

Effects of Intermittent Fasting on Human Metabolism and Evaluation of Its Effectiveness in Weight Loss

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Abstract:

Intermittent Fasting (IF), a dietary modification through time-restricted feeding, has gained significant attention in the past few years owing to its advantages in metabolic health and weight management. Available evidence suggests that IF can improve insulin sensitivity; lower the levels of blood glucose and fat; prevent body fat accumulation; and reduce the risk of obesity-related chronic disease by mitigating oxidative damage and affecting the activity of antioxidant enzymes. However, a number of gaps in knowledge remain regarding IF, especially its long-term safety and the generalisability of IF. This paper discussed the effects of IF on metabolism and body health through the mechanism of high-intensity, nutrient-strong IF. It mentioned that IF led to improved insulin sensitivity, lower blood lipid levels and inhibition of body fat accumulation, and was easier to stick to than daily calorie restriction. Other clinical studies with longer intervals and durations also reported significant effects of IF on weight loss and body health. Long term strict IF is unfavorable for some patients – in particular the elderly and the chronically ill – due to the potential for nutritional and metabolic problems. This study serves as an important reference for the use of IF in health and weight loss management, and offers potential directions for future research. Even though IF showed clear benefits, its safety in the long term and applicability across different populations still need to be validated. Future investigations may look into the long-term effects of IF in different populations, and its potential application in various health conditions.

Keywords: Intermittent fasting; weight loss; dietary modification.

1. Introduction

IF is a time-restricted eating protocol used for dietary regulation with alternating cycles of fasting and eating. The two most popular types of IF are the 16/8 protocol (where an individual eats in an eight-hour period, skips several hours for a snack and then fasts for 16 hours), the 5:2 diet (where an individual fasts for two days a week, with little to no restrictions on the remaining five days), and alternate-day fasting (where an individual fasts every other day). IF has been touted lately as a health intervention that can benefit metabolic health and wellbeing, while also playing a role in weight loss efforts. Studies have shown that IF leads to weight loss, and is also a great strategy for bolstering metabolic health, as well as enhancing autophagy and the rate at which we can slow the aging process. Intuitively, it makes sense to recognise that fasting is a healthful practice that one could likely benefit from, but the scientific literature has still widely supported these notions, which have finally reached a crescendo of noise in the media. At present, there are studies to show that IF acts on several metabolic pathways through a myriad of mechanisms – one of which includes improving insulin

sensitivity and lowering glucose levels, not to mention reducing body fat accumulation. Another mechanism by which IF works is through the reduction of oxidative damage and modulation of antioxidant enzyme activity, both of which reduce exposure to oxidants resulting in a reduced risk of chronic disease [1,2].

Due to lower meal frequency and caloric intake, which characterises IF, and a reduced blood insulin concentration, in patients, food consumption results in better sensitivity of the cells to insulin and lower glucose blood levels [1,3]. As a consequence, IF has important implications in the prevention and treatment of type 2 diabetes (T2D). IF affords a protective effect against aging and chronic disease due to higher production of antioxidant enzymes and lower levels of free radicals and, consequently, reduced oxidative stress (OS) [3,4]. It also has important effects on lipid metabolism, decreasing the levels of accumulation of body fat and release of blood lipids, with implications for cardiovascular health [1].

As far as weight loss is concerned, several clinical studies provide evidence that IF can help control weight, or help people reduce total calorie intake and hence lose body fat. Clinical trial data shows that IF is as effective as daily cal-

orie restriction in terms of weight loss, and even better in terms of ease of adherence and reduced hunger [2,3].

IF might not be appropriate for everyone, and its safety is also a concern. Some longer-term (ie, several months to years), severely restrictive IF regimens may lead to the development of chronic, irreversible nutritional and metabolic problems in some people. Thus, while there’s an understandable desire to start a regimen today, the safety of IF as a therapy remains an open question that should be fully evaluated both by the scientific community and by those considering its use. Guidance by a healthcare provider can ensure appropriateness and safety, depending on individuals’ medical conditions and needs [2,4].

With its potential benefits and the range of possibilities that it offers for self-control around food, it is need to carefully evaluate the impact of IF on human metabolism, energy loss and weight loss. The aim of this article is to evaluate the literature and the available data about IF, and to provide an overall assessment, in order to help individuals and physicians better understand the applications and implications of IF to their daily lives and dietary habits. This study will focus on the classification of IF and its effects on metabolism, including its effects on glucose metabolism, lipid metabolism and OS; the relationship between IF and weight loss; the assessment of its effectiveness; and the safety of IF, including its side effects and the extent to which it can be applied. By performing these analyses, this study hopes to provide more compelling support for the scientific use of IF, and also provide reference for the future development of relevant fields.

2. Metabolic Effects of IF

2.1 Glucose Metabolism

A particularly important area that has been studied relates to the effects of IF on glucose homeostasis – specifically, its impact on lowering blood glucose levels. It has been shown that IF reduces glucolipotoxicity as a result of significant improvements in insulin sensitivity. This major impact helps in the prevention (or management) of T2D. When the body becomes more insulin sensitive, there has been an overall increase in the effectiveness of one’s insulin. This in turn readily facilitates the uptake and utilisation of glucose by the cells of the human body, and thus it reduces the risk of hyperglycemia. The fasting state produced by IF significantly lowers blood glucose and post-prandial glucose variability; the mechanisms shown for this improvement involve reduction of insulin resistance, hence the overall beneficial impact on improving glucose metabolic health [5].

2.2 Lipid Metabolism

IF’s effects on lipid metabolism have also attracted significant attention. IF has been demonstrated to reduce blood lipid levels and body fat deposition, enhancing cardiovascular health.(Figure 1) IF can lower LDL-C and total cholesterol, while increasing HDL-C. All these factors reduce the risk of atherosclerosis and cardiovascular disease. Patterson et al. demonstrated that IF significantly reduced body fat stores by enhancing fat oxidation and reducing the size and number of fat cells [6].

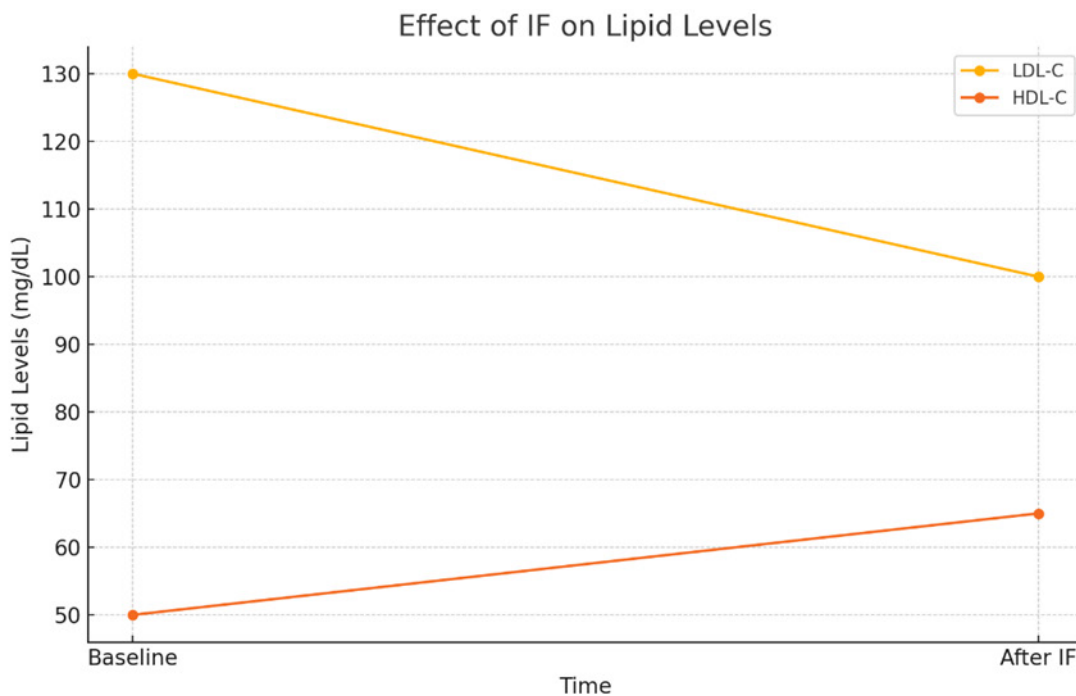


Fig. 1 Effect of IF on Lipid Levels.

2.3 Oxidative Stress

It's been described as a pathological condition driven by the production of excessive amounts of free radicals and reduced production of antioxidants. Many chronic diseases have been linked to OS, with one study suggesting that IF 'is beneficial in reducing OS and enhancing major

antioxidant enzymes, helping the cellular health. Some of the mechanisms of the influence of IF on OS have been reported. It has been described that IF decreases the level of free radicals and increases the activity of intracellular antioxidants. Conclusively, IF helps to reduce OS.

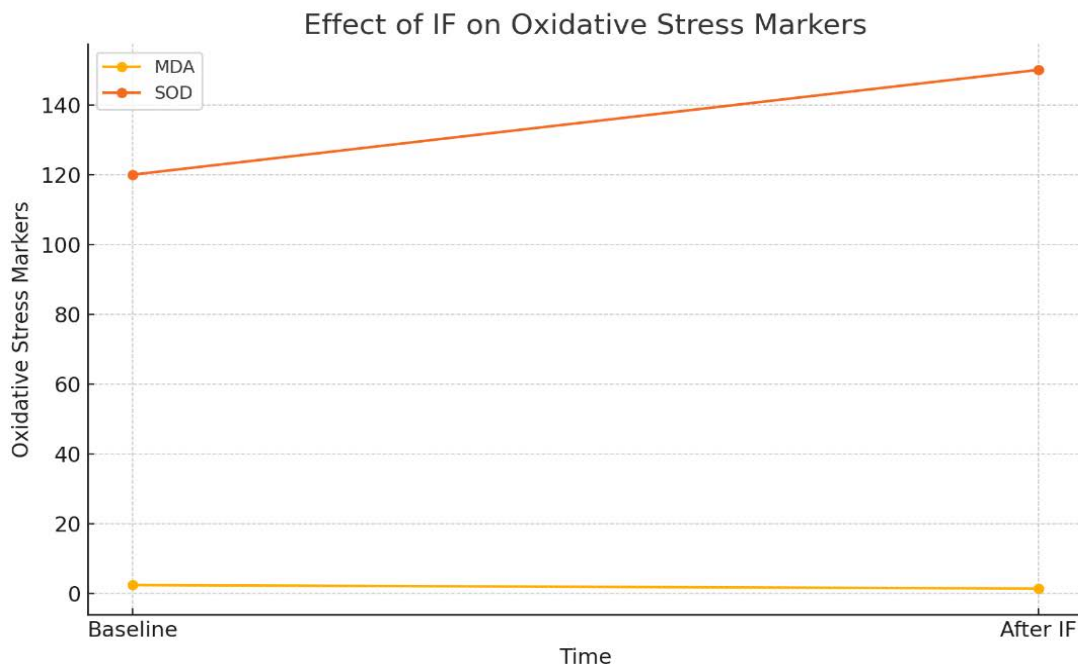


Fig. 2 Effect of IF on OS Markers.

de Cabo and Mattson reported that IF activates intracellular antioxidant responses to improve the capability of animals to resist stress which is linked to age. (Figure 2) For example, IF up-regulates the expression of SOD and GPx, increases anti-OS capacity [3]. Another study by Whitaker et al. showed that IF was found to improve brain pathology and memory function in the AD model mice [7].

3. Associations with Weight Loss

3.1 Clinical Studies

It is recognized that IF can help with weight loss because it limits daily eating – essentially a form of time-restricted caloric restriction, designed in a way that still allows us to eat a full set of meals and snacks within a shorter period of time. All restrictive eating will probably lead to weight loss and fat reduction, but the issue with conventional daily caloric restriction is that it isn't usually adhered to. There is mounting clinical trial data showing how IF is as effective in weight loss as daily caloric restriction methods, and even better in some cases. For example, people

were less likely to quit an IF eating pattern, because they weren't limiting the kinds or amounts of foods they were eating during the fasting cycle; they were just limiting the period of time during which they ate.

3.2 Data Analysis

Many meta-analyses have demonstrated the considerable weight loss effects of IF in various populations. For example, in a randomised controlled trial of several hundred participants who were randomised to either an IF group or a control group, the average weight loss in the IF group was significantly higher than in the control group. Participants not only lost weight but also had significant reductions in reported percent body fat and waist circumference. Other health biomarkers that seem to benefit from IF include blood pressure and markers of inflammation. In fact, a recent study demonstrated that while an 8-hour time restricted diet (16:8) had some health benefits in the short term, long-term observation could reveal a greater risk of cardiovascular death.

3.3 Assessment of IF

IF has been generally accepted standard methods to assess body composition, which includes body weight, body fat percentage, body mass index (BMI), waist circumference circle, as presented in Table 1. All of these parameters are parameters related to body composition and can reflect the effects of IF on body composition and body health through comprehensive evaluation. If we consider the percentage of body fat as a sign of health, we can also infer the effects of IF on body composition and health from the body weight. de Cabo and Mattson made a summary based on evidence that IF not body fat, but alsoolic health and reducing theid levels in the blood important signals of health.

4. Association with Weight Loss (Effectiveness)

4.1 Clinical Studies

From a clinical perspective, IF leads to weight loss as the restriction of feeding time results in a decrease of total calorie intakes and triggers the mechanisms associated with weight loss. Overall, these dietary interventions have shown better weight losses and diet adherence when compared with traditional daily calorie restriction.

A randomised controlled trial of Catenacci and colleagues,

where subjects were asked to adhere to an IF diet (accompanied by decreased carbohydrate consumption) or a control group (no time restriction and carbohydrate-rich diet) for one year showed significantly better weight loss with the IF group: ‘Over the 12-month study period, subjects in the IF diet group lost more weight and were more likely to adhere to with controls.

Besides weight loss, IF has also resulted in significant decreases in body fat percentage and waist circumference, as shown by a study of Tinsley and Boutenko in 2014. Such factors are of importance for the prevention of obesity and the treatment of metabolic syndrome [8].

4.2 Clinical Studies

Multiple meta-analyses have shown the same effects of weight loss in the general population when IF is used. In a meta-analysis of randomised controlled trials, Mollasadeghi et al showed that IF produced much greater weight loss than percent body fat and BMI, as well as similar or even better weight-loss effects than daily calorie restriction. Similarly, in a large, real-world clinical trial of IF, Schwarzfuchs et al showed that, in addition to lowering weight, IF produces many beneficial health effects on a wide range of health factors, such as blood pressure and inflammatory markers (see Figure 3) [9, 10].

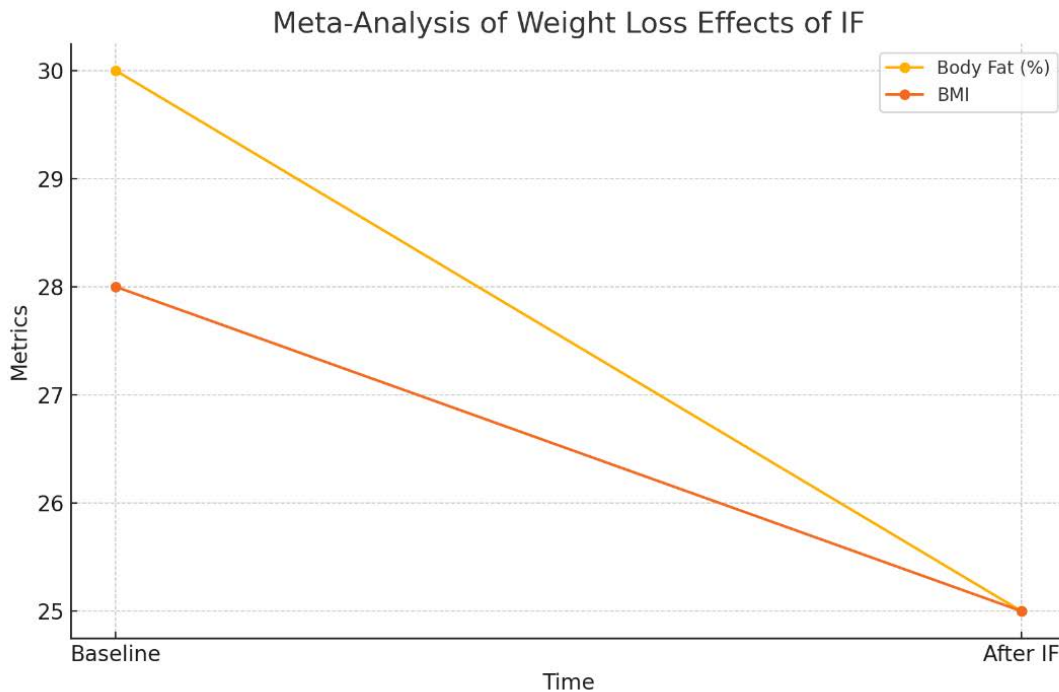


Fig. 3 Meta-Analysis of Weight Loss Effects of IF.

4.3 Assessment of Metrics

Indicators for the weight loss effect of IF may include body weight, body fat percentage, BMI and waist circumference. These are important indicators for the effects of IF to body composition and health status. Afiri et al. reported, with the data from Varady et al., that IF reduced body weight and body fat percentage effectively, by adding that IF also improved insulin sensitivity and blood lipid levels. Weinandy and Weiss also reported that IF reduced the risk of cardiovascular disease and metabolic syndrome by lowering visceral fat amount and improving metabolic health [11].

5. Safety

5.1 Side Effects

Despite its numerous health advantages, IF, particularly its prolonged (months to years) practice, can have detrimental side effects and cause chronic irreversible nutritional and metabolic problems. Populations susceptible include frail older individuals and younger people with existing chronic illnesses such as cardiovascular disease and diabetes. For instance, Horne et al suggested that prolonged IF can lead to malnutrition, bone loss and endocrine disruption. Likewise, a study by Anderson et al reported that IF might be associated with various gastro-intestinal discomforts including bloating, constipation and heartburn.

5.2 Applicability

The applicability of IF varies depending on age, gender, and health status. IF is generally safe and efficacious in most adults; however, the safety, tolerability, and efficacy of IF in children, adolescents, pregnant and lactating women, and increasing number of patients with certain comorbidities with chronic diseases all warrant more caution. In a review article, Rynders et al. pointed out that children and adolescents are primarily in the period of growth and development and IF might interfere their normal development and nutrient intake. Moreover, some patients with specific metabolic disorders or dietary treatments should cautiously undertake IF under strict clinical supervision as indicated [12].

6. Conclusion

In various forms, IF is a type of dietary control by time-restricted eating that has received much public attention in recent years with regard to metabolic health benefits and ways to promote weight management. Studies have shown that IF has positive effects on human metabolism through various pathways. Firstly, IF has been demonstrated to significantly improve the sensitivity of insulin and lower the level of blood glucose, which is important

in the prevention and management of T2D. Secondly, IF is beneficial for cardiovascular health by reducing body fat accumulation and blood lipid levels while increasing the level of fat oxidation. Thirdly, it reduces the risk of chronic disease and decreases the degree of ageing by lowering the level of oxidative damage and modulating antioxidant enzyme activity.

Data from clinical trials and analyses of the literature suggest that IF is indeed an effective means of losing weight. IF is as effective as, and indeed better than, daily caloric restriction for weight loss when it comes to the overall effectiveness of dietary adherence and, more importantly, hunger. To date, several clinical trials on adults have demonstrated that subjects using IF genuinely lose weight, as evident through metrics such as body weight, body fat percentage, waist circumference, blood pressure and inflammatory markers.

But IF is not the panacea – it is not good for all populations. Some studies have found that chronic and severe IF can cause nutritional and metabolic problems in some people, especially frail older adults and younger people with pre-existing chronic conditions. In particular, studies have suggested that IF can lead to issues such as malnutrition, bone loss and endocrine disruption if done over the long term. For these reasons, those who wish to try IF should do so with the help of a medical professional to ensure it is a good fit and safe for them.

To summarise, the IF is shown to be a promising dietary modification for improving health and weight loss outcomes, but further research and validation are needed to explore its long-term safety and applicability. Future research should further explore the long-term effects of IF in different populations, and evaluate IF's potential for gaining application as a health or weight-loss management tool. This will provide a more solid scientific basis for individuals and clinicians to put IF into practice to achieve optimum health and weight loss.

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