# The Mechanism and Coping Strategies of Sleep Disturbance during Perimenopause

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**Abstract.** Many women suffer from menopausal symptoms, especially the sleep disturbances, which is harmful to health and living standard. This review aims to provide the information about mechanism of how lacking estrogen and progesterone affects the sleeping quality. Estrogen can control body temperature, regulation of cortisol and depression and progesterone have impact on nervous system and breathing. Those impacts play pivotal role in sleeping quality, so that understanding the mechanism is extremely useful for establishing effective treatment. Also, the review provides the corresponding treatment, including hormone therapy, CBTI, and aerobic exercise. Overall, hormone therapy supplies the deficient hormone directly, which is the most effective method for treating perimenopausal sleep disorders, CBTI is a non-pharmacological approach, and aerobic exercise offers additional benefits for sleep and general health. Further research is warranted to compare the results of different treatments in the long term and to make some plans for more Individualized treatment which can be more effective and lead to better outcomes.

**Keywords:** Sleep disturbance; Perimenopause; Estrogen; Progesterone.

## 1. Introduction

Perimenopause is a crucial period of transition which women experience from reproductive age to menopausal. This period always comes along with complexed mental and physical changes, among all these changes, sleep disorders is the most overwhelming and common symptom. According to some research, almost from 16% to 47% of women suffer from sleeping disturbances, such as sleep fragmentation, RLS (restless leg syndrome) as well as nocturnal polyuria during this transitional period [1]. Long-term poor sleeping quality not only detrimental to people's living standard, but also results many chronic diseases, such as cardiovascular risks.

The sleeping disturbances can be result of hormone disorder. For example, lacking estrogen and progesterone can play a pivotal role in poor sleeping quality. For the mechanism, estrogen play an important role in both level of depression and temperature homeostasis,which affect the sleeping quality. Moreover, progesterone is a neuroactive steroid which binds to the receptors. This influences the sleep and circadian rhythm. For the treatment, oral therapy and transdermal application are the ways of the estrogen treatment. Also the combined hormone therapy (HT) can improve the sleep quality both objectively and subjectively.

Although many studies have revealed the relationship between hormone changes and sleeping disturbances during the perimenopause, there is no conclusion regarding the precise neuroendocrine pathways linking estrogen and progesterone and have no highly effective treatment for improving sleeping quality. Therefore, this review aims to integrate current findings on mechanisms and treatment, to clarify the precise mechanism and provide proper treatment.

## 2. The Effect of Estrogen on Sleep

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The function of the estrogen is boosting the metabolism of norepinephrine (NE), serotonin (5 HT) and acetylcholine and increase the time of REM sleep in human. In perimenopause, there is a decrease of estrogen. Some research has shown that estrogen decreases the sleep latency, reduces the number

of awakenings after people fall asleep, increases the total sleep time and decreases the number of cyclic spontaneous arousals. Estrogen also has impact on the core body temperature during sleep. In mammals, estrogen acts as a thermoregulatory hormone that controls the timing of the lowest body temperature at night. Stopping the secretion of estrogen leads to time move earlier and change the depth of temperature drop. Both changes make more sleeping disturbances [2].

Moreover, estrogen has a direct impact on mood through its central. Estrogen can affect the regulatory process of the neurotransmitters, because there are receptors of estrogen in CNS. It mainly involves in 5-HT, serotonin and NE, norepinephrine and also involves in GABA(Gamma-Aminobutyric Acid) in some extent, which may result in an antidepressant effect. For 5-HT, Estrogen enhances postsynaptic responsiveness to 5-HT, while also boosting the quantity of 5-HT receptors and facilitating its uptake. Hence, since the estrogen decreases in menopausal transition, it can lead to depression which is detrimental to decrease sleeping quality. For NE, estrogen decrease the reactivity of monoamine oxidase, MAO. MAO can breakdown the NE. When the concentration of MAO decrease, the amount of NE can rise. GABA is the main inhibitory neurotransmitter, which can stabilize neural activity, helping to promote calmness and reduce anxiety [3]. All effects can promote anti-depression.In the perimenopause, the estrogen decreases in women's body, so that perimenopausal women are more likely to depress. Many mechanism indicate that depression can lead to poor sleeping quality, In patients with depression, dysregulation of the norepinephrine (NE) system manifests as overactivity of the locus coeruleus (LC), leading to heightened arousal and frequent nighttime awakenings. At the same time, hypofunction of the serotonin (5-HT) system, due to reduced activity of the raphe nuclei, results in decreased slow-wave sleep and dysregulated REM sleep, such as shortened REM latency [4].

Estrogen also affects the sleeping quality by controlling the regulation of cortisol. The level of cortisol indicates the occur of sleep awakening, higher cortisol lower sleeping quality. Menopausal women have higher level of cortisol in earlier sleep, which is higher than cortisol of usual morning cortisol spike. This suggests that cortisol levels, which typically remain low at night, may begin to rise earlier than normal during menopause, potentially interfering with sleep. Menopause renders women more prone to cortisol surges in response to relatively minor stresses, eventually leads to sleep disorders [3].

## 3. The Effect of Progesterone on Sleep

Progesterone also has impacts on sleeping quality and nervous system. Firstly, When progesterone enter body , it have a sedative effect. The mechanism is that progesterone can stimulate the benzodiazepine receptors which also triggers the production of GABA receptors associated with NREM sleep. GABA (gamma-aminobutyric acid) is the primary inhibitory neurotransmitter in the central nervous system, slowing down neuronal activity and thereby promoting relaxation and sleep. Therefore, the decline in progesterone levels during perimenopause directly weakens its inherent hypnotic and calming effects. Secondly, progesterone have impact on breathing. Progesterone enhances respiratory drive, has been used to treat mild obstructive sleep apnea. In a similar manner, before menopause, when progesterone levels are naturally low, the prevalence of sleep apnea is also increased [3].

## 4. Treatment

### 4.1. MHT

Menopausal Hormone Therapy (MHT), formerly known as Hormone Replacement Therapy (HRT), is a treatment that employs estrogen, either alone or in combination with progestogen, to address menopausal symptoms and counteract the adverse health effects of estrogen deficiency. It is the only solution that can comprehensively address all the related issues caused by estrogen deficiency after menopause. The essence of MHT is a therapeutic measure taken to compensate for

ovarian failure caused by aging. All types of MHT can improve chronic insomnia during perimenopause. Some research reveal that sleep disorders in the perimenopausal period, particularly those concomitant with vasomotor symptoms (e.g., hot flashes and night sweats), MHT is considered the most effective therapeutic option. However, its effect in women without VMS is less clear [4]. The use of MHT must follow the principle of individualization and weigh the pros and cons. For women under 60 years old or within 10 years of menopause without contraindications (such as known or suspected history of breast cancer, coronary heart disease, thrombosis, etc.), the benefits of MHT usually outweigh the risks. The treatment plan should use the lowest effective dose and the shortest course of treatment.

The single estrogen regimen is a type of MHT, suitable for women who have had their uteruses removed. It is usually administered continuously, including oral or transdermal administration. oral estrogen, have to pass through the liver after entering the body. This can reduce the amount of hormone that is actually available in the blood and cause fluctuations in hormone levels, which may make it harder to keep sleep regulation stable. In contrast, hormones delivered through the skin, such as 17β-estradiol patches, are absorbed directly into the bloodstream. This keeps blood estrogen levels more stable and closer to natural physiological changes, allowing the hormone to act more effectively on brain regions that control sleep, and thereby improve sleep quality.

Studies have also found that, regardless of the route of administration, combining estrogen with a progestin has a clearer effect on improving sleep, which supports the idea that both the delivery method and hormone combination work together. For example, transdermal delivery combined with hormones, such as 17β-estradiol patches plus micronized progesterone, significantly improved sleep problems (SMD = -0.22, 95% CI: -0.37 to -0.06, P = 0.007) and was more effective than estrogen alone. Oral delivery combined with hormones, such as oral combined estrogen plus medroxyprogesterone acetate, also improved sleep (SMD = -0.10, 95% CI: -0.13 to -0.07, P < 0.00001), but the effect was weaker than the transdermal combination [5].

### 4.2. CBT-I

Cognitive Behavioral Therapy for Insomnia (CBT-I) is a multi-component treatment that includes behavioral, cognitive, and educational strategies, and it is believed to address the key factors that contribute to the persistence of insomnia. Recognized as a first-line approach for insomnia disorder , CBTI has been shown to be as effective as hypnotic medications in the short term, while in the long term it demonstrates greater effectiveness and better tolerability than hypnotics.

CBT-I is a highly effective treatment for decreasing sleep quality of menopausal women compared to other treatment such as SRT. In a research, information about insomnia symptoms and sleep characteristics was gathered through the Insomnia Severity Index (ISI, a seven-item self-report instrument for rating the severity of insomnia) and the consensus sleep diary,comparing the global insomnia, sleep quality, sleep latency, and wake after sleep onset between two different kind of treatment (CBTI and SRT).

Result showed that Result showed that the remission rate of CBTI is 54%–84% and SRT account for 38%–57%,Aslo,the CBT-I leads to the greatest improvements across all measures. Specifically, CBTI leads to the largest and most sustained reduction in ISI that finally decrease from almost 15 to 7, significant improvements in sleep quality, shorter sleep latency, and less wakefulness after sleep onset. These benefits are not only observed immediately after treatment but also maintained at the 6-month follow-up, whereas SHE shows minimal effects and SRT demonstrates moderate improvements. Hence the higher rates of remission and more pronounced improvements in sleep quality indicate that CBTI could be a more effective treatment choice for the majority of women. People can choose different treatment according to their own needs and situation [6].

Patients' cognitive distortions often revolve around hormonal issues. For example: "It's impossible to sleep well unless hormone levels return to normal." "Every night's hot tide is bound to ruin my sleep." CBT-I may enhance the self-regulation ability of sleep, reduce the frustration and

anxiety after waking up at night, reconstruct cognition, and thereby maximize the improvement of sleep quality.

### 4.3. Aerobic Exercise

In recent years, to find therapies that are effective, safe, economical, and forward-looking, some researchers have shown from the perspective of exercise health promotion that aerobic exercise not only improves cardiopulmonary function and endocrine secretion but also enhances sleep quality by reducing neural sensitivity and alleviating anxiety and depression. Its advantages include high accessibility, and few side effects. It is noticeable that it appears to have a particularly strong effect on sleep disorders in menopausal women. Some results showed that, compared with the control group, aerobic exercise had a significant effect on improving sleep disorders in menopausal women. because consistent aerobic activities, such as jogging or aerobics, have been shown to increase serum estradiol levels, mitigate somatic symptom and regulate negative emotion which are positively associated with better sleep quality.

A study reveals that all forms of aerobic exercise (static, dynamic, or a combination of both )can help improve sleep disorders in menopausal women. However, their effects differ, with static exercise being the most effective, followed by dynamic exercise and the combined form. Static exercises, such as stretching and yoga, help improve sleep in menopausal women by relaxing muscles, regulating breathing, and reducing anxiety and depression. Their mechanism is similar to progressive muscle relaxation training and can also increase brain γ-aminobutyric acid levels, reduce sympathetic activity, and activate the parasympathetic nervous system, thereby relieving vasodilation symptoms and improving sleep quality. Dynamic exercises have higher intensity and, through greater movement range and muscle engagement, can enhance cardiopulmonary function, increase blood flow, and promote sweating, supporting overall physiological regulation [7].

High-intensity exercise can be difficult for menopausal women in poor physical condition to maintain. In contrast, low- to moderate-intensity aerobic exercise makes it easier to increase the duration of each session and the number of sessions per week. By doing so, menopausal women can significantly raise their daily and weekly total exercise volume, which helps improve hormone secretion, reduce symptoms of menopause, and enhance sleep quality. In menopausal women, those who exercised for at least 225 minutes per week were more likely to fall asleep than those who exercised less than 180 minutes per week.

## 5. Conclusion

To sum up, many women during menopausal transition often have some sleeping disturbances, which is quite detrimental to their living quality and sometimes leads to chronic diseases. Understanding the specific mechanism of how lacking estrogen and progesterone result in poor sleeping quality is crucial for developing proper treatment. This review mainly explain the mechanism of relationship between both lower estrogen and progesterone and poor sleeping quality during menopause and synthesis three kind of treatment including MHT, CBTI, and aerobic exercise.

MHT provides the supplement of estrogen and progesterone directly and have shown this is an effective measure. However, its use is sometimes limited by safety concerns, Especially monotherapy with estrogen. CBT-I, on the other hand, is supported by strong evidence as a first-line, non-pharmacological treatment. It improves sleep onset and maintenance without pharmacological risks, making it suitable for a broad population. Moving on to aerobic exercise, although this is not specific for improving sleeping quality, this is also shown to be a effective supplementary approach.

Nevertheless, there is a lack of research providing personalized strategies tailored to different symptom patterns and individual needs. Therefore, future research should pay attention to study different treatment catering people with various condition and needs. Moreover, focusing on how to integrate different interventions is also indispensable for providing effective treatment for women.

Establishing such strategies is crucial for providing comprehensive care and improving the life quality of menopausal women.

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