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This ACADEMIC HIGHLIGHTS section of *The Journal of Clinical Psychiatry* presents the highlights of the teleconference series “Current Management Approaches for Insomnia,” which was held in June, September, and October 2020. This activity was prepared and independently developed by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Eisai Inc.

The teleconference was chaired by **Russell P. Rosenberg, PhD**, Atlanta School of Sleep Medicine and Technology and NeuroTrials Research, Inc., Georgia. The faculty was **Andrew D. Krystal, MD**, Department of Psychiatry and Behavioral Sciences, University of California San Francisco.

CME Objectives

After studying this article, you should be able to:

- Routinely include sleep history and use screening tools as part of patient assessment
- Develop an effective evidence-based treatment plan for patients with insomnia

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Diagnosing and Treating Insomnia in Adults and Older Adults

Russell P. Rosenberg, PhD,
and Andrew D. Krystal, MD

Insomnia, the most prevalent sleep-wake disorder, is defined as difficulty falling or staying asleep that is associated with significant impairment or distress in daytime function and occurs despite an adequate opportunity for sleep.^{1,2} This report, based on presentations given by Russell P. Rosenberg, PhD, and Andrew D. Krystal, MD, will address how to distinguish chronic insomnia from medical or psychiatric disorders and develop an effective evidence-based treatment plan for patients with insomnia.

RISK FACTORS FOR AND DIAGNOSIS OF INSOMNIA

According to Dr Rosenberg, about one-third of adults report symptoms of insomnia, and 6%–10% meet diagnostic criteria for insomnia disorder.¹ This condition may result in interpersonal and occupational problems¹ and has a deleterious effect on quality of life.³ Decreased attention and concentration are common, and a higher rate of accidents is associated with insomnia.¹ People who almost always experience difficulty falling asleep are more than twice as likely as people who never have issues initiating sleep to die from a motor vehicle injury.⁴ The presence of insomnia is a risk factor for cardiovascular disease, type 2 diabetes mellitus, gastroesophageal reflux disease, asthma, and thyroid disorders.⁵

Risk Factors for Insomnia

Dr Rosenberg explained that women are more likely than men to experience insomnia and that insomnia symptoms increase with age.⁶ He stated that the disorder is thought to be associated with hyperarousal throughout the day and night, as evidenced by neuroendocrine, autonomic, neuroimmunologic, electrophysiologic, and neuroimaging studies.⁷

Therefore, insomnia may result from the interplay between a genetic vulnerability for an imbalance between arousing and sleep-inducing brain activity, psychosocial or medical stressors, and perpetuating mechanisms including dysfunctional sleep-related behaviors, learned sleep-preventing associations, and a tendency to worry/ruminate.⁷

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Dr Rosenberg is a consultant and member of the speakers/advisory boards for Jazz, Eisai, and Harmony BioSciences and has received grant/research support from Jazz, Eisai, and Avadel. Dr Krystal is a consultant for or receives research support from Adare, Axsome Therapeutics, Big Data, Eisai, Evecxia Therapeutics, Ferring, Galderma, Harmony Biosciences, Idorsia, Janssen, Jazz, Millenium, Merck, Neurocrine Biosciences, Pernix Therapeutics, Otsuka, Sage Therapeutics, and Takeda and has received grant/research support from Janssen, Axsome Therapeutics, Reveal Biosensors, The Ray and Dagmar Dolby Family Fund, and the National Institutes of Health.

Review Process

The faculty member(s) agreed to provide a balanced and evidence-based presentation and discussed the topic(s) and CME objective(s) during the planning sessions. The faculty's submitted content was validated by CME Institute staff, and the activity was evaluated for accuracy, use of evidence, and fair balance by the Chair and a peer reviewer who is without conflict of interest.

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insomnia²) has the same criteria but occurs for less than 3 months. Criteria in both the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5),¹ and the International Classification of Sleep Disorders, 3rd Edition (ICSD-3),² include the following:

- Distress or impairment is caused by the insomnia
- The problem occurs despite adequate opportunity to sleep
- The difficulty cannot be better explained by other physical, mental, or sleep-wake disorders
- The problem cannot be attributed to substance use or medication

Insomnia Interview and Assessment Tools

Dr Rosenberg stated that the cornerstone of the insomnia evaluation is a detailed history obtained during the patient interview.^{6,9} Key points that should be covered to ensure a thorough evaluation are the following: (1) the nature of the complaint (sleep onset, sleep maintenance, early-morning awakening, nonrestorative sleep quality, or a combination), (2) the patient's sleep-wake schedule and routines, and (3) functional impairment (including safety issues) and distress. If possible, an interview with the patient's bed partner, family member, or significant other is helpful. To see more details from Dr Rosenberg's presentation, see the on-demand activity "Prevalence, Impact, and Burden of Insomnia and Discussing It With Patients" in this series at CMEInstitute.com. Dr Rosenberg also advised using tools such as the Epworth Sleepiness Scale,⁹ an actigraph,¹⁰ sleep diaries,⁹ and physical and mental status examinations to assess patients for insomnia. Polysomnography is used when the diagnosis is uncertain and there is reasonable clinical suspicion of sleep apnea or movement disorders, when initial treatment fails, or arousals from sleep occur with violent or injurious behavior.¹¹



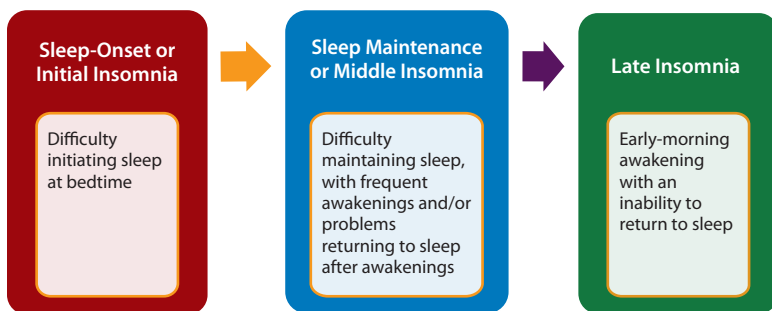
Patient Perspectives

Here, a person describes how nightly rumination about life circumstances contributed to insomnia, which has now become another source of worry itself: "It feels like no matter how tired I am, whenever my head hits the pillow, my body is jolted awake by distressing thoughts and fears about my life and future. For context, I'm 24 and planning to go to law school in a few months. I fear that my lack of sleep will lead to irreversible health issues down the road (like dementia)."⁶

Diagnostic Criteria for Insomnia

Individuals with insomnia disorder may have trouble falling asleep, staying asleep, or both (Figure 1). To meet criteria for persistent insomnia disorder¹ or chronic insomnia,² symptoms must occur a minimum of 3 days per week for 3 months.¹ Episodic insomnia¹ (or short-term

Figure 1. Manifestations of Insomnia



Based on American Psychiatric Association.¹

THE BIDIRECTIONAL RELATIONSHIP BETWEEN INSOMNIA AND COMORBID DISORDERS

Insomnia is commonly comorbid with psychiatric, medical, and neurologic disorders.^{12,13} Insomnia and comorbid conditions have a bidirectional relationship, ie, the status of each impacts the other,

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potentially affecting the treatment course and outcome.¹ The National Comorbidity Survey Replication¹⁴ reported that 92% of people with insomnia in the past 12 months had at least 1 other disorder; the mean number of other disorders among those with insomnia was 3.2.

Dr Rosenberg noted that, for years, insomnia was thought to occur secondary to various disorders; therefore, it did not receive the attention it warranted because the comorbid disorder seemed to play the primary role in the insomnia problem. It was believed that treatment for the other disorder(s) would resolve the insomnia.¹ However, our thinking has evolved from that strategy toward the treatment of insomnia as a separate condition.¹³

Psychiatric Disorders and Insomnia

Insomnia and mental illnesses may share common causes, and insomnia may be a factor in someone developing a mental illness.¹⁵ Dr Rosenberg presented results from the National Comorbidity Survey Replication,¹⁶ which revealed that 4 sleep problems (difficulty initiating or maintaining sleep, early morning awakening, nonrestorative sleep) were significantly comorbid with 1 or more anxiety disorders, mood disorders, impulse-control disorders, or substance use disorders.



Patient Perspectives

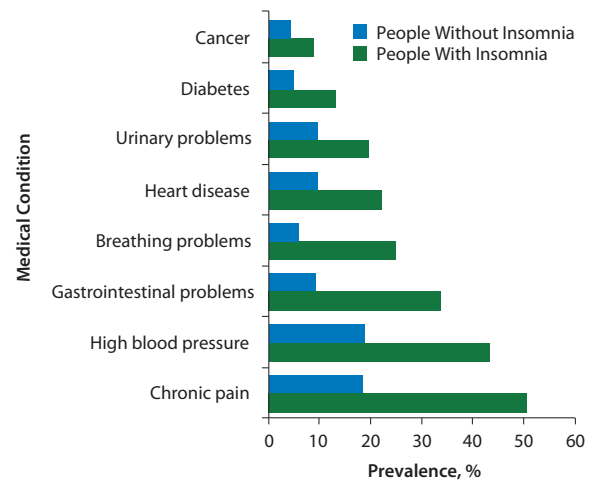
Here, a person with insomnia and anxiety describes the impact of the disorders:

"I struggle out of bed, never feeling well-rested but unable to go back to sleep. I trudge through my day, anxious and dreading the most basic of chores and responsibilities. Do I check the mail? What if I have to talk to someone on the way? I don't think I have the energy to buy groceries. If I do housework, what if I start something I can't finish? I should do homework, but for some reason it's scary. My brain is always in a fog. All day I want nothing more than a nap, but I tell myself to wait. Keep a schedule, stay awake until it's time for bed. And then I can't sleep. Anxious thoughts run through my head. I feel worthless. Everything hurts. I have to read a book until I pass out to stop the torrent of dread and general self-loathing that always hits me just when I'm trying to relax. Fatigue by day, insomnia by night. Awesome."¹⁷

Medical Disorders and Insomnia

Dr Rosenberg stated that people with insomnia report higher rates of several medical conditions than do those without insomnia, and people with medical disorders have a higher prevalence of insomnia than people without those medical problems. In a survey¹⁸ of 772 individuals, results showed that people with chronic insomnia had a higher incidence of heart disease, high blood pressure, breathing problems, urinary problems, chronic pain, and gastrointestinal problems (Figure 2). He also cited a population-based study¹⁹ of 3,282 participants in which those with any medical disorders were more than twice as likely to have insomnia as those without medical disorders.

Figure 2. Prevalence of Medical Conditions in People With and Without Insomnia



Data from Taylor et al.¹⁸

Neurologic Disorders and Insomnia

Dr Rosenberg reported on results from a large survey¹⁸ that showed that people with chronic insomnia had a higher incidence of neurologic disease than those without insomnia. He added that comorbid insomnia is common in patients with disorders such as Parkinson disease (PD) and Alzheimer disease (AD).²⁰ According to Dr Rosenberg, insomnia may occur on its own or may occur because of factors associated with the neurologic condition, such as pain, depression, or medications.

Problems in the sleep-wake cycle have been found to influence the risk of developing AD through accumulation of amyloid- β (A β) in the brain.^{21,22} Once A β accumulates, increased wakefulness and altered sleep patterns develop. Thus, explained Dr Rosenberg, sleep disorders and neurodegenerative disease may influence each other in ways that have important implications for the treatment of both conditions. He also cited a review²³ of insomnia as a risk factor in both PD and AD, indicating that insomnia and neurodegenerative disorders have a complex and bidirectional relationship.

To read more about the associations between insomnia and other conditions, see the on-demand activity “The Bidirectional Relationship Between Insomnia and Comorbid Disorders” in this series at CMEInstitute.com.

OPTIMIZING TREATMENT FOR INSOMNIA

Dr Krystal discussed new agents for insomnia that have emerged in recent years with highly specific pharmacologic effects.²⁴ The newer agents include those with relatively limited negative effects on brain function, primarily affecting sleep systems and having reduced impact on other functions than older agents that have wide-ranging neural effects. According to Dr Krystal, this advancement paves the way for a new paradigm for managing insomnia

Table 1. Matching Insomnia Treatments to Patient Presentation

Treatment	Patient Presentation
CBT-I	<ul style="list-style-type: none"> Increased arousal Decreased homeostatic drive
BZs/Non-BZs	<ul style="list-style-type: none"> Sleep-onset insomnia Comorbid depression/anxiety
Doxepin	<ul style="list-style-type: none"> Sleep-maintenance insomnia, especially in last third of the night Vulnerability to substance use disorder Required to wake up and function in the night
DORAs	<ul style="list-style-type: none"> Sleep-onset and sleep-maintenance insomnia, last quarter of the night Required to wake up and function in the night
Ramelteon	<ul style="list-style-type: none"> Sleep-onset insomnia Vulnerability to substance use disorder
Off-Label Treatments	
Antidepressants	<ul style="list-style-type: none"> Treatment-resistant insomnia Comorbid depression, anxiety, pain
Antipsychotics	<ul style="list-style-type: none"> Treatment-resistant insomnia Comorbid psychosis, depression

Based on Krystal,²⁴ Minkel and Krystal,²⁵ and Hassinger et al.²⁶
 Abbreviations: CBT-I = cognitive-behavioral therapy for insomnia, BZs = benzodiazepines, DORAs = dual orexin receptor antagonists.

in which clinicians aim to select interventions that best target the specific type of sleep problem of each patient.

Dr Krystal outlined the differences between treatments and explained that awareness is needed of the specific effects of interventions and of the patient subpopulations who would optimally benefit from each type of treatment (Table 1).^{24–26}

Cognitive-Behavioral Therapy for Insomnia

A first-line treatment for insomnia is CBT-I, or cognitive-behavioral therapy for insomnia.^{9,27–29} Dr Krystal explained that CBT-I targets factors such as sleep drive dysregulation, sleep-related anxiety, and sleep-interfering behaviors, thereby restoring homeostatic regulation of sleep and helping to diminish maladaptive sleep-related thoughts through cognitive restructuring.³⁰

Certain features of patient presentation can suggest usefulness of CBT-I. Dr Krystal cited a study³¹ that tested the hypothesis that biomarkers of homeostatic sleep drive and arousal would be predictors and correlates of CBT-I response. Results suggested that both decreased homeostatic sleep drive and elevated arousal can be effectively targeted with CBT-I. Results from trials^{32,33} in patients with insomnia and depression indicated that CBT-I combined with antidepressant therapy is beneficial for people who have insomnia occurring with depression, although other treatments are needed to improve depression symptoms. Finally, those with objectively determined short sleep duration (< 6 hours) are less likely to improve with CBT-I than those who sleep at least 6 hours.^{34,35}

Benzodiazepines and Nonbenzodiazepines

Dr Krystal outlined the mechanisms and effects of benzodiazepines (BZs) and nonbenzodiazepines (non-BZs).

Commonly prescribed BZs that are approved by the United States Food and Drug Administration (FDA) for the treatment of insomnia are triazolam, flurazepam, estazolam, quazepam, and temazepam. Zolpidem, zaleplon, and eszopiclone are non-BZs. Evidence indicates that both classes are useful when nonspecific effects are desired, such as for patients with comorbid anxiety, depression, or pain, or for patients with sleep-onset difficulties.²⁴ Eszopiclone and zolpidem CR also have evidence for benefit in sleep maintenance.²⁵

Selective H1 Histamine Receptor Antagonists

Evidence supports that histamine drives wakefulness via H1 receptors.³⁶ As a result, blocking the H1 histamine receptors has the potential to enhance sleep.²⁵ However, Dr Krystal noted, the antihistamines that clinicians have used for years were not specific H1 antihistamines; they had other pharmacologic effects that either detracted from or added to their sleep effects and also led to side effects that are not linked specifically to the H1 mechanism.²⁵

Doxepin, a tricyclic antidepressant used in dosages of 75–150 mg/d, is approved for the treatment of insomnia in dosages of 3–6 mg/d; this agent is a more potent and selective H1 antagonist than other medications referred to as “antihistamines.”²⁵ Unique effects of selective H1 antihistamines are evident in the profile of doxepin 3–6 mg, which has stronger effects on sleep maintenance than on sleep onset³⁷ and has therapeutic effects in the last third of the night, without significant adverse effects in the morning.²⁵ It would be useful in abuse-prone patients with sleep maintenance difficulties because it does not have abuse liability.

Selective Orexin Antagonists

Dr Krystal discussed the FDA-approved hypocretin-orexin receptor antagonists suvorexant and lemborexant.³⁸ These medications have a highly specific effect, blocking only the 2 orexin receptors, which are important mediators of wakefulness.²⁴ Because they block both orexin receptors, these agents are sometimes referred to as dual orexin receptor antagonists (DORAs).

According to Dr Krystal, data suggest that the DORAs have robust effects on sleep onset and sleep maintenance,^{39–41} improving sleep in the last quarter of the night without substantial morning impairment. This effect is like that of doxepin 3–6 mg for the same reason: they block a single wake-promoting system that is active in the last quarter of the night while others are not (hypocretin/orexin release drives histamine release in the last quarter of the night, so blocking either achieves the same effect).⁴² Also like doxepin 3–6 mg, the DORAs do not prevent awakenings and do not raise the arousal threshold; they have a relatively limited impact on systems other than sleep and, as a result, are associated with fewer side effects and less

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impairment than the BZs and non-BZs in patients' ability to arise and function. Unlike doxepin, the DORAs improve sleep onset, but they also have abuse liability and are listed as controlled substances by the Drug Enforcement Administration.^{43,44}

Selective Melatonin Receptor Agonists

Dr Krystal discussed agents that produce pharmacologic effects through agonism of melatonin receptors, including the hormone melatonin (available "over the counter" as a supplement) and ramelteon.²⁴

Melatonin appears to have a greater effect on patients with circadian rhythm disorders than on patients with insomnia; however, meta-analyses suggest that melatonin has a modest therapeutic effect on sleep onset in patients with insomnia.^{24,45} Dr Krystal stated that ramelteon has been shown to be effective for sleep-onset difficulties.^{24,37} The agent has relatively limited adverse effects, especially regarding motor and cognitive impairment, and is without abuse potential.⁴⁶

Antidepressants

The antidepressants that are most often used off-label for the treatment of insomnia include trazodone, mirtazapine, amitriptyline, and higher-dose doxepin.²⁴ According to Dr Krystal, despite their relatively widespread use for the treatment of insomnia, limited data exist on the efficacy and safety of these drugs.²⁴ For example, he noted, in a 14-day study,⁴⁷ trazodone 50 mg/d failed to show sustained therapeutic effect versus placebo.²⁵ Dr Krystal also mentioned the side effects of antidepressants due to their nonselective mechanisms of action, which vary depending on the drug. Adverse effects may include weight gain, orthostatic hypotension, dry mouth, constipation, blurred vision, urinary retention, cognitive impairment, cardiotoxicity, sexual dysfunction, and potentially delirium.²⁶

Antipsychotics

Dr Krystal discussed the antipsychotics often used off-label for insomnia, including quetiapine, olanzapine, risperidone, and lurasidone.²⁴ Limited data on the efficacy and safety of these drugs are available in the treatment of insomnia. Their side effect profiles, inferred from use in psychiatric conditions, can be quite significant, including extrapyramidal side effects (eg, tardive dyskinesia, parkinsonism), weight gain, insulin resistance, orthostatic hypotension, dry mouth, constipation, and sexual dysfunction.²⁶ According to Dr Krystal, like antidepressants, antipsychotics are most beneficial for patients with insomnia in whom nonspecific effects could be advantageous, such as patients with comorbid mania or a psychotic condition, or for patients with treatment-resistant insomnia.²⁴

For more information from Dr Krystal's presentation, see the on-demand activity "Optimizing Treatment for Insomnia" in this series at CMEInstitute.com.



Case Practice Question

Discussion of the best response can be found at the end of the activity.

A 58-year-old attorney specializing in family law presents to the clinic with a complaint of difficulty staying asleep. He began having sleep maintenance problems when he attended law school. He would often wake feeling that he was unprepared for class, and then he would stay awake studying for hours in the middle of the night. The insomnia remitted during his late 30s, but he relapsed with both sleep onset and sleep maintenance difficulties when his law partner decided to leave the practice. Currently, he has mild depression and coronary artery disease. He has used zolpidem 10 mg, and, while it helps him initiate sleep, he awakens about 3:30 AM or 4:00 AM and has difficulty getting back to sleep until 1 or 2 hours have passed. Which pharmacologic agent is best for you to consider next?

- Benzodiazepine
- Antihistamine
- Dual orexin receptor antagonist
- Antipsychotic



Patient Perspectives

Here, a person with insomnia described their relief at receiving a medication that began to treat their insomnia:

"I've suffered intermittently throughout my life, but just recently got over my worst chronic episode yet . . . I just stopped sleeping at night; couple that with the fact that it's always been impossible for me to sleep during the day, and it made for stretches of about 3 solid days with no sleep at all, and when I would get some it would be about 1–3 hours. This went on for months and I felt like I was losing my mind . . . I cycled through countless prescriptions and only found [that] the fifth or so one that I landed on did anything at all. I started getting 4 hours of sleep a night with [a nonbenzodiazepine] after about 4 months of staying awake for 3 days and then crashing for 1–3 hours, only to do it all over again. Needless to say, those 4 hours each night felt like a godsend."⁴⁸

CHALLENGES IN MANAGING INSOMNIA IN OLDER PEOPLE

Up to 50% of older adults have difficulty initiating and maintaining sleep, which is associated with an increased risk of morbidity and mortality and has a negative impact on quality of life and functioning.⁴⁹ Older adults also have an increased risk for psychiatric effects of insomnia.⁵⁰ Dr Krystal stated that managing late-life insomnia is a challenge for clinicians because of concerns about residual daytime sleepiness and medication side effects. Elderly patients are more likely to have impaired drug metabolism, to be taking other medications that may interact with insomnia treatments, and to be more vulnerable to the adverse effects of sleep medications.^{50,51} Older patients (aged 65 years or older) have double the risk of experiencing adverse drug reactions compared with younger people.⁵²

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Risk-Benefit Analysis

Dr Krystal explained that the choice of a medication for an individual should take into account a careful risk-benefit analysis,⁵³ requiring clinicians to know the expected benefits and risks of various insomnia treatments based on the available data from placebo-controlled trials. He stated that clinicians should consider if a study addresses the type of sleep problem the patient has and if it was conducted in a sample having a similar age as the patient with an age-appropriate dose.

Additionally, Dr Krystal cited several studies^{7,9-12} that have examined insomnia treatments in patients with comorbid conditions that are common in older adults, such as chronic low back pain, chronic obstructive pulmonary disease, rheumatoid arthritis, and menopausal sleep disturbance. Because treating sleep problems has an impact on coexisting conditions, he explained, clinicians should know which drugs have specific therapeutic effects to improve those conditions.

Treatment Overview for Insomnia in Older Adults

Dr Krystal focused his presentation on pharmacologic and nonpharmacologic approaches that may be used individually or in combination.³⁸ The initial treatment that is recommended by guidelines is CBT-I, but if this option is ineffective or the patient is not able or willing to try it, then clinicians should discuss the benefits, harms, and costs of medication options with the patient.^{28,38}

Few drugs have shown efficacy for both sleep onset and sleep maintenance in older adults,⁵³ but Dr Krystal stated that some BZs and non-BZs and 2 DORAs have done so.²⁴ The BZs are commonly used but are not recommended for elderly patients according to Beers Criteria.³⁸

In pooled data from 3-month studies⁵⁴ in elderly patients, suvorexant improved sleep onset and maintenance compared with placebo. Lemborexant treatment significantly improved both sleep onset and sleep maintenance, including in the second half of the night, compared with both placebo and zolpidem extended-release.⁴² The ability to improve sleep later in the night, seen with lemborexant as well as suvorexant, without significantly increasing daytime sedation is important because many older adults have sleep difficulties toward the end of the night.

According to Dr Krystal, another drug that may reduce early-morning awakenings is doxepin.⁵⁵ Doxepin has a favorable side effect profile, with a study⁵⁶ reporting that rates of any adverse events were 52% for placebo versus 32% for doxepin 3 mg in older adults. Impairment of memory and balance is minimal with doxepin.⁵⁶ Compared with placebo, doxepin improved sleep in the last third of the night.⁵⁶ Although the recommended dose for older adults is 3 mg,⁵⁷ Dr Krystal noted that in his clinical experience, he finds that many older patients receive benefit from doses below 3 mg. At doses of 1 mg and 3 mg in elderly patients, doxepin can improve sleep in the early morning without residual daytime sedation, but it does not have robust effects on sleep onset.⁵⁶

Ramelteon is an FDA-approved drug that targets type 1 and 2 melatonin receptors³⁸ and has a favorable risk-benefit profile in older adults; it has efficacy for sleep onset but not sleep maintenance.⁵³

Antidepressants, antipsychotics, anticonvulsants, over-the-counter drugs, and herbal supplements are often used off-label for insomnia without any robust evidence of efficacy, and they have side effects that could be dangerous in elderly patients.

For more from Dr Krystal's presentation, see the on-demand activity "Challenges in Managing Insomnia in Older People" in this series at CMEInstitute.com.

Insomnia Treatment in Cognitively Impaired Older Adults

Little research has been conducted on treatment for insomnia among older adults with mild cognitive impairment or Alzheimer disease (AD), but these patients often experience sleep disturbances. He noted that a recent study⁵⁸ of suvorexant in 277 patients with insomnia and mild-to-moderate probable AD showed significant efficacy for sleep maintenance ($P < .02$) and a trend for efficacy in sleep onset ($P < .09$). Melatonin in varying dosages has been examined in studies in patients with AD and insomnia,^{59,60} with no evidence of efficacy. A small study⁶¹ of mirtazapine 15 mg in patients with AD and sleep disorders did not show benefit but rather found worsening daytime sleepiness in the mirtazapine group. Preliminary evidence for the efficacy of trazodone was found in a study⁶² of 30 patients with AD and sleep disturbance based on assessing sleep with actigraphy. According to Dr Krystal, patients may have inconsistent results with certain medications, and each treatment will need to be personalized.

CONCLUSION

Individuals with insomnia may experience difficulty with sleep onset, sleep maintenance, or both. Insomnia is the most prevalent sleep-wake disorder and may result in social and occupational problems and diminish quality of life. Insomnia disorder is often comorbid with psychiatric, medical, and neurologic disorders. Diagnosis should entail patient interview, assessment tools, and criteria. Selection of treatment for patients with insomnia should weigh efficacy for the patient's specific complaint(s) as well as other features such as safety profile and abuse liability. Cognitive-behavioral therapy for insomnia is a first-line recommendation, but some patients are unable or unwilling to try it or may not respond to it. Older adults with insomnia disorder require careful consideration of medications' risk-benefit profiles.

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Disclosure of off-label usage: The faculty members have determined that, to the best of their knowledge, trazodone, mirtazapine, amitriptyline, quetiapine, olanzapine, risperidone, lurasidone, and melatonin are not approved by the US Food and Drug Administration for the treatment of insomnia.

**Clinical Points**

- To assess patients for insomnia disorder, interview them about sleep problems and use tools and diagnostic criteria.
- Recognize the bidirectional relationship between insomnia and comorbid conditions.
- Treat insomnia and the comorbid condition simultaneously.
- CBT-I is first-line treatment for insomnia and appears to benefit patients with low homeostatic sleep drive and elevated arousal.
- Optimal medication treatment for insomnia requires selection of an agent to address the type of sleep difficulty experienced by the patient.
- Agents with nonspecific effects, including benzodiazepines and nonbenzodiazepines, are generally associated with a higher rate of undesired side effects than highly specific agents (eg, doxepin 3–6 mg, ramelteon, orexin antagonists) that can target specific insomnia problems with fewer adverse effects.
- Older adults with insomnia are at increased risk for adverse effects from medications due to their metabolism, coadministered medications, and comorbid conditions.

**Discussion of Case Practice Question**

The preferred response is c. *Dual orexin receptor antagonist*. Insomnia is often comorbid with depression and heart disease. This patient may have significant adverse events when taking a benzodiazepine and has had an inadequate response to a nonbenzodiazepine. Antihistamines are not reliably used for insomnia treatment, and their effect is mostly limited to sleep maintenance. The safety of antipsychotics is unproven. DORAs have been shown to improve sleep onset and maintenance and are well tolerated by all adult age groups.

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POSTTEST

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1. **You've been treating a 23-year-old woman for depression for 6 months. Sleep has not been problematic in the past, but during her clinic visit, she reports trouble getting to sleep and waking up in time for work. Which of the following assessments is not recommended for this patient's evaluation at this time?**
 - a. Epworth Sleepiness Scale
 - b. Sleep diary
 - c. Polysomnography
 - d. Sleep history
2. **A 45-year-old woman with a history of sleep onset and maintenance problems presents to your clinic. She has previously been prescribed 6 mg of doxepin at bedtime. Which one of the following statements is true regarding her treatment?**
 - a. Doxepin has been shown to improve sleep maintenance but is not the best choice when a patient has both onset and maintenance difficulties.
 - b. Doxepin has been shown to produce more adverse effects than other antihistamines because of its nonselective action.
 - c. This patient has been sober for 1 year, and doxepin is not the best choice for her due to its abuse liability.
 - d. There is no formulation of doxepin that has been FDA-approved for treating insomnia.

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