Insomnia and Other Sleep Disorders in Older Adults

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KEYWORDS

• Geriatric psychiatry • Geriatrics • Insomnia • Sleep disorders
• Age-related changes in sleep • Treatment of insomnia • CBT-I

KEY POINTS

- Sleep disturbances are associated with many poor health outcomes in older adults, including increased risk for falls, cognitive decline, and all-cause mortality.
- Insomnia is often related to underlying medical, psychiatric, or environmental factors. A thorough medical and psychiatric history and an understanding of sleep environment and psychosocial stressors are essential when evaluating sleep disturbances.
- Many medications can cause or contribute to insomnia and other sleep disorders. It is critical to review patients' medication lists and if feasible, discontinue or reduce the dosages of agents that may be contributing to sleep disturbances.
- Cognitive behavioral therapy for insomnia is the first-line treatment for adults with chronic insomnia and is available in many different modalities.
- Benzodiazepines, "Z-drugs," and significantly anticholinergic medications such as diphenhydramine should be avoided in older adults. Providers should carefully weigh the potential adverse events and side effects of agents that do have evidence for effective use in older adults.

Abbreviations	
CBT-I	Cognitive Behavioral Therapy for Insomnia

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INTRODUCTION

Approximately half of older adults (typically defined as age 65 years and older) report sleep disturbances.[1,2] Several common sleep disorders are more prevalent in older adults than in younger individuals. This increased prevalence is associated with various correlates of aging, including sleep architecture changes, medical, psychiatric and neurocognitive diseases, untreated or undertreated pain, medication side effects, and stressors such as social isolation, racial discrimination, bereavement, and caregiving responsibilities.[3–6]

Sleep disturbances are associated with poor health outcomes in older adults, including increased fall risk, higher rates of depression, poorer control of chronic medical conditions, greater morbidity from acute medical illness, increased risk for cognitive decline, and increased all-cause mortality, even after controlling for factors such as medication use, age, mobility, and baseline health status.[3,7–12] In other words, sleep disturbances may not only be symptoms of medical, psychiatric, and neurocognitive disorders but may also be risk factors for developing or worsening these conditions.[3,13]

With the worldwide population of people aged 65 or older projected to more than double from 727 million in 2020 to over 1.5 billion in 2050, sleep symptoms will be encountered by many providers with increasing frequency.[14] It is vital for those who care for older adults to understand age-related sleep changes and have a framework for prevention, diagnosis, and treatment of insomnia and other disorders that impact this population so significantly.

Although insomnia is the primary focus of this article, the authors also review other sleep disorders that are more prevalent in older age, some of which are associated with cognitive impairment and/or neurodegenerative disorders. These include advanced sleep–wake phase disorder (ASWPD), rapid eye movement (REM) sleep behavior disorder (RBD), obstructive sleep apnea (OSA), restless leg syndrome (RLS), and periodic limb movement disorder (PLMD).[15–18]

AGE-RELATED CHANGES IN SLEEP AND CIRCADIAN RHYTHMS

Developmental changes in sleep occur throughout the lifespan, and older adults experience normal, age-related changes in sleep and circadian rhythms.[19] Sleep architecture refers to the classification of sleep into different stages, as measured by brain wave patterns, eye movements, and muscle tone.[20] Sleep consists of three non-REM stages known as N1, N2, and N3 and REM sleep.[20,21] Compared with younger persons, older adults spend more time in N1 and N2, the “shallow” stages of sleep in which awakenings can occur more readily, and less time in stage N3 (deep, slow-wave sleep) and REM sleep[22–24] (**Box 1**).

The National Sleep Foundation recommends 7 to 8 hours of sleep for older adults, similar to the 7 to 9 hours recommended for those under age 65 years.[25] Evidence suggests that older adults who sleep between 6 and 9 hours have improved mental and physical health, cognition, and quality of life compared with those with shorter or longer durations.[4]

Sleep efficiency (SE)—defined as the percentage of time in bed spent sleeping compared with the total time spent in bed—continues to decrease after age 60.[19] This is particularly relevant to insomnia, as decreased SE essentially represents increased time spent in bed trying to fall and stay asleep. Improvement in SE is a key measure in evaluating the efficacy of insomnia treatment, and SE is used to implement sleep restriction therapy (SRT), a major component of cognitive behavioral

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Box 1
Age-related changes in sleep and circadian rhythms

- Increased N1 sleep
- Increased N2 sleep
- Decreased N3 sleep
- Decreased REM sleep
- Earlier typical bedtimes
- Earlier circadian preference (greater "morningness")
- Shorter nighttime sleep duration
- Greater sleep fragmentation
- Increased time awake after sleep onset
- More frequent napping
- Decreased sleep efficiency

therapy for insomnia (CBT-I). Reduced SE has been associated with increased risk for falls, frailty, and death.[8,26,27]

The sleep–wake cycle changes with age. Circadian rhythms, intrinsic 24-hour cycles that govern the sleep–wake cycle and other physiologic processes, become less effective at responding to external cues or "zeitgebers" ("time givers" in German) that signal when one should sleep or wake, and thus the sleep–wake cycle becomes less consistent.[7] Many older adults have less exposure to these cues. For example, older adults, especially those who have Alzheimer's disease and/or live in institutional settings, have substantially less exposure to bright light, the strongest entrainer of circadian rhythms.[28] Further, dim light melatonin onset, the time at which the pineal gland releases endogenous melatonin in response to dim light, typically 2 to 3 hours before one's habitual bedtime, commonly occurs earlier in the day in healthy older adults. This can be accompanied by a "phase advanced" sleep–wake cycle, that is, the individual falls asleep earlier and wakes up earlier than is typical.[7,29–31] Older adults may also struggle to stay awake during the day and engage in more frequent napping, which can alter circadian rhythms.[13,32]

There are also sleep parameters that do not change significantly in older age. Total daily sleep duration decreases by about 10 minutes per every decade of life, but it does not decrease significantly past age 60. Sleep-onset latency, the amount of time it takes to transition from wakefulness to sleep, increases but only by approximately 10 minutes in total between the ages of 20 and 80, an effect that levels off by age 60.[19] Healthy older adults often have more frequent awakenings but they fall back asleep in a similar amount of time as their younger counterparts.[33]

INSOMNIA DISORDER

Insomnia is the most prevalent sleep disorder, and symptom burden increases with age, particularly for women.[15,34] Although insomnia can manifest as a primary disorder, it is frequently comorbid and multifactorial in origin (**Box 2**).[35] "Comorbid insomnia" refers to insomnia that is directly related to an underlying medical, psychiatric, or environmental cause.[36] A thorough medical and psychiatric history and an understanding of sleep environment and psychosocial stressors are essential when evaluating sleep disturbances **Box 2**.

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Box 2
The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for insomnia disorder[15]

- Dissatisfaction with sleep quantity or quality, associated with one or more of the following:
  - Difficulty initiating sleep
  - Difficulty maintaining sleep—characterized by frequent awakenings or problems returning to sleep after awakenings
  - Early morning awakening with inability to return to sleep
- Clinically significant distress or functional impairment
- Occurs at least three nights per week and be present for at least 3 months, despite adequate opportunity for sleep
- Cannot be attributable to the physiologic effects of a substance nor be explained predominantly by a coexisting psychiatric or medical illness.

MEDICAL, PSYCHIATRIC, AND ENVIRONMENTAL FACTORS IMPACTING INSOMNIA AND OTHER SLEEP DISTURBANCES

Medical Comorbidities

The more comorbidities an older adult has, the more likely he or she is to report a sleep complaint.[37] Common medical conditions strongly associated with insomnia and reduced sleep quality include heart disease, cancer, hypertension, neurodegenerative disorders, respiratory disease (including OSA), urinary issues, diabetes, chronic pain, and gastrointestinal disorders.[38–40] When evaluating a sleep concern, clinicians should screen for shortness of breath, somatic pain, nocturia, gastrointestinal symptoms, and limitations in mobility, all of which may compromise sleep and should be addressed.[41]

The Effects of Medications on Sleep

Almost 40% of older adults take five or more prescription medications.[42] Many medications can cause, or contribute to, insomnia and other sleep disturbances, including RLS and RBD. **Table 1** shows an abbreviated list of common medications that may disturb sleep. The effects of withdrawal from medications may also interfere with sleep.

Medications with anticholinergic or antihistaminic properties, anticonvulsants, antispasmodics, benzodiazepines, and opiates can all cause daytime somnolence that can interfere with the sleep–wake cycle. Benzodiazepines and opiates can also worsen OSA, cause cognitive impairment, and increase fall risk.[43] These medications should be avoided in older adults whenever possible.

Providers should discontinue unnecessary medications and consider reducing the dosage of agents that may be contributing to sleep disturbance but are medically necessary. It is also important to avoid a prescribing cascade wherein medications such as hypnotics or stimulants are used to treat sleep-related side effects of other medications.[43] Reviewing the timing of medication administration is prudent; stimulating medications and diuretics should be taken as far from bedtime as possible, and sedating medications should be taken closer to bedtime.[28]

Psychiatric Conditions

Anxiety and depression are the most common psychiatric conditions in which older adults report difficulties with sleep onset or maintenance.[47] The association between insomnia and mood disorders is bidirectional; sleep disturbances can be both risk factors and consequences of anxiety and mood disorders. If left untreated, insomnia may

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Table 1
Adverse sleep effects of medications commonly prescribed to older adults[4,28,43–46]

Medications	Effect(s) on Sleep	Possible Mechanism(s)
Beta-adrenergic blockers	Somnolence or insomnia	Vasodilatation through alpha-1 blockade (sedation); high beta-2 and 5-hydroxytryptamine receptor occupancy (insomnia); inhibition of melatonin production (insomnia)
Angiotensin-converting enzyme inhibitors	Insomnia	Cough
Angiotensin II receptor blockers	Insomnia	Unknown
Dopamine agonists	Somnolence (low doses) or insomnia (higher doses)	Dopamine agonism
Dopamine antagonists	RLS	
Antihistamines	RLS	
Melatonin	RLS	
Levothyroxine	Insomnia	Effects on hypothalamic-pituitary-adrenal axis; increasing histamine in hypothalamus and cerebral cortex
Loop diuretics	Insomnia	Nocturia
SSRIs/SNRIs	Daytime sedation, insomnia RLS RBD	Inhibition of serotonin and norepinephrine reuptake
Tricyclic antidepressants	RBD	
Mirtazapine	RBD Nightmares	
Psychostimulants (eg, methylphenidate)	Insomnia RLS	Sympathomimetic effects
Pseudoephedrine, ephedrine	Insomnia RLS	Sympathomimetic effects
Beta-agonists (inhaled and oral)	Insomnia	Sympathomimetic effects
Corticosteroids	Insomnia	Effects on hypothalamic-pituitary-adrenal axis; effects on cytokines

Abbreviations: RBD, rapid eye movement sleep behavior disorder; RLS, restless leg syndrome; SNRIs, serotonin and norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

also diminish treatment response to psychiatric illness and is associated with longer time to recovery, higher likelihood of relapse, higher health care utilization, and more frequent suicidal ideation.[48–50]

Other comorbid psychiatric conditions, notably bipolar affective disorder and post-traumatic stress disorder, are also strongly associated with sleep disturbances.[51,52]

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Sleep Environment

Environmental factors such as noise, light, temperature, bedroom environment, disruptive medical care, social interaction, and sleep–wake patterns can all contribute to sleep disturbance.[43] The use of light-emitting devices such as smart phones, tablets, and e-readers before bed has been shown to alter circadian rhythms, which may potentiate poor sleep.[53]

Bereavement

The loss of a loved one is a common occurrence in older patients, and there is a strong relationship between bereavement and decreased sleep quality, especially with "complicated grief" or the DSM-5's persistent complex bereavement disorder, which is characterized by at least 12 months of clinically significant distress or functional impairment that is outside of sociocultural norms, in response to the death of a loved one. Grief therapy has been shown to partially improve sleep symptoms in bereavement.[54]

EVALUATION AND DIAGNOSIS

Taking a Sleep History

The evaluation of the older patient with sleep difficulties begins with gathering a thorough sleep, psychiatric, and medical history and should incorporate collateral information from a bed partner or caretaker if possible. A sleep history should identify chief sleep complaints, which commonly include one or more of the following: inability to fall asleep, inability to stay asleep, waking too early, poor sleep quality, too little sleep, work or lifestyle interfering with sleep, or inability to sleep without medications. The daytime consequences should be elicited.[55] Sleep-onset latency or time awake after sleep onset greater than 30 minutes is considered clinically significant in adults, although quantification is not necessary for diagnosis.[56]

An assessment of current sleep behaviors is the next task of a sleep history. This can be done retrospectively during a clinical interview, or prospectively with the use of a sleep diary, such as the Consensus Sleep Diary.[57] Pertinent data include bedtime, time the individual actively tries to fall asleep, sleep latency, wake time, time the individual gets out of bed to start the day, timing and number of nighttime awakenings, daytime naps, differences in weekday/weekend behavior, an inventory of prescription and over-the-counter (OTC) medications and their effectiveness, substance use (including alcohol, caffeine, nicotine, and other substances), presleep activities (e.g., use of electronics, exercise, food and liquid intake), perceived cause of insomnia (e.g., stress, nocturia, environmental factors), coping response to poor sleep, and factors that improve or worsen sleep.[55]

Drawing on collateral from a bed partner and/or caretaker, clinicians should assess for symptoms such as abnormal breathing and nocturnal movements that could be indicative of OSA, RLS, PLMD, or RBD.

Diagnosis

Many sleep disorders can be diagnosed clinically using DSM-5 criteria alone. However, several screening tools are practical supplements for assessment of sleep disturbances and can also be used to monitor treatment response. The Insomnia Severity Index consists of seven items that assess symptoms over the prior 2 weeks.[58] The Pittsburgh Sleep Quality Index measures seven domains of sleep over the prior month, yielding a global sleep quality score.[59] Either can typically be administered in 10 minutes or less. Another important and simple screening tool is the STOP-Bang

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questionnaire, which is used to stratify risk for OSA. It consists of eight yes/no items regarding clinical features of sleep apnea.[60]

In-laboratory polysomnography (PSG) or home sleep testing is not necessary to diagnosis insomnia but may be indicated when there is suspicion for another primary sleep disorder that may better explain the symptoms or a comorbid sleep disorder, such as OSA. PSG may also be indicated to assess for RBD or PMLD or when insomnia is refractory to treatment.[55]

TREATMENT OF INSOMNIA

Non-Pharmacological Interventions

Given the increased potential for adverse medication side effects in older adults, non-pharmacological interventions for insomnia are first line.[61] Behavioral approaches target thoughts, feelings, and behaviors that cause, perpetuate, and exacerbate poor sleep. They include sleep hygiene education (SHE), SRT, stimulus control therapy (SCT), relaxation techniques (RT), cognitive therapy (CT), and CBT-I. All have demonstrated sustained efficacy for older adults, including those with medical and psychiatric comorbidities.[62–64] Multimodal CBT-I combines several of these approaches. Mindfulness training is emerging as another evidence-based option for treating insomnia in older adults.[65]

Sleep Hygiene Education

Sleep hygiene education is the mostly widely disseminated behavioral treatment strategy, given its low resource intensity (**Box 3**). The drawback of SHE is that it is generally not efficacious as a stand-alone treatment of chronic insomnia and may delay the use of more effective treatment **Box 3**.[66]

Multimodal Cognitive Behavioral Therapy for Insomnia

The American College of Physicians endorses CBT-I as the first-line treatment for adults with chronic insomnia.[68] It has also been found to reduce concurrent depression and suicidality.[69] CBT-I consists of 6 to 10 sessions and includes components of SRT and SCT; it may also encompass SH, CT, and RT.

Box 3
Sleep hygiene recommendations[67]

- Avoid caffeine past noon
- Avoid naps past noon
- Avoid exercise within 2 hours of bedtime
- Avoid tobacco or nicotine products, especially within 2 hours of bedtime
- Avoid alcohol use, especially within 2 hours of bedtime
- Avoid heavy meals within 2 hours of bedtime
- Do not take over-the-counter sleep medications or supplements unless directed by a health care provider
- Go to sleep and wake up at the same time every day
- Maximize comfort of sleeping environment by controlling temperature and noise
- Avoid spending more than 20 minutes awake in bed; engage in an activity that does not involve a light-emitting device until sleepy, and then go back to bed

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One barrier to CBT-I is a scarcity of trained clinicians to deliver individual treatment, which has resulted in the development of alternate delivery models such as group therapy, abridged protocols, and telephone, video, and application-based therapies. In older adults, the choice of CBT-I modality should weigh technology literacy, Internet access, and vision and hearing impairment, any of which could limit implementation.[66] However, a 2018 randomized placebo-controlled trial of Internet-based CBT found decreased rates of attrition with each decade above the study's average age of about 44 year old, diminishing the frequent assumption that older age limits one's ability to use digital CBT-I modalities.[70]

PHARMACOLOGIC TREATMENT OF INSOMNIA

General Principles

If non-pharmacological interventions for insomnia are not sufficiently effective, pharmacologic options may be considered. Although several medications are commonly prescribed for insomnia in the general population, particular care must be taken when selecting one for the aging adult.

The American Academy of Sleep Medicine (AASM) Clinical Practice Guideline for pharmacologic treatment of insomnia published in 2017 is used by many providers as a guide for insomnia treatment in adults.[71] Although this publication serves as a compendium of insomnia treatment data, it should be used cautiously with older adults. As the authors acknowledge, these guidelines do not contain independent analyses of efficacy in older adults and data are not stratified by age. Moreover, hypnotics are associated with an increased risk for adverse events in older adults and the starting doses listed in the guidelines do not take into account the changes in pharmacokinetics and pharmacodynamics that emerge with aging.

Many of the medications recommended by the AASM guidelines are found on the American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, which presents a list of medications to avoid in older adults when possible and is used widely by health care providers who treat this population.[72] Medications used for insomnia that are listed in the Beers Criteria include benzodiazepines, benzodiazepine receptor agonists (also known as "Z-drugs"), antihistamines, and other anticholinergic medications.

There is limited evidence for the efficacy of benzodiazepines and Z-drugs for chronic insomnia.[61] More importantly, their use can result in hangover effects, dependence, tolerance, and rebound insomnia on discontinuation. They also confer an increased risk for severe complications in older adults, including infection, depression, falls, hip fractures, car accidents, cognitive impairment, delirium, and overall mortality risk.[71,73–75]

Antihistamines, such as diphenhydramine, are sedating and unfortunately are components of many popular OTC "PM" products. Many antihistamines, particularly those used in OTC sleep aids, have anticholinergic effects such as urinary retention and constipation that are detrimental to aging adults. Anticholinergic drugs are associated with cognitive impairment and can precipitate delirium.[76,77] Antihistamines that are significantly anticholinergic should not be used in older adults.

The choice of an agent should weigh treatment goals, symptom target (sleep onset, sleep maintenance, or both), previous response to treatment, patient preference, comorbid conditions, contraindications, medication interactions, side effects, cost, and availability of other treatments.[78] Generally, medications for insomnia should be used at the lowest effective dose, dosed only intermittently rather than every night, and used in the short term—ideally for less than 1 month. When a medication is discontinued, it should be done gradually to reduce the risk of withdrawal symptoms, including

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rebound insomnia. Medications with shorter elimination half-lives should be favored to mitigate daytime sedation and other side effects.[13]

Food and Drug Administration (FDA)-Approved Medications for Treatment of Insomnia with Evidence Supporting Their Use in Older Adults

Orexin receptor antagonists

Suvorexant was the first dual orexin receptor antagonist (DORA) FDA-approved for the treatment of sleep-onset and sleep maintenance insomnia. It inhibits the binding of orexin A and B, both wakefulness-promoting neuropeptides, to orexin receptors. Suvorexant increases time spent in all sleep stages, preserves sleep architecture, and improves sleep maintenance, with more modest improvements in sleep onset.[79,80] Suvorexant was well tolerated over 3 months in older patients and has not been associated with significant daytime impairment such as residual sleepiness, gait instability, or memory complaints.[81] The effects of suvorexant on sleep apnea have not been well studied, so coordination with a sleep medicine specialist is advisable when there is a diagnosis or suspicion for OSA.[80]

Another DORA, lemborexant, has subsequently been FDA-approved. Comparisons between the two DORAs suggest that lemborexant may be slightly more efficacious than suvorexant but has a greater risk of daytime somnolence and higher rates of discontinuation due to adverse effects.[82]

Ramelteon

Ramelteon is a melatonin receptor agonist approved in the United States for treatment of sleep-onset and sleep maintenance insomnia. RCTs in older adults demonstrate mixed results. One meta-analysis of 13 trials with adults and older adults reported small but statistically significant improvements in subjective sleep-onset latency and subjective quality of sleep.[83] Ramelteon does not have a significant effect on sleep maintenance insomnia.[80] It does not cause central nervous system depression and is not associated with significant rebound insomnia, withdrawal effects, memory impairment, or gait instability.[80,84,85]

Doxepin

Doxepin, a tricyclic antidepressant, is the only antidepressant that is FDA-approved for insomnia, although limited to doses of 3 to 6 mg (sold as brand-name Silenor) for this indication, far less than the 75 to 150 mg typically used to treat depression. Its mechanism of action is antihistaminic; histamine is a key neurotransmitter for wakefulness.[86] At doses below 25 mg, doxepin is highly selective for H1 receptors, with minimal anticholinergic effects. The Beers Criteria notes that at doses $\leq$ 6 mg, the safety profile of doxepin is comparable to that of placebo.[72] Three RCTs in older adults using doses of 1 mg, 3 mg, and 6 mg showed efficacy for sleep maintenance insomnia with no significant hangover effects or memory impairment. Reports of the most common side effects—somnolence, nausea, and dizziness—were similar to placebo.[80] Patients with impaired renal function may have delayed clearance of doxepin, and the medication is not recommended for individuals with severe sleep apnea.[80]

Non-FDA-Approved Medications for Treatment of Insomnia

Melatonin

Endogenous melatonin production is generally reduced in aging.[61] Exogenous melatonin is sold as an OTC sleep aid, and it is used commonly due to its availability, low cost, and relatively low burden of adverse events and side effects.[87,88] Although it is approved in Europe for short-term treatment of insomnia in adults 55 years and older,

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it is not FDA-approved for any indication in the United States.[61] Some data suggest that it is effective for chronic insomnia, however the data are considered of "very low" quality as per the AASM Clinical Practice Guideline.[71]

A 2018 review of pharmacologic management of insomnia in older adults found that melatonin slightly improves sleep onset and duration, but these effects are limited by variability in dosing and product quality. There is little consensus on appropriate dosing of melatonin. Doses between 3 and 5 mg are typical, but some studies indicate that 0.3 to 0.5 mg can be effective, and doses of 10 mg or more are used in certain clinical situations, for example, treatment of circadian dysregulation in patients with visual impairment and treatment of RBD.[80] A 2020 review found that short-term use of melatonin was associated with improvement in sleep quality and sleep-onset latency but had an inconsistent effect on total sleep time. The authors concluded that there was inadequate evidence to confirm its efficacy for insomnia.[87] Because of its circadian phase-shifting properties (i.e., its ability to reset the timing of the internal biological clock), melatonin has a greater impact on insomnia associated with circadian misalignment such as shift work or jet lag.[89]

A limitation of currently available data is that many studies do not specify the timing of melatonin administration. When timing is noted, it can range from 15 minutes to 2 hours before bedtime. This raises an important consideration in the use of melatonin; administering melatonin when endogenous melatonin levels are already high often has minimal impact.[87,88] There is no clear consensus, but given that most preparations of melatonin take 45 to 60 minutes to become bioavailable, and perhaps longer in older adults, the drug should be administered at least an hour before the individual's typical bedtime and should be administered at the same time each night.[88]

Given the lack of high-quality evidence and variability in formulations, further research is required to establish detailed guidelines for melatonin use in older adults. However, given some evidence for its effectiveness and its relatively low risk of causing adverse events, it is worth considering before agents associated with more risk.

Trazodone

Trazodone is an antidepressant that is not FDA-approved for insomnia but is commonly prescribed by providers who treat sleep disorders in older adults, in doses typically ranging from 25 to 100 mg.[61] Its mechanism of action is via its moderate antihistamine activity. Trazodone is often seen as a preferable choice given its very low anticholinergic activity. The clinical practice guidelines from AASM suggest that its harms outweigh its benefits and recommend that clinicians do not use trazodone for sleep-onset or maintenance insomnia.[71] Salient risks in aging adults include dizziness, orthostatic hypotension, and psychomotor impairment.[90] Parkinsonism has also been reported in elderly patients taking trazodone.[91] Patients and families should be alerted of these increased risks and encouraged to monitor for side effects.

Mirtazapine

Mirtazapine is another antidepressant with an antihistaminic mechanism of action that has been shown to have some efficacy for insomnia in limited case series and open-label studies but is not FDA-approved for that use.[92] In the aging adult, mirtazapine can be a useful agent for treating insomnia with comorbid depression, particularly if poor appetite is a symptom, however it is not recommended for primary insomnia without depression, given conflicting evidence, risk of weight gain, and possible habituation to its sedative effects.[61]

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OTHER NOTEWORTHY SLEEP DISORDERS IN THE AGING ADULT

It is important to recognize that insomnia in older adults can co-occur with and obfuscate the diagnosis of other sleep disorders. Moreover, patients with overlapping sleep disorders typically do not improve unless all conditions are addressed.

Obstructive Sleep Apnea

OSA is characterized by recurrent episodes of upper airway obstruction during sleep.[15] It is the most common breathing-related sleep disorder, and its frequency increases with age.[15,93] Over half of older Americans are at high risk for OSA, although most of the cases are undiagnosed.[94] Frequent underdiagnosis may be attributable to changes in clinical presentation of older adults with OSA; after the age of 60, the disease is equally as common in females as in males, obesity is not a significant risk factor, witnessed apneas and snoring are less frequently reported, and daytime sleepiness and nocturia are more common.[95,96]

OSA is associated with cognitive impairment and incidence of dementia, among many other medical and psychiatric consequences.[93,97] Importantly, treatment of this disorder with positive airway pressure is associated with lower odds of Alzheimer's dementia diagnosis, making screening, diagnosis, and treatment critical.[97] The STOP-Bang questionnaire is a useful tool for clinicians to stratify risk for OSA and triage for referral for PSG, which confirms a diagnosis.[15,60]

Rapid Eye Movement Sleep Behavior Disorder

RBD is characterized by a lack of the atonia that is normally present in REM sleep, resulting in acting out dreams with vocalizations and/or complex motor behaviors.[15] This can result in injury to the individual or to a bed partner. Most cases of RBD have an onset between ages 50 and 70.[4]

As noted in **Table 1**, RBD is associated with several medications, and treatment may begin with lowering or discontinuing offending agents if feasible. High-dose melatonin (6 to 12 mg) is the first-line treatment of RBD. Clonazepam (0.25 to 2 mg) is a commonly used second-line treatment but should be prescribed cautiously in older adults given its substantial risks and side effects.[98]

Importantly, if a patient has RBD, is not on a medication likely to cause it, and does not have another known medical condition associated with RBD, providers should consider the possibility that the patient may have or may ultimately develop a neurodegenerative disorder. There is substantial risk for an individual with idiopathic RBD to manifest Parkinson's disease or dementia with Lewy bodies in particular.[99,100] One longitudinal study of 93 patients who had idiopathic RBD and no parkinsonian or cognitive symptoms yielded an estimated 17.7% 5-year risk of developing a neurodegenerative disease. The risk was 40.6% at 10 years, and 52.4% at 12 years.[100]

Restless Leg Syndrome and Periodic Limb Movement Disorder

RLS is defined by an urge to move one's legs in response to an uncomfortable sensation in the legs that occurs at rest and is at least partially relieved by movement. The urge is worse at night (or only occurs at night), which presents a challenge for sleeping.[15] RLS worsens steadily with age until about 60 and occurs in up to 20% of adults aged 65 and older.[16,101] With late-onset RLS (after age 45), progression of symptoms is often rapid and commonly related to aggravating factors, such as medications.[102] It may share similar features with anxiety disorders, drug-induced akathisia, leg cramps, positional discomfort, tic disorders, and peripheral neuropathy, and thus a broad differential should be considered.[103] RLS may also be comorbid with

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any of these conditions. RLS is diagnosed based on the presence of clinical symptoms.

PLMD is characterized by repetitive contractions of the legs that occur during sleep and often overlaps with a diagnosis of RLS.[15] Up to 90% of those diagnosed with RLS demonstrate periodic leg movements in sleep.[104] PLMD is diagnosed when PSG shows more than 15 periodic limb movements per hour, and the patient reports sleep disturbance or other functional impairment.[105]

The etiologies of RLS and PLMD are uncertain, but disturbances in iron metabolism and in the central dopaminergic system are theorized to play a role.[15,103] RLS is associated with iron deficiency, with or without anemia, and ferritin levels less than 50 μg/L.[103] Iron replacement is recommended when ferritin is $\leq$ 75 μg/L.[106] Neither RLS nor PLMD has a poor prognosis if sleep disruption is addressed, and neither is associated with increased risk for neurodegenerative disorders.[103]

Withdrawing potentially offending medications (selective serotonin reuptake inhibitors and other antidepressants, dopamine-blocking medications, and sedating antihistamines) when feasible may improve symptoms. Bupropion is an antidepressant that may be less likely to induce or exacerbate RLS.[107]

Behavioral measures such as regular exercise and limiting alcohol and caffeine should be used and are often effective in individuals with intermittent symptoms. Alpha-2-delta ligands (such as gabapentin) have recently been recommended as the first-line pharmacologic treatment of RLS and PLMD, supplanting dopaminergic agents, which have been associated with worsening of symptoms with chronic use.[108]

Advanced Sleep–Wake Phase Disorder

ASWPD is a circadian rhythm sleep–wake disorder in which sleep quality and duration are normal but both sleep onset and wake times are "advanced" such that an individual chronically falls asleep and wakes up earlier than is desired or socially acceptable. These individuals may attempt to stay up later in the evening to maintain a "normal" sleep schedule, believing they will be able to wake up later accordingly. However, they are likely to still wake up early, given their earlier circadian phase, resulting in less total sleep time and daytime sleepiness.[15,109] A thorough sleep history and the use of a sleep diary for at least 7 days can be useful in making this diagnosis. Depression and insomnia should be excluded, as both can also cause earlier sleep onset and early morning awakening—although these conditions can be comorbid.[109]

Factors that can contribute to the development of ASWPD in older adults include altered exposure to zeitgebers (such as light, meals, activity, and social rhythms), decreased responsiveness to evening light (which would normally delay sleep), and increased responsiveness to morning bright light, which advances the internal circadian phase and makes awakening for the day more likely.[109]

The first-line treatment of ASWPD is bright light therapy in the evening.[109] There is no substantial evidence for pharmacotherapy as treatment of ASWPD. Theoretically, melatonin administration late at night or in the early morning could be used to phase delay the circadian clock, which may improve ASWPD symptoms, but there are no data to support its efficacy for this purpose.[109,110]

SUMMARY

Insomnia and other sleep disorders are prevalent in older adults and are associated with distress and negative health outcomes. A thorough sleep history and review of medical and psychiatric history, medication list, and collateral history from bed

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partners or caregivers are crucial to effective diagnosis and treatment planning. Nonpharmacological treatment of insomnia, particularly CBT-I, should be implemented first whenever possible. Some pharmacologic treatments for insomnia are effective but should be chosen with great caution given substantial risks for adverse events, side effects, and medication interactions.

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