

CRITICAL ANALYSIS OF INTERMITTENT FASTING

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ABSTRACT

Introduction: *Intermittent fasting (IF) is an alternative dietary pattern that imposes the complete or partial restriction of all sources of calories for a specific period in time. In-between these periods there is a restricted time window to consume calories in the form of food, drinks, etc. IF is one of the most popular regimens amongst dieters worldwide. Despite the popularity of this dietary pattern, there are plenty of misconceptions regarding both the benefits and health risks of IF.*

Review Results: *Intermittent fasting does not appear to produce any metabolic advantages or disadvantages compared to other methods for calorie restriction despite the effects on hormones, meal skipping, and the effect of continuous fasting on energy expenditure. It is as effective as continuous energy restriction in improving body weight and cardiovascular risk factors. IF might also provide benefits against oxidative stress and inflammation. Its effect on autophagy is not yet investigated in humans. Despite the benefits for weight loss and metabolic health, certain population groups such as women with normal and low body weight might experience worsened glucose tolerance due to fasting. There is also a risk for hypotonia, hypoglycemia, menstrual problems, and others.*

Conclusion: *IF is as effective as continuous calorie restriction and there do not appear to be any metabolic advantages or disadvantages related to fasting. Long-term adherence might be an issue for a significant percentage of dieters. Currently, there is a lack of evidence for the long-term safety and effectiveness of IF regimens.*

Keywords: *intermittent fasting, weight loss, metabolic effect, alternate-day fasting, health risks*

INTRODUCTION

Intermittent fasting (IF) is an alternative dietary pattern that imposes the complete or partial restriction of all sources of calories for a specific period in time. In-between these periods there is a restricted time window to consume calories in the form of food, drinks, etc. This time-restricted feeding reduces the person's ability to consume more calories, which can lead to energy deficit and weight loss.

There are three main groups of IF regimens. The first and most commonly practiced is when the caloric intake is restricted only to a few hours per day. Examples include 16:8, 18:6, 20:4, and 22:2. The latter is also known as the warrior diet and restricts your daily intake of calories to just a couple of hours or one meal in total. 16:8 is the most prevalent which restricts the caloric intake to 8 hours per day, while the

remaining 16 hours, including the period of sleep, is the period of fasting.

The second group of regimens requires fasting from 1 to 3 days per week. The most common pattern is 5:2, which includes 2 days of complete or partial caloric restriction and 5 days of normal eating each week. Thus, each period of fasting lasts about 36 hours, including the two periods for sleep, before and after the day for fasting.

The last and most restrictive pattern is called alternate-day fasting, which requires fasting every other day. Again, each period of fasting lasts about 36 hours, including the two periods for sleep, before and after the day for fasting.

According to the annual survey of the International Food Information Council, IF is one of the most common diets worldwide (1). The 2019 Food and Health Survey revealed that about 10% of all

people following a diet, are following IF. A study performed on the US population reported that about 14% of all Americans following a diet are practicing IF (2).

Despite the popularity of this dietary pattern, there are plenty of misconceptions regarding both the benefits and health risks of IF. Most people are unaware of the potential risks of IF for certain population groups, while others are often concerned for the wrong reasons. This review will critically assess the current evidence on IF in regards to the most commonly perceived advantages and disadvantages and attempt to separate reality from misbelief.

The review will address the metabolic effects of IF as well as the claims for a metabolic advantage over other weight-loss diets. We will focus on weight loss and related benefits, as well as other possible advantages. Furthermore, we will point out the contraindications against IF as well as risk groups that should avoid the diet.

METHODS

A literature search was performed using PubMed, MEDLINE, and the reference lists of the selected articles. The keywords used were: intermittent fasting AND weight loss* OR health benefits* OR health risks* OR metabolic effect. The search resulted in a total of 45042 articles from the last 30 years. The first 100 articles were reviewed and based on title and abstract relevance, 21 articles were selected.

Metabolic Effects of IF

Intermittent fasting is most commonly used as a weight-loss regimen by people aiming to lose fat and improve their health and physique. However, most supporters of the regimen also claim that it has metabolic advantages over other weight-loss diets and it results in fat loss without the need for a caloric deficit.

One of the main theories behind these claims is that IF stimulates the release of growth hormone (GH) and results in higher amplitude and frequency of GH pulses. GH has a well-known role on human adipose tissue and especially abdominal fat storage. The hormone stimulates the process of lipolysis and the release of free fatty acids into the bloodstream where they can be oxidized and used for energy. A study in nine healthy men reported that 24 hours of fasting results in a 2-fold rise in GH production rate, while 56 hours of fasting increased the GH secretion 5-fold (3).

However, a systematic review of 40 clinical trials reveals that such metabolic advantage does not occur despite the effect on GH (4). The review reported that there is no physiological benefit of IF over continuous dieting and if the caloric deficit is the same, so

is the rate of weight loss. That's likely because, even though GH may increase the mobilization of fatty acids from the adipose tissue, it is the energy deficit that will be the determinant of how much of those acids will be oxidized for energy.

On the other hand, there are concerns that skipping meals and fasting might have a negative effect on the metabolism. For example, IF regimens such as 16:8, 18:6, etc., often involve skipping breakfast. Indeed, epidemiological studies have previously suggested that people who skip breakfast tend to be overweight or obese more often than those who eat breakfast regularly (5).

However, correlation does not necessarily mean causation. A meta-analysis of 13 randomized clinical trials revealed that the addition of breakfast in those who are overweight and skipping it does not solve the problem with the extra body weight (6). On the contrary, body weight increased due to higher caloric intake in those who added breakfast and it resulted in worsening obesity.

Skipping more than one meal and fasting for more than a day is also often the subject of concern because of a presumed negative effect on metabolism. When losing weight there is a natural metabolic adaptation, which results in a lower resting energy expenditure (REE) and basal metabolic rate (BMR). If the weight is regained, so is the BMR as part of the adaptation.

However, this adaptation is often called starvation mode or even metabolic damage, implying that it is a permanent condition that will prevent further weight loss and result in rapid weight gain once caloric intake is increased.

Studies suggest that the effect of short-term fasting on the metabolism is rather minor, and sometimes even beneficial. A study in healthy individuals fasting for at least 3 days revealed only an 8% reduction in REE (7).

Another study in 11 individuals who fasted for 48 hours reported an increase in REE with 3.6% (8). Again, a study in 11 healthy individuals who fasted for 3 days reported a 14% increase in REE (9).

A reason for these increases in REE during short-term fasting might be the significant release of nor-epinephrine which triggers the sympathetic nervous system and the metabolism (10).

Weight Loss and Related Health Benefits

A systematic review and meta-analysis, which included 6 studies, showed that IF is effective in treating overweight and obese patients, and it is comparable to the effectiveness of continuous energy restriction (11).

Another systematic review and meta-analysis of 11 randomized controlled trials also concluded that the effect of IF and continuous energy restriction is the same and both strategies can successfully reduce weight but long-term trials for IF are needed (12).

A third systematic review and meta-analysis of trials that lasted only more than 6 months once again confirm the effectiveness of IF. It has also comparable effectiveness to continuous energy restriction when it comes to improving lipid profile, glucose tolerance, and insulin levels (13). However, the meta-analysis warns that there is a lack of long-term trials lasting more than 12 months.

Yet, IF might have some disadvantages when it comes to hunger control and sustainability. Sustainability is indeed one of the most important factors for the success of a weight-loss diet (14).

Short-term studies reveal that individuals on IF tend to compensate for the hunger from the period of fasting by choosing more calorie-dense foods in the period when food consumption is allowed (15). The effect did not result in overcompensation and caloric surplus, so the subjects remained in a caloric deficit and lost weight. Unfortunately, the rates of hunger do not lower with time, which calls into question long-term adherence to IF (16).

Long-term studies are required to assess the safety and effectiveness of IF. According to a systematic review of randomized trials, IF can lead to benefits regarding body weight in the short term, including a lower incidence of cardiovascular conditions and diabetes (17). However, its long-term benefits and effects remain unknown. Thus, IF can't be recommended as a health intervention in people with obesity or related problems.

Autophagy and Other Health Benefits

Apart from the effects on weight loss and related health benefits, IF might also provide additional advantages. One cellular process often associated with fasting is autophagy. It is a defensive lysosomal pathway for intracellular degradation of macromolecules as well as recycling damaged organelles and misfolded proteins. The purpose of the process is to ensure cellular homeostasis and optimal function (18).

Dysfunction in the process of autophagy is considered to play a role in the pathogenesis of multiple chronic and debilitating processes including aging, carcinogenesis, neurodegenerative conditions, etc.

Currently, there are only *in vitro* and animal studies suggesting that short periods of complete energy restriction and fasting stimulate the process of autophagy in tissues such as the nerve tissue and might provide benefits for neurodegenerative conditions (19).

Unfortunately, there is no evidence in humans, apart from indirect benefits for oxidative stress and inflammation observed in a few clinical trials. One study in ten subjects on alternate-day fasting regimen reported that there were significantly increased levels of certain antioxidants, while indicators of neuroinflammation were decreased (20). Studies also show decreased levels of TNF- α , IL-6, and CRP in participants following a prolonged IF regime (21, 22).

Contraindications and Risk Groups

Despite the fact that weight loss can improve glucose tolerance and benefit insulin sensitivity, studies reveal that IF might have the opposite effect in certain population groups. A study in people with normal BMI revealed that in women, but not in men, 3 weeks of IF leads to a worse glucose tolerance than before which is an indicator of insulin resistance (23).

Furthermore, IF might have other negative effects on women who are with normal BMI or underweight including problems with the menstrual cycle and fertility. Despite multiple anecdotes of such effects, currently, there are no human studies to support it. However, animal studies show that IF can lead to changes in the hypothalamic-pituitary-ovarian axis in female mice, dysregulated menstrual cycle, and infertility (24).

Women are also more likely to experience hypotension and hypoglycemia while fasting, which makes IF an inappropriate regime for weight loss in this population group. Certain gastrointestinal conditions such as gastritis and ulcers might also be worsened during fasting. Furthermore, children, adolescents, and pregnant women should avoid IF.

There is only one trial investigating the effect of IF on patients with eating disorders (25). The study revealed that patients suffering from binge-eating disorder experience improvement in their condition and symptoms of depression after 8 weeks. However, there was no improvement in self-perception and purgative behavior.

CONCLUSION

Intermittent fasting appears effective for achieving weight loss and related health benefits in the short term, but it might not be a suitable dietary approach in some population groups. The method is as effective as continuous calorie restriction and there do not appear to be any metabolic advantages or disadvantages related to fasting. However, long-term adherence might be an issue for a significant percentage of dieters. Currently, there is a lack of evidence for the long-term safety and effectiveness of IF regimens.

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