THE CARLAT REPORT
ADDICTION TREATMENT

A CE/CME Publication

CURRENT COVERAGE OF TOPICS IN ADDICTION MEDICINE

Bachaar Arnaout, MD
Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Sleep Disorders and Addiction

Learning Objectives
After reading these articles, you should be able to:

1. Identify ways for clinicians to diagnose and treat obstructive sleep apnea in patients with substance use disorders.

2. Evaluate the effectiveness of pharmacologic and non-pharmacologic treatments for managing insomnia in substance-using patients.

3. Discuss the benefits and drawbacks of non-addictive sleep medications.

Sleep Apnea in Patients With Substance Use Disorders: A Primer

Rehan Aziz, MD
Associate Professor of Psychiatry and Neurology, Rutgers University—Robert Wood Johnson Medical School

Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

A 55-year-old male patient you have been treating for alcohol use disorder has been struggling with withdrawal following detox. He tells you his spouse is complaining about his severe and disruptive snoring, and he says he feels "wiped out" all day, even falling asleep at work. He then admits that, to stay alert, he has been regularly taking Adderall supplied by a colleague and now has strong cravings to have a beer to "take off the edge" after work.

In Summary

- Substance use can mask, exacerbate, or trigger obstructive sleep apnea (OSA), which is the most common type of sleep apnea.
- A continuous positive airway pressure (CPAP) machine is the gold standard treatment for OSA.
- When treating patients with SUD, choose medications that will either improve OSA or will help patients tolerate CPAP treatment.

He is at risk for relapse, and you suspect sleep apnea might be a risk factor.
What do you do next?

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Q&A With the Expert

Treating Insomnia With Addiction

Eric Hermes, MD

Assistant Professor, Department of Psychiatry, Yale School of Medicine, New Haven, CT

Dr. Hermes has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CATR: With substance use disorders (SUDs) that are comorbid with chronic insomnia, what would you say are some of the main treatment challenges?
Dr. Hermes: The first thing I'd say is that chronic insomnia has a high comorbidity rate with SUDs as well as general psychiatric conditions and medical conditions, including chronic pain, COPD, heart disease, and diabetes to an extent. These comorbidities often take precedence, and treating insomnia becomes sort of a sideshow. Clinicians have limited time, and getting into the ins and outs of treatment options for insomnia usually doesn't happen. For instance, SUD clinicians don't usually receive special training about managing insomnia, and sleep disorders may not be high on their list. So, I think insomnia ends up being a secondary issue, and that means the focus may be more on the easier treatment regimens, like psychopharmacology—sometimes to the detriment of behavioral treatment options.

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Sleep Apnea in Patients With Substance Use Disorders: A Primer

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Basics of sleep apnea

There are three types of sleep apnea: obstructive sleep apnea (OSA), central sleep apnea, and mixed. Of these, OSA is by far the most common, and that's what we'll focus on in this article.

OSA is caused by excessive relaxation of the throat during sleep, which in some people causes enough obstruction to impede the flow of air. The apnea causes them to reflexively wake up enough to temporarily open the airway, after which they fall back to sleep. Dozens or hundreds of such mini-awakenings can occur, and patients may not remember them. They may wake up thinking that they have slept all night, but they still feel exhausted.

Risk factors for OSA include obesity and enlarged tonsils (mainly a cause in children). The prevalence of diagnosed and treated OSA is around 2%–4%, but milder forms probably affect many more people. OSA's prevalence is higher in patients with a substance use disorder (SUD). While substances can aggravate OSA, the causality often works the other way: OSA may cause fatigue and depression, which can then lead to substance use as a coping mechanism.

OSA is diagnosed through a comprehensive sleep evaluation conducted by a sleep specialist, who is commonly a pulmonologist. This involves reviewing a patient's medications, substance use history, sleep logs, collateral history, and—crucially—polysomnography (PSG) results, the gold standard for OSA. For PSG, the patient is kept in a sleep lab overnight and physiologic variables are monitored. The main outcome measure of PSG is the apneo-hypoxia index (AHI), which is the average number of disordered breathing events per hour. Typically, OSA is defined as an AHI of 5 or greater with associated symptoms (eg, excessive daytime sleepiness, fatigue, or impaired cognition) or an AHI of 15 or greater with or without associated symptoms. Instead of PSG, home sleep testing may be used for uncomplicated adult patients (Kapur VK et al, *J Clin Sleep Med* 2017;13(3):479–504).

The main treatment for sleep apnea is continuous positive airway pressure (CPAP), administered via a small machine that provides low levels of air pressure through a mask to keep the airway passages open during sleep. If an individual is overweight, even a 10% reduction in weight can be beneficial. Sometimes surgical procedures are recommended to correct airway anatomy.

Stress to the patient the negative impact of substance use on sleep, as it can mask, exacerbate, or trigger OSA.

How to screen substance-using patients for OSA

Screen not just patients complaining of fatigue, but all your patients with an SUD. Start by asking, "Do you snore?" If they say no, ask if anybody else has told them that they snore. Ask, "Do you wake up feeling like your sleep is nonrestorative? Do you feel sleepy throughout the day?" Depending on your level of suspicion for

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Welcoming Our New Editor-in-Chief

We're pleased to introduce Bachaar Arnaout, MD, as the new editor-in-chief of *The Carlat Addiction Treatment Report*. Dr. Arnaout is an assistant professor of psychiatry at the Yale School of Medicine. He completed medical school at the Jagiellonian University in Kraków, Poland, and trained in psychiatry at St. Luke's-Roosevelt Hospital Center in New York, where he also completed the Intensive Psychoanalytic Psychotherapy Program at the William Alanson White Institute of Psychiatry, Psychoanalysis & Psychology. He then trained in addiction psychiatry at the Yale School of Medicine.

Dr. Arnaout holds board certification in psychiatry, addiction psychiatry, addiction medicine, hospice and palliative medicine, and brain injury medicine. Dr. Arnaout's academic interests include the psychotherapy and psychopharmacology of addiction and co-occurring disorders, and medical education. He has co-edited two books on addiction psychotherapy that draw on the theoretical framework of motivational interviewing: *Handbook of Motivation and Change: A Practical Guide for Clinicians* (American Psychiatric Publishing, Inc., 2010) and *Motivational Interviewing in Clinical Practice* (American Psychiatric Association Publishing, 2017).

Sleep Apnea in Patients With Substance Use Disorders: A Primer
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OSA, ask about two other symptoms commonly seen in the disorder: morning headache and frequent nighttime urination.

If you suspect OSA, refer to a sleep specialist. Patients might ask what they should expect at a sleep evaluation, so being knowledgeable on the subject might encourage them to follow up. Say, "The specialist will take a thorough sleep history and go over all the factors in your life that might be interfering with sleep. If the specialist suspects sleep apnea, you'll do a sleep study where you sleep in a special room while having your brain waves, breathing, and oxygen level monitored." Also mention that the main treatment, CPAP ("a special small breathing machine"), will likely prevent serious health problems (especially cardiac ones) and give patients more years to live. In addition, CPAP has been shown to improve depressive symptoms (Economou NT, *PLoS One* 2018;13(6):e0197342).

Effects of substances on OSA

While screening for sleep apnea is important, the vast majority of your sleep apnea patients will have already been diagnosed by the time you see them. Sleep apnea may be one of a long list of medical problems, which in these patients commonly include hypertension, hyperlipidemia, diabetes, and other ailments associated with obesity. Add an SUD to this list, and you have a pretty complicated patient.

What's a good approach in these cases? First, you should explain to your patient how substances can aggravate OSA.

Alcohol and benzodiazepines. Alcohol and other sedatives excessively relax the muscles of the throat, which worsens airway obstruction. In addition, sedatives impair the natural arousal reflex that allows the airway to open up for drawing the deep breaths the body needs. This is a double whammy for sleep apnea patients. Indeed, research has shown that alcohol increases the duration and frequency of apneas in OSA and increases the extent of hypoxemia. There's even some evidence that in patients with benign chronic snoring, alcohol can actually induce OSA (Issa FG et al, *J Neurol, Neurosurg, and Psychiatry* 1982;45(4):353–359).

Opioids. Patients who are taking opioids, whether prescribed for chronic pain or as replacement therapy, are in a special risk category because they are vulnerable to central sleep apnea. Central sleep apnea is a relatively uncommon condition seen mostly in patients who are taking very large doses of opioids (morphine equivalent >200 mg), particularly if they are also on benzodiazepines (Correa D et al, *Anesth Analg* 2015;120(6):1273–1285). But even in patients taking smaller opioid doses, try to avoid using benzos.

Tobacco. Surveys have shown an association between cigarette smoking and sleep apnea, with possible mechanisms including airway inflammation and sleep instability from overnight nicotine withdrawal (Franklin KA et al, *J Thorac Dis* 2015;7(8):1311–1322).

Cannabis. Oddly, there is some preliminary evidence that THC can improve OSA (Carley DW et al, *Sleep* 2018;41(1):zsx184). Nonetheless, the American Academy of Sleep Medicine has stated that "medical cannabis and/or its synthetic extracts should not be used for the treatment of OSA due to unreliable delivery methods and insufficient evidence of effectiveness, tolerability, and safety" (Ramar K et al, *J Clin Sleep Med* 2018;14(4):679–681).

Thoughtful prescribing for sleep apnea patients

Your goal is to avoid meds that may worsen the condition, while selecting meds that will either improve it or will help patients tolerate CPAP treatment. (For a good review on psychiatric management of OSA patients, see: Heck T and Zolezzi M, *Neuropsychiatr Dis and Treat* 2015;11:2691–2698).

Antipsychotics

Try to avoid sedating antipsychotics, such as quetiapine, olanzapine, and chlorpromazine. Second-generation antipsychotics are associated with a near doubled risk of severe OSA—though the mechanism is unclear (Shirani A et al, *Sleep Med* 2011;12(6):591–597). So, these are not the patients who should be getting those little 25 mg doselets of Seroquel for sleep.

Antidepressants

It's well-known that many antidepressants decrease the amount of rapid eye movement (REM) sleep. And since apneas occur more frequently during REM, decreasing REM might theoretically decrease the number of apnea episodes. However, neither tricyclics or SSRIs have been consistently shown to improve OSA. Fortunately, these meds do not worsen the condition.

Benzodiazepines

While there's no solid evidence that benzos worsen OSA, common sense dictates they might, so you should avoid them if possible. Patients who are on benzos should limit their use to shorter-acting agents not taken too late in the day.

Non-benzodiazepines

Because non-benzos have fewer muscle relaxant effects than benzos, they are thought to be safer in OSA. Some experts actually advocate their use on the grounds that they help patients sleep while using the intrusive CPAP machines, thereby improving adherence with OSA treatment. For example, one study randomly assigned 152 OSA patients to eszopiclone (Lunesta) 3 mg or placebo for 2 weeks. Patients taking Lunesta used CPAP for more nights and for more hours per night than those taking placebo, and there were no differences in side effects between the groups (Lettieri CJ, *Ann Intern Med* 2009;151(10):696–702).

Stimulants

Since OSA causes daytime sedation, modafinil (Provigil) is recommended by most experts. Ideally, this should be explored only after CPAP intervention since patients who adhere to and respond well to CPAP will see resolution or improvement of daytime sedation. While stimulants also work well to treat fatigue, you should avoid them if possible because of the potential for misuse and diversion.

CATR VERDICT: Make screening for OSA a part of your routine for patients with SUDs. And when prescribing meds for them, avoid psychotropics, such as sedating antipsychotics and benzodiazepines, that might worsen the condition.

Expert Interview
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CATR: And then it becomes a potential issue for the patient?

Dr. Hermes: Exactly. For the patient, chronic insomnia is often primarily a behavioral disorder. Chronic insomnia is technically defined as having affected the patient for at least 3 months. But if you've had trouble sleeping for a couple of weeks or even days, cognitive and behavioral issues can start to reinforce the problem, where you have negative thoughts that drive behaviors and thereby perpetuate the insomnia. Pharmacologic treatment is really good at putting people to sleep, but it doesn't address these cognitive and behavioral issues that are part and parcel with chronic insomnia.

CATR: The theme of this month's issue is sleep and addiction, but we also know that chronic insomnia can be comorbid with many additional mental health disorders we see in our patients. How can treating the insomnia help there?

Dr. Hermes: First, we know that there are strong associations between insomnia and many mental health disorders. Most critically, we know that independent of all other comorbidities, insomnia increases the risk of suicidal ideation and attempts. We also know that treating insomnia reduces risk when it comes to some of the other comorbid disorders. For instance, the treatment of comorbid insomnia will improve depression and reduce posttraumatic stress disorder scores (Krakow B et al, *Am J Psychiatry* 2001;158(12):2043–2047; Manber R et al, *Sleep* 2008;31(4):489–495). Treating insomnia will also likely reduce the risk of relapse in patients with SUDs.

CATR: So, let's talk about behavioral interventions. What's your approach? Does cognitive behavioral therapy for insomnia (CBTi) really work?

Dr. Hermes: There have been multiple systematic reviews showing that CBTi has an incredibly strong evidence base. It's a very powerful treatment, with treatment effects at 3, 6, and 12 months after a course of therapy has been completed (Smith MT et al, *Amer J Psychiatry* 2002;159(1):5–11). According to the American Academy of Sleep Medicine, CBTi is a recommended first-line treatment for chronic insomnia.

CATR: If CBTi is so effective, then why are clinicians quick to prescribe medication?

Dr. Hermes: Some clinicians may not be aware of what CBTi is or that it has such a strong evidence base. There are not a lot of providers out there who are trained to deliver CBTi. Also, it is a time-consuming process for both the provider and the patient—it involves showing up for therapy once a week for 6 weeks, and often as many as 9 to 12 weeks. Then the patient has to go home and actually do the CBTi activities. These are sometimes difficult, as with any therapy. So, there are these barriers, but in the end—if it's available—providers should really try to use CBTi as a first-line treatment.

"Benzodiazepines are a last-line option for insomnia. There is much higher risk of benzo use disorder in the SUD population, particularly with those who have an alcohol use disorder. It's less of a question that benzo use will throw a patient with an AUD into relapse and more about the high potential for a new SUD involving the benzo."

Eric Hermes, MD

CATR: Has CBTi been validated for patients with SUDs?

Dr. Hermes: Yes, there have been some studies that have validated CBTi in substance-using populations. I think most of those populations were for alcohol use disorder (AUD) and sorted in terms of what stage of treatment a patient was in, whether it was early sobriety or after years of sobriety (Currie SR et al, *Addiction* 2004;99(9):1121–1132).

CATR: For those who aren't trained in CBTi, can you give us some basics?

Dr. Hermes: CBTi is sort of a mish-mash of different behavioral and cognitive activities. One of those is sleep hygiene, and that's really the bare bones of learning practices that promote good sleep habits. But sleep hygiene education as a stand-alone intervention does not have a particularly strong evidence base—it's necessary, but not sufficient by itself. The most powerful component of CBTi seems to be "sleep restriction," which involves getting patients to stay up late to ensure they are indeed tired when they hit the bed, and then locking down consistent wakeup times in the morning. Doing that basically allows them to reset their sleep cycle. This can take as little time as a couple of days (Edinger JD and Means MK, *Clinical Psychol Review* 2005;25(5):539–558).

CATR: I've heard that fixing the wakeup time is the most vital component when using sleep restriction. Do you agree?

Dr. Hermes: Yes, I think locking down wakeup time is also quite beneficial. Many practitioners I talk to will work on sleep hygiene practices first, which serves as preparation for getting patients to set up a wakeup time as part of sleep restriction activities. But as we've learned, it's not always easy having people stay up late to ensure they're ready for sleep and then getting them to wake up at a consistent time. It'll take constant reminders and working with patients to troubleshoot difficulties.

CATR: Considering the challenges of dealing with patients who are new to recovery—maybe they're just coming off detox—would it be a good idea to delay CBTi until they stabilize, using a non-benzodiazepine drug to help them sleep in the interim?

Dr. Hermes: Yes, I don't know if CBTi would be appropriate for most people in early sobriety. Obviously, during early sobriety, patients are most focused on their recovery activities. It might be difficult for these patients to also focus on CBTi activities. So, helping them initially—at least for a few weeks—with a pharmacological solution makes sense.

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Non-Addictive, Pharmacological Options for Sleep

Daniel Carlat, MD
Publisher, The Carlat Addiction Treatment Report

Dr. Carlat has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

In this month's interview with Dr. Eric Hermes, we learned about his approach to treating insomnia in patients with substance use disorders, with a focus on cognitive behavioral therapy. In this article, we'll look at some non-addictive pharmacological options. That means we're not going to review any of the benzodiazepines or the non-benzodiazepines (eg, "Z drugs"), such as Ambien, Sonata, or Lunesta. While the non-benzos are probably less addictive than benzos, they often seem to make their way into recreational drug cocktails when in the hands of patients with SUDs, so they're best avoided in this population if possible.

Sedating antidepressants

Trazodone. Trazodone, which is an antidepressant that has never been FDA-approved for insomnia, turns out to be the second most prescribed sleeping pill in the U.S. (Bertisch SM et al, *Sleep* 2014;37(2):343–349). It is typically started at 25 mg–50 mg, but some patients will respond to 12.5 mg, while others require doses greater than 150 mg. Usually once patients are using those higher doses, they will start requesting to switch to something else. You've probably been prescribing trazodone for many years, but chances are slim that you've actually seen data for its effectiveness in insomnia. A recent meta-analysis should ease your mind. An analysis of 7 trials evaluating trazodone found that it is more effective than placebo, and that both high and low doses are helpful, with the main effect seen for sleep maintenance as opposed to sleep initiation (Yi XY et al, *Sleep Med* 2018;45:25–32).

Mirtazapine. Mirtazapine (Remeron) is a very effective triple-use medication that can target depression, anxiety, and insomnia. Though only FDA-approved for depression, it works for anxiety at doses used for insomnia. There is some credible evidence that it is more effective for sleep at low doses (15 mg) than high doses (30 mg and higher) (Savarese M et al, *Arch Ital Biol* 2015;153(2–3):231–238). The putative reason for this is that at low doses mirtazapine is primarily an antihistamine, whereas at higher doses it increases norepinephrine release, which can be stimulating. However, some psychiatrists say they haven't seen this dosing effect in their practices, so it might just be psychopharmacology lore. The unfortunate drawback is that mirtazapine causes weight gain in many patients, a side effect that you can't prevent by using low doses. Orthostatic hypotension is an under-appreciated side effect, especially in the elderly.

Doxepin. Doxepin (Silenor) is a tricyclic that has been around for a long time as an FDA-approved treatment for depression and anxiety. At low doses (10 mg–20 mg of generic doxepin, or 3 mg–6 mg of Silenor), it is an effective hypnotic with relatively few anticholinergic side effects.

Amitriptyline. Amitriptyline (Elavil) is another sedating tricyclic, with insomnia doses typically in the 25 mg–75 mg range. It has the bonus of being effective for a range of pain issues, including fibromyalgia, migraine headaches, diabetic neuropathy, and post-herpetic neuralgia. So you can potentially avoid two classes of addictive medicines with this drug: benzos and opiates.

The antihistamines

Diphenhydramine (Benadryl and others). The effective and starting dose is 25 mg–50 mg, though it can be effective at doses as low as 6.25 mg. Next-day grogginess seems to be a common problem with diphenhydramine, as well as pretty rapid development of tolerance—sometimes within a few days. In terms of anticholinergic side effects, the one we're most concerned about is cognitive impairment, which is primarily a problem in older patients with long-term use.

Doxylamine (NyQuil and others). Think of doxylamine as very similar to diphenhydramine; it works just as well and is usually dosed at 25 mg. Use doxylamine for patients who tell you diphenhydramine doesn't work for them—they may well respond to this alternative.

Hydroxyzine (Atarax, Vistaril). Hydroxyzine has been around since 1956 and has FDA indications for pruritis, anxiety, and sedation before surgery. Confusingly, there are two versions of hydroxyzine: hydroxyzine HCL (Atarax) and hydroxyzine pamoate (Vistaril). During medical training, some of us might recall being taught that Atarax is the version to use for itching while Vistaril is better for anxiety. But there's no truth to this rumor,

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Non-Controlled Drugs Used for Insomnia

Drug	Dose for Insomnia	Significant Side Effects
Preferred agents		
Trazodone	25–200 mg QHS	Dizziness, hypotension, priapism
Mirtazapine	7.5–30 mg QHS	Weight gain, constipation
Doxepin	3–20 mg QHS	Anticholinergic effects, sexual dysfunction, fatal overdose
Ramelteon	8 mg QHS	Dizziness, headache, change in taste
Melatonin	1–5 mg 1–2 hours before bedtime	Dizziness, headache
Non-preferred agents (use only in selected patients)		
Clonidine	0.1–0.4 mg QHS	Lightheadedness, rebound hypertension
Doxylamine	25 mg QHS	Anticholinergic effects
Diphenhydramine and hydroxyzine	25–100 mg QHS	Anticholinergic effects
Amitriptyline	25–75 mg QHS	Anticholinergic effects, hypotension, sexual dysfunction, fatal overdose
Gabapentin	100–1200 mg QHS	Dizziness, diplopia, ataxia
Quetiapine	25–100 mg QHS	Weight gain, lipid abnormalities, tardive dyskinesia

Note: Daytime sedation is a common potential side effect of all hypnotics.

Expert Interview
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CATR: Let's talk about pharmacological solutions, either as an interim step before beginning CBTi for chronic insomnia or for simply treating acute, short-term insomnia. What do you recommend for patients who have a comorbid SUD?
Dr. Hermes: First, I think the key is talking clearly with patients up front about the benefits and especially the risks of pharmacologic insomnia treatment. Make that the first conversation. Talk about what the plan would be if, in a few weeks, the prescription isn't working, and explain what the probabilities are around that. Then, talk about side effects and the short-term risks, which are pretty minimal. Most of the sedative-hypnotic medications are well-tolerated. The risks in my mind are more long-term involving how patients come off these medications.
CATR: Should they still need medication in a few weeks, do you then tell them what the plan would be next?
Dr. Hermes: Yes, at that initial talk, you want to at least introduce the idea of starting CBTi. I actually don't use the word "therapy," though. I tend to use the term "training," such as, "We should begin that training soon." I don't even use the term "CBTi." I'll tell patients, "If you feel you still need the drugs for your insomnia in 2 or 3 weeks, we can try an effective training regimen instead. It will be more of a commitment, but it really works, and it doesn't involve medication."
CATR: What medications do you usually consider: benzodiazepines, the Z drugs, or another medication?
Dr. Hermes: Well, I put them all in a group of sedative-hypnotics, and within that group I personally define them as the benzos, the non-benzo GABA-agonists [Z drugs (eg, zolpidem)], antihistamines, and "others," such as sedating antidepressants. In substance-using populations, I'll usually start with a sedating antidepressant such as trazodone. I'll do that because in most of the populations I treat, the risk of going from acute pharmacologic treatment to chronic pharmacologic treatment in substance-using populations is high. After the sedating antidepressants or the antihistamines, I would go to the Z drugs and then—if necessary—the benzos. With antihistamines, I will use a drug like Benadryl with patients that have more of a middle insomnia picture after something like trazodone has failed. This is usually not very well-tolerated because of the morning grogginess, so I will mainly use it short-term—say, a week—as I am trying to get the patients into CBT. I will use hydroxyzine for more early insomnia.
CATR: Since many patients are familiar with Ambien (zolpidem), is that typically what they ask for first?
Dr. Hermes: Yes, it's a household name at this point and the most commonly prescribed sleep drug, so usually patients will know it if not request it. When they ask, I will start a conversation to educate them about how there are less risky drugs that we should consider first. But it can be a challenging conversation, since most people know Ambien, and many patients have been on it and like its effectiveness.
CATR: So, how do you have that conversation with the patient?
Dr. Hermes: I'll start the discussion with, "Where do you want to be in 3 months? A year? Do you still want to be taking this medication? Most of these drugs will work very well, especially in the short term, but for some people they are difficult to stop." This allows me to discuss drugs that are less likely to evolve into chronic use, and then dovetail that into introducing the idea of an "effective training regimen" with CBTi.
CATR: Can you tell us more about why you mention benzodiazepines as a last-line option for an SUD patient?
Dr. Hermes: Simply put, it's because of the much higher risk of benzo use disorder in the SUD population, particularly with those who have AUD. I think that's the worry. It's less of a question that benzo use will throw a patient with an AUD into relapse. It's more about the high potential for a new SUD involving the benzo.
CATR: But isn't that also the case with those who have an AUD and are also taking zolpidem?
Dr. Hermes: I think the risk of relapse is lower with zolpidem, but it does happen. As I remember, there are some early studies showing that those in AUD recovery didn't risk zolpidem misuse, but the bulk of the evidence shows that there is a connection (Griffiths RR and Johnson MW, *J Clinical Psych* 2005;66(9):31–41). I see many patients with an AUD who find it very, very difficult to quit the zolpidem.
CATR: How about the use of melatonin?
Dr. Hermes: Most people I see are already on melatonin, usually at a lower dose than is recommended. I have never really seen melatonin work, but this may just be the population I see. I generally don't even increase the dose and will just start another agent and try to get them to stop the melatonin in order to simplify the medication regimen. Interestingly, patients will usually stay on it of their own accord. I think this is more about it being a "natural substance" than its efficacy for insomnia.
CATR: Thank you for your time, Dr. Hermes.

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Non-Addictive, Pharmacological Options for Sleep
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which is an artifact of Vistaril's unique availability as a fast-acting injection for anxiety. At any rate, hydroxyzine is a favorite among inpatient psychiatrists for use as a "prn" for anxiety, but it works well for insomnia too. Prescribe 25 mg–100 mg at bedtime and warn patients about next-day sedation.

The melatonin receptor agonists
Melatonin. The melatonin you can buy at the drugstore is the synthetic form of the natural hormone, which is secreted by the pineal gland. Its blood levels typically rise at sunset and peak in the middle of the night. A recent meta-analysis of 12 studies comparing melatonin to placebo concluded

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CE/CME Post-Test

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Below are the questions for this month's CE/CME post-test. This page is intended as a study guide. Please complete the test online at www.carlataddictiontreatment.com. Note: Learning objectives are listed on page 1.

1. Polysomnograph tests measure the apneo-hypoxia index (AHI), the average number of disordered breathing events per hour. Which AHI measure is typically associated with a diagnosis of obstructive sleep apnea (OSA)? (LO #1)

   a. 1 or greater with associated symptoms
   b. 3 or greater without associated symptoms
   c. 5 or greater with associated symptoms
   d. 8 or greater without associated symptoms

2. According to Dr. Hermes, using cognitive behavioral therapy for insomnia (CBTi) to establish a consistent wakeup time in the morning can allow patients with insomnia to reset their sleep cycle in under a week's time. (LO #2)

   a. True
   b. False

3. What effect do the non-benzodiazepine medications, such as eszopiclone, have on OSA? (LO #1)

   a. They are likely to increase the duration and frequency of apneas in patients with OSA
   b. They often decrease the amount of rapid eye movement sleep, which helps to decrease patients' number of apnea episodes
   c. They can help patients using continuous positive airway pressure (CPAP) machines to sleep, which can improve adherence to OSA treatment
   d. They are associated with a near doubled risk of severe OSA

4. According to Dr. Hermes, which of the following statements about CBTi is true? (LO #2)

   a. Patients can learn CBTi in as little as 3 sessions over the course of a few weeks
   b. CBTi is most effective if patients rise only when they feel refreshed in the morning
   c. CBTi treatment effects have been shown to last up to 12 months after a course of therapy has been completed
   d. CBTi is most effective for drug-using patients in the early stages of sobriety

5. Hydroxyzine HCL (Atarax) is more favorable than hydroxyzine pamoate (Vistaril) for treating anxiety and insomnia. (LO #3)

   a. True
   b. False

Non-Addictive, Pharmacological Options for Sleep

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that melatonin improves insomnia in patients with sleep onset difficulties (Auld F et al, *Sleep Medicine Reviews* 2017;34:10–22). Additionally, a few small studies have found that a newer extended-release melatonin product may aid in maintaining sleep. The dose is highly variable, and the meta-analysis reported that the doses used in clinical trials ranged from 0.3 mg to 10 mg, with most between 2 mg and 5 mg. Don't forget to tell your patients to take their melatonin several hours before sleeping; it's unlikely to work if taken right at bedtime.

Ramelteon (Rozerem). Ramelteon is a prescription product approved for insomnia and is a melatonin receptor agonist. Although it clearly outperforms placebo in clinical trials (see the 2014 meta-analysis: Kuriyama A et al, *Sleep Med* 2014;15(4):385–392), patients often don't feel like it's working because they don't detect a sedating sensation. Often patients say it doesn't start working for several days, so you have to encourage them to stick with it for a while. There's no notable next-day sedation. Prescribe it 8 mg at bedtime. Since it's not available generically, it may be hard for some patients to obtain.

Other sedating drugs

Gabapentin (Neurontin). Even though gabapentin has gotten bad press recently related to the possibility of recreational use, it's not as addictive as the benzos, and the majority of those who get into trouble with it are also misusing opioids. Gabapentin is a highly popular medication, in part because it causes few drug interactions; therefore, prescribers feel comfortable using it in patients on multiple medications. There's no question that some patients find gabapentin sedating. For insomnia, start at 100 mg QHS and titrate upward as needed.

Quetiapine (Seroquel). Prescribed at 25 mg–100 mg at bedtime, quetiapine, for better or worse, has become a go-to sedative for those who shouldn't take benzos.

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THE CARLAT REPORT:
ADDICTION TREATMENT

P.O. Box 626
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This Month's Focus:
Sleep Disorders and Addiction

Next month in *The Carlat Addiction Treatment Report:*
Addiction in Older Adults

Non-Addictive, Pharmacological Options for Sleep

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We worry about the potential for weight gain and hyperlipidemia. It's not clear that weight gain on quetiapine is dose-dependent, but it's likely that very low doses don't cause much weight gain. For example, in one study of 534 adults on quetiapine doses of 100 mg or less, the average weight gain was 2.2 pounds after 12 months. While this was not a controlled trial, this amount of weight gain is lower than what's usually reported for quetiapine at antipsychotic doses. But even at low doses, you should monitor weight and lipids periodically.

Clonidine. Clonidine (Catapres) is an alpha-2 agonist that was initially used for hypertension. Over time, it has become clear that it's also helpful for hyperarousal states, such as ADHD, opioid withdrawal, anxiety, and insomnia. Clonidine is a favorite of child psychiatrists treating insomnia in children, but it likely works as well for adults. Start most patients on 0.1 mg at bedtime, and increase as needed up to about 0.4 mg. Since it relaxes blood vessels, it can cause lightheadedness, which you should warn patients about (though this is rarely a problem for patients taking it at bedtime). Another issue to watch out for is rebound hypertension after suddenly stopping the medication. Be sure to taper the dose gradually when discontinuing clonidine in patients who use it chronically.

CATR VERDICT: There are plenty of non-addictive hypnotics for your patients with SUDs. Just go down the list and you'll find something that works. If you don't, it's probably because your patient is trying to wear you down until you unleash the "good stuff"!