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Effects of Intermittent Fasting on Weight Loss and Metabolic Health

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Abstract

Introduction and Purpose: Intermittent fasting (IF) has become a popular strategy for combating obesity and improving metabolic health. This dietary regimen alternates between periods of fasting and eating, aiming to enhance cellular health and increase longevity. With obesity rates doubling globally since 1990 and metabolic diseases on the rise, IF offers a potential solution by promoting metabolic benefits and reducing obesity-related conditions.

Material and Method: This review examines various IF methods, including alternate-day fasting, the 5:2 diet, and time-restricted eating. The analysis focuses on the impact of these fasting methods on body weight, insulin sensitivity, and lipid profiles, based on a compilation of studies that explore the physiological effects and health outcomes associated with IF.

Results: IF has shown to be effective in reducing body weight and improving metabolic parameters. Studies indicate significant benefits in insulin sensitivity and lipid profiles, with some variations across different IF protocols. Physiological insights reveal that IF leads to a metabolic switch from glucose-based to ketone-based energy, which plays a critical role in its effectiveness.

Conclusions: Intermittent fasting appears to be a viable alternative to continuous calorie restriction for weight loss and metabolic enhancement. It not only aids in weight management but also offers additional health benefits such as improved insulin sensitivity and better lipid profiles. However, more long-term studies are needed to fully understand its benefits and potential risks. Future research should focus on optimizing fasting protocols and exploring their long-term effects on health and disease.

KEYWORDS: intermittent fasting; intermittent fasting and metabolic health

INTRODUCTION

Intermittent fasting (IF) has garnered considerable attention as a method for weight management. It involves alternating between periods of eating and fasting, emphasizing both timing and overall food intake.[1] Latest research indicates that in 2022, 1 in 8 people in the world were living with obesity. In addition, since 1990, the global adult obesity rate has more than doubled. There were 2.5 billion adults over the age of 18 who were overweight, with 890 millions of them classified as obese.[2] Additionally, IF may enhance metabolic health and decrease the likelihood of obesity, as well as related conditions like nonalcoholic fatty liver disease, diabetes, and cancer.[3] This dietary approach promotes metabolic and cellular health, potentially delaying the onset of age-related diseases and enhancing longevity.[4,5] However, there is limited data from human studies regarding the beneficial effects of time-restricted heating.

PURPOSE OF STUDY

This review aims to thoroughly analyze the effects of intermittent fasting (IF) on body weight, insulin sensitivity, and lipid profiles by evaluating a variety of studies that have explored the efficacy of different IF methods, such as alternate-day fasting, the 5:2 diet, and time-restricted eating. The primary objective is to systematically assess the impact of IF not only on weight loss but also on enhancing metabolic functions, potentially mitigating obesity-related conditions, and improving overall health outcomes. This review also seeks to explain the physiological mechanisms through which IF exerts its effects, considering its potential to delay the onset of age-related diseases and enhance cellular health. By integrating findings from diverse clinical trials and observational studies, this review addresses the growing need for effective dietary strategies against the backdrop of a global obesity epidemic and associated metabolic diseases. This is particularly important at a time when obesity rates are at historic highs and the medical community is urgently seeking sustainable, effective interventions.

METHODS OF INTERMITTENT FASTING

Intermittent fasting methods generally fall into three main categories: alternate-day fasting (ADF), the 5:2 diet, and time-restricted eating (TRE).[6] ADF consists of a cycle between days of no food intake at all and days where eating is allowed without restrictions. The 5:2 approach limits calorie intake to approximately 500 for women and 600 for men on two non-sequential days of the week, permitting normal eating on the other days. TRE differs by establishing a consistent daily schedule, restricting food intake to a specific timeframe each day, such as the 16:8 method, which confines eating to an 8-hour period and fasting for the remaining 16 hours.[7] This is the most popular model of time-restricted diet, however, the hours can be adjusted according to individual preferences, work, etc. The methods are presented in Table 1. [6,7]

Main Intermittent fasting schemes

DIET	FEED DAY Energy Allowance	FAST DAY Energy Allowance	Weekly Fast Days	Feeding Window
ADF Alternate-Day Fasting	normal eating	0%	$\frac{3}{4}$	Open
5:2	normal eating	25% women 500kcal men 600kcal	2	Open
TRF Time-Restricted Feeding	normal eating	normal eating	7	<10h

Table 1

Weight reduction through IF is generally comparable to that achieved through daily calorie restrictions. IF may offer additional advantages like increased insulin sensitivity, independent of weight loss. Given the variability in individual responses to different IF regimens, no singular approach is deemed universally effective.[8] Other analyses indicated that IFD notably reduces BMI, fasting glucose levels, and insulin resistance measures compared to control diets. Also, notable biochemical changes included increased adiponectin levels and reduced leptin levels, suggesting potential metabolic benefits. This evidence suggests that intermittent fasting may offer considerable advantages for glycemic control and weight management in adults.[9]

Physiology of intermittent fasting

The main source of energy on which IF is based are ketones. The shift from glucose-based energy to ketones, which are derived from fatty acids, acts as a pivotal moment that transitions metabolism from synthesizing lipids and cholesterol and storing fat to activating fat breakdown through fatty acid oxidation. [10] Glucose falling approximately 6 hours post-meal, then decrease and remain low until the following day. [11] However, for this reaction to occur, decreasing glucose is not enough. The metabolic switch occurs only after 10-14 hours after the glycogen stores in their liver are empty. Some research even claims up to 36 hours after stopping food intake. This timing varies based on the amount of food consumed, the initial level of liver glycogen and exercise during the fasting period. After liver's glycogen reserves are used up, fats stored in adipocytes are broken down into free fatty acids (FFAs) through lipolysis. These FFAs are subsequently released into the bloodstream. The FFAs are transported to liver to produce the ketones acetone. Gene called SIRT1 which is activated during the shift from glycogenolysis to ketone production play an important role in the process. It contributes to decreasing glucose production, prevents liver fat accumulation, and regulates energy expenditure. [4] As a result, ketones are produced and therefore able to encourage the growth of new mitochondria, enhance synaptic flexibility and boost cellular resilience against stress by stimulating producing of BDNF (brain-derived neurotrophic factor). The products of metabolic switch also stimulate realising GLP-1 (glucagon-like

peptide 1) into blood. Hormone which improves glucose removal from the bloodstream as well as enhances insulin sensitivity in cells.[12] Additionally, adenosine triphosphate (ATP) is another product ketones are metabolized into. This process is conducted in cells with elevated metabolic rates, such as muscle cells and neurons. This mechanism allows ketones to act as a vital energy source, sustaining the function of both muscle and brain cells during fasting and prolonged physical activity. Increasing evidence indicates that certain organ systems demonstrate comparable cellular and molecular reactions to aerobic exercise and intermittent fasting (IF), such as the inhibition of mTOR, activation of autophagy, and promotion of mitochondrial biogenesis.[4] Research also outlining the function of autophagy in cancer and its prospective use as a therapeutic target. [13]

Effects of intermittent fasting on bodyweight

Chronic overeating results in the accumulation of excess fat tissue, termed obesity, and is associated with various metabolic alterations, including insulin resistance and type 2 diabetes mellitus.[14] Regulating caloric consumption can potentially reverse these metabolic shifts. Intermittent fasting is an effective strategy for facilitating weight loss. Studies indicate that this approach aids in reducing body weight. [1,5,9,15,16,17,18,19] However, there are differences in the findings of various studies. Some research indicates no significant change in weight with lean mass largely preserved.[9] In contrast, other studies report a considerable decrease in body weight, approximately 8 kg, after eight weeks of alternate day fasting (ADF). Unfortunately, these studies do not offer details on changes in body composition.[20] According to another research, presented results are more specific and include information regarding alterations in body composition such as an approximate reduction of 4 kg in body weight, including 3 kg of fat mass and 1 kg of lean mass.[15]. Other studies have shown a decrease in both body weight and fat mass, with lean mass remaining stable [17,18]. These findings relate to obese individuals, but similar outcomes are observed in non-obese groups. For instance, after a four-week ADF regimen, there was a 4.5% decrease in body weight along with an improvement in the fat-to-lean mass ratio [5]. When comparing the effectiveness of intermittent energy restriction (IER) with continuous energy restriction (CER), both methods show similar effectiveness in promoting short-term weight loss and

metabolic improvements. However, more long-term research is needed to provide definitive conclusions. [21,22,23]

Effects of intermittent fasting on glucose metabolism and insulin sensitivity

Excessive calorie consumption has become increasingly prevalent in modern diets, contributing to a rise in obesity and related health issues. This trend towards higher calorie intake often stems from easily accessible processed foods high in sugar and fat, exacerbating lifestyle diseases.[10] This phenomenon leads to glucotoxicity. Nonphysiologically, potentially irreversible harm within pancreatic beta-cells caused by prolonged exposure to excessively high glucose levels, resulting in impaired insulin secretion and deteriorating glucose control.[24] Intermittent fasting has been found to offer benefits for managing blood sugar levels in individuals with metabolic syndrome, significantly enhancing insulin sensitivity. It can serve as a supportive treatment strategy to mitigate the consequences of abnormal glucose levels and therefore the risk and progression of chronic illnesses such as atherosclerotic and cardiovascular diseases, along with insulin resistance and diabetes, which can lead to various vascular and neurological issues, including strokes.[25] While there may be some varying findings, the majority of research suggests that intermittent fasting leads to a reduction in insulin levels and improves insulin sensitivity.[15,16,26] Definitely, may enhance insulin resistance conditions better than not following any specific, structured eating plan.[27] Some research presents the superiority of IF in lowering insulin levels over calorie-restricted diets.[21,22] However, no significant or clinically meaningful differences in insulin sensitivity was found between those practicing long-term Alternate Day Fasting (ADF) and the control group of non-obese people.[5] That presents a pattern that IF may affect differently based on level of insulin resistance.

Effects of intermittent fasting on lipid profiles and cardiovascular disease

Increased triglycerides (TG) in the blood, and reduced levels of high-density lipoprotein (HDL) in the blood are two of five factors indicating metabolic syndrome [28] and both concern lipid profile. In addition, the condition contributes to the proliferation of illnesses such as type 2 diabetes, heart diseases, strokes, and various other health complications. What contributes to developing diseases mentioned above is sedentary lifestyle

and consuming a high-calorie-low fibre diet.[29] Modifying one's diet could offer protection against developing DM2 and heart-related conditions. This process often co-occurs with not only affecting lipid profile but also weight body reduction. [1,17,30] Compared to individuals who do not follow any diet, those who adhere to intermittent fasting (IF) and energy-restricted diets (ERD) see notable improvements in their levels of lipid profile.[31] Whereas, comparing IF and ERD the findings are still nonconclusive. Both diets have similar potential to improve the physical measurements, body composition, and lipid profile of overweight or obese adults. [21, 23] Research on specific lipid classes presents a decrease in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). However, not significant change in high-density lipoprotein cholesterol (HDL-C) levels is observed. [18,31] Whereas, the others demonstrate a positive impact of IF on HDL-C levels.[19,32,33] IF has been demonstrated to effectively decrease the risk of cardiovascular disease (CVD) not only in overweight or obese individuals but also in metabolically healthy, non-obese patients. Significant improvements in blood lipid levels were observed after more than six months of ADF intervention.[5]

Conclusions

This comprehensive review on the effects of intermittent fasting (IF) on weight loss and metabolic health reveals a multifaceted impact. IF, encompassing methods like alternate-day fasting (ADF), the 5:2 diet, and time-restricted eating (TRE), offers a promising alternative to traditional calorie restriction diets. The evidence consistently shows that IF can lead to weight loss, with some studies highlighting its superiority in improving insulin sensitivity and lipid profiles. Intermittent fasting's physiological impacts, particularly its ability to switch metabolism from glucose-based to ketone-based energy, play a crucial role in its health benefits. This metabolic switch not only supports weight loss but also stimulates the breakdown of fats, reduces inflammation, and enhances cellular health. Notably, the shift to ketone production and utilization promotes improvements in cellular resilience, which may delay aging and mitigate age-related diseases. In terms of weight management, IF has shown comparable or even superior results to continuous energy restriction, especially in the context of significant body weight reduction and metabolic improvements. The variability in

individual responses suggests that personalization of IF regimens could enhance their effectiveness and sustainability. For metabolic health, IF has been shown to improve glucose control and insulin sensitivity, making it a viable intervention for individuals with metabolic syndrome and type 2 diabetes. Additionally, intermittent fasting positively influences lipid profiles, reducing the risk of cardiovascular diseases. While the current body of research provides substantial evidence supporting the benefits of IF, long-term studies are necessary to fully understand its impact on health, sustainability, and potential risks. Future research should focus on the mechanisms underlying the health benefits of IF, the optimal fasting protocols for different populations, and the long-term effects of IF on health and disease. In conclusion, intermittent fasting emerges as a beneficial strategy for weight loss and metabolic health improvement, offering a feasible alternative to traditional dieting methods. Its potential for widespread application in public health and individual wellness needs further exploration to optimize its implementation and understand its full scope of benefits and limitations.

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