

Insomnia and the menopause: Where are we and where are we going?

Insônia e menopausa: Onde estamos e para onde vamos?

Insomnio y menopausia: ¿Dónde estamos y hacia dónde vamos?

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Abstract

The menopause, marked by a decrease in ovarian follicles and changes in female sex hormones, can trigger symptoms such as facial flushing and sleep disturbances. Hormonal fluctuations, notably a decrease in estrogen and progesterone, are associated with night-time awakenings and difficulty maintaining uninterrupted sleep. This condition has a negative impact on quality of life, leading to conditions such as obesity, diabetes, cardiovascular disease, and depression. The transition to menopause intensifies sleep disorders, especially insomnia, which is often associated with hot flashes. Despite the lack of clear evidence on the efficacy of hormone therapy, its use persists, highlighting the need for personalized approaches. Therapeutic strategies, such as the fusion of hormone therapy with sleep hygiene and cognitive-behavioral therapy, are emerging as promising. Some recommendations include adjustments to sleep habits, regular exercise, and a balanced diet. In conclusion, menopause significantly influences sleep disorders in women, affecting various aspects of physical and emotional health. Comprehensive therapeutic strategies, including behavioral changes, hormone therapy, and nutritional support, show promise for improving quality of life during this inevitable transition in female aging.

Keywords: Menopause; Sleep wake disorders; Sleep hygiene.

Resumo

A menopausa, marcada pela diminuição dos folículos ovarianos e alterações nos hormônios sexuais femininos, pode desencadear sintomas como rubor facial e distúrbios do sono. As flutuações hormonais, nomeadamente uma diminuição do estrogênio e da progesterona, estão associadas a despertares noturnos e à dificuldade em manter um sono ininterrupto. Esta condição tem um impacto negativo na qualidade de vida, levando a condições como obesidade, diabetes, doenças cardiovasculares e depressão. A transição para a menopausa intensifica os distúrbios do sono,

especialmente a insônia, que está frequentemente associada a afrontamentos. Apesar da falta de evidências claras sobre a eficácia da terapia hormonal, o seu uso persiste, destacando a necessidade de abordagens personalizadas. Estratégias terapêuticas, como a fusão da terapia hormonal com a higiene do sono e a terapia cognitivo-comportamental, estão emergindo como promissoras. Algumas recomendações incluem ajustes nos hábitos de sono, exercícios regulares e uma dieta balanceada. Concluindo, a menopausa influencia significativamente os distúrbios do sono nas mulheres, afetando diversos aspectos da saúde física e emocional. Estratégias terapêuticas abrangentes, incluindo mudanças comportamentais, terapia hormonal e suporte nutricional, mostram-se promissoras para melhorar a qualidade de vida durante esta transição inevitável no envelhecimento feminino.

Palavras-chave: Menopausa; Distúrbios do sono-vigília; Higiene do sono.

Resumen

La menopausia, marcada por la disminución de los folículos ováricos y cambios en las hormonas sexuales femeninas, puede desencadenar síntomas como enrojecimiento facial y alteraciones del sueño. Las fluctuaciones hormonales, concretamente una disminución de los estrógenos y la progesterona, se asocian con despertares nocturnos y dificultad para mantener un sueño ininterrumpido. Esta condición tiene un impacto negativo en la calidad de vida, dando lugar a condiciones como obesidad, diabetes, enfermedades cardiovasculares y depresión. La transición a la menopausia intensifica los trastornos del sueño, especialmente el insomnio, que a menudo se asocia con sofocos. A pesar de la falta de pruebas claras sobre la eficacia de la terapia hormonal, su uso persiste, lo que destaca la necesidad de enfoques personalizados. Las estrategias terapéuticas, como la fusión de la terapia hormonal con la higiene del sueño y la terapia cognitivo-conductual, se perfilan como prometedoras. Algunas recomendaciones incluyen ajustes en los hábitos de sueño, ejercicio regular y una dieta equilibrada. En conclusión, la menopausia influye significativamente en los trastornos del sueño en la mujer, afectando varios aspectos de la salud física y emocional. Las estrategias terapéuticas integrales, incluidos cambios de comportamiento, terapia hormonal y apoyo nutricional, son prometedoras para mejorar la calidad de vida durante esta transición inevitable en el envejecimiento femenino.

Palabras clave: Menopausia; Trastornos del sueño-vigilia; Higiene del sueño.

1. Introduction

Sleep is a fundamental and necessary process for maintaining life (De Beritto et al., 2020). The states of sleep and wakefulness are generated by neuronal circuits regulated by circadian mechanisms. Thus, the onset and maintenance of sleep require the suppression of the ascending arousal systems that generate the waking state (Baranwal et al., 2023). Sleep deprivation, whether due to insomnia or another sleep disorder, results in an increase in oxidative stress leading to alterations in regular functional connectivity in neural networks such as the medial prefrontal cortex, temporoparietal junction, precuneus, and hippocampus (Atrooz et al., 2020; Ning et al., 2022).

Perimenopause is characterized by the deterioration of ovarian function, which leads to endocrine dysfunction in a progressive and non-linear way. This event is related to the natural aging process and occurs between the ages of 50 and 53, depending on the population (Grisotto et al., 2022). Lifestyle habits directly interfere with the menopause process, which is described as the last cycle of the menstrual period, symbolizing the end of the reproductive period (Marjoribanks et al., 2017). Post-menopause is manifested by the end of menstruation for a period of more than 11 months (Grisotto et al., 2022).

During puberty and menopause, concentrations of female sex hormones change and women tend to suffer from sleep disorders, the main one being insomnia, which significantly affects quality of life and general well-being (Morssinkhof et al., 2020). Insomnia is therefore exacerbated by underdiagnosis and inadequate treatment (Thongchumnum et al., 2023). Both a short (<6 hours) and a long (>9 hours) period of sleep, as well as frequent snoring, have been associated with a higher risk of ischemic stroke and numerous cardiovascular diseases (Beverly Hery et al., 2020).

Hormonal changes in the hypothalamic-pituitary-gonadal axis, which maintain ovarian follicle development and estrogen secretion, are of paramount importance in this process (Salão et al., 2015). The menopause is preceded by perimenopause, in which the gradual loss of oocytes, the altered response to gonadal steroid feedback, as well as wide hormonal fluctuations and irregular menstrual patterns, culminate in what is characterized as the menopause itself, in which menstruation ceases, oocytes are depleted and gonadal steroids fall (Santoro et al., 2021). The physical and psychological changes resulting

from the aging process and the menopause create recurrent insomnia, with difficulty falling asleep being the main symptom for these women (Santoro et al., 2015; Cavadas et al., 2010).

During menopause, the deficiency in estrogen levels makes women in this period more susceptible to developing sleep disorders, such as insomnia (Lizcano et al., 2014). In this way, estrogen hormone replacement can serve as a protective therapy against sleep disorders. In addition, estrogen receptors regulate various aspects of glucose and lipid metabolism, meaning that dysfunctions in this hormone favor the appearance of metabolic syndrome and cardiovascular alterations in menopausal women (Morssinkhof et al., 2020).

Hormone therapies are effective for vasomotor and vaginal symptoms of the menopause (Santoro et al., 2021). In short, a balanced diet, physical exercise, and maintaining healthy lifestyle habits, such as a good diet and quitting smoking, are crucial measures for maintaining bone health, osteoporosis is also present during menopause, so the recommendation of medication is indicated for patients at high risk of fractures (Stuenkel et al., 2015). Hormone Replacement Therapy (HRT) should be prescribed for a short period of time and at the minimum dose after careful analysis of the best formulation, the best route of administration, and the most appropriate monitoring for the patient (Cavadas et al., 2010).

Therefore, it is clear that the hormonal changes that occur during menopause due to alterations in the hypothalamic-pituitary-gonadal axis also alter the functional connectivity of brain areas related to the ascending inhibition system, consequently helping in the development of sleep disorders such as insomnia. Thus, this review aims, through an analysis of the available literature, to analyze and describe how hormonal oscillations during menopause alter the quality, quantity, and variability of sleep, contributing to the development of insomnia.

2. Method

This article presents a narrative literature review based on the analysis of scientific articles published from 2013 to 2023, in PubMed and ScienceDirect, about insomnia in women during menopause. In the application of the first set of criteria, titles that did not mention the theme “insomnia and menopause” were excluded, as well as articles that were not included in the research period from 2013 to 2023 and articles that were not found in English. The second set of criteria was applied, from which were excluded the abstracts that did not address sleep disorders in menopause. In the PubMed database, 124 articles were found through the keywords ((Insomnia disorders) OR (Sleep disorders) AND (Menopause) OR (Perimenopause) AND (Treatments)), and 15 were selected following the first exclusion criteria. In the Science Direct database, 434 articles were found using the keywords (Insomnia Disorders) AND (Menopause) AND (Treatments) AND (Hormone therapy), with a filter for review articles, selecting systematic reviews, of which only 56 studies. The second set of criteria was applied, from which abstracts that did not address the topic of sleep disorders and menopause were excluded, which led to the exclusion of 5 articles in the Pubmed database and 13 articles in the Science Direct database. Among the remaining articles, 1 was a duplicate, covering the Pubmed and Science Direct databases. In total, 37 articles originally in English remained.

3. Discussion

3.1 How does menopause affect sleep?

Menopause is a physiological phase inherent to the aging of women, characterized by the gradual decrease in ovarian follicles and changes in the concentrations of female sex hormones. Typically manifested around the age of 51, the transition from perimenopause to menopause is accompanied by vasomotor symptoms, such as hot flushes and facial flushing, as well as sleep disturbances (Caretto et al., 2019).

Fluctuations in sex hormone levels show a clear association with the prevalence of sleep disorders and even depressive symptoms, notably manifested first during puberty and then during the transition from perimenopause to menopause in women. Thus, female sex hormones may play a significant role in the propensity to develop sleep disorders (Morssinkhof et al., 2020).

The hormonal effect of menopause is magnanimous because, presumably, the decrease in endogenous estrogen - which is relevant in the clinic because it is related to sleep - and progesterone is responsible for the symptoms of nocturnal awakenings and difficulty in maintaining uninterrupted sleep at night, with the evolution of this clinic being conceptualized as a gradual increase during the transition from menopause to post-menopause. Corroborating this hypothesis, an increase in menopausal symptoms has been observed in response to the suppression of sex hormones by oral contraceptives (Morssinkhof et al., 2020). The persistent presence of an unsatisfactory sleep pattern is associated with a significant decrease in quality of life, a reduction in positive affect, and a general decline in life satisfaction. Furthermore, such an inadequate sleep pattern represents a substantial risk factor for the development of chronic conditions such as obesity, diabetes, cardiovascular disease, and even depression (Avila et al., 2023). Conditions that even represent an under-quantification of their potential effects, as they are a factor in excluding candidates from populations in studies on the subject (Tansupswatdikul et al., 2014).

Still on the implications of sleep problems on patients' quality of life, the intrinsic implications between the components of the triad of sex hormones, depression, and sleep on each other are proven: there is a quantitatively majority intersection of unsatisfactory subjective sleep and depressive mood, with depressed patients showing longer sleep onset latency, more time lost in superficial sleep, as well as having altered proportions of delta sleep; in contrast, the relationship between depression and sex hormones only occurs as some concatenation in the clinical reasoning of hormone suppression being carried out, in which sleep and depression problems are associated with this in much more discrete numbers. Thus, the two-dimensional relationship between sleep and depression is more certain, a direct relationship between sex hormones and sleep is factual, to the detriment of the association of the former with depression, and it is an important question to ask how sex hormones fit into this scenario more specifically, with hypotheses raised that estrogen is associated with better sleep quality, that a longer REM latency in the transition from the luteal to the follicular phase of the menstrual cycle predicts a worse mood, and that hormonal intervention may lead to an improvement in depressive symptoms, all of which are worthy of future investigation and conjecture (Morssinkhof et al., 2020). Therefore, the predominant identification of sleep disorders during periods of hormonal fluctuations in women suggests a direct impact on quality of life and highlights the importance of a comprehensive preventive and therapeutic approach (Haufe et al., 2022).

Recent research has revealed that estrogen influences the regions responsible for sleep regulation in the brain, indicating that changes in estrogen levels are a central factor in sleep disorders. In this respect, the role of hormones in this regulation is well-founded: steroid receptors are found in areas of the brain that regulate sleep, where they influence cholinergic, serotonergic, dopaminergic, and adrenergic sleep-regulating neurotransmitters; as well as the potential importance of estrogen in the restoration of circadian hormones such as growth hormone, prolactin, cortisol and melatonin and the role of this hormone in the regulation of *g*-aminobutyric acid (GABA), all of which converge to its prominent central position in sleep regulation (Tansupswatdikul et al., 2014).

In this context, menopause is an undoubted risk factor for respiratory sleep disorders, and factors such as age, diet, and exercise can be disregarded, so the relationship between the two is that the severity of sleep disorders increases as the menopause progresses. As far as body temperature regulation is concerned, the first occurrences of hot flashes are at the beginning of the perimenopause, and they are the result of a drop in endogenous estrogen and progesterone, a conclusion presumed from studies in which, with the suppression of sex hormones, there was an increase in hot flashes in patients (Morssinkhof et al., 2020). In addition, the decrease in progesterone during menopause has been associated with a series of impacts on the central nervous system, as evidenced by accumulated clinical data (Pan et al., 2022).

The close relationship between sleep problems and reduced levels of reproductive hormones in menopausal women has prompted consideration of hormone therapy (HT) as an approach to alleviating these symptoms. However, in order to accurately establish the safety and efficacy of HT, further studies are needed to confirm its effects (Lindberg et al., 2020).

3.2 Sleep problems and menopause

Estudos chegaram à conclusão de que as taxas de prevalência de distúrbios de sono é maior em mulheres, sendo 1,6 vezes maior do que em homens. Por causa disso, a probabilidade de um indivíduo do sexo feminino apresentar insônia é relativamente superior que a de um do sexo masculino, principalmente durante a transição da menopausa (Cheng et al, 2021).

Among the signs and symptoms of menopause, sleep problems are one of the most uncomfortable. As a result, they are complained of by 40 to 60% of women going through this period (Baker et al, 2018).

There is plenty of conclusive evidence in the literature to confirm the existence of a significant increase in the rate of reports of these symptoms. One of these is the Women's Health Study (SWAN), which presented data reinforcing the idea that the prevalence of sleep disorders increases during this transition (Caretto et al, 2019).

Among these disorders are conditions related to the constriction of the upper respiratory tract and the absence of a breathing pattern during the night, which are better known as sleep-disordered breathing (SDB). It is known that the endocrine changes that women face during menopause are intrinsically related to the onset of these conditions. In addition, recurrent awakenings are responsible for respiratory instability and the increased collapsibility of soft tissues can lead to obstruction of the upper respiratory tract, as well as increase the risk of weight gain (Lindbeg et al, 2020).

During this transition, there are mood swings, a reduction in the level of general life satisfaction, and an increased likelihood of developing psychiatric disorders. All these factors lead to a considerable reduction in the quality of life of these women. Furthermore, it is possible to conclude that there are consequences of recurrent awakenings together with the difficulty of maintaining continuous sleep, symptoms that are very common at this stage of life (Haufe et al, 2022).

3.3 Can menopause treatment improve sleep?

The menopause, or climacteric, is a period that marks the change from the reproductive phase, with the end of the menstrual cycle, to the non-reproductive phase. It is an inexorable event in a woman's aging process, linked to changes in physiology and hormonal balance. These changes occur around the age of 45 and a half, and many women begin to notice physiological and behavioral changes that have a negative impact on their quality of life and social relationships. (Lomônaco et al, 2015; Ning et al, 2022).

Among the many comorbid conditions that occur during this period is insomnia, which is intensified by hot flashes. This further emphasizes the importance of specialized medical care in order to provide adequate hormone replacement so that women can go through this phase with minimal impact on their physical and emotional health (Lomonaco et al, 2015).

Often, in the period of transition to menopause, there is a significant oscillation in sex hormones, notably seen with a drop in estrogen levels, which is intrinsically related to sleep problems such as obstructive sleep apnea, sleep fragmentation, and excessive daytime sleepiness, which can be related to the development of diseases such as depression, cardiovascular disease, diabetes, and obesity. (Marjoribanks et al, 2017; Cintron et al, 2017).

In recent years, there has been a considerable increase in the life expectancy of women, who live one-third of their lives after menopause and may suffer from its various symptoms over the years. Although there is no scientific evidence that hormone therapy (HT) is effective in balancing menopausal symptoms, such as vasomotor symptoms (hot flushes) - which have an inverse relationship with sleep quality - it is known that the use of information for the application of HT is complex due to the diversity

of available studies concerning the age at which HT is started, the amount and type of estrogen used, contraindications and auxiliary therapies (Cintron et al., 2017).

In addition, the concerns addressed in the Women's Health Initiative (WHI) report in 2002 influenced the guidelines to recommend shorter exposure to HT. However, a decade after the WHI, the use of low-dose HT remains stable, gynecology professionals still prefer HT, and guidelines continue to endorse HT as the most effective treatment for relieving menopausal symptoms, including sleep disturbances (Citron et al., 2017).

A wide range of therapeutic approaches are currently employed for the management of sleep disorders, ranging from hormone replacement therapy, pharmacological therapy, and alternative therapies such as acupuncture, as well as the application of techniques derived from respiratory physiotherapy (Lialy et al., 2023). These therapeutic strategies aim to treat sleep disorders such as insomnia, obstructive sleep apnea, and other related conditions. Thus, a meticulous analysis of multiple factors is necessary in order to select the most effective therapeutic approach, emphasizing the importance of a personalized and targeted approach to meet the individual needs of each female patient (Cheng et al., 2021).

3.4 Tips for sleeping better with menopause

A mix of therapeutic approaches is emerging as a promising avenue in the context of treating sleep disorders in menopausal women. Among such approaches, the synergistic fusion of hormone replacement therapy with sleep hygiene strategies stands out, as does the implementation of cognitive-behavioral therapy (Silvestri et al., 2019). Changes in behavior and sleep habits play a crucial role in improving sleep quality. It is recommended that you get between 7 and 9 hours of sleep a night, maintain regular sleep and wake times, establish a consistent bedtime routine, exercise regularly, and adopt a disciplined routine (Baranwal et al., 2023).

In addition, it is essential to abstain from substances that can alter sleep, such as caffeine and alcohol. Even exposure to artificial light in the afternoon should be avoided, as these practices are associated with a fragmented sleep pattern and poor quality. These guidelines aim to improve sleep quality by promoting habits and behaviors that favor a more effective and restorative rest (Baranwal et al., 2023).

Nutritional strategies also play a key role in the management of sleep disorders associated with menopause, especially in dealing with obesity and overweight. In addition, certain foods, such as soy, fish, whole grains, vegetables, and fruit, have been identified for their ability to attenuate symptoms such as depression and vasomotor manifestations, which are correlated with sleep disorders in postmenopausal women (Laudisio et al., 2021).

The inclusion of nutritional support is, therefore, a considerable additional alternative since a thorough analysis carried out by means of a systematic review showed encouraging and promising results regarding the effects of nutritional interventions on sleep disorders related to menopause (Polasek et al., 2023).

4. Conclusion

The physiological phase of menopause, characterized by the reduction of ovarian follicles and changes in female sex hormones, triggers noticeable manifestations such as facial flushing and disturbances in sleep patterns. The hormonal oscillations prominent in this phase of life, especially the decrease in estrogen and progesterone, correlate with nocturnal awakenings and difficulties in maintaining continuous sleep. This complex confluence of physiological changes has a detrimental influence on overall quality of life, associated with a predisposition to pathological conditions such as cardiovascular disease and depressive states.

The complex interrelationship between sex hormones, sleep, and depression highlights the need for comprehensive therapeutic approaches. Thus, the synergistic combination of hormone therapy with sleep hygiene practices and cognitive-

behavioral modalities appears promising. In addition to measures involving careful changes in sleep habits, adherence to regular exercise routines, and a nutritionally balanced diet.

Building on the intricate connections between hormonal changes during menopause, sleep disturbances, and mental health, future research should focus on multi-disciplinary approaches that encompass not only medical but also lifestyle interventions. Emphasis should be placed on longitudinal studies to understand the long-term effects of hormone therapy combined with lifestyle adjustments. Moreover, the potential role of alternative medicine, such as herbal supplements and mindfulness practices, in mitigating menopausal symptoms warrants exploration. Personalized medicine, taking into account individual differences in hormonal profiles and response to therapy, could revolutionize treatment strategies. Lastly, increasing awareness and education about menopause in society is essential to destigmatize this natural phase of life, ensuring women receive the support and understanding they need during this transition.

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