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Chapter 4

Intermittent fasting: a precautionary alternative remedy for people with obesity

Madison Gaia Martinez Uzarraga, Silvana Carolina Delgado Ortega, Viviana Medina Moreno, Valeria Esquivel Barbosa, María Guadalupe Haros Saucedo, Gilberto Mercado Mercado

Abstract

Intermittent fasting (IF) has become popular due to the ease of reducing body weight by alternating periods of fasting with unrestricted eating; however, its frequent practice may have consequences unknown to most users. The IF diet triggers adaptive cellular responses that cause a decrease in inflammatory markers that go hand in hand with alterations in metabolic and physiological processes that could help treat and prevent obesity and associated diseases. This chapter narrates, focuses and analyzes the different types of IF and their contributions to health improvement. Thus, the hypothesized intermittent fasting regimens offer promising approaches to improve population health.

Keywords:
Intermittent fasting; calorie restriction; health; obesity; metabolism.

Introduction

Currently in Mexico, 70% of Mexicans are overweight and almost a third suffer from obesity, which is why these have been identified as a problem and the challenge of the coming decades (Llamas et al., 2024). Both pathologies are considered as chronic diseases, among their main characteristics we can find an excessive accumulation of fat mass as a consequence of the excessive consumption of calories, representing an energetic imbalance as they are stored and not expended (Templeman et al., 2018).

One of the alternatives that have been put into practice is the restriction of energy and comprehensive intervention on lifestyle to generate a moderate weight loss (Canicoba, 2020), however, since obesity is a precursor of multiple chronic diseases such as diabetes mellitus, hypertension and heart disease, it has been required to implement an effective diet for weight loss with good metabolic results, which is why intermittent fasting is an alternative option to regulate obesity (Ederra Unzu, 2021).

The subject of weight loss is a very current topic, we can see that there is a global trend to consume healthy foods because of the interest and awareness of consumers, although this is not the only reason. That is why every day there are more diets and different techniques to lose weight, however, we are going to focus on the effectiveness of intermittent fasting for weight loss. Most diets focus on what to eat, while intermittent fasting revolves around when to eat (Fung, 2016). As discussed above, with fasting, food intake is only allowed for a certain period of time, either for hours or days, depending on the type of fasting being performed.

Intermittent fasting (IF)

IF is a practice that has been performed throughout the history of human beings, dating back to the time of the cavemen, who unconsciously practiced it due to the lack of food that could not be found to subsist, therefore, they could spend long periods fasting between meals (Song and Kim, 2023). This practice has been recommended since the 5th century, where Hippocrates recognized the healing aspects of a diet based on IF, as well as Socrates, Plato and Aristotle who considered it as a good practice to maintain and improve their healthy body (Brogi et al., 2024). Likewise, IF is also used from the spiritual, medicinal, therapeutic, nutritional and even as a way of life point of view; but nowadays this temporary food restriction is focused on an improvement in the health of the body (Nye et al., 2024).

IF is a process of caloric restriction, daily by a voluntary act of refraining from ingesting calorie-dense foods, beverages and/or supplements during specific and recurrent periods (Ke et al., 2024; Elsworth et al., 2023). It should be emphasized that AI is not generic and should not be confused with starvation, i.e., a state of chronic uncontrolled non-voluntary nutritional deficiency that can result in death. Therefore, it is important to determine that this restriction can occur during one or more days per week, continuous (12, 16, 24 and 48 h) or alternated, generating changes in eating habits in a conscious manner; where healthy foods (fruits and vegetables), hydrating liquids and non-caloric stimulants (water, tea, coffee, infusions) are included, as well as physical activity, provoking adaptive cellular responses during the fasting period so that the cells participate in specific tissue processes of growth and plasticity, with important metabolic effects, resistance to stress and suppression of inflammation (Brogi et al., 2024). Also, it is important to highlight that while sleeping, the body is fasting, which eliminates toxins and undesirable metabolites inducing an increase in the amount of urine (Benjamin et al., 2015).

Metabolism in intermittent fasting

Previously mentioned, IA induces the coordinated alteration of metabolic and transcriptional mechanisms after 12 to 36 h (Mattson et al., 2017). The organism, when it senses the need for glucose and fatty acids, the cell produces molecular mechanisms causing the body to enter a physiological state of adipose tissue lipolysis, whereby triglycerides are hydrolyzed to increase the production of free fatty acids (FFA), glycerol, and ketone bodies (KB; acetoacetate and β-hydroxybutyrate (βHB)). These metabolites are produced in the liver and are transported to the brain and many tissues to be used for their energy needs (Brogi et al., 2024; Ke et al., 2024). In the liver FFA are oxidized to βHB and acetoacetate to become energy through β-oxidation, involving an increase in circulating FFA and other changes related to glucose and FFA metabolism (Benjamin et al., 2015; Morselli, et al., 2010). Also, KB function as receptor coactivators and activators by peroxisome proliferator 1a (PGC-1a), fibroblast growth factor (Gälman et al., 2008), nicotinamide adenine dinucleotide (NAD+) with energy production and sirtuins (Brito et al., 2019). In addition, IF regulates mitochondria functions, whereby peroxisome proliferator-activated receptor alpha (PPAR-α) induces the expression of genes that regulate AG oxidation in muscle cells and suppresses the expression of proinflammatory cytokines (IL-6 and Tumor Necrosis Factor α (TNFα) (Longo & Mattson, 2014). During IF, autophagy of body tissues is also promoted, which has been considered an optimal intervention to improve health and increase longevity, which in turn influences lipid metabolism by altering the activities of some anorexigenic and oroxigenic hormones, involved in the

regulation of appetite and satiety mechanisms, such as ghrelin, leptin, insulin, amylin, peptide YY (PPY), cholecystokinin (CCK) and glucagon-like peptide (GLP-1) (Table 1) (Benjamin et al., 2015).

Table 1. Effect of IF on hormones involved in appetite and satiety.

Hormona	IF	Reference
Ghrelin	Low	Coultihno et al., 2018; Sutton et al., 2018
Leptin	Low	Shabkhizan et al., 2023; Parr et al., 2020
Insulin	Low	Cienfuegos et al., 2020; Trepanowski et al., 2018
Amylin	Sin cambios	Shabkhizan et al., 2023; Hutchison et al., 2019
PPY	Low	Shabkhizan et al., 2023
CCK	Sin cambios	Zouhal et al., 2020; Coultihno et al., 2018
GLP-1	Low	Shabkhizan et al., 2023; Sutton et al., 2018

AI: intermittent fasting; PPY peptide YY; CCK: cholecystokinin; GLP-1: glucagon-like peptide.

Source: own elaboration

Leptin is associated with proinflammatory processes, so in the IF this protein decreases inducing increased insulin sensitivity, in this sense, in the IF its production and secretion decreases due to low triglyceride reserves; while ghrelin can stimulate neurogenesis (neuronal regeneration and development) (Table 1) (Brogi et al., 2024; Longo and Mattson, 2014). Ghrelin is secreted before meals and peaks at the onset of meals, which its concentrations are elevated in IF (Ke et al., 2024; Elsworth et al., 2023).

On the other hand, insulin secretion is reduced in IFs (Benjamin et al., 2015), due to caloric reduction of up to 75 % (Longo & Mattson, 2014). Some studies report that in 12-week IF postprandial insulin decreases (Brogi et al., 2024; Sutton et al., 2018); while amylin is secreted to reduce food intake and favor energy balance (Nye et al., 2024). Similarly, PPY is secreted in small amounts in both pancreatic islet F cells and the large intestine by significantly reducing caloric reserve intake over periods of more than 12 weeks (Liu et al., 2020). Other proteins that are reduced by low caloric content are CCK and GLP-1, which, because they are not synthesized by duodenal cells, cause weight loss by reducing glucagon secretion and inducing insulin secretion (Morselli et al., 2010).

Types of Intermittent Fasting

Currently, there are different modalities of IF depending on the duration of caloric restriction, which can be classified into short-duration IF, long-duration IF and extended IF for long periods of time. Short-duration AIs are performed more frequently and on a daily basis for the ease of a weight loss or to treat their diseases such as type II diabetes mellitus or other metabolic diseases but with relevant care (Nye et al., 2024; Fung, 2016). Table 2 shows the classification of the different types of IF fasting according to the duration time.

Table 2. Relationship of schedule in short-term intermittent fasting.

IF	Funtion	References
Fasting on alternate days		
5:2	Normal food intake for 5 days a week and limit for 2 days to an intake of 500-600 Kcal in a single meal or spread out over a day	Warchalowski, 2020
Alternating fasts		
12:12	12 h window to eat and undergo another 12 h without ingestion. Works as prevention against obesity	Hall, 2020
16:8	Ingesta durante 8 h/d, sin consumir en el periodo de 16 h. Coloquialmente conocido como “saltarse la cena”	Ramírez-Harris, 2018
12:12	Combination with a low-carbohydrate diet for a greater effect on weight loss	Nye, Cherrin, Meires, 2024
20:4	Ayuno estricta que tienen la opción de comer durante cuatro h/d y mantener en ayunas durante 24 h	Hall, 2020
Extended IF		
2–3 days	Avoidance of food intake for 2–3 days	Ramírez-Harris, 2018
7–14 days	Avoidance of total food intake for 7 to 14 days. Allows the body to adapt quickly to the fasting conditions, allowing an easy and gradual transition	Elsworth et al., 2023
>14 days	Prolonged fasting longer than 14 days. It is advisable to follow up with a doctor	Elsworth et al., 2023

*IF: Intermittent fasting.

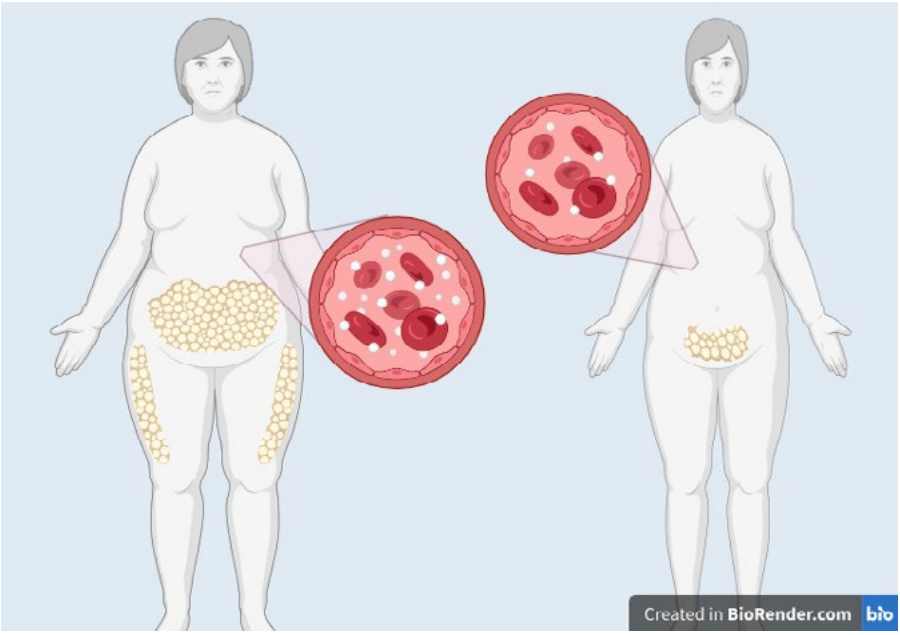
Source: own elaboration

In the table above you can see that depending on the time of fasting are the effects it generates in the body. Therefore, when fasting is considered to be used over long periods of time or in a more persistent way, it is important to constantly consult a doctor to avoid the consequences of this type of diet, which is very often performed by people without the supervision of medical personnel.

Benefits of IF in obesity

IF has a number of benefits to the body, including improved cognition, mitochondrial biogenesis and resistance to injury and disease, increased parasympathetic system, reduced blood pressure and resting heart rate (Varady et al., 2022). It also decreases the amount of glycogen, lipid accumulation, leptin production and inflammation. At the same time, it increases insulin sensitivity and improves muscular endurance and efficiency, improves the central nervous system and the metabolic system (Nye et al., 2024; Morselli et al., 2010). Taking the last point, it decreases the suffering of overweight and/or obesity and does not lead to malnutrition if controlled within 6 months (Song and Kim, 2023; de Cabo & Mattson, 2019). Studies have found that by increasing leptin levels and decreasing ghrelin levels, IF helps control appetite and reduce caloric intake (Hannaford et al., 2013), whereby, by limiting feeding windows, it facilitates the mobilization of stored fat since, during periods of fasting (Figure 1), the body consumes its glycogen stores and eventually begins to use fat as a source of energy, which can result in a significant reduction in adipose tissue (Anton et al., 2018; Duncan et al., 2020; Longo & Panda, 2016). IF may also positively influence the composition of the gut microbiome, favoring species that promote better metabolic health (Clemente et al., 2012).

Figure 1. Effect of blood glucose and decrease in abdominal fat.



Source:

Table 3 shows the results of the implementation of the FI. IF helps to increase thermogenesis and norepinephrine activity, favoring lipolysis (Varady & Hellerstein, 2009) and reducing LDL and triglyceride levels (Harvie & Howell, 2017; Harvie et al., 2013; Tinsley & La Bounty, 2015).

Table 3. Some studies conducted with IF.

IF regimen	Duration	Results	Reference
15 days: alternate-day fasting	20-hour fasting intervals	↓ glucose ↑ adiponectin ↓ leptin	Halberg et al., 2005
22 days: no caloric intake every other day	(36-hour fasting intervals)	↓ insulin ↓ weight change	Heilbronn 2005
1 day: water only	28-hour fasting interval	↓ glucose ↓ weight change ↓ insulin ↑ LDL ↑ HDL ↓ TG	Horne 2013

IF regimen	Duration	Results	Reference
12 weeks: weight-loss diet with alternate-day modified fasting	25% of energy needs	↓ TG ↓ CRP ↑ adiponectin ↓ weight change	Varady 2013
weight-loss diet with alternate-day modified fasting, 25% of energy needs	8 weeks	↓ weight change ↓ glucose ↓ insulin ↓ leptin	Hoddy 2016
1 meal per day	8 weeks	↓ weight change ↓ glucose ↓ LDL ↑ HDL ↑ TG	Carlson 2007; Stote 2007
3 day fast (25% to 30% of caloric needs), 3 day usual diet, and 1 day ad libitum intake	3 days fast, 3 days usual diet, and 1 day ad libitum intake	Viable weight loss strategy in obesity	Eshghinia and Mohammadzadeh, 2013
2 days fast and 5 days usual diet	2 days fast (25% of usual calorie intake) and 5 days usual diet	Effective for weight loss and insulin sensitivity	Harvie et al, 2011
12 wk	16 h daily fast	Effective for weight loss and glycemic control in Type2 Diabetes Mellitus	Kahleova et al., 2014

↓ decrease; ↑ increase; Abbreviations: CRP, C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; TNF-α, tumor necrosis factor-α; h: hours; wk: week.

Source: own elaboration

An alarming fact, currently children and adolescents under eighteen years of age, suffer from overweight or obesity, a fact that leads us to think that the new generations do not have a correct healthy eating habits style (Song and Kim, 2023). The above, generates a reflection that society lives in an environment where a large amount of hypercaloric and ultra-processed foods are ingested, and the realization of physical activity every day is less due to the existence of numerous means of transport and entertainment devices that are present 24 hours a day and make unnecessary the use of their own feet (Stockman et al., 2018; Varady et al., 2022).

Considerations to take into account when practicing IF

Adopting the IF as a diet style to achieve weight loss should take into consideration possible risks if it is not monitored by physicians and nutritionists, because in excess it can cause dehydration, hypoglycemia, fatigue, dizziness, migraines and in extreme cases malnutrition (Garegnani et al., 2023). To understand the role of IF it is important to mention that this practice does not generate the same result with people with obesity, since there are factors that influence the results, among them are age, nutritional status of the person, gender, period with the disease, circadian rhythm, implementation of drugs for the control of obesity, to mention some of them (Stockman et al., 2018). Likewise, the type of IF influences the outcome, as was the case in a study conducted by the Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai, Thailand, where 108 participants with obesity and type 2 diabetes mellitus of both sexes were grouped into three AI groups: 16:8 and 14:10, and a control group. Anthropometric measurements (weight, height, waist and hip circumference) were measured at week zero, six and twelve. The weight change in both groups was significant compared to the control group where the percentage weight change was -0.55%. The 16:8 group had -4.02% weight change while the 14:10 group obtained -3.15% (Sukkriang & Buranapin, 2024; Varady et al., 2022). Another study with 131 patients with obesity, three groups were divided, the first group performed IF 5:2, the second group applied daily caloric restriction (70% of energy needs every day) and the third group with daily caloric restriction with meal replacement (70% of energy needs every day, partially with protein-rich meal replacement); with this, it was demonstrated that IF 5:2 was superior to caloric restriction for weight loss (Kang et al., 2022).

Conclusions

Based on scientific evidence related to this work, it is concluded that the present benefits of IF are optimal for the treatment of obesity as a dietary intervention, however, possible risks should be taken into consideration if they are not controlled and supervised. Performing IF can provide flexibility that allows the public to choose the one they consider convenient for their lifestyle or healthy goals.

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Ayuno interminente: remedio alternativo precautivo en las personas con obesidad

Jejum intermitente: um remédio alternativo preventivo para pessoas com obesidade

Madison Gaia Martinez Uzarraga
Universidad de las Américas | Ciudad Juárez | México
Km3705641@gmail.com
Nutrition student in her fifth semester at the campus in Ciudad Juárez, Chihuahua.

Silvana Carolina Delgado Ortega
Universidad de las Américas | Ciudad Juárez | México
silvanastanton@yahoo.com
Nutrition student in her fifth semester at the campus in Ciudad Juárez, Chihuahua. She has experience in participating in local research meetings.

Viviana Medina Moreno
Universidad de las Américas | Ciudad Juárez | México
vm4000619@gmail.com
Nutrition student in her fifth semester at the campus in Ciudad Juárez, Chihuahua. She has experience in participating in local research meetings.

Valeria Esquivel Barbosa
Universidad de las Américas | Ciudad Juárez | México
valeriaesquivel638@gmail.com
Nutrition student in her fifth semester at the campus in Ciudad Juárez, Chihuahua.

María Guadalupe Haros Saucedo
Universidad de las Américas | Ciudad Juárez | México
Maria_HS_18@outlook.com
B.S. in Chemistry, graduated from the Universidad Autónoma de Ciudad Juárez. Currently teaching at Universidad de las Américas, Campus Cd. Juárez.

Gilberto Mercado Mercado
Universidad de las Américas | Ciudad Juárez | México
gilberto.mercado@uacj.mx
Professor and researcher at the UACJ-ICB Ciudad Juárez, Coordinator of research and nutrition degree at the Universidad Vizcaya de las Américas campus Juárez and member of the National System of Researchers and Researchers of the Secretariat of Science, Humanities, Technology and Innovation for 6 years.

Resumen

El ayuno intermitente (IF) se ha popularizado debido a las facilidades de reducir el peso corporal a partir de alternar periodos de ayuno con alimentación sin restricciones; sin embargo, su práctica frecuente puede contraer consecuencias aun desconocidas para la mayoría de los usuarios. La dieta de IF desencadena respuestas celulares adaptativas que provocan una disminución de los marcadores inflamatorios que van de la mano de la alteración en procesos metabólicos, y fisiológicos que podría ayudar a tratar y prevenir

la obesidad y las enfermedades asociadas. Este capítulo narra, centra y analiza los diferentes tipos de IF y sus contribuciones a la mejora de la salud. Así, la hipótesis de los regímenes de ayuno intermitente ofrece enfoques prometedores para mejorar la salud de la población.
Palabras clave: Ayuno intermitente, restricción calórica, salud, obesidad, metabolismo.

Resumo

O jejum intermitente (IF) tornou-se popular devido à facilidade de reduzir o peso corporal alternando períodos de jejum com alimentação irrestrita; no entanto, sua prática frequente pode ter consequências desconhecidas pela maioria dos usuários. A dieta IF desencadeia respostas celulares adaptativas que causam uma diminuição nos marcadores inflamatórios que acompanham as alterações nos processos metabólicos e fisiológicos que poderiam ajudar a tratar e prevenir a obesidade e as doenças associadas. Este capítulo narra, enfoca e analisa os diferentes tipos de IF e suas contribuições para a melhoria da saúde. Assim, os regimes hipotéticos de jejum intermitente oferecem abordagens promissoras para melhorar a saúde da população.
Palavras-chave: Jejum intermitente; restrição calórica; saúde; obesidade; metabolismo.