Approach to insomnia in patients with dementia

Jennifer Molano, MD

Bradley V. Vaughn, MD

Summary

Insomnia occurs in one-fourth to one-third of patients with dementia, and can lead to patient and caretaker distress and early institutionalization. An array of effects from the disease, medication, behaviors, and mood issues may play a role in influencing sleep. This perplexing issue can be handled effectively with appropriate evaluation and understanding of basic sleep-wake physiology. For most patients, appropriate timing of cues, modifying behavior, and optimizing medications can improve the patient's and caregiver's quality of life. In this article, we review signs that may help the clinician recognize insomnia early and approach the issue in a logical manner.

Approximately 1 in 3 normal individuals may complain of insomnia.¹ The diagnosis of insomnia is defined as difficulties with sleep onset, sleep maintenance, nonrestorative sleep, or early morning awakenings for at least 1 month resulting in daytime sequelae.² The consequences of insomnia are substantial, and associated with decreased daytime functioning and quality of life as well as increased consumption of health care resources.¹ For seniors, the complaint of insomnia becomes an even greater challenge due to the potential for many contributing factors. People may note more awakenings during the night as part of normal aging. The key is determining if these awakenings lead to a daytime issue.

In patients with dementia, the prevalence of insomnia ranges from 20% to 35%.³ The consequences of insomnia are similar but also include increased unwanted behaviors and agitation that may lead to increased caregiver burden, risk for falls, and early nursing home placement.⁴ Both physiologic and environmental factors may be associated with insomnia.

Most clinicians find sleep issues end up being a “doorknob” conversation, with a patient or caregiver mentioning sleep difficulties at the end of a visit. Addressing sleep issues requires time, but optimizing sleep offers an opportunity to make a difference to the patient and the patient's family. Clinicians may wish to schedule another visit to focus on sleep. Another strategy is to ask the patient and caretaker if they are satisfied with the patient's sleep early in

Department of Neurology (JM), The University of Cincinnati College of Medicine, Cincinnati, OH; and Department of Neurology (BVV), University of North Carolina, Chapel Hill.

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Correspondence to: vaughnb@neurology.unc.edu

Table 1 Questions to ask the patient and caregiver

1. Consistency of sleep schedule
2. Bedtime and wake-up time during the week and on the weekends
3. Time to fall asleep after bedtime
4. Frequency and causes of nighttime awakenings
5. Time to return to sleep after a nighttime awakening
6. Frequency and duration of daytime naps
7. Caffeine and alcohol use
8. Medical and psychiatric factors that may be associated with insomnia, e.g., pain, nocturia
9. Environmental factors that may be associated with insomnia
10. Symptoms of other sleep disorders, e.g., snoring, dream enactment behavior

the visit or on a previsit questionnaire. This way, the clinician can concentrate on assessing the basic drivers for sleep, look for medications, supplements, or affective issues that may be disrupting sleep, and ask about other treatable sleep disorders. This article reviews tips that may improve effectiveness in recognizing and managing insomnia in those with dementia. While some of these tips can be applied to those with normal cognition, special considerations in those with dementia are also discussed.

Address sleep early in the visit

All of us understand how busy practice has become. We have competing demands, regulations, and unfunded mandates, yet a couple of proactive questions may allow you to focus easily on sleep issues that are key to the patient and caregiver. These 2 questions should be “Are you satisfied with sleep?” and “Are you tired or sleepy during the day?” Asking these questions early allows the clinician to focus on these issues thoroughly. If the patient or caregiver answers affirmatively, then the clinician can ask about scope and effect of the sleep disturbance on both the patient and caregiver.

An essential part of the assessment for insomnia includes a thorough history on the patient’s sleep schedule and behaviors. In those with dementia, it is also important to have a caregiver who can confirm or correct this information. Clinicians should ask about bedtime, time it takes to fall asleep, the number of nighttime awakenings, time it takes to fall back asleep after a nighttime awakening, and wake-up times both during the week and the weekends. It is also useful to know the frequency and duration of naps plus quantity and duration of caffeine consumption. In addition, understanding other triggers for insomnia such as nocturia or pain can assist in facilitating the management of insomnia in patients with or without dementia (table 1).⁵

The effect of the patient’s sleep on the caregiver can be asked at the initial visit but may be more useful to ask during a follow-up visit, after a physician–patient relationship has been established. If it is discovered that a patient’s sleep disturbance is affecting the sleep and quality of life of the caregiver, recommending respite care or assistance at home may be beneficial.

Look for alterations in the sleep-wake cycle: Circadian and homeostatic drivers

The sleep-wake cycle is guided by 2 predominant drivers: the circadian rhythm and the homeostatic drive for sleep⁶ (figure). Alterations in these physiologic mechanisms can be associated with insomnia in those with dementia.

The circadian rhythm is slightly longer than 24 hours (24.2 hours), requiring adjustment of the clock on a daily basis for our bodies to remain synchronized with our environment. Cues that adjust the circadian rhythm are bright light, activity, social interactions, and food.⁷ Of

Figure The 2-process model for sleep/wake

This graph represents a cartoon of the circadian rhythm's influence to promote wakefulness and the accumulation of the homeostatic drive for sleep. If the circadian drive to be awake is more than the homeostatic drive to sleep, the person is awake, but once the homeostatic drive supersedes the circadian drive, then sleep is more likely.

these, light is the most powerful. Timing of these cues during periods that we wish to be awake promotes the brain to anticipate that wakefulness is needed at the prescribed time. For example, exposure to bright light in the morning (after the temperature nadir, usually at 4 AM) would advance the clock to promote an earlier awakening. Bright light in the evening would delay the clock to promote evening wakefulness and later sleep onset. Although evidence is limited, encouraging light during the day and a darker environment at night may help with maintaining an appropriate circadian rhythm.

In addition, regularly timed meals, activity, and social interactions may also help.⁷ The circadian rhythm follows closely with the body's temperature curve, with a falling body temperature associated with sleep and a rising temperature associated with awakening. The temperature peak is typically in the evening and typically starts to fall around 9 PM (figure). The drop in temperature facilitates sleep onset and maintenance.

Sleep onset is also facilitated by the pineal gland releasing melatonin in response to darkness. The melatonin secretion decreases with age. While the duration of the circadian rhythm stays consistent in older adults, further alterations in the circadian rhythm can occur in those with dementia and lead to more sleep difficulties.⁸ In patients with Alzheimer disease, for example, tau pathology in the suprachiasmatic nucleus and other structures associated with circadian rhythms is associated with an irregular sleep-wake rhythm,^{2,8} and "sundowning" or increased behaviors such as agitation and aggression at nighttime may be heightened by circadian rhythm dysfunction. Recent studies implicate alterations in circadian rhythms as a feature present prior to the development of mild cognitive impairment and dementia in older women.⁹ This work suggests that the circadian system may be more vulnerable to express degeneration in certain types of diseases. Yet more research is needed to determine if correcting circadian rhythm alterations is a modifiable risk factor that may delay the progression of cognitive decline.

Decreased daytime light exposure also may be a contributing factor in irregularities in the sleep-wake cycle in these patients.¹⁰ Many individuals with dementia typically become more isolated and less engaged with the outside environment with fewer daily activities. Some patients with dementia display an inconsistent sleep-wake cycle as the cause of their daytime sleepiness and an inability to fall asleep or stay asleep at night. These patients may benefit from full spectrum bright light of 1,000 lux and above delivered during the day, as well as daytime activities and exercise.¹¹ Patients with dementia can respond to these interventions, though persistent, active involvement by the caregiver may be required.⁹

In addition to the circadian rhythm, the homeostatic drive for sleep is also important. This drive is related to the accumulation of physiologic substances during wakefulness that promote sleep and eventually overwhelm the circadian drive to stay awake⁶ (figure). Both mental and

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physical activity may play a key role in building this drive and promoting sleep. Someone who is very inactive may not build up their homeostatic drive as well as a person who is very active. For the clinician to measure this, actigraphy can measure daily activity over a 1- to 3-week period.³

Adenosine is one of the major components of the homeostatic driver.⁶ Two common maladaptive behaviors that can be associated with sleep onset and sleep maintenance insomnia include daytime napping and afternoon caffeine use, both of which can lead to decreased effectiveness of adenosine in the brain. Napping during the day is a common event and may be encouraged by some caregivers as a time to attend to other chores or rest themselves, leading to a cycle of less sleep at night and more daytime issues.¹⁰ Caffeine is also used as a strategy to combat fatigue. Although caffeine may have a blood half-life of 4–6 hours, the pharmacodynamics effect for some people may be much longer. Caffeine sensitivity may change through life and some individuals are more caffeine sensitive in their later years.

Be cautious with medications that may affect the sleep-wake cycle

The regulation of wake and sleep is related to a complex neuronal network but uses some common themes. Wakefulness is primarily produced by the reticular activity system and activation of the monoaminergic nuclei, primarily acetylcholine and monoamines such as norepinephrine, serotonin, and histamine. GABA and glycine are the predominant neurotransmitters that induce sleep.⁶ During REM sleep, the brainstem cholinergic system again becomes more active with continued decreased activation of the monoaminergic systems.⁶ In addition, increased glycine activation leads to the inhibition of the lower motor neurons that is associated with the muscle atonia in REM sleep.⁶ In those with dementia, alterations in the neurotransmitters can be seen. For example, patients with Alzheimer disease are known to have decreased acetylcholine production from the basalis nucleus, which may be associated with a disrupted sleep-wake cycle.⁸

These neuronal networks are susceptible to medications. Wake-promoting medications such as acetylcholinesterase inhibitors such as donepezil or rivastigmine, or combined selective serotonin and norepinephrine reuptake blockers such as venlafaxine, may produce insomnia if taken at night. In addition, sedating medications such as anxiolytics and muscle relaxants may cause the patient to sleep during the day and thus not build up the need for sleep at night. Patients and caregivers also may try energy supplements, caffeine, or medications to stay awake during the day, as well as alcohol or supplements at night to help with sleep. In addition to education on optimizing the circadian rhythm and homeostatic drive, the clinician also should review the patient's medication list to determine if adjustments could be made to optimize the sleep-wake cycle. For patients who are prescribed aspirin for vascular issues, adjusting the timing to evening may enhance the nighttime drop in body temperature.

While medications have been used to assist with the onset and maintenance of sleep, the safety and efficacy of hypnotics in patients with dementia have not been well-established. Although controversial, melatonin (0.5–6 mg) may be helpful in some patients to promote sleep at night and can be dosed approximately 2 hours prior to the desired bedtime.^{12,13}

Sedative hypnotic agents, especially benzodiazepines and benzodiazepine receptor agonists, are widely used as short-term treatment for general insomnia. Although most of these agents increase N2 or the intermediate stage of sleep, they do not appear to have a major effect on

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sleep maintenance in older individuals.¹⁴ Unfortunately, these agents can cause daytime sedation, confusion, and memory problems, and are associated with a higher risk of hip fractures. They also have not been tested in patients with dementia. Antidepressants such as selective serotonin reuptake inhibitors or trazodone have also been frequently used in individuals with dementia, but these agents have no evidence-based data to support their use.¹⁵ These medications have undesirable side effects of daytime somnolence, dizziness, and weight gain. Antihistamines are widely found in many over-the-counter sleep aids, but should be avoided if possible due to anticholinergic effects that may worsen cognitive impairment. Low-dose doxepin (1 mg and 3 mg), found to decrease the amount of wake time and improve sleep latency and overall sleep efficiency in elderly with insomnia, again, has not been studied in individuals with dementia.¹⁶ Due to cardiac side effects, neuroleptics are not recommended as hypnotics, but may be needed short term to mitigate the threat of harm in the face of unmanageable aggression.

Keeping these cautions in mind, the benefits of starting a medication for insomnia may outweigh the risks. As always, the risks and benefits should be discussed with patients and their caregivers, with the goal of maintaining quality of life and daytime functioning. The medications ideally should be used short term, as the addition of nonpharmacologic treatments provides a better long-term strategy.

Think about affective disorders and psychological stress

Mood disorders are very common in patients with dementia, ranging from 32% to 92%.¹⁷ Patients with dementia are prone to develop depression and anxiety early in the course of the disease, and some researchers suggest mood disorders may be a prodrome to dementia.¹⁸ Depression and anxiety can be a driver of insomnia for both the patient and the caregiver. Determining whether a mood disorder is a major contributor to symptoms can be challenging. With increasing age, the circadian rhythm naturally shifts to earlier and this shift may be confounded by the classical early waking associated with depression. In addition, depression and anxiety may lead to further behaviors that promote insomnia. Patients with cognitive impairment and depression are more socially withdrawn, more agitated, and less involved with activity, which makes them more likely to disrupt their sleep-wake patterns. These patients may benefit from treatment of both the insomnia and the affective disorder. Studies of younger individuals show that treatment of the insomnia and depression helps both the depression and insomnia, beyond treatment of only the insomnia or depression alone.¹⁹ The insomnia and mood in this group may also respond to therapies that improve the insomnia such as cognitive-behavioral therapy, establishing a routine, and exercise. In addition to nonpharmacologic treatments, medication management of depression may be necessary, but is beyond the scope of this article.

Investigate other sleep disorders

Patients with dementia may not present with the same symptoms of sleep disruption as individuals who are not cognitively impaired. Thus, if the patient or caregiver identifies sleep as an issue, further questions regarding the type of disturbance may prove helpful in identifying the source.³ Caregivers should be asked about snoring, pauses in respiration, excessive movements, or dream enactment behaviors, since these symptoms may prompt the clinician to order polysomnography (table 2).⁴

Table 2 Indications for overnight polysomnography

1. Snoring
2. Observed repetitive respiratory pauses
3. Excessive movement in sleep
4. Dream enactment behavior or potentially injurious nocturnal events
5. Stereotypic events

Snoring and pauses in breathing may be features of a sleep-related breathing disturbance. These patients should be considered for polysomnography to evaluate possible obstructive or central sleep apnea.² For patients with insomnia and dementia, some may be able to respond to conservative therapies such as sleeping in the lateral position, weight loss, and avoidance of alcohol. Others may need an oral appliance or continuous positive airway pressure. Both of these therapies require training the patient and caregiver to assure device comfort and compliance.

Patients with excessive movements may have a movement disorder, or in some cases, restless legs syndrome.² The latter is frequently associated with insomnia and medications such as dopamine agonist, gabapentinoid agent, and optimization of ferritin above 50 µg/L provide benefits in normal individuals.²⁰ Nocturnal events of altered consciousness and stereotyped behaviors may be a clinical manifestation of nocturnal seizures and would be an indication for polysomnography with extended EEG.

Dream enactment behavior is an important and potentially dangerous clue to the patient with dementia.² Due to the potential for injuries, the patient and bed partner's safety is paramount if violent dream enactment behavior is present. To confirm the diagnosis of REM sleep behavior disorder (RBD), which has been associated with synucleinopathies such as Parkinson disease, multiple system atrophy, and dementia with Lewy bodies, the clinician should order polysomnography with surface EMG of all 4 limbs and simultaneous recording of video to determine if the patient has a loss of the muscle atonia that typically occurs during REM sleep. The clinician should also review medications such as antidepressants to look for secondary causes for RBD. Polysomnography can also determine if the dream enactment behavior is due to a different cause, such as sleep-disordered breathing. For most patients with dementia, melatonin may be a good alternative to the traditional clonazepam therapy in those with RBD.²¹ Safety measures such as placing a mattress on the floor, padding the furniture, or having the caregiver sleep in another room is also recommended.²¹

Treatment and the role of the caregiver

Caregivers are central to managing a patient with dementia. Active involvement by the caregiver may be important not only in obtaining information about the patient's sleep patterns and behaviors, but also in assisting in improving their sleep quality. If someone with dementia has obstructive sleep apnea, for example, the caregiver should be educated on the proper technique of placing the mask on the patient. Caregivers also should be educated on the importance of assistance in keeping the patient awake during the day to allow for a better chance of sleeping during the nighttime. Caregivers need to participate with the therapies and provide support to maintain daily routines.²² Since increased sleep disturbances in those with dementia may lead to increased caregiver burden and sleep disruption, it is also important to ensure that the caregiver has enough social and community support to complete these nonpharmacologic tasks. Clinicians, therefore, must assess the effect of sleep on the caregiver and advise good habits that promote healthy sleep and activity for the caregiver as well.

DISCUSSION

Insomnia in patients with dementia can be associated with decreased quality of life, increased health care costs, increased nursing home placement, and increased caregiver burden.

Table 3 Good sleep practices

During the day
1. Get exposure to bright light and participate in activity
2. Socialize
3. Optimize the timing of medications to optimize sleep and wakefulness drugs at night, alerting agents in the day
4. Avoid caffeine and alcohol
5. Give plenty of signals of appropriate the approaching sleep/wake expectation (wind down period in evening, a board showing what activity is coming up)
During the night
1. Make the bedroom for only sleep or intimacy
2. Keep the bedroom relatively dark and quiet (a low level night light may help)
3. A low level constant white noise can help mask outside noise
4. Allow the body temperature to drop (take a hot shower at night; keep a cool environment in the bedroom)
5. Make sure the bed is comfortable
6. Change or clean pillows, sheets, and comforters on a regular basis

Clinicians should be proactive and ask about sleep satisfaction. Asking about factors that may be driving the insomnia in these patients, including alterations in the sleep-wake cycle, medications, as well as underlying other sleep disorders or other medical and psychiatric conditions, is important. Treatments may include pharmacologic and nonpharmacologic interventions, as well as education on good sleep practices (table 3). Caregiver support may be important in treating these patients, especially in adhering to nonpharmacologic interventions such as keeping the patient awake during the daytime hours. However, physicians should be aware that increased caregiver burden may result from such active involvement.

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