

Clinicians' Forum

From time to time, the editors of *Menopause Management* field interesting clinical questions and dilemmas. In this forum, our Editorial Advisory Board members, experts in a range of fields related to midlife women's health, tell readers how they handle these situations.

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Question: Outside of the effect of vasomotor symptoms, does menopause itself have a direct impact on duration or quality of sleep? What is the impact of vasomotor symptoms? Does exogenous estrogen therapy enhance sleep? What is your approach to counseling postmenopausal women complaining of insomnia?

Answers:

Sleep complaints are very commonly associated with menopause. One-fourth to one-half of menopausal women complain of a sleep-related problem. This compares with 15% of the general population. Estrogen has many properties

that are biologically sleep maintaining. It is surprising, therefore, to note that there is little formal polysomnographic (PSG) evidence of sleep disturbance in a general population-based prospective study other than what is associated with age-related changes.^{1,2}

While the standard sleep electroencephalogram may be normal, menopause is associated with increased arousability when exposed to nighttime stressors.³ In clinical estrogen replacement trials, estrogen has been shown to decrease latency time to sleep onset, increase total sleep time and decrease spontaneous arousals. The subjects most affected by estrogen therapy (ET) are those in the subset that is experiencing the most vasomotor symptoms. While not all arousals are associated with measurable vasomotor changes, those patients who experience hot flashes are the ones most likely to have disturbed sleep. ET in those patients would improve sleep.^{4,5}

In fact, sleep symptoms, given their medical implications, may be one of the major remaining reasons for prescribing hormone therapy (HT).

There are several ways in which menopause has an effect on sleep. The first is the development of menopause-related depression. Insomnia and depression are closely linked in a "chicken and egg" way. Insomnia is difficulty initiating sleep at the beginning of the night or reinitiating sleep after waking up. It is "learned" and self-perpetuating. One bad night tends to lead to others due to performance anxiety over the possibility of not sleeping.

Since insomnia is often the precursor to depression, treating it can prevent depression. Patients who experience vasomotor symptoms are the ones most likely to develop insomnia, and therefore go on to depression. Increased

arousals from vasomotor symptoms create the setting in which sleep-maintenance insomnia develops. Estrogen itself may also have an antidepressant effect.⁶

Cognitive/behavioral and nonmedical treatments have been shown to be the most effective ways to treat insomnia in the long term.⁷ Sedating medications, while relatively safe for long-term use, do not ultimately "teach" someone how to go back to sleep following an interruption. Preventing arousals in the first place, such as with ET, is an appropriate part of therapy, but ultimately learning to go back to sleep following sleep disruptions is the long-term approach to insomnia therapy.

The second, less well recognized, effect is sleep apnea. Apnea triples in incidence immediately after menopause. This is only partially due to menopause-associated weight gain. Estrogen has an effect on airway neuromuscular function.⁸ The significance of this is to not write off all sleep disruptions that occur after menopause to simple hormonal deficiency effects. Snoring and daytime sleepiness should be tip-offs for doing a sleep study.

Menopause's third effect on sleep is the increase in general pain and the development of fibromyalgia (FM). FM is characterized by poor-quality sleep, like depression and insomnia, in a "chicken and egg" manner. Poor sleep leads to increased pain sensitivity that will, in turn, make for more disrupted sleep.⁹ There is a 7:1 predominance of women to men in FM sufferers. Menopause is a common time for FM to develop. While ET has not been reported to improve FM, any method of improving sleep is beneficial. Similarly, discontinuing ET may well make FM worse in some patients.

Finally, sleep disruptions due to menopause may make existing sleep disorders worse. This is particularly true of restless legs syndrome (RLS). RLS can create insomnia by creating an



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uncomfortable condition in the legs while lying in bed. Menopause may mark the time that patients need to increase RLS medications to maintain sleep.

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Many epidemiologic studies have found increased reports of sleep disturbance during the menopausal transition. It is generally believed that hot flashes produce arousals and awakenings from sleep, leading to fatigue and, possibly, impaired performance. However, this notion is challenged by two recent laboratory investigations. In one study, symptomatic and asymptomatic postmenopausal women and premenopausal women of similar ages were recorded under controlled laboratory conditions.¹ They were screened to eliminate those with any drug use, sleep, physical, or mental disorder, or body mass index over 30. There were no group differences whatsoever on any sleep stage

measure, sleep or fatigue questionnaires, or performance test. When hot flashes occurred (mean = 5.2 ± 2.9 SD/night), they tended to follow, rather than precede, arousals and awakenings. These data provide no evidence that hot flashes produce sleep disturbance in symptomatic postmenopausal women.

These findings are strongly supported by those of a large, recent epidemiologic investigation. The Wisconsin Sleep Cohort Study measured sleep quality by complete laboratory PSG and by self-reports in a probability sample of 589 premenopausal, perimenopausal, and postmenopausal women.² Sleep quality was not worse in perimenopausal or postmenopausal women nor in symptomatic versus asymptomatic women on any measure.

Thus, whereas the majority of epidemiologic studies find increased reports of sleep disturbance during menopause, this is not supported by laboratory investigations. This apparent contradiction may be partially resolved by a recent study conducted in our laboratory. Eighteen symptomatic and 6 asymptomatic postmenopausal women and 12 eumenorrheic women of similar ages were recorded on warm (30° C ambient), neutral (23° C), and cold (18° C) nights. When data were examined for the entire night, the same findings reported above were obtained: there were no significant differences among the groups and no evidence of hot flash-induced sleep disturbance. However, when data were examined by halves of the night, a different picture emerged. We divided the data because most rapid eye movement (REM) sleep occurs in the second half of the night and it has been previously reported that thermoregulatory effector responses (eg, hot flashes) are suppressed during REM. These analyses showed that, during the first half of the night, the women with hot flashes had significantly more arousals and awakenings than the other two groups, and the 18° C

ambient temperature significantly reduced the number of hot flashes. These effects did not occur in the second half of the night. In the first half of the night most hot flashes preceded arousals and awakenings. In the second half of the night, this pattern was reversed. Since the previous laboratory studies did not analyze data by halves of the night, the discrepancy with the epidemiologic studies may be partially explained.

Given the above data, the most logical, conservative treatment for hot flash-induced sleep disturbance, if present, is to lower the room temperature to 64° F for the first 4 hours of sleep. Most home thermostats can do this. Additionally, the practice of paced respiration prior to bedtime may be beneficial.

Although estrogen definitely ameliorates hot flashes, its effects on sleep are less clear. Therefore, given the recent findings from the Women's Health Initiative (WHI), the risks of estrogen use will probably outweigh the benefits for many women requesting treatment for disturbed sleep.

The incidence of sleep disordered breathing (apnea) increases significantly during menopause. Progesterone is a respiratory stimulant and has been used to treat mild obstructive sleep apnea. Patients suspected of having sleep apnea—those who snore, are obese, have a large neck circumference, and complain of daytime sleepiness—should be referred to an accredited sleep-disorders center for evaluation and treatment.

— Robert Freedman, PhD



Robert Freedman, PhD

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Sleep problems, especially insomnia, in menopausal women are either induced by menopause or coincide with the menopause period. Typical symptoms include trouble falling asleep (long sleep latency), difficulty staying asleep (excessive or prolonged awakenings), awakening involuntary too early in the morning, or not feeling restored from sleep.^{1,2} The consequences of this poor-quality sleep, like fatigue, sleepiness, irritability, mood disorders, memory troubles, lack of concentration or disability in daytime functioning,³ may mimic climacteric symptoms. The same woman may suffer from some or all forms of insomnia.

Insomnia is reported by 25% of women and severe insomnia by 15% of women between 50 and 64 years of age. In the age groups over 65, the prevalence of insomnia and severe insomnia is 25% and 16%, respectively.⁴ According to another study the risk for sleep disturbance in postmenopausal women was 3.4, and in perimenopausal women 1.5, compared with premenopausal women.⁵ However, studies assessing sleep by objective measurements have shown few changes connected with menopause.⁶⁻⁸

Sleep and Climacteric Symptoms

Several studies support an association between self-reported sleep problems and climacteric symptoms.^{7,9,10} A European study of over 5,000 women reported an unambiguous correlation between insomnia and vasomotor symptoms.¹⁰ In a more recent study with 12,600 US women of multiethnic origins, an odds ratio for sleep problems in women with climacteric symptoms was 2.0 compared with asymptomatic women.⁹

The previous data about the relationship between objectively measured sleep quality with PSG and climacteric symptoms is sparse. Shaver et al¹¹ reported longer times sleeping and longer

REM latency in symptomatic women compared with asymptomatic women. In a study by Erlik and colleagues¹² hot flashes caused arousals. Three other studies could not characterize any specific abnormalities in PSG in connection with climacteric symptoms.^{7,13,14} The study by Woodward and Freedman⁶ was the first to obtain objective measures of vasomotor symptoms during the sleep-recording night. They found that vasomotor symptoms disrupted sleep by causing nocturnal awakenings, increasing sleep stage changes and lowering sleep efficiency, although a recent study by the same research group¹⁵ could not repeat the findings.

Effect of HT on Sleep Quality

HT has been found to be an effective treatment to control menopausal sleep problems. In a Swedish study¹⁶ alleviation of vasomotor symptoms was significantly associated with improvement in sleep quality. In another study of postmenopausal women who were both symptomatic and asymptomatic for vasomotor symptoms,¹⁷ estrogen facilitated falling asleep and decreased nocturnal restlessness and awakenings, as well as decreased tiredness in the morning and during the daytime. The degree of improvement in vasomotor symptoms was an important predictor of the degree of improvement in sleep disturbance. However, the subset of women with at least some degree of insomnia in the absence of vasomotor symptoms also reported improved sleep quality during HT use. The same finding was evident in a recent large, randomized, placebo-controlled study of the WHI,¹⁸ which evaluated the long-term effects of HT on the quality of life. This study's enrollment excluded climacterically moderate or highly symptomatic women.

The beneficial results of HT on subjective sleep quality are easily explained in women with vasomotor symptoms, in whom sleep problems can be regarded

secondary to vasomotor symptoms. As for asymptomatic women, two explanations can address these findings. First, women may underestimate or not recognize



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their symptoms. In that case, alleviation of the vasomotor symptoms again plays an important role in improving sleep quality. Second, decreased hormone levels associated with menopause may interfere with sleep regulation in the central nervous system, causing sleeping disturbance. By replacing hormone levels with HT, at least some of these symptoms may be abolished.

The findings about the effects of HT on objective sleep quality have not been as unanimous as those concerning the effect of HT on subjectively measured sleep quality. HT has been shown to increase REM sleep¹⁹⁻²¹ and reduce awakenings.^{12,19,22-23} Also, a decrease in nocturnal wakefulness during the entire night^{19,24} or in the first sleep cycles²¹ has been reported, as well as a shortening of sleep latency,^{20,25} an improvement in sleep efficiency^{22,24} and a reduction of the rate of cyclic alternating patterns of sleep.²² In some studies no improvements whatsoever have been found.²⁶⁻²⁸ In the largest study to date, postmenopausal women on HT had worse sleep quality compared with their counterparts who do not take HT, as they had less short wave sleep, more stage 1 sleep, and their sleep was more fragmented.¹³

Treating Sleep Disturbances During Menopause

In women with climacteric vasomotor symptoms, the first-line treatment for insomnia should be HT. Additionally, women whose insomnia is indispensably related to mood symptoms benefit from HT.¹⁷ A subset of women who do not have vasomotor symptoms may also

benefit from HT,¹⁷ but careful screening of other underlying reasons for sleep problems is crucial. In case of contraindications or fears about HT, other treatment alternatives, such as relaxation therapies or improvement of sleep hygiene, as well as antidepressants, dietary isoflavones and soy foods, should be considered. However, although the effectiveness and safety of these treatments, at least in the long run, are still unproven. In sleep-disordered breathing, nasal continuous positive airway pressure remains the treatment of choice until more information about HT, especially about progesterone, is available.

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It is well documented that around the age of menopause—compared with before menopause—more women report sleep disturbance. Data from cross-sectional studies comparing sleep variables by menopausal status or monitoring concurrent hot flash activity and sleep reveal that sleep disruption is associated

with menopausal hormone changes in some, but not all menopausal women, and predominantly in those women with hot flash symptoms. Sleep problems separate from hot flash activity during menopause are reported, but contributing factors are difficult to disentangle. Besides being influenced by ovarian hormonal changes, contributors to sleep problems are likely the concurrent aging of sleep regulation mechanisms, making sleep less stable; sleep-related physiology changes such as sleep-disordered breathing or periodic leg movements; and other aging phenomena such as urinary bladder control. As well, social factors producing stress or life strain, or various combinations of such factors, could be at play.



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Vasomotor Symptoms

There is ample evidence that women with vasomotor symptoms tend to have disturbed sleep, both reported or measured by PSG, raising questions about whether sleep disruptions are concurrent with or a consequence of hot flashes. However, PSG sleep disruptions have been shown to both precede and follow physically measured hot flash activity. Body-temperature-regulating brain centers are close to sleep-regulating centers and could be concurrently disturbed by hypothalamic-pituitary-ovarian hormone fluctuations or levels. Alternatively, the temperature-regulating axis might trigger hot flash/sweat activity with ensuing discomfort to the point of affecting sleep; perhaps both dynamics occur.

Most investigators who have specifically manipulated HT have concluded that HT affects perceived and PSG sleep positively, but mainly in conjunction with reducing hot flash/sweat activity or other symptoms.

Other Contributors

In midlife women denying significant sleep problems prior to perimenopause, we assess possible contributors to the perceived sleep disturbance, most particularly hot flash activity, psychological distress (anxiety, depressed mood) and life strain (ie, challenging life events). We observed from our studies of midlife women reporting insomnia that some women exhibit substantial hot flash activity but little coexisting psychological distress or life strain. Other women reported high psychological distress and life strain but little hot flash activity. Actually, the former group showed PSG sleep disturbance while the latter group tended to have normative PSG patterns in spite of reporting insomnia. If menopausal symptoms appear dominant, we counsel women to seek treatment for hot flashes (eg, with HT or natural compounds). If psychological distress and high life strain appear dominant, we encourage stress management behavioral treatments for insomnia. Both approaches are relevant, especially for women with both substantial menopausal symptoms and stress/strain; in any case, behavioral treatments are not likely to do any harm. Indeed, HT in combination with psychological treatment has been observed to be more effective than HT alone in alleviating insomnia.

Treatments

Behavioral treatment recommendations for insomnia include what I call the four R's: Regularize, Ritualize, Relax and Resist Sleep-Interference Behaviors. A very important component of sleep efficiency is *regularizing* sleeping hours and restricting them to consistent placement on the 24-hour light/dark cycle, thereby strengthening the entrainment of sleep and wake. Regardless of what time one goes to sleep, the important element is to get up at the same time every day. *Rituals* to prepare for sleep and using the bedroom only for sleep

play a conditioning role. Techniques for *relaxation* (eg, warm baths or the practice of mindful relaxation techniques such as progressive muscle relaxation, deep breathing, or creative imagery as self-taught or learned through books, videotapes or the Internet) prime the body through the mind to allow sleep to override arousal. *Resisting behaviors that interfere with sleep* include counseling to avoid caffeinated beverages or foods or large meals (small snacks are encouraged), and to avoid strenuous exercise or intensive mind/emotional stimulation close to bedtime.

Alleviation of symptoms interfering with sleep, especially hot flashes and behavioral strategies, occasionally used in combination with short-acting hypnotics to break cycles of insomnia, can go a long way in helping midlife women sleep better.

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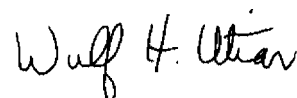
From the Editor

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abuse, implement the support system for immediate referrals, assess safety, assist with reporting if necessary, document appropriately, and provide ongoing clinical care.⁶

Perhaps a Different Ending

My primary objective in writing this editorial is to trigger awareness of IPV and DV, and to remind you that these issues might lie behind an unusual or persistent presentation in some of your patients. We are the front line and often the only defense for victims of abuse. I strongly recommend that you access the resources referred to in this editorial. I certainly wish that all those years ago I had an awareness of DV and IPV and that these resources were available to me. Perhaps the outcome for my own patient might have been better.



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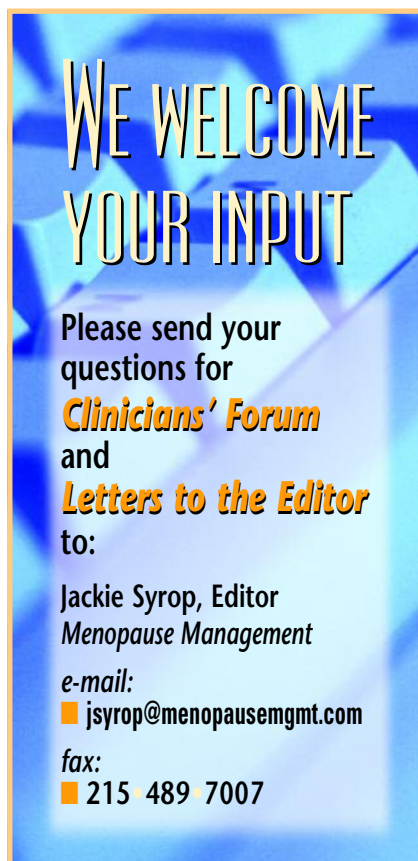
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