AMA Journal of Ethics®
October 2024, Volume 26, Number 10: E763-770

CASE AND COMMENTARY: PEER-REVIEWED ARTICLE

When Should Pharmacological Interventions for Insomnia Be Recommended?

Brandon Peters, MD and Maxwell Sarver, MD

Abstract

This commentary on a case describes how social determinants of health also contribute to insomnia and then suggests how to balance risks and benefits of different strategies for managing chronic insomnia. Behaviorally induced insufficient sleep syndrome can exacerbate morning side effects of prescription sleep aids, and there are potentially serious long-term risks (eg, dementia, falls, death) associated with chronic benzodiazepine use. Before trying sleeping pills, chronic insomnia should be treated with cognitive behavioral therapy.

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Case

Dr D sees CC, a 46-year-old patient who struggles to sleep well. CC is a parent and works between 55 and 60 hours per week at 2 jobs. CC's family lives where there is frequently noise outside of their home at night. CC has trouble falling asleep and trouble staying asleep, with sleep interrupted by periods of wakeful anxiety. In total, CC probably logs about 5 hours of sleep per night.

Over the years, CC has tried over-the-counter melatonin, a dietary supplement, and diphenhydramine (an antihistamine). CC is currently on eszopiclone, a central nervous system depressant, which Dr D prescribed, but CC would like to change, since the eszopiclone makes them feel "hung over" in the morning. CC asks Dr D, "May I get a prescription for something else? You once prescribed benzos and they worked really well."

Dr D considers whether a benzodiazepine (eg, alprazolam, clonazepam, or diazepam) would be appropriate. Dr D also wonders, "With these drugs, I'm treating the symptom of insomnia, when they work, but not the causes of CC's long-term life stress, worry, and environment. Do the short- and long-term side effects of these drugs balance or outweigh the risks of untreated lack of sleep?"

Dr D considers how to respond to CC's request.

Commentary

When reviewing this scenario, it is easy to identify with a patient who, facing pressure from both professional and personal demands, discovers that their own sleep suffers. Sleep is a pillar of health and well-being, affecting nearly every aspect of optimal wakeful function. It is sacrificed or lost—to the detriment of an individual and the broader society—sometimes with serious adverse consequences. At what potential cost should opportunities for adequate sleep quantity and quality be protected, restored, or enhanced? Pharmacological interventions are frequently employed, but their use can be limited.[1] Honest accounting of how these medications work and their potential for both short- and long-term harms should, we argue, prompt wider use of important alternatives for managing chronic insomnia, including cognitive behavioral therapy for insomnia (CBTI). The rest of this commentary explores how to optimize the clinical assessment of insomnia, normative data and basic sleep concepts that contextualize patients' experiences of insomnia, and treatment strategies that promote best outcomes with the least risk to both the individual and society.

Clinical Assessment of Insomnia

When clinically assessing someone's sleep, it is important to start by conducting an interview to understand the basics of their sleep routine.[2] This query should ascertain the typical bedtime, the average time it takes to initially fall asleep (ie, sleep-onset latency, or SOL), the average total time spent awake in the night after initially falling asleep and before the final awakening (ie, wakefulness after sleep onset, or WASO), and the typical time to get out of bed at the end of the sleep period (usually at morning awakening).[3] It is also useful to learn how bedtime and final wake time vary on days off from work, such as weekends, as significant variance may be present and contributes to a recurring circadian misalignment known as social jet lag.[4] A useful assessment framework is the SATED (satisfaction, alertness, timing, efficiency, and duration) questionnaire.[5] Symptoms and signs of other sleep disorders, including sleep apnea, restless legs syndrome, and delayed sleep phase syndrome, may also be relevant.[2,6]

In this example, a caregiver with multiple jobs may have a behavioral sleep restriction, leading to a discrepancy between the opportunity and ability to sleep. When prolonged wakefulness (self-reported SOL or WASO of more than 30 minutes) intrudes into this limited window for potential sleep, insomnia may contribute to further difficulties. Insomnia is caused by predisposing (ie, genetics), precipitating (eg, stressors, environment), and perpetuating (eg, poor sleep habits, altered relationship to sleep, untreated anxiety) factors.[7] Chronic insomnia is insomnia that occurs at least 3 nights per week and lasts for at least 3 months.[8] It may be associated with unrefreshing sleep, fatigue, decreased energy, headache, pain, malaise, dyspepsia, cognitive dysfunction, and mood complaints.[9] Insomnia is the most common sleep complaint encountered in the primary care setting, affecting 1 in 10 people.[9]

Normal sleep is enhanced by optimizing the factors that influence the homeostatic sleep drive and circadian rhythm, including a consistent sleep-wake schedule and obtaining 15 to 30 minutes of morning light exposure.[10] The average sleep need for adults is 7 to 9 hours, and those aged 65 years and older may need an average of 7 to 8 hours.[11] CC's only getting 5 hours of sleep per night, as reported in the case, indicates a significant compromise for a 46-year-old. This self-assessment can be supported with longer-term sleep logs kept by CC over several weeks or the integration of data from data collection devices worn by CC, although few studies have objectively assessed device performance among individuals with insomnia.[12]

Contextualizing Risks of Insomnia

Beneficence is an ethical imperative to act in the patient's best interests[1]—in this case, to correct sleep deficiencies. Insomnia is a known risk factor for depression, anxiety, alcohol or drug use, suicide, chronic pain, and social and occupational dysfunction.[13,14,15,16] In addition, chronic sleep deprivation can have serious health consequences, affecting everything from metabolism to immune system and cardiovascular function.[17,18,19] Moreover, as the first author (B.P.) has written elsewhere, based on studies of cognitive performance[20]:

> Studies have shown that sleep deprivation can profoundly affect memory and performance. Attention, concentration, and vigilance become impaired. People who sleep less than 7 hours per night have reaction times that are similar to those who are completely sleep deprived for one or even two nights. This leads to errors, accidents, and impaired work performance. The scary thing is that when you are chronically sleep deprived, you may not even recognize the level of impairment.[21]

Sleep loss thus leads to chronic, insidious problems that undermine health and quality of life as well as to immediate risks that threaten life itself. These effects may be due, at least in part, to disturbance of the glymphatic system, a perivascular network that flushes metabolites from the brain's tissues during sleep.[22]

Given these potential consequences, a medical professional might be quick to reach for the prescription pad to deliver relief. There is little guidance from the national medical academies (eg, the American Academy of Sleep Medicine, the American College of Physicians) with regard to when pharmacological interventions, especially benzodiazepine agents, are preferred due in part to a paucity of longitudinal efficacy and safety data.[23,24] In this scenario, the patient is currently on eszopiclone, a non-benzodiazepine hypnotic with a half-life of approximately 6 hours (closer to 9 hours in the elderly), and is having a "hangover" effect in the morning, likely due to behaviorally induced insufficient sleep, and so requests a benzodiazepine.[25] Contrary to the impulse to accede to this request, the ethical standard of nonmaleficence (*primum non nocere*, or "first, do no harm") must give a clinician significant pause.[1]

Benzodiazepine Medications

Historically, benzodiazepines were used in the management of both acute and chronic insomnia in adults. This routine use was the result of several studies that showed benefits of short courses of benzodiazepines; however, the study populations were primarily nonelderly adults, and long-term follow-up results were lacking.[26] A more recent, large-scale study in the United Kingdom evaluated the all-cause mortality associated with the use of hypnotics over a 7.6 year period and demonstrated a more than 3-fold greater hazard of mortality with any sleep aid exposure.[27] Among the studied sedatives, benzodiazepines notably had the highest prescription rates and the highest individual mortality rate; there was also a dose-dependent increase in mortality.[27] While this study could only demonstrate correlation and not causation, there are several known adverse effects of all classes of benzodiazepines. These include increased risk for car crashes, cognitive decline, and falls or fractures.[26] Long-acting benzodiazepines (eg, diazepam, clonazepam) are generally better tolerated but may cause the morning hangover effect with associated cognitive impairment,[28] while short-acting benzodiazepines (eg, temazepam) have less of a hangover effect but have a higher risk of fractures.[29]

Benzodiazepines have also been shown to have a risk of dependence with long-term use. Dependence can lead to several risky or maladaptive behaviors, including driving under the influence, use in addition to other sedatives, rebound insomnia or anxiety with discontinuation, or replacement with other substances after discontinuation by a physician.[30] Interestingly, although clinicians often encounter these issues in elderly patients, the 12-month prevalence of a diagnosed hypnotic or anxiolytic use disorder is only 0.04% in those age 65 years and older, which may indicate that benzodiazepine use is an underrecognized problem by primary care clinicians.[31]

In addition, the long-term use of benzodiazepine medications has been associated with cognitive decline and dementia.[32] While benzodiazepines are known to cause short-term cognitive defects, several studies have demonstrated that, even after discontinuation, several domains of cognitive function continue to be impaired in long-term users.[33,34] Because there is some debate as to whether insomnia or anxiety can be early presentations of dementia,[35] it is unclear if benzodiazepines are causing cognitive decline or if they are being used to treat these prodromal symptoms.

Overall, the risks of benzodiazepine use for treatment of insomnia have been viewed as outweighing the benefits in the majority of cases, causing them to be listed on Beer's Criteria with a strong recommendation against their use, particularly in the elderly with known cognitive deficits or in those at high risk of falls.[36] The American Academy of Sleep Medicine recommends against long-term use of hypnotic medications, including benzodiazepine receptor agonist medications like eszopiclone, except in very specific circumstances,[23] which this patient has not met. What is an ethical sleep caregiver to do?

Cognitive Behavioral Therapy

Since 2016, the American College of Physicians has recommended that all adult patients with chronic insomnia receive CBTI as their initial treatment.[24] Despite this recommendation, the prevalence of medication use remains high, with an estimated 8.4% of adults in 2020 reporting the use of a sleep aid every day or most days in the prior month, according to the Centers for Disease Control and Prevention.[37] Awareness of and access to CBTI are both paramount to delivering the gold standard of medical care for treatment of chronic insomnia. CBTI is a structured 6-week program that reinforces changes in sleep habits while addressing sleep-disruptive thoughts, emotions, and social pressures.[38] It may be delivered one-on-one by a therapist, in a shared medical appointment workshop, through online or app-based programs, or via bibliotherapy.[39] Key elements of CBTI include sleep consolidation, stimulus control, cognitive restructuring, relaxation training, and sleep hygiene advice. Significant improvement occurs within weeks, and long-term skills are provided that yield ongoing benefits even years beyond the training.[40] CBTI has no side effects.

The ethical principle of justice should inform the administration of CBTI, as it unfortunately still represents a scarce health resource that is unevenly distributed. In 2016, it was estimated that there were 752 behavioral sleep medicine practitioners capable of delivering CBTI worldwide; 88% live within the United States; and more than half live in just 12 states.[41] There are many cities, regions, states, and countries with no sleep medicine practitioners. Technology must be leveraged to amplify limited CBTI expertise and address these unmet needs.[42]

For patients who are unable or unwilling to engage in CBTI, the benefits afforded by the use of medications may outweigh the risks of potential harms associated with insomnia and sleep deprivation. As necessary, clinicians should venture to engage in shared decision-making to determine when and what pharmacotherapy should be employed. In this case, the use of a short-acting benzodiazepine (eg, temazepam) may be preferable if CBTI is not possible. Regular follow-ups with reassessment of need via a risk-benefit discussion may help mitigate undesirable consequences.

Finally, a broader perspective on the presented scenario appeals to the social determinants of health.[43] How can society best support the factors conducive to the sleep of individuals to optimize community well-being? CC's socioeconomic situation, which necessitates their working multiple jobs, may indicate lack of livable wages, education, or employment opportunity. Social support networks, or the lack thereof, may add to the burden of caregiving and other inequalities. The noise of the neighborhood—and even the safety of the built environment—are additional influences on this individual's sleep.

Conclusion

Sleep loss has extensive and serious consequences, with detrimental effects that extend from the individual to society at large. The ethical treatment of chronic insomnia requires universally extending access to CBTI and (when possible) avoiding the use of benzodiazepine medications and their inherent risks. Yet, in specific circumstances, pharmacotherapy may have a role. Moreover, we must advocate for social change that promotes healthy sleep by according it a central place in the lives of individuals and implementing public health policy to protect this most basic, undeniable, and ubiquitous good.

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Brandon Peters, MD is a double-board-certified neurologist and sleep medicine physician at Virginia Mason Franciscan Health in Seattle, Washington. He was previously a sleep fellow at Stanford University, where he also trained in cognitive behavioral therapy for insomnia. He is the creator of the online *Insomnia Solved* program.

Maxwell Sarver, MD is a second-year internal medicine resident at Virginia Mason Medical Center in Seattle, Washington. He also works as a primary care physician at Eastgate Public Health, where he aims to improve insomnia management in a resource-limited setting.

Editor's Note

The case to which this commentary is a response was developed by the editorial staff.

Citation

AMA J Ethics. 2024;26(10):E763-770.

DOI

10.1001/amajethics.2024.763.

Conflict of Interest Disclosure

Authors disclosed no conflicts of interest.

The people and events in this case are fictional. Resemblance to real events or to names of people, living or dead, is entirely coincidental. The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.

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ISSN 2376-6980