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Intermittent fasting in women of reproductive age: hormonal impacts and clinical implications

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ABSTRACT

OBJECTIVE

To investigate the impact of intermittent fasting (IF) on the female hormonal system in women of reproductive age, with emphasis on the hypothalamic-pituitary-ovarian axis and the metabolic hormones involved in menstrual and reproductive regulation.

METHODS

This study is an integrative literature review. Articles published between 2009 and 2024 were searched in PubMed, SciELO, the National Library of Medicine, and ScienceDirect databases. Studies including healthy women and those with polycystic ovary syndrome (PCOS), aged 18-45 years, were eligible if they evaluated the effects of IF on reproductive hormones (gonadotropin-release hormone (GnRH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol) and metabolic hormones (insulin, leptin, ghrelin). Data synthesis followed the Whittemore and Knafl (2005) framework, using a descriptive and comparative analysis to identify patterns and inconsistencies across studies.

RESULTS

Evidence suggests that mild to moderate IF protocols, when combined with adequate caloric compensation, do not surpass the critical energy threshold required to suppress GnRH secretion, thus maintaining stable LH, FSH, and estradiol levels in eumenorrheic women. More intensive or prolonged fasting protocols tended to reduce LH and estradiol levels, particularly under metabolic stress conditions. In women with PCOS, IF was associated with significant improvements in insulin sensitivity and increased menstrual regularity, indicating a beneficial modulation of the reproductive axis secondary to metabolic enhancement. Variations in leptin and ghrelin reflected adaptive physiological responses to altered feeding patterns, without persistent endocrine dysfunction.

CONCLUSION

Intermittent fasting exerts variable effects depending on metabolic status and the intensity of caloric restriction. Moderate, well--balanced protocols appear safe and metabolically advantageous, particularly for women with PCOS, whereas prolonged or severe regimens may increase the risk of menstrual disturbances and functional hypothalamic amenorrhea.

KEYWORDS

Intermittent fasting; Menstrual cycle; Endocrine system.

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INTRODUCTION

Intermittent fasting (IF) has gained popularity in recent years as a strategy for weight loss and health promotion. It consists of the alternation between periods of feeding and fasting, commonly ranging between 16 hours of fasting and 8 hours of feeding, or alternatively 24-hour fasting protocols on alternate days.[1]

Studies suggest that this practice may provide significant metabolic benefits, such as improved insulin sensitivity, reduced inflammation, and weight loss.[2-4] However, the influence of intermittent fasting on female hormones remains a field under exploration and raises controversies.[5]

The menstrual cycle is a cyclical physiological process, with an average duration of 28 days (ranging from 21 to 35), divided into three main phases: the follicular phase, ovulation, and the luteal phase. This cycle is regulated by complex hormonal interactions coordinated by the hypothalamic–hypophysis–ovarian axis, which integrates metabolic and neuroendocrine stimuli. [6-7]

During the follicular phase, an increase in follicle-stimulating hormone (FSH) promotes the growth of ovarian follicles and the synthesis of estradiol, which stimulates endometrial proliferation. When estradiol levels reach a critical threshold, a surge of luteinizing hormone (LH) occurs, responsible for ovulation and the release of the mature oocyte. In the luteal phase, the corpus luteum begins to secrete progesterone and small amounts of estradiol, preparing the endometrium for possible implantation. In the absence of fertilization, regression of the corpus luteum leads to a decline in these hormones and the onset of a new menstrual cycle.[6-7]

The hypothalamic–pituitary–ovarian axis is highly sensitive to changes in energy balance, making the study of the effects of intermittent fasting on sex hormones relevant. [8] Even subtle alterations in these hormones may affect ovulation, menstrual cyclicity, and fertility, making it essential to understand whether IF represents a benign, neutral, or potentially adverse modulating factor for female reproductive health. [9-11]

To date, there is no consistent evidence that intermittent fasting directly alters levels of estradiol, progesterone, LH, or FSH in healthy women.[9,10,12,13] Preliminary studies indicate that IF may impact key hormones such as estrogen and luteinizing hormones.[9-13] However, recent studies suggest that possible hormonal variations may occur transiently and depend on the duration of fasting, body composition, and the phase of the menstrual cycle.[13-15] From this perspective, it is of utmost importance to investigate the hormonal changes caused by intermittent fasting in women of reproductive age and their clinical and reproductive implications.

This review has the general objective of synthesizing and critically analyzing the available scientific evidence on the effects of IF on sex and metabolic hormones in women of reproductive age, identifying possible endocrine alterations and their implications for reproductive function.

Among the specific objectives, this review sought to identify the different IF protocols applied in women of reproductive age, describe their main characteristics and duration, and analyze their effects on serum levels of GnRH, LH, FSH, estradiol, insulin, leptin, and ghrelin. In addition, it aimed to compare the results between healthy populations and those with associated metabolic conditions, such as polycystic ovary syndrome, and to integrate the available evidence in order to identify gaps and guide future investigations on the endocrine effects of IF in women.

METHODS

This study is an integrative literature review. A comprehensive search was conducted across the following databases: PubMed, SciELO, ScienceDirect, and the National Library of Medicine. The search was carried out in English and Portuguese, using the following descriptors: "intermittent fasting," "female hormones," "women of reproductive age," "hormonal impact," "consequences of intermittent fasting," and "menstrual cycle."

Eligibility criteria were defined based on the objective of the integrative review and the methodological scope proposed by Whittemore and Knafl (2005).[16] The following were included: (i) published studies available in full text; (ii) investigations conducted in women of reproductive age (18–45 years), either healthy or with associated metabolic conditions, such as polycystic ovary syndrome (PCOS); (iii) studies that evaluated intermittent fasting protocols, including time-restricted feeding (16/8), the 5:2 regimen, alternate-day fasting (ADF),

and one meal a day (OMAD); (iv) clinical trials, observational studies, and reviews (systematic, meta-analyses, or narrative) that analyzed the effects of intermittent fasting on female sex hormones, such as estradiol, GnRH, LH, and FSH, as well as metabolic hormones such as insulin, leptin, and ghrelin.

Studies conducted in men, adolescents, pregnant women, lactating women, postmenopausal women, continuous caloric restriction protocols without intermittent fasting, and publications that did not present specific hormonal outcomes were excluded.

Data were independently extracted by one reviewer and subsequently organized and compared descriptively, allowing the identification of convergences, divergences, and gaps among the studies.

The data was independently extracted by one reviewer, organized and compared descriptively, allowing the identification of convergences, divergences, and gaps between studies.

The synthesis was conducted in a narrative and integrative manner, according to the model proposed by Whittemore and Knafl (2005), encompassing data reduction, data display, data comparison, and conclusion.[16] The results were grouped according to the types of fasting protocols and the hormones evaluated (LH, FSH, GnRH, estradiol, insulin, leptin, and ghrelin), allowing a critical analysis of methodological consistency and the main reported findings.

RESULTS AND DISCUSSION

Study Selection

A total of 54 articles were identified through database searches (PubMed n = 14; SciELO n = 14; ScienceDirect n = 13; and the National Library of Medicine n = 13). Of these, 42 articles were excluded for not meeting the eligibility criteria. In total, 12 articles were included in the analysis and descriptive synthesis of this integrative review.[3,9-11,13-23] Additionally, the literature was complemented with textbooks on medical physiology and other relevant articles used to contextualize intermittent fasting and the current scientific evidence within the field of endocrinology.[1,2,4,5-8,12,14-16] Totalizing, 23 articles included in the descriptive structure of this integrative review.[1-23]

Alterations in Female Sex Hormones caused by IF

According to the Endocrine Society Guideline on Functional Hypothalamic Amenorrhea (FHA), menstrual disturbances observed in women exposed to energy restriction result from an adaptive neuroendocrine response that suppresses the pulsatility of the gonadotropin-releasing hormone (GnRH) through activation of the hypothalamic–hypophysis–adrenal (HPA) axis. This mechanism reflects a physiological prioritization of metabolic homeostasis and survival over reproductive function in situations of energy deficit or stress. [11]

The guideline emphasizes that acute or chronic nutritional deprivation—whether due to excessive physical exercise, restrictive eating behaviors, or psychological stress—activates corticotropin-releasing hormone (CRH)-secreting neurons in the paraventricular nucleus. This activation leads to increased cortisol secretion and inhibition of hypothalamic GnRH stimulation, resulting in reduced levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol.[11] This adaptive response was experimentally demonstrated by Loucks and Thuma (2003), who showed that when energy availability falls below approximately 30 kcal/kg of lean body mass per day, there is a significant reduction in LH pulse frequency, reflecting suppression of GnRH secretion. This finding established a physiological threshold required for the maintenance of female reproductive function.[17]

In contrast, Redman et al. (2009) demonstrated that a moderate caloric restriction of 25%, maintained for six months in normal-weight women, did not impair ovulatory function or gonadotropin secretion, with preservation of normal LH pulse frequency and physiological levels of estradiol and progesterone. Participants remained eumenorrheic throughout the intervention, with no cases of amenorrhea, indicating that moderate and sustained energy restriction does not exceed the critical threshold required to suppress GnRH.[19]

Similarly, both Zangeneh et al. (2015) and the uncontrolled study by Li et al. (2021), included in the review by Floyd et al. (2022), observed that none of the intermittent

fasting protocols evaluated (Ramadan fasting or the 16:8 regimen) resulted in significant changes in LH levels in women with PCOS. LH levels remained basally elevated in most patients, reflecting pituitary hyperstimulation mediated by insulin resistance and hyperandrogenism. Despite reported metabolic improvements, including reductions in insulin levels, HOMA-IR, and the free androgen index, the hypothalamic–hypophysis–ovarian (HHO) axis showed no measurable changes in LH secretory pulsatility following fasting. These findings suggest that modification of hypothalamic GnRH pulsatile drive may require greater weight loss or a longer duration of intervention to be achieved.[4,13,18]

In this context, IF, particularly when associated with prolonged periods of food abstinence or inadequate caloric compensation, may act as a metabolic and psychosocial stressor, modulating the activity of kisspeptin/neurokinin B/dynorphin (KNDy) neurons and reducing the frequency of GnRH pulses.[11] However, most clinical studies evaluating intermittent fasting protocols in women employ moderate and compensatory energy restrictions that do not reach the critical threshold described by Loucks and Thuma, which helps explain the absence of significant hypothalamic suppression observed in these interventions.[17]

Alterations in Metabolic Hormones caused by IF

The study by Harvie et al. (2013) evaluated 115 overweight women and investigated the effects of intermittent fasting with intermittent energy and carbohydrate restriction (IECR), comparing it with continuous daily energy restriction (DER). The study found a significant reduction in fasting serum insulin levels in the IECR groups compared with the DER group. This improvement was observed within the first weeks of the intervention, even before substantial differences in weight loss emerged, suggesting a metabolic effect independent of weight reduction. The authors proposed that IF enhances insulin sensitivity, possibly due to the alternation between periods of restriction and refeeding, which optimizes glucose metabolism and reduces hepatic fat accumulation. This results in lower chronic insulin exposure, a mechanism that could be beneficial for hyperinsulinemic conditions such as PCOS, although patients with this condition were not included in the study.[2]

Regarding serum leptin, a significant reduction was observed across all groups following the weight loss period, with a more pronounced decrease in the IF IECR groups. Despite the expected fluctuations between fasting and refeeding days, no sustained increase in ghrelin levels was observed, suggesting physiological adaptation to the dietary pattern.[2]

A systematic review and meta-analysis by Cioffi et al. (2018), which analyzed 11 clinical trials in adults (predominantly overweight women), found that intermittent fasting protocols (the 5:2 regimen and alternate-day fasting) resulted in a significant reduction in fasting insulin levels (WMD = −0.89 µU/mL; p = 0.009) compared with continuous caloric restriction. The authors observed that the benefit on insulin was statistically modest and dependent on the overall energy deficit, with no evidence of clinical superiority between the dietary approaches. Leptin and ghrelin were not quantitatively assessed and were mentioned only as potential theoretical mediators of energy balance.[20]

The randomized controlled trial conducted by Jakubowicz et al. (2013) evaluated 93 overweight women with metabolic syndrome, comparing two isocaloric dietary patterns of 1,400 kcal/day: one with a higher caloric intake at breakfast (50%) and another with a higher intake at dinner (50%). Although the study did not include classicain IF periods, the group with greater morning caloric intake experienced a prolonged overnight fasting period (~15 hours), resembling an early time-restricted feeding pattern.[21]

The results showed a marked reduction in fasting insulin levels (−51%) in the group that concentrated caloric intake in the morning, in contrast to smaller reductions observed in the high-calorie dinner group. Plasma ghrelin levels decreased by 9% in the morning-intake group and by only 4.9% in the evening-intake group, accompanied by a subjective reduction in hunger (−28%) and increased satiety (+31%). These findings suggest that circadian distribution of food intake, characterized by higher daytime caloric consumption and prolonged overnight fasting, aligns orexigenic hormones with metabolic rhythms, thereby reducing appetite and improving glycemic ef-

ficiency. No significant changes in leptin levels were observed, possibly due to the relatively short study duration (12 weeks) and the stability of fat mass.[21]

The study by Kim et al. (2021) descriptively evaluated the effects of intermittent fasting on insulin secretion and circadian rhythm. Protocols such as alternate-day fasting (ADF), time-restricted feeding (TRF), and the 5:2 regimen demonstrated sustained reductions in fasting insulin levels, accompanied by improvements in peripheral insulin sensitivity. The review emphasized that fasting alters the temporal pattern of insulin secretion by reducing its amplitude and shifting its peak to earlier phases of the day, reflecting an adaptive pancreatic response to restricted eating windows. Thus, the metabolic improvements induced by intermittent fasting appear to be mediated by temporal optimization of insulin secretion and restoration of cellular metabolic sensitivity, rather than solely by an absolute caloric deficit.[9]

In the randomized controlled trial conducted by Talebi et al. (2024), which compared an early time-restricted eating protocol (14 hours of fasting and 10 hours of feeding), either alone or combined with probiotic supplementation, with a conventional hypocaloric diet in obese women with polycystic ovary syndrome, no significant differences were observed between groups in metabolic or reproductive outcomes. All interventions led to similar reductions in body weight, body mass index, glucose levels, insulin, and HOMA-IR, as well as modest clinical improvements in hirsutism and acne. However, there were no statistically significant changes in serum levels of LH, FSH, total testosterone, SHBG, or menstrual regularity. These findings suggest that short-duration, moderate-intensity intermittent fasting does not exert a measurable impact on the hypothalamic-pituitary–ovarian axis and is limited to metabolic benefits comparable to those achieved with continuous caloric restriction.[22]

In contrast, in the retrospective study conducted by Feyzioğlu, Güven, and Avul (2023), an 8-hour time-restricted feeding protocol (eating between 1:00 p.m. and 9:00 p.m.) was applied for six weeks in women with PCOS. The results revealed significant improvements in metabolic parameters, including reductions in glucose, insulin, HOMA-IR, LDL cholesterol, and triglycerides, along with increased HDL levels and decreased fecal calprotectin, suggesting improvements in insulin resistance and intestinal permeability. Concurrently, significant reductions were observed in serum levels of LH, FSH, estradiol, AMH, prolactin, total and free testosterone, DHEAS, and the free androgen index (FAI), accompanied by an increase in SHBG and a decrease in the proportion of patients with hyperandrogenism. These findings indicate that an 8-hour time-restricted feeding protocol may beneficially modulate both metabolic and reproductive axes, possibly through reductions in intestinal inflammation and the mechanisms of hyperinsulinemia, well recognized in the pathophysiology of PCOS[23]

CONCLUSION

Intermittent fasting, when implemented in a mild to moderate manner and with adequate caloric compensation, appears to be a metabolically beneficial and safe intervention for women of reproductive age.[2,9,20,21] The available evidence consistently demonstrates improvements in insulin sensitivity and inflammatory profiles, without significant suppression of the hypothalamic-pituitary–ovarian axis.[2,4,9,13,18-20,22,23]

Short-term or moderate-intensity protocols do not exceed the critical energy threshold described in functional hypothalamic amenorrhea, thereby preserving gonadal function.[11,17,19] However, prolonged or excessively restrictive regimens, particularly in contexts of low body weight or heightened psychophysiological stress, may trigger reversible reproductive dysfunction.[11,17]

Therefore, the impact of intermittent fasting on female sex hormones depends on the balance between energy deficit, intervention duration, and baseline metabolic profile.[17,19,22,23] Further long-term clinical trials incorporating direct assessments of GnRH and LH pulsatility are needed to define the safe threshold between metabolic adaptation and the risk of reproductive suppression, thereby guiding individualized clinical use of this strategy across different female phenotypes.[11,17,22,23]

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