CASE STUDIES
in Lifestyle
Medicine

Cindy Geyer, MD

In Search of a Good Night's Sleep:
Hormones, Mind, Movement,
and Breath

Abstract: *Sleep disturbances are common in postmenopausal women and contribute to increased morbidity and mortality. Sleep apnea may be underdiagnosed in women, and other conditions such as insomnia and restless legs may coexist with sleep apnea. This case illustrates the complex interplay of anatomical, hormonal, metabolic and psychological factors that can interfere with restorative sleep, and the importance of both diagnostic testing and clinical history in identifying which combination of therapies will be most beneficial in improving sleep quality and quantity.*

Keywords: Cognitive behavioral therapy; insomnia; menopause; Restless legs; sleep apnea

NK is a 71-year-old woman with whom I have worked for 17 years, who presented 5 years earlier newly concerned about disrupted sleep and daytime fatigue. She described falling asleep around 11 PM with the light on, then awakening several hours later to go to the bathroom. Although she was able to get back to sleep, she would then toss and turn, at times have very vivid

dreams with occasional nightmares, and did not always feel refreshed in the morning. She was unsure if she snored, but denied gasping for air. By 2 to 5 PM she experienced a significant decrease in her energy. She had a 10-year history of bruxism for which she used a bite guard. Her past medical history was otherwise notable for a herniated disc at L4-5 with radicular symptoms, post spinal fusion with good results. She had seasonal allergic rhinitis. She was recently post

progesterone, Wellbutrin, loratidine as needed, a multivitamin, and occasional calcium supplement. She was divorced, active on many nonprofit boards and philanthropic organizations, and frequently traveled overseas.

Her lifestyle habits included regular walking, swimming during the summer months, and Pilates. Her diet was typically black coffee in the morning followed by yogurt or a smoothie with almonds, fruit, greens, and prunes. She

The risk of sleep apnea in women increases with age and with menopause, not solely explained by increases in body weight.

Moh's resection of a basal cell carcinoma on her forehead and had a prior history of melanoma resection. She underwent thymus irradiation as a child. She had 2 uncomplicated pregnancies and deliveries, and she went through menopause at age 53. Her medications included transdermal estradiol, oral

would sometimes skip lunch and eat a chocolate bar in the afternoon. A typical dinner would be fish and vegetables or salad. She did not drink alcohol and had been actively involved in alcoholic anonymous for many years. At the time her physical exam was notable for an alert woman who appeared younger

DOI: 10.1177/1559827617747222. From Canyon Ranch Lenox, Lenox, Massachusetts. Address correspondence to: Cindy Geyer, MD, Canyon Ranch Lenox, Lenox, MA 01240; e-mail: cgeyer@canyonranch.com.

For reprints and permissions queries, please visit SAGE's Web site at <http://www.sagepub.com/journalsPermissions.nav>.

Copyright © 2017 The Author(s)

than her stated age, with a height of 5'6 inches, weight of 146 pounds, body mass index 23.6, and waist-hip ratio 0.85. Her blood pressure was 116/80, pulse 66 and regular. She had narrow nasal passages, which were patent with clear nasal discharge. Her oral airway was well visualized with a Mallampati score of 1. Her neck, heart, and lung exam were normal. Laboratory data were notable for a normal blood count with a ferritin level of 87 mg/mL. Thyroid-stimulating hormone (TSH) was 4.04 μ IU/mL with free T4 and free T3 in the midrange of normal and negative thyroid antibodies. Her estradiol level was <6.0 pg/mL.

Because of her symptoms, she underwent home screening for sleep apnea using peripheral artery tonometry. The results were notable for poor sleep continuity, with 7 awakenings during the night. She had moderate obstructive sleep apnea (OSA) with an apnea-hypopnea index (AHI) of 24.3. Some of her episodes were associated with oxygen desaturation, with the lowest recorded oxygen saturation of 88%. There was a slight positional component, with more events recorded in the supine sleeping position. Both rapid eye movement and deep sleep were decreased as a percentage of total sleep time. These results were reviewed, and it was recommended that she follow-up with a full polysomnogram (PSG) for continuous positive airway (CPAP) titration. She was encouraged to implement nasal lavage with saline, nasal strips, and positional therapy to avoid the supine sleeping position in the interim. Her estradiol dose was increased from 0.025 mg to 0.0375 mg. She was also started on low-dose levothyroxine when her repeat TSH went up to 5.29 μ IU/mL.

She returned 18 months later for follow-up. She reported that her busy schedule had kept her from pursuing additional evaluation for her OSA. She had been under significant stress, and she noted a marked increase in daytime sleepiness, fatigue, anxiety/depression, and forgetfulness. She also related 2 minor motor vehicle accidents that she attributed to being distracted. She denied falling asleep at the wheel. She felt her chocolate cravings had increased. She was referred for full PSG and her results

confirmed moderate sleep apnea with an AHI of 24.9. She was also noted to have periodic limb movements with a periodic limb movement (PLM) index of 39.4. Repeat estradiol level was now 29.1 pg/mL, and her TSH was 1.53 μ IU/mL. She was prescribed CPAP; however, over the next year and a half, she had significant difficulty tolerating the mask. She would find herself ripping it off in the middle of the night, averaging less than 2 hours of use. She tried a full face mask, nasal pillows, and changing to Bi-PAP, yet she continued to have difficulty. She described her bed "looking like World War II" in the morning from her tossing and turning. Her course was also complicated by severe sinusitis from a dental implant that eroded into her maxillary sinus. She was treated with numerous rounds of antibiotics followed by surgery to drain her sinus, repair the defect from the implant, and repair a deviated septum.

Because of her difficulty tolerating her mask and the hope that the septal repair may have improved her OSA, a follow-up in room sleep study was done. She again showed poor sleep continuity, awakening 10 times during the night. While her AHI was still moderate at 28.1, she was now shown to have a striking positional component: her supine AHI was 53, while on her side her AHI ranged from 1 to 4 (normal). Positional therapy was reinforced, and she was referred to an otolaryngologist who specialized in temporomandibular joint concerns for more in-depth assessment of her airway and her jaw. She was found to have a separation in her jaw with malocclusion, which was addressed with modification of her upper and lower night guards. In addition, NK realized that as a child her sleep had been chronically disrupted because of being exposed to her parents' alcohol use, numerous late night parties, and frequent arguing; she remembered going to bed tense and being very sensitive to noise. She did some additional work with a behavioral therapist focusing on cognitive-behavioral approaches to sleep, addressing prior trauma, and engaging in breath-based relaxation techniques including biofeedback. The new oral appliance and her ongoing work with

the behavioral therapist resulted in improved quality of sleep, mood, daytime energy, and alertness. Additional follow-up to consider includes another sleep study to confirm efficacy of the oral appliance in treating her OSA, and the possibility of pharmacologic treatment for her PLMs if she continues to experience unrefreshing sleep.

Recent years have seen numerous studies linking sleep quality, quantity, and timing with adverse health outcomes, including higher risk of cardiometabolic disease,^{1,2} mood disorders,³ chronic pain,⁴ risk of cognitive decline,⁵ and higher risk of accidents/poorer work performance.⁶ Sleep apnea often goes undiagnosed, particularly in lean women. The risk of sleep apnea in women increases with age and with menopause, not solely explained by increases in body weight.^{7,8} Women may be more likely to present with atypical symptoms such as insomnia, depression, or restless sleep.⁹ In addition, women may be more likely to have a phenotype of prolonged partial upper airway occlusion during sleep,¹⁰ which is underdiagnosed by standard AHI criteria or home studies. Nonetheless, partial upper airway occlusion may be equal to OSA in its impact on significant daytime sleepiness and adverse cardiometabolic outcomes.¹¹ It can be diagnosed by documenting sustained flow limitation in nasal prongs in conjunction with increased respiratory effort (mattress sensors), and responds well to nasal CPAP therapy. Sleep onset and sleep maintenance insomnia also increase in the menopause transition, and there appears to be a bidirectional relationship between sleep disruption, anxiety, and depression.¹² Hormonal factors contributing to decrease in sleep quality may include increased vasomotor symptoms, loss of progesterone's sedative and anxiolytic effects along with progesterone's benefit on respiratory drive and genioglossal tone, loss of estrogen's effect on sleep continuity,¹³ and decreased melatonin.¹⁴ The incidence of hypothyroidism increases in women after menopause, and may also contribute to incidence and severity of OSA.^{15,16}

The most recent review of women in the KEOPS trial found that both oral conjugated estrogens and transdermal

estradiol with cyclic progesterone were better than placebo at improving overall sleep quality along with specific domains of sleep latency, satisfaction, and efficiency as measured by the Pittsburgh Sleep Quality Index scores. Improvements in global sleep quality correlated with reduction in vasomotor symptoms, while improvements in sleep latency and efficiency did not. Transdermal estradiol resulted in better improvement in sleep disturbance than oral conjugated estrogens.¹⁷ Studies on the impact of hormone therapy (HT) on incidence and severity of OSA have been more mixed. While some studies have shown reduced incidence and severity of OSA in women on HT,^{18,19} a more recent review suggests this may be related to a “healthy user bias” in women using HT.²⁰ Nonetheless, a conversation about sleep should be factored in as an important variable in the discussion of the pros and cons of HT.

As NK’s story illustrates, more than one factor can be contributing to decreased sleep quality: not only did she have OSA, she had evidence of PLMs and childhood exposure to emotional stressors. While home sleep tests offer data on sleep-related breathing disorders, the gold standard PSG includes electroencephalogram, electromyogram, and electrocardiogram. In NK’s case, the diagnosis of sleep apnea was helpful but incomplete in understanding her fragmented sleep. NK’s reports of both bruxism and restlessness are important: these symptoms often occur together and some believe they have a common etiology.²¹ The ability to review brain waves, lower extremity movement, and bruxism with a PSG improved our understanding of additional contributors to NK’s unrefreshing sleep and may have partially explained her difficulty in tolerating CPAP therapy. While treatment of coexisting OSA often results in improvement in PLMs,²² conversely the treatment of underlying restlessness may be necessary to improve tolerance of CPAP therapy.²¹ A comprehensive review of the treatment of PLMs is included for more in-depth reading.²³ Supplemental iron and vitamin C have been shown effective if serum ferritin is <75 ng/mL

(care should be taken to evaluate possible causes of blood loss or malabsorption of iron). Exercise and stretching may also be beneficial in reducing symptoms of PLMs.²⁴

NK was already being treated with HT and did not present with significant vasomotor symptoms; an initial increase in her estradiol dose to obtain measurable serum estradiol levels did not seem to improve her sleep quality. Any additional increase in dose would need to be weighed against potential risk of long-term HT. Because she had a normal body mass index, it is unlikely that weight loss would improve her OSA. In people who are overweight or obese, weight loss may improve AHI scores and reduce cardiometabolic risk,²⁵⁻²⁷ but weight loss alone may not be enough to resolve sleep apnea. However, exercise may independently improve overall sleep quality and reduce cardiovascular risk independent of any impact on AHI scores.²⁸

Addressing the psychological contributors to poor sleep quality is critical. Cognitive-behavioral therapy is considered the gold standard for insomnia,^{29,30} but there is a shortage of qualified professionals providing CBT-i (cognitive-behavioral therapy for insomnia). Growing evidence suggests that online CBT-i may be an effective strategy for people who do not have access to a psychologist or psychiatrist in person.^{31,32} Recognizing and addressing previous trauma and/or posttraumatic stress disorder are also important aspects of working with people to improve sleep quality. CBT-i has shown benefit in improving sleep quality for people with posttraumatic stress disorder and may also positively influence nightmares, depression, and psychosocial impairment.^{33,34}

In summary, it is increasingly clear that there exists a bidirectional relationship between poor quality and quantity of sleep and the risk for anxiety and depression, chronic pain, cognitive impairment, weight gain, and cardiometabolic risk. Sleep deprivation may also negatively affect people’s ability to follow through with their health intentions regarding food choices and exercise.³⁵⁻³⁷ Assessing sleep in

postmenopausal women is crucial as part of a whole person, lifestyle-centered approach. It is important to maintain a high index of suspicion for sleep disordered breathing in women, since they are less likely to present with classic symptoms and may be at higher risk of prolonged partial upper airway occlusion. In addressing sleep apnea, referral to an otolaryngologist for an in-depth assessment of airway anatomy should be considered, especially if CPAP is not tolerated. Treating coexisting sleep apnea, maintaining a serum ferritin >75, and incorporating exercise and stretching may help symptoms of periodic limb movements. Cognitive-behavioral therapy for insomnia is the gold standard for both sleep onset and sleep maintenance insomnia, and may be beneficial in people with posttraumatic stress disorder. By identifying and addressing the multifactorial contributors to decreased sleep quality and quantity in our patients, we will be better able to support their health and well-being.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Not applicable, because this article does not contain any studies with human or animal subjects.

Informed Consent

Not applicable, because this article does not contain any studies with human or animal subjects.

Trial Registration

Not applicable, because this article does not contain any clinical trials. [AJLM](#)

References

1. Shivashankar R, Kondal D, Ali MK, et al. Associations of sleep duration

- and disturbances with hypertension in metropolitan cities of Delhi, Chennai, and Karachi in South Asia: cross-sectional analysis of the CARRS Study. *Sleep*. 2017;40. doi:10.1093/sleep/zsx119.
2. Barger LK, Rajaratnam SMW, Cannon CP, et al. Short sleep duration, obstructive sleep apnea, shiftwork, and the risk of adverse cardiovascular events in patients after an acute coronary syndrome. *J Am Heart Assoc*. 2017;6. doi:10.1161/JAHA.117.006959.
 3. Müller MJ, Kundermann B, Cabanel N. Eveningness and poor sleep quality independently contribute to self-reported depression severity in psychiatric inpatients with affective disorder. *Nord J Psychiatry*. 2016;70:329-334.
 4. Marshansky S, Mayer P, Rizzo D, Baltzan M, Denis R, Lavigne GJ. Sleep, chronic pain, and opioid risk for apnea [published online July 19, 2017]. *Prog Neuropsychopharmacol Biol Psychiatry*. doi:10.1016/j.pnpbp.2017.07.014.
 5. Leng Y, McEvoy CT, Allen IE, Yaffe K. Association of sleep-disordered breathing with cognitive function and risk of cognitive impairment: a systematic review and meta-analysis. *JAMA Neurol*. 2017;74:1237-1245.
 6. Rosekind MR, Gregory KB, Mallis MM, Brandt SL, Seal B, Lerner D. The cost of poor sleep: workplace productivity loss and associated costs. *J Occup Environ Med*. 2010;52:91-98.
 7. Dancey DR, Hanly PJ, Soong C, Lee B, Hoffstein V. Impact of menopause on the prevalence and severity of sleep apnea. *Chest*. 2001;120:151-155.
 8. Mirer AG, Young T, Palta M, Benca RM, Rasmuson A, Peppard PE. Sleep-disordered breathing and the menopausal transition among participants in the sleep in midlife women study. *Menopause*. 2017;24:157-162.
 9. Valipour A. Gender-related differences in the obstructive sleep apnea syndrome. *Pneumologie*. 2012;66:584-588.
 10. Anttalainen U, Tenhunen M, Rimpilä V, et al. Prolonged partial upper airway obstruction during sleep—an underdiagnosed phenotype of sleep-disordered breathing. *Eur Clin Res J*. 2016;3. doi:10.3402/ecrj.v3.31806.
 11. Anttalainen U, Polo O, Vahlberg T, Saareanta T. Women with partial upper airway obstruction are not less sleepy than those with obstructive sleep apnea. *Sleep Breath*. 2013;17:873-876.
 12. Jehan S, Masters-Isarilov A, Salifu I, et al. Sleep disorders in postmenopausal women. *J Sleep Disord Ther*. 2015;4:1000212. doi:10.4172/2167-0277.1000212.
 13. Tal JZ, Suh SA, Dowdle CL, Nowakowski S. Treatment of insomnia, insomnia symptoms, and obstructive sleep apnea during and after menopause: therapeutic approaches. *Curr Psychiatry Rev*. 2015;11:63-83.
 14. Jehan S, Jean-Louis G, Zizi F, et al. Sleep, melatonin and the menopausal transition: what are the links? *Sleep Sci*. 2017;10:11-18.
 15. Takeuchi S, Kitamura T, Ohbuchi T, et al. Relationship between sleep apnea and thyroid function. *Sleep Breath*. 2015;19:85-89.
 16. Petrone A, Mormile F, Bruni G, Quartieri M, Bonsignore MR, Marrone O. Abnormal thyroid hormones and non-thyroidal illness syndrome in obstructive sleep apnea, and effects of CPAP treatment. *Sleep Med*. 2016;23:21-25.
 17. Cintron D, Lahr BD, Bailey KR, et al. Effects of oral versus transdermal menopausal hormone treatments on self-reported sleep domains and their association with vasomotor symptoms in the recently menopausal women enrolled in the Kronos Early Estrogen Prevention Study (KEEPS) [published online August 21, 2017]. *Menopause*. doi:0.1097/GME.0000000000000971.
 18. Galvan T, Camuso J, Sullivan K, et al. Association of estradiol with sleep apnea in depressed perimenopausal and postmenopausal women: a preliminary study. *Menopause*. 2017;24:112-117.
 19. Bixler EQ, Vgontzas AN, Lin HM, et al. Prevalence of sleep disordered breathing in women: effects of gender. *Am J Respir Crit Care Med*. 2001;163(3 pt 1):608-613.
 20. Mirer AG, Peppard P, Palta M, Benca RM, Rasmuson A, Young T. Menopausal hormone therapy and sleep-disordered breathing: evidence for a healthy user bias. *Ann Epidemiol*. 2015;25:779-784.
 21. Silva C, Peralta AR, Bentes C. The urge to move and breathe—the impact of obstructive sleep apnea syndrome treatment in patients with previously diagnosed, clinically significant restless legs syndrome. *Sleep Med*. 2017;38:17-20.
 22. Phillips B. The many disorders comorbid with restless legs syndrome. <https://www.medscape.org/viewarticle/734547>. Accessed November 24, 2017.
 23. Winkleman J, Armstrong M, Allen RP, et al. Practice guideline summary: treatment of restless legs syndrome in adults: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. *Neurology*. 2016;87:2585-2593.
 24. Aukerman MM, Aukerman D, Bayard M, Tudiver F, Thorp L, Bailey B. Exercise and restless legs syndrome: a randomized controlled trial. *J Am Board Fam Med*. 2006;19:487-493.
 25. Kuna S, Reboussin DM, Borradaile KE, et al. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. *Sleep*. 2013;36:641A-649A.
 26. Araghi MH, Chen YF, Jagielski A, et al. Effectiveness of lifestyle interventions on obstructive sleep apnea (OSA): systematic review and meta-analysis. *Sleep*. 2013;36:1553-1562.
 27. Hamilton GS, Joosten SA. Obstructive sleep apnoea and obesity. *Aust Fam Physician*. 2017;46:460-463.
 28. Kelley GA, Kelley KS. Exercise and sleep: a systematic review of previous meta-analyses. *J Evid Based Med*. 2017;10:26-36.
 29. Lam S, Macina LO. Therapy update for insomnia in the elderly. *Consult Pharm*. 2017;32:610-622.
 30. Wang M, Wang SY, Tsai PS. Cognitive Behavioral therapy for primary insomnia: a systematic review. *J Adv Nurs*. 2005;50:553-564.
 31. Meaklim H, Cunningham D. Web-based cognitive behaviour therapy for insomnia shows long-term efficacy in improving chronic insomnia [published online September 29, 2017]. *Evid Based Ment Health*. doi:10.1136/eb-2017-102726.
 32. Ho FY, Chung KF, Yeung WF, et al. Self-help cognitive behavioral therapy for insomnia: a meta-analysis of randomized controlled trials. *Sleep Med Rev*. 2015;19:17-28.
 33. Talbot LS, Maguen S, Metzler TJ, et al. Cognitive behavioral therapy for insomnia in posttraumatic stress disorder: a randomized controlled trial. *Sleep*. 2014;37:327-341.
 34. Ho FY, Chan CS, Tang KN. Cognitive-behavioral therapy for sleep disturbances in treating posttraumatic stress disorder symptoms: a meta-analysis of randomized controlled trials. *Clin Psychol Rev*. 2016;43:90-102.
 35. Hogenkamp PS, Nilsson E, Nilsson VC, et al. Acute sleep deprivation increases portion size and affects food choice in young men. *Psychoneuroendocrinology*. 2013;38:1668-1674.
 36. Hui SK, Grandner MA. Association between poor sleep quality and stages of change of multiple health behaviors among participants of employee wellness program. *Prev Med Rep*. 2015;2:292-299.
 37. Chen J, Liang J, Lin X, et al. Sleep deprivation promotes habitual control over goal-directed control: behavioral and neuroimaging evidence [published online November 6, 2017]. *J Neurosci*. doi:10.1523/JNEUROSCI.1612-17.2017.