Insomnia is a troubling and under-treated problem

Consider gabapentin or eszopiclone to help wakeful women get some sleep at last

These problems occur in association with impairment of daytime functioning.

In young adulthood, men and women display an equivalent prevalence of symptoms of insomnia. Perimenopausal and postmenopausal women, however, report a rate of insomnia much higher than what is reported by age-matched men.1

Our patients who suffer insomnia symptoms—in particular, those perimenopausal and postmenopausal women—would be deeply appreciative if we used our clinical skills to help guide them to a peaceful night’s sleep. Here are 1) strategies for addressing their needs through pharmacotherapy and 2) useful lifestyle tips to improve their chances of good sleep (see “How you can improve sleep hygiene,” page 8).

Hormone therapy

Gynecologists are expert, of course, at using estrogen and progestin hormone therapy to treat menopausal symptoms, such as moderate and severe hot flushes. In perimenopausal and postmenopausal women, these hot flushes often occur concurrently with insomnia.

A recent survey, for example, found that the majority of women who reported hot flushes also reported symptoms of insomnia.2 And another group of researchers showed that women who have moderate-to-severe hot flushes are more likely than women who experience mild hot flushes to have greater nighttime wakefulness and a greater number of long-awake episodes.3

Estrogen therapy, in addition to reducing the severity of hot flushes, has been reported to reduce sleep latency and to increase the quantity of rapid eye movement (REM) sleep—thereby improving postmenopausal patients’ perception of the quality of their sleep.4

Non-estrogen treatment

Many women do not want to take estrogen, however; in others, estrogen therapy is contraindicated. This need not be a roadblock: Women in whom the symptoms of troubling insomnia predominate but who report few hot flushes may, in fact, benefit more from a non-estrogen treatment for insomnia. In my gyn practice, I’ve found that the agents gabapentin and eszopiclone—each with its own mechanism of action—are of value for treating insomnia in perimenopausal and postmenopausal women.

Gabapentin

Well known by its brand name,
Neurontin, gabapentin is approved by the Food and Drug Administration for the treatment of seizures and postherpetic (shingles) neuralgia. The drug has also been— but is not FDA-approved—to treat diabetic neuropathy, chronic pain, and restless legs syndrome. In addition, clinical trials have shown that gabapentin is effective for treating insomnia and hot flushes—although, again, these are not FDA-approved indications.

To treat insomnia in my peri- menopausal and postmenopausal patients, I start gabapentin at a dosage of 100 mg nightly, increasing it to 300 mg nightly. Occasionally, a patient reports the need to take as much 600 mg nightly before the quality of her sleep improves.

The most common side effects reported with gabapentin are somnolence, drowsiness, dizziness, and a “spacey” feeling—most often, during the first 1 to 3 weeks of treatment or when the dosage is escalated. Side effects tend to subside after 4 weeks of treatment.

Because gabapentin reaches its peak serum level 2 to 3 hours after ingestion of an oral dose, it is best to recommend that your patient take the drug a few hours before going to bed. Gabapentin has a half-life of 5 to 7 hours, allowing a single dose taken near bedtime to last throughout the night.

For cooling hot flushes. In addition to being effective for the treatment of insomnia, gabapentin has been reported, as I noted, to alleviate hot flushes. Dosages required to achieve this effect are greater than what is typically prescribed for insomnia:

- In two clinical trials in which gabapentin was evaluated for treating hot flushes, researchers reported that a dose of 300 mg, three times daily, reduced hot flushes better than placebo did.
- In a third clinical trial, gabapentin was prescribed as a single, 600-mg dose at bedtime. Investigators reported that gabapentin reduced hot flushes almost as well as low-dosage transdermal estradiol.

Eszopiclone
This drug (sold as Lunesta) is a non-benzodiazepine gamma-aminobutyric acid (GABA) type A-receptor agonist that is FDA-approved for treating both sleep-onset and sleep-maintenance insomnia. A typical starting dosage is 2 mg at night, increased to 3 mg as needed. Note: If your patient is simultaneously taking a drug that inhibits the cytochrome P450 3A4 (CYP3A4) enzyme system (e.g., ritonavir and other protease inhibitors, ketoconazole, verapamil, dilitiazem, fluconazole), begin the dosage of eszopiclone at 1 mg nightly and do not increase it!

For comparison, consider the half-life of four of the most commonly prescribed sleep medicines:

- eszopiclone, 5 to 7 hours
- zolpidem (Ambien), 1.5 to 2.4 hours
- extended-release zolpidem (Ambien CR), 1.5 to 2.4 hours (although the active drug is released from its matrix over a longer duration)
- zaleplon (Sonata), 1 hour.

Because eszopiclone and extended-release zolpidem have the longest-lasting effects, they are most likely to maintain sleep throughout the night. The most common side effects of eszopiclone are a persistent metallic taste, somnolence, headache, dizziness, and unpleasant dreams.

Eszopiclone (as well as extended-release zolpidem) is approved for long-term use. Non-benzodiazepine
GABA_α_ agonists such as eszopiclone are not considered addictive.

Notable research. In a 6-month trial, eszopiclone, 3 mg nightly, was associated with improvements in sleep, quality of life, and work performance, compared with placebo.10 In a trial of more than 400 perimenopausal women who had symptoms of insomnia, eszopiclone, 3 mg nightly for 4 weeks, improved sleep onset, sleep maintenance, sleep duration, sleep quality, and daytime functioning, also compared to placebo.11 Eszopiclone also improved depressive symptoms as recorded by the Montgomery-Åsberg Depression Rating Scale.11

The latter finding is significant. Investigators have reported that insomnia and mood disturbances, such as depression and anxiety, exhibit an association in some mid-life women.12,13 The two problems may influence each other: Insomnia increases the risk of daytime mood disturbance while emotional distress increases the chance that a woman will experience insomnia.14

In a study, perimenopausal and postmenopausal women who experienced the combination of hot flashes, insomnia, and mild depression with or without anxiety were randomized to eszopiclone, 3 mg nightly for 11 weeks, or to placebo pill.15 Compared with placebo, eszopiclone alleviated insomnia, nocturnal (but not daytime) hot flushes, and symptoms of depression and anxiety and improved quality of life.

Note: During nights that follow cessation, for any reason, of eszopiclone treatment, sleep latency and episodes of wakefulness may increase.

“… and in the morning wake … new-created”

Literature is filled to overflowing with reflections on the nature of sleep. D. H. Lawrence depicted it as a profound restorative in the poem “Shadows.” Here is an excerpt:

And if tonight my soul may find her peace in sleep, and sink in good oblivion, and in the morning wake like a new-opened flower then I have been dipped again in God, and new-created.

As I said: How appreciative your patients will be if you can help them feel like a “new-opened flower,” come morning! 😊

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References