

INTERMITTENT FASTING IN MANAGEMENT OF OBESITY

Upasanaba Jadeja¹, Divyesh Vadasmia¹, Piyush Makwana³, Mina Varlekar³, Harsiddh Thakar³, Rajesh Mohan²

1.Associate professor,. 2. Professor 3. Assistant professor; GMERS medical college, Himmatnagar, Gujarat.

Abstract: Fasting- voluntary abstinence for food is practiced since centuries in human evolutionary practices for various reasons. Intermittent fasting is the term used to describe multiple strategies of time related diet restriction such as alternate day fasting, two meals a day diet, one meal a day diet, 16:8 diet etc. Obesity is emerging as new epidemic in the world affecting all age groups. Guidelines for management of obesity include calorie restriction along with lifestyle modification. There has been increased interest in identifying alternative dietary weight loss strategies that involve restricting energy intake to certain periods of the day or prolonging the fasting interval between meals (i.e., intermittent fasting). Here, we summarize the current evidence for intermittent fasting strategies as treatments for overweight and obesity. Although there are no large, randomized control trials examining the relationship between intermittent fasting and weight loss related outcomes, current human studies suggest that, this diet could reduce the risk for obesity and related cardiovascular complications. It may lead to improvement in weight control, hypertension, dyslipidemia and diabetes. There may be multiple mechanisms through which intermittent fasting may exert its effect including reducing oxidative stress, optimization of circadian rhythms and ketogenesis. This review evaluates various studies regarding the effects of intermittent fasting on obesity and related disorders.

Keywords: intermittent fasting; obesity; alternate day fasting; 16:8 fasting; time restricted feeding.

Author of correspondence: Dr. Upasanaba Jadeja,

Introduction: Obesity is not only a risk factor for many non communicating diseases such as coronary artery disease, hypertension, diabetes mellitus, cancer etc but also impacts mental health of person causing poor self image and low self esteem. Obesity along with poor diet are important, modifiable contributors to the rise of cardiovascular disease with an estimated attributable risk of 13% to cardiovascular mortality.¹ Caloric restriction is considered as an important strategy of dietary intervention which involves limiting calories consumed during a given period. Caloric restriction is linked to improvement in weight, blood pressure and insulin sensitivity in humans.² In intermittent fasting, time period during which food can be consumed is restricted whether amount of food is not restricted. Intermittent fasting focuses on the timing of when one can consume meals, either within a day or a week. Many different types of intermittent fasting are alternative day fasting, 2 days in a week fasting, one meal a day fasting, two meals a day fasting and 16:8 fasting. In alternative day fasting, subset may consist of 24-hour fasts followed by a 24-hour eating period that can be done several times a week such as a 5:2 strategy when there are 2 fast days mixed into 5 nonrestrictive days. For time restricted fast

programs, variations include 16-hour fasts with 8 hour feeding times, 20-hour fasts with 4-hour feed times or other similar versions. While both caloric restriction and intermittent fasting may result in overall decreased caloric intake, this is not integral to intermittent fasting. Intermittent fasting has been linked to better glucose control in both humans and animals.^{3,4} Intermittent fasting diet may be easier to follow for people who can't restrict calories during their meal. Similar to calorie restriction diet, intermittent fasting may also reduce overall calorie intake, therefore it is plausible that intermittent fasting could also confer cardiovascular benefits. It has also shown potential benefit in slowing the progression of neurodegenerative diseases like Alzheimer's and Parkinson's.⁵ In this review, we explore the potential benefits of intermittent fasting for improving obesity and cardiovascular health.

Alternate Day Fasting (ADF): in this type of intermittent fasting, fasting days are observed in which limited or no food is consumed which are followed by days of normal caloric intake. In 2007, Varady and Hellerstein reviewed alternate day fasting studies in animals and concluded that

this fasting regimen was as effective as simple caloric restriction in decreasing fasting insulin and glucose concentrations.⁶ Alternate day fasting in animals also reduced total plasma cholesterol and triglyceride (TG) concentrations, and had beneficial effects on cancer risk factors such as cell proliferation. In a study of overweight men with type II diabetes, subjects in both caloric restriction and intermittent fasting regimens experienced weight loss with intermittent fasting subjects losing 1.1% of body fat with a mean 6.5% weight loss after 12 weeks.⁸ Another study included 74 obese male and female whose mean age was 45 years. This study by K K Hoddy and colleagues divided subjects in three groups according to fasting regime. All subjects took full caloric intake in one day followed by only 25% caloric intake in next day. Next day subjects could take food in either lunch, dinner or small meals which could improve tolerability of this regime. All subjects showed weight loss of ADF-lunch 3.5±0.4 kg ADF-dinner for 4.1 ± 0.5 kg ADF-small meals 4.0 ± 0.5 kg.

2 days a week fast: In this regime, fasting is observed for any two days of week, for rest of the week normal non restricted diet is followed. A study on 107 women was done according to this diet regime. Harvie et al⁹ showed effect of intermittent fasting in 107 overweight and obese premenopausal women. Weight of subjects reduced from mean (95% CI) 81.5 (77.5 to 85.4) kg to 75 (71.2 to 78.8) kg in the intermittent fasting group. They also compared the result with caloric restricted diet. Both approaches achieved comparable weight loss and improvements in a number of risk markers for cancer, diabetes and cardiovascular disease, for example reductions in fasting insulin, insulin resistance, leptin, the leptin: adiponectin ratio, free androgen index, inflammatory markers, lipids, blood pressure, increases in SHBG, IGFBP-1 and 2.

Time restricted feeding (TRF): Time-restricted feeding is a dietary approach that consolidates all calorie intake to 6- to 10-h periods during the active phase of the day, without necessarily altering diet quality and quantity. Moro et al¹⁰ was done on athletic men who were doing resistant training for minimum 5 years and compared effects of time restricted eating versus normal eating without time restriction on different body weight and measurement parameters. Thirty-four

resistance-trained males were randomly assigned to time-restricted feeding (TRF) or normal diet group (ND). TRF subjects consumed 100 % of their energy needs in an 8-h period of time each day, with their caloric intake divided into three meals consumed at 1 p.m., 4 p.m., and 8 p.m. The remaining 16 h per 24-h period made up the fasting period. After 8 weeks, a significant decrease in fat mass was observed in the TRF group (-16.4 vs -2.8 % in ND group), while fat-free mass was maintained in both groups (+0.86 vs +0.64 %). The study concluded that TRF with 16 h of fasting and 8 h of feeding, could be beneficial in resistance trained individuals to improve health-related biomarkers, decrease fat mass, and at least maintain muscle mass.

Mechanisms: There are several proposed mechanisms for how intermittent fasting could lead to reduce fat mass and cause better cardiovascular outcomes.

The Oxidative Stress Hypothesis The Oxidative Stress Hypothesis states that decrease energy intake cause mitochondria to produce fewer free radicals.¹¹ The findings of a study¹² detected a marginal increase (2.7%) in SIRT3 expression due to the intermittent fasting diet which suggest that intermittent fasting may have some benefits on biological pathways that directly affect metabolism and potentially longevity, even in healthy individuals.

Circadian Rhythm Theory Eating and fasting at appropriate times as per evolution and biological clock may have advantageous effects on overall health of human and other animals. Feeding in most animals is confined to a defined period, leaving short periods of fasting that coincide with sleep. Fasting enables organisms to enter alternative metabolic phases, which rely less on glucose and more on ketone body-like carbon sources. Both intermittent and periodic fasting result in benefits ranging from prevention to the enhanced treatment of diseases. One circadian example relevant to intermittent fasting is decreasing insulin levels later in the day.¹³ Taking dinners late at night time are associated with higher postprandial glucose levels than daytime meals, increasing the risk of diabetes. Sleep quality and quantity decreases with night time eating, which also leads to increased insulin resistance, obesity and cardiovascular disease.^{14,15} Intermittent fasting especially time restricted

feeding when synchronised with biological clock of body, may help in improving metabolic health .

Ketogenesis during fasting:One important fact is that when body enters a state of fasting, it goes into a state of ketogenesis. There is rise of β -hydroxybutyrate levels during fasting in overweight subjects according to a study.¹⁶ Ketone levels typically become detectable in blood around 6-8 hours after fasting, which detects change in metabolism of body towards utilization of fat and reduction in storage of fat, which is indicated by reduction in levels of low density lipoproteins (LDL). Just after the meal, insulin is secreted which ensures utilizing glucose as principle source of energy after meals. This glucose is utilized by adipose tissue for lipogenesis. Thus, insulin promotes lipogenesis. Reducing frequency of feeding, such as in two meals a day or one meal a day diet, also causes reduction in frequent spikes of insulin secretion, further preventing lipogenesis and utilizing fat as energy source. This change from using glucose as

Table:1^(7,8,9,10)

energy to using fatty acids and ketones for energy is called intermittent metabolic switching.

Calorie restriction during fasting: fasting reduces caloric intake and this simply induces weight loss if regularly followed. This is a simple mechanism which also explains weight loss in overweight individuals due to intermittent fasting.

Comparing intermittent diet with calorie restriction diet: Both types of diets would be not easy to follow because they induce a state of starving in individuals. Any kind of diet should be done in observation of experienced doctor or dietician to prevent adverse effects such as hypoglycaemia. Calorie restriction eating (CRE) involves close monitoring of amount and type of food to be consumed. Intermittent fasting allows freedom from counting calories during each meal and does not need restriction of type or amount of food to be consumed during meals, which gives freedom of eating satisfying amount and type of meal to the individual.

Study title	Participants	Intervention duration	Type of intervention	Results
Moro et al	34 resistant trained males	8 weeks	Time restricted feeding	Reduced fat mass in study group
Harvie et al	107 overweight and obese female, mean age – 40 years	24 weeks	2 days a week fast	Lost 6.4 kg
Hoddy et al	74 male and female mean age 45 years , obese	8 weeks	Alternate day fast with ADF lunch, dinner or small meals	ADF-lunch 3.5±0.4 kg ADF-dinner for 4.1 ± 0.5 kg ADF-small meals 4.0 ± 0.5 kg
Ash et al	51 male, mean age 54 years, overweight, type -2 DM	12 weeks	Alternate day fast	Mean weight loss of 6.4±4.6kg Reduction in waist circumference 8.1±4.6cm Loss of body fat 1.9±1.5%

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