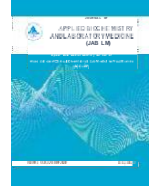




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REVIEW ARTICLE: Current Topics

Title: Short Term Intermittent Fasting: Another Path to Weight Loss

L. Shaini^{1*}, Bishnupriya Panda^{1*}

1. Professor & HOD, Department of Biochemistry, RIMS, Imphal, Manipur

1. Postgraduate resident, Department of Biochemistry, RIMS, Imphal, Manipur



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INTRODUCTION
In the third world where we are leading a sedentary life style, we have to underscore the need of weight loss for minimizing the risk factors leading to obesity induced morbidity. Both overweight and obesity significantly increase the chances of coronary heart disease (CHD) which can be reduced markedly by a weight loss of only 5 to 10 percent¹. Till now, it has been well established that reducing calorie intake to an optimum level helps in increasing the overall life span also in human. Hence, for combating the increased risk for CHD, various measures have been adopted for reducing the daily calorie intake to an optimum level and achieving a better cardiovascular health. These regimens are increasingly including alternate day fasting (ADF)² and other forms of intermittent fasting (IF) procedures. Recent studies have also indicated that the increase in life span is proportional to the reduced calorie intake along with its duration barring the critical point of starvation. The duration is important as it has been evident that the effect of short term reduction in daily calorie intake is not long lasting. Most

ABSTRACT

Both overweight and obesity pose high risk for development of cardiovascular diseases. The risk decreases significantly with a moderate decrease in the weight. Intermittent fasting (IF) comes to rescue in achieving these goals. Now-a-days it is quite a popular weight loss regime. The study is a systematic review of the most recent evidence on IF's effects on weight loss and the potential role it plays in reducing the morbidity. Seven recent randomized control trials on humans were taken into account with different intermittent fasting regimes. The intervention trials showed that intermittent fasting is successful in achieving short term weight loss in normal weight, over weight and in obese individuals but to maintain this weight loss strict diet adherence is required.

interestingly, intermittent fasting has been found to augment the life span significantly without a significant reduction in calorie intake^{3,4} although different regimens for reducing daily calorie restriction (CR) are still in abundance that recommend significant weight loss⁵. However, the major drawback of these CR regimens is the non-compliance of people due to unsuccessful adoptive efforts for maintaining this strict regimen in which they are not allowed to take the foods they wish throughout the whole day. Due to these adversaries related to CR, the IF process is gaining popularity for achieving a decent weight loss and thus a better cardiovascular profile among many people as it proposes an energy restriction for only 1–3 days per week allowing free food consumption according to one's habitual food habit for the rest of the period in the week⁶. In the above context this review presents a timely information on the recent developments in the concept of IF and its long lasting impact on maintenance of an optimum body weight with a significant increase in life span and its overall beneficial effects on the primary treatment of obesity.

*Correspondence:

shiny15thokchom@gmail.com

drbp2014.bp@gmail.com

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DIFFERENT INTERMITTENT FASTING REGIMES PROPOSED: -

1. Alternate Day Fasting (ADF)

It involves fasting days alternate with normal feeding days. No energy-containing foods or beverages are consumed during fasting days followed by alternating days where foods and beverages are consumed ad libitum. As the study conducted by Johnson JB et al in 2007 showed that 9 of the 10 participants complied with the ADCR (Alternate day calorie restriction) regimen after joining the study and the result was reflected by a progressive weight loss in them. Thus, the clinical advantage of the ADCR diet was evident in all 9 subjects who completed the regimen and successfully came out with a significant improvement in the quality of life⁷.

An alternate day fasting regimen is better than the continuous calorie restriction method in those people who feel a continuous hunger followed by an inevitable extra food intake which happens to be the commonest side effect of the continuous calorie restriction regimen. In contrary to this regimen people on alternate day fasting method are free to take their food of choice in adequate quantity on the non fasting dates and so are less prone to premature abandoning of this regimen due to non compliance. Another advantage of the alternate day fasting method is the avoidance of the daily fatigue that is associated with regular calorie restriction in the continuous calorie restriction method⁸.

2. Modified Fasting Regimens

Different modified regimens for calorie restriction during intermittent day fasting methods have been adopted. One of the commonest method is to allow 20 to 25 percent of the daily calorie need during the fasting days with normal calorie intake on non fasting days. This method has been successfully adopted using a 5 : 2 dietary regimen in which the calorie restrictions are advised on two consecutive days with normal food intake on the rest of the five days of the week. A successful use of this method has found to induce significant weight loss with about 25% of energy restriction per day⁹.

The effectivity of intermittent fasting regimens are comparable with the continuous calorie restriction procedure. It has been reported that intermittent fasting regimens bring out a reduction of about 3 to 8 percent in body weight within a period of 3 to 24 weeks of its initiation. In comparison to this about 4 to 14 percent of weight reduction has been observed in the continuous calorie restriction method within the period of 6 to 24 weeks of initiation. Furthermore, significant reductions in the visceral fat mass, fasting insulin levels and insulin resistance have been observed in comparable manner in both regimens¹⁰. Hence, as the effects are comparable in both methods, the intermittent fasting methods have been better adopted in people due to its better compliance.

3. Time Restricted Feeding

The term describes an eating pattern restricted food intake within a time window of 6- 8 hours per day¹⁰. However, till now there is scarcity of studies on humans that investigated the final effect of this regimen in a significant weight loss. In a case control study involving 29 men with normal weight a prescribed night time fasting interval of ≥ 11 hours with a two weeks per study condition was undertaken. The study reported a significant weight change difference between the case population (-0.4 kg) and controls (+0.6 kg) i.e with a net difference of 1.3% weight loss¹¹.

4. Religious Fasting

Many religions come with spirituality hand in hand with fasting. Muslims observe fast during the holy month of Ramadan, Hindu people also follow different fasting regimes throughout the year, followers of older days saints in churches also hold routine fasting. A meta-analysis using a cohort of 30 students showed that the low-density lipoprotein and fasting blood glucose levels were significantly reduced in the entire group after their Ramadan fasting compared to levels prior to it¹².

A study conducted by Horne BD et al, on 448 subjects who underwent coronary angiography, showed that subjects who reported routine fasting exhibited significantly lower prevalence of diabetes ($p = 0.048$) and were associated with lower risk of coronary artery disease than the non-fasting subjects (64% vs. 76% CAD; $p=0.010$)¹³.

Table 1: Different Dietary Regimes

Alternate Day Fasting	Alternating fasting days without any intake of energy-containing foods and eating days without any caloric restriction as per choice of the participants.
Modified Fasting Regimens	This allows a reduced calorie intake upto 20 to 25 percent of the daily requirement on certain prefixed days and normal eating for other days. 5:2 regime included under this (2 days fasting and 5 normal eating days).
Time-Restricted Feeding	In this method the calorie intake is limited to a window period of 6- 8 hours per day. It induces fasting periods on a routine basis
Religious Fasting	This includes a wide variety of fasting periods depending on different religious and spiritual customs (The most common example is fasting during Ramadan).

A clinically significant weight loss will be a 5% reduction in weight for the prevention and treatment of obesity in adults who adopt and sustain physical activity combined with a proper diet regime¹⁴. Hence, IF can be an option for short-term weight loss intervention. Certain difficulties are encountered while adhering to the IF regimes. Some studies showed that participants reported negative side effects, such as feeling cold, irritable, low energy, hungry or drowsiness episodes. Even ADF is not appropriate for individuals such as type 1 diabetes, pregnant and breastfeeding women and elderly, who need regular food intake¹⁵. Certain religious fasting regimes like Ramadan, feeding pattern is in biologic opposition to human circadian rhythms and therefore unlikely to be pursued as a desirable weight loss intervention.

DISCUSSION

Effect on weight

In a study conducted by Johnson JB et al (2007) on 10 subjects with asthma having a BMI>30, an alternate day fasting dietary regimen was conducted. The study period was of 2 months during which the participants were allowed to consume food of their own choice on alternate day.

A total calorie intake of 20 percent less than the normal limit was allowed on the intervening days. 9 of the subjects adhered to the diet and were found to lose an average weight by 8% of their initial weight with a significant improvement in their asthma related symptoms within 2 weeks of diet initiation. Clinical findings showed decreased levels of serum cholesterol and triglycerides, striking reductions in markers of oxidative stress and increased levels of the antioxidant uric acid⁷.

Trepanowski JF et al observed the effect of alternate day fasting in metabolically healthy obese adults and compared it with daily calorie restriction taking these key indicators into account like weight loss, weight maintenance and risk indicators for cardiovascular disease. In a randomized control clinical trial that divided 100 participants into 3 groups with an 1 year study period. The regimens compared were i) alternate-day fasting, ii) a continuous calorie restriction of 75% of energy requirement per day and iii) a no-intervention control group with no dietary restrictions who enjoyed their normal food habits during the study period. In this trial the initial 6-month weight-loss phase was followed by a 6-month weight-maintenance phase.

Mean weight loss was similar for participants in the alternate-day fasting group (6.8%, 6.0%, BMI= 34±4) and those in the daily calorie restriction group (6.8%, 5.3%, BMI= 35±4) at month 6 and month 12 compared to control group. Mean LDL cholesterol levels significantly increased among the participants in the alternate-day fasting group relative to those in the daily calorie restriction group. No significant differences were observed between the intervention groups in blood pressure, heart rate, triglycerides, fasting glucose, fasting insulin, insulin resistance, homocysteine concentrations and C-reactive protein after a period of 6 or 12 months¹⁶.

Several studies have reported different pitfalls and advantages of different regimens adopted for restricting calorie intake till now and a look into these are of much help for taking a decision for an effective implementation of a selected calorie restriction regimen at large. Horne et al (2013) reported that in spite of good effectivity in weight reduction the commonest side effect with continuous calorie restriction diet is an induction of higher hunger followed by additional eating in many and so although it seems to be effective during initial phases the final success of this regimen depends mainly of a strict control and discipline on the participants. As its remedial approach alternate day fasting regimen is a better option considering that people can eat in their usual ways on non-fasting days¹⁷.

The usefulness of the alternate day fasting regimen has been also reviewed extensively. In a study that was undertaken to find out the effectivity of this model of dietary restriction in non-obese people along with any improvement in their longevity 16 non obese people were with eight men and eight women were subjected to an alternate fasting for a period of 22 days. The study population selected was a good reflection of the heterogeneity of society as seven of them enjoyed a sedentary life habit with three participants engaged in moderate activity level and the other three going through very active life with an exercise 5 times per week. The study population was reported to lose about 2.5% of their initial body weight (P = 0.001) and 4% of initial fat mass (P = 0.001). An increased catabolic activity was found with an increase in oxidation of the lipid reserve of upto 15 grams in non-obese subjects without any change in appetite on non-fasting days. The researchers did not find any significant alterations in the appetite inducing hormone ghrelin and blood glucose with a significant reduction in the fasting insulin level upto 57 percent with a p value < 0.001 signifying that the change was significant. At the end of their study the researchers suggested including one additional small meal on fasting days to make it more compliant for the participants¹⁸.

The pros and cons of alternate day fasting are now evident as more studies are reporting them on various study population. The major advantage of this regimen is that the regular anxiety linked to daily calorie restriction and food restriction is alleviated a lot and so people tend to comply better with this regimen with full liberty to take their foods of choice during the non restricted days. Furthermore, many people practise taking foods at long intervals during the day and they show much better compliance with the alternate day fasting regimen. In the contrary, this regimen is not suitable for those people who are used to take their foods at frequent regular intervals. This regimen is also not advised for those people who should not have long fasting periods like patients suffering from diabetes mellitus, patients on hypoglycemic agents, pregnant population, breastfeeding mothers, elderly people, sick people and people taking medicines every day at regular intervals. The overall weight loss in alternate day fasting is maximally observed after six months, after which it reaches a plateau phase. After reaching the plateau phase the reduced weight has to be maintained by continuing the dietary restrictions as well as the regular exercise as suitable for age and lifestyle^{15, 19}.

Some important changes in the biochemical parameters that signify regulation of feeding behaviour in the brain were also observed with alternate day fasting. Changes in the mu (μ) opioid receptor characteristics, activation of the meso-corticolimbic dopamine system and reduction of D2 dopamine receptor expression signify that this food intake method plays a significant role in regulating the appetite regulating mechanism in the brain also⁸.

Studies related to the effects of alternate day fasting methods in obese people have been also of much interest. Obese people with BMI > 30 kg/m² and within the age range of 18 to 55 showed different outcomes when they were randomly assorted to two different dietary regimens namely to zero calorie alternate day fasting and a continuous calorie restriction method with 400 kcal less per day. At the end of 8 weeks of study period in 14 adults a baseline change in lean fat mass was more distinctly observed in the alternate day fasting group. However, no significant changes were observed between the two dietary regimens in the context of total body weight, BMI and blood lipid levels. At the end the researchers opined that alternate day fasting is an effective, safe and more compliant method for achieving a lower lean body mass²⁰.

Studies have also been conducted to underscore the effectiveness of the time restricted feeding regimen. In one such case control study undertaken by Gabel et al (2018) 23 Obese participants (case group) were subjected to a normal food intake between 10 am to 6 pm with an 8 hour time period of restricted food intake. The study period was 12 weeks with control group having no restrictions. The outcome indicated a significant reduction in body weight in the case group with a p < 0.05. Interestingly, the systolic blood pressure showed a significant reduction in the case group with restricted food intake. However, no significant difference was observed in visceral and lean fat mass between the case and control groups. The study finally suggested that an 8 hour restricted dietary intake regimen for 12 weeks could provide a mild reduction in caloric intake and body weight²¹.

The results of short term intermittent fasting have also been reported in recent years. A continuous 2 day fasting with normal food intake for rest of the five days in the week was repeated for 3 cycles in a non obese overweight adult male. A decrease of about 1.3 kilogram in body weight was observed at the end of 3 cycles without any significant reduction in the body fat ratio. A significant reduction was observed in high sensitive C reactive protein signifying the beneficial effect of this type of fasting on inflammatory markers. No changes were observed in glycated hemoglobin and waist hip ratio. However, this short term 48 hrs fasting was accompanied by a resultant increase in serum uric acid, blood pressure, fasting blood glucose level and body temperature which somehow underscore some of its side effects as well²².

Table 2: Different Types of Human Interventions

Sl. No.	Study conducted by	Type of study	Types of Intermittent Fasting regimes	Results of the study
1.	Johnson JB et al ⁷	Clinical Trial	Alternate day calorie restriction	Patients showing weight reduction (8% of initial weight), improvement in asthma related symptoms and pulmonary function
2.	Varady K. et al ¹⁵	RCT	Alternate day fasting	Alternate day fasting group has a decrease in body mass by 3.6 ± 0.7 kg as compared to the control group
3.	Bhutani S. et al ¹⁹	RCT	Alternate day fasting and exercise combined	Fasting or exercise alone are not fully effective. Exercise show maximum benefit when they are accompanied with alternate day fasting regimen.
4.	Catenacci VA et al ²⁰	RCT	Comparison between alternate day fasting and daily calorie restriction	No significant between-group differences observed in weight and body composition
5.	Trepanowski JF et al ¹⁶	RCT	Alternate day fasting on weight loss	There was no significant difference in the Mean weight loss between the alternative fasting regimen and continuous dietary restriction regimens.
6.	Gabel K et al ²¹ 2018	Clinical Trial	Time restricted fasting	There was significant reductions in both body weight and energy intake in the participants undergoing time restricted food intake pattern.
7.	Ooi S et al ²² 2019	Case Report	Modified Fasting Regimen; 5:2	An intermittent fasting regimen of 3 weeks showed a reduction of 2% in initial body weight along with 3.6% decrease in the initial fat mass.

LIMITATIONS AND FUTURE HOPES

At present we have limited amount of data related to the area of study. More amount of human intervention trials needs to be undertaken to explore the nature of intermittent fasting in long term cases; especially in obese, hypertensive and diabetics, where lifestyle modification is of primary importance. We have very little evidence about the effects of intermittent fasting on mental health of study participants, their sleep pattern, physical activities and bowel habits. More evidences are required linking the effects of IF on chronic diseases like Alzheimer's, cardiovascular diseases and cancer.

CONCLUSION

In general laboratory practice, patients are usually asked to maintain an overnight fasting of 8-12 hours, before collecting blood sample for various tests, which indicates that fasting helps the metabolic indicators to achieve the steady state in chronic diseases. Therefore, by adopting intermittent fasting regimes, a healthy metabolic state can be achieved. Many human intervention trials showed that intermittent fasting is successful in achieving short term weight loss in normal weight, over weight and in obese individuals, but to maintain this weight loss strict diet adherence is needed. The review showed that patients with metabolic diseases like diabetes, asthma and cardiovascular complications, improved with the intermittent fasting regimes, with better metabolic compliance.

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