseline after 3 wk. This could be due to the already low glucose concentrations of their population or that 3 wk of alternate-day fasting was insufficient to produce this response. Halberg et al. (12) observed that normal-weight persons fasted for 20 h periods and then ate their habitual diet ad libitum on alternate days, after 2 wk, the insulin-mediated glucose uptake increased which implied improved insulin sensitivity. However, animal data indicate that ADF is just as efficacious in

Table 3 – Plasma glucose and lipid concentrations at baseline and at the end of the trial

Biochemical index	Before	After
FBS (mmol/L)	5.9 ± 1.05	$5.23 \pm 0.92^*$
Total cholesterol (mmol/L)	6.12 ± 1.1	$5.42 \pm 1^*$
LDL cholesterol (mmol/L)	3.99 ± 0.96	$3.34 \pm 0.87^*$
HDL cholesterol (mmol/L)	1.43 ± 0.38	$1.30 \pm 0.31^{**}$
Triacylglycerols (mmol/L)	1.59 ± 0.6	1.69 ± 0.7

* $p < 0.0001$, ** $p < 0.005$

decreasing fasting glucose and insulin concentrations as is daily CR (13).

Total and LDL-cholesterol concentrations decreased by 13.3% and 16.9%, respectively, after 4 wk of diet. These modulations in total and LDL-cholesterol concentrations are similar to those observed by Varady et al. (7) that showed 21.2% and 24.8% reduction in total and LDL-cholesterol respectively after 8 wk treatment.

No changes in Triacylglycerol concentrations were observed throughout the 4 wk trial. HDL-cholesterol concentrations showed reduction ($P < 0.005$) throughout the trial. Heilbronn et al. observed that the changes in lipid concentrations were sex specific. The women had an increase in HDL cholesterol concentrations, and only the men had a decrease in triacylglycerol concentrations. There is no clear explanation for these sex-based differences (14). Findings from Varady et al. reported no changes in HDL (4). This lack of benefit effect of ADF on HDL cholesterol is not surprising because this

cardioprotective lipid parameter is generally increased in response to exercise training (15). The next step in the ADF field will be to incorporate an exercise program into this diet to test more benefits effects in lipid profile.

It should be noted that this trial and other ADF trials did not have control groups and included limited subjects. A randomized controlled trial with larger groups is needed to test these findings.

CONCLUSION

These findings suggest that ADF is a viable diet option to help obese individuals lose weight and decrease systemic blood pressure and some CAD risk factors.

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REFERENCES

1. Suzuki K, Simpson KA, Minnion JS, Shillito JC, Bloom SR. The role of gut hormones and the hypothalamus in appetite regulation. *Endocrine* 2010;57(5):359-72.
2. Lau DC. Diabetes and weight management. *Prim Care Diabetes* 2010;4 (Suppl 1):S24-30.
3. Gomes F, Telo DF, Souza HP, Nicolau JC, Halpern A, Serrano CV Jr. Obesity and coronary artery disease: role of vascular inflammation. *Arq Bras Cardiol* 2010;94(2):255-66.
4. Varady KA, Bhutani S, Church EC, Klempel MC. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. *Am J Clin Nutr* 2009;90(5):1138-43.
5. Redman LM, Heilbronn LK, Martin CK, de Jonge L, Williamson DA, Delany JP, et al. Pennington CALERIE Team. Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss. *PLoS One* 2009;4(2):e4377.
6. Chaston TB, Dixon JB. Factors associated with percent change in visceral versus subcutaneous abdominal fat during weight loss: findings from a systematic review. *Int J Obes (Lond)* 2008;32:619-28.
7. Varady KA, Hellerstein MK. Alternate-day fasting and chronic disease prevention: a review of human and animal trials. *Am J Clin Nutr* 2007; 86:7-13.
8. Malik VS, Hu FB. Popular weight-loss diets: from evidence to practice. *Nat Clin Pract Cardiovasc Med* 2007;4:34-41.
9. Das SK, Gilhooly CH, Golden JK, Pittas AG, Fuss PJ, Cheatham RA, et al. Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial. *The American journal of clinical nutrition* 2007;85(4):1023.
10. Johnson JB, Summer W, Cutler RG, Martin B, Hyun DH, Dixit VD, et al. Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma. *Free Radical Biology and Medicine* 2007;42(5):665-74.
11. Heilbronn LK, Civitarese AE, Bogacka I, Smith SR, Hulver M, Ravussin E. Glucose tolerance and skeletal muscle gene expression in response to alternate day fasting. *Obes Res* 2005;13:574-81.
12. Halberg N, Henriksen M, Soderhamn N, Stallknecht B, Ploug T, Schjerling P, et al. Effect of intermittent fasting and refeeding on insulin action

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- in healthy men. *Journal of Applied Physiology* 2005;99(6):2128.
13. Anson RM, Guo Z, De Cabo R, Iyun T, Rios M, Hagepanos A, et al. Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistance to injury from calorie intake. *Proceedings Of The National Academy Of Sciences Of The United States Of America* 2003;100(10):6216.
 14. Heilbronn LK, Smith SR, Martin CK, Anton SD, Ravussin E. Alternateday fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism. *Am J Clin Nutr* 2005;81:69–73.
 15. Ellison RC, Zhang Y, Qureshi MM, Knox S, Arnett DK, Province MA. Lifestyle determinants of high-density lipoprotein cholesterol: the National Heart, Lung, and Blood Institute Family Heart Study. *Am Heart J* 2004;147:529–35.