Treatment of Insomnia in Anxiety Disorders

January 05, 2012 | Sleep Disorders [1], Anxiety [2], ADHD [3], Comorbidity In Psychiatry [4], Generalized Anxiety [5], Major Depressive Disorder [6], Addiction [7], Alcohol Abuse [8]
By Gregory M. Asnis, MD [9], Elishka Caneva, MD [10], and Margaret A. Henderson, MD [11]

How often do insomnia and anxiety disorders coexist? And how best to treat patients with comorbid insomnia and anxiety? Answers here.

Insomnia is highly prevalent in psychiatric disorders, and it has significant implications. This review focuses on insomnia in the context of anxiety disorders. The prevalence of comorbid insomnia in anxiety disorders is addressed and the clinical implications associated with insomnia are discussed as well as when and how to treat this important comorbidity. Just how specifically insomnia relates to and possibly affects anxiety disorders is highlighted by the fact that insomnia is one of the defining criteria in a number of the DSM-IV-TR anxiety disorders. For example, difficulty in falling or staying asleep is a criterion for PTSD, acute stress disorder, and generalized anxiety disorder (GAD). The relationship of insomnia to anxiety disorders is also influenced by comorbid major depression. The severity of insomnia is increased when an anxiety disorder is comorbid with a major depressive disorder (MDD). This is highly relevant because 58% of MDD patients have a lifetime anxiety disorder. The presence of insomnia has a deleterious effect on daytime functioning and negative effects on quality of life, including social and work relationships. Also, there is clear evidence that the presence of insomnia in anxiety disorders is associated with increased morbidity. For example, in patients with PTSD, insomnia is associated with an increased likelihood of suicidal behavior, depression, and substance abuse as well as nonresponsiveness to treatment. In addition, insomnia as an early symptom in traumatized patients increases the risk of the development of PTSD 1 year later.

Early assessment

It is important to carefully assess for insomnia early in the evaluation of patients with anxiety disorders and to aggressively treat this complicating comorbidity. Insomnia is an underrecognized and undertreated problem. Patients rarely report their symptoms of insomnia spontaneously to their doctor. Adding to the problem of detecting insomnia is the finding that doctors rarely inquire about insomnia in their patients. Thus, a carefully taken history is an important first step in the assessment of insomnia. Self-rating sleep questionnaires and direct clinical interviews are used to obtain a history of potential sleep disorders (eg, insomnia). A number of well-validated sleep questionnaires have been widely used. The most widely used and validated questionnaire is the 19-question Pittsburg Sleep Quality...
Index. The questions cover sleep quality, sleep problems, sleep medications, and so on, within the past month. Another widely used questionnaire is the Leeds Sleep Evaluation Questionnaire (LSEQ). The LSEQ consists of 10 self-rating questions that cover sleep and aberrant sleep behaviors.

Besides self-rating questionnaires that depend on memory of sleep disturbances, a sleep log or diary can confirm questionable sleep disturbances prospectively. The use of a sleep log allows for an analysis of day-to-day sleep patterns, such as the time that the patient went to bed, sleep latency, and nighttime awakenings. The log is filled out by the patient shortly after awakening in the morning (see Morin for an example of a sleep log). If at all possible, monitoring for up to 2 weeks is highly recommended because it allows for sleep abnormalities that might show marked day-to-day variability and would more likely be detected by extensive monitoring.

What is already known about insomnia in patients with anxiety disorder?

Anxiety disorders frequently coexist with insomnia. The latter is believed to be part and parcel of various anxiety disorders and is one of the defining criteria of a number of them.

What new information does this article provide?

Our article clarifies new approaches to considering insomnia in anxiety disorders. The presence of insomnia should be considered a comorbid illness and treated on its own. Pharmacotherapy, cognitive-behavioral therapy, and a combination of both are discussed. Insomnia is an added pathology that brings increased morbidity to patients with anxiety disorders. Our review suggests that successful treatment of insomnia actually increases the responsiveness of anxiety disorders to many antianxiety treatments.

What are the implications for psychiatric practice?

When evaluating patients with anxiety disorders, psychiatrists should carefully evaluate for the presence of insomnia. Patients infrequently bring up this symptom on their own. If insomnia is present, aggressive treatment early in the course of therapy is highly suggested.

If the presence of insomnia is suspected, interviewing a spouse, a significant other, or a caregiver is helpful. Some patients who believe they have insomnia symptoms appear to have “sleep state misperception,” where their partners clearly state that their sleep is normal. These “others” can also report problems that are likely not obvious to the patient:

• Apnea spells or excessive snoring as seen in obstructive apnea
• Excessive body movements as seen in periodic leg movement disorder and restless legs syndrome
• Various sleep-related behaviors (sometimes violent and aggressive) as seen in rapid eye movement behavior disorder (RBD)
• Sleepwalking

Referral to a sleep specialist and sleep polysomnography has been recommended if pharmacological or nonpharmacological options are not working. Referral is also warranted for patients with insomnia in whom a specific sleep disorder, such as obstructive sleep apnea, periodic limb movements, narcolepsy, or RBD, is suspected. Even when a visit to a sleep laboratory is suggested, the cost of an overnight visit is often prohibitive—more than $1000 per night; usually 2 nights are required with the first being an adaptation night for the patient. Insurance frequently does not cover these costs. If it is found that the patient has sleep apnea, a sleep movement disorder, RBD, or a number of other sleep disorders, specific nonhypnotic treatments may be required (eg, continuous positive airway pressure for sleep apnea is the treatment of choice).

Before beginning treatment of anxiety disorder-associated insomnia symptoms, rule out any
concurrent medical illness, medication treatment, or substance use that might be inducing or worsening insomnia. Many medical illnesses, such as cardiovascular disorders (eg, congestive heart failure), pulmonary disorders (eg, emphysema), endocrinopathies (eg, thyroid disorders), GI disorders (eg, acid reflux), and neurological disorders (eg, pain syndromes), are associated with insomnia.  

Carefully assess the use of medications for medical and psychiatric disorders that may be implicated in insomnia as well as caffeine or alcohol use. Even small amounts of the latter have been associated with increased nighttime awakenings. One should be highly suspicious of alcohol or substance use or abuse in patients with anxiety disorders because these are frequently comorbid.  

Various medications are associated with insomnia, including psychostimulants (eg, ephedrine found in cold medication, amphetamines used in ADHD), bronchodilators (eg, theophylline, albuterol), pain medication (eg, oxycodone), and antidepressants (eg, SSRIs).  

Before providing any significant intervention for insomnia, a careful evaluation regarding behaviors that might contribute to insomnia should be made. Daytime naps, late nighttime snacks or meals, watching television in bed, nighttime exercise, or excessive light or loudness in the bedroom should be identified and modified. Eliminating these behaviors can lead to significant sleep improvements. A 13-item self-rating questionnaire by Mastin and colleagues can help elicit sleep hygiene information. 

Pharmacological options 

The treatment of insomnia in patients with anxiety disorders is, for the most part, the same as the treatment of insomnia per se: pharmacological, nonpharmacological, or a combination of the two. The primary treatment of insomnia is pharmacological because of the rapid onset of action (eg, hypnotics are usually effective within days to 1 week of use). The most common nonpharmacotherapy, cognitive-behavioral therapy for insomnia (CBT-I) takes considerably longer.  

Currently, the FDA has 11 approved drugs for the treatment of insomnia:  

- Nonbenzodiazepines: eszopiclone, zolpidem, zolpidem ER, and zaleplon  
- Benzodiazepines: estazolam, flurazepam, quazepam, temazepam, and triazolam  
- A tricyclic antidepressant: low-dose sinequan  
- A melatonin agonist: ramelteon  

In recent years, nonbenzodiazepines have become the most recommended of the approved hypnotics. (There has been less and less reliance on benzodiazepines.) Not only are nonbenzodiazepines effective in treating insomnia (equivalent to the benzodiazepines), but there is a notion that they are safer than benzodiazepines.

Both nonbenzodiazepines and benzodiazepines are associated with adverse effects that include fatigue, dizziness, ataxia, and the development of dependence and tolerance with long-term use. Although head-to-head studies comparing these classes of hypnotics have been minimal, a recent meta-analysis supports the finding of reduced adverse effects for the nonbenzodiazepines. The nonbenzodiazepines typically have a shorter half-life and are more selective at the γ-aminobutyric acid receptor, factors that are partially responsible for less residual daytime sedation and other adverse effects.

In the treatment of anxiety disorders with comorbid insomnia, the latter should be treated concurrently with, but independently of, the anxiety disorder per se. The idea that one should wait to see whether the insomnia resolves with only the treatment of the anxiety disorder is no longer valid. Clinical experience has shown that without targeted insomnia treatment, insomnia frequently persists.

When adding a hypnotic to an antidepressant in the treatment of anxiety, the risk to benefit ratio must be considered. Pollack and colleagues looked at a large group of patients with GAD comorbid with insomnia (N = 595). The patients received either 10 mg of escitalopram coadministered with 3 mg of eszopiclone or the escitalopram with placebo. Those in the active hypnotic treatment group had a significant response in their insomnia by the first week. The combination of medications was well tolerated with no significant increase in adverse effects.

Most surprisingly, the anxiety scores for those patients who received the hypnotic significantly improved starting at week 4 even after removing insomnia symptoms from the anxiety assessment. The time to onset of the anxiolytic response was also reduced. In addition, the combination treatment led to a slightly better symptom response and remission rate for the anxiety disorder. Similar results were reported in a 12-week open-label study (N = 27) undertaken by Gross and
The researchers evaluated ramelteon (8 mg/d), a melatonin agonist, in patients who had GAD comorbid with insomnia and whose condition was partially responsive to an SSRI or a serotonin norepinephrine reuptake inhibitor. The hypnotic was well tolerated, effective for insomnia, and appeared to facilitate the treatment of GAD.

A double-blind placebo-controlled study by Fava and colleagues evaluated the efficacy and safety of zolpidem extended-release (12.5 mg/d) versus placebo in patients with comorbid GAD and insomnia who were being treated with escitalopram (10 mg/d). Sleep measures improved significantly by the end of week 1, and there was no added burden of adverse effects. Zolpidem did not show a beneficial anxiolytic effect.

Approximately 50% of patients with insomnia continue to have insomnia 3 years after initial diagnosis, and many patients require months to years of treatment. Nonbenzodiazepines for primary insomnia were found to have continued efficacy and to be well tolerated with no evidence of abuse or withdrawal symptoms on discontinuation of use after 12 months. Ramelteon was also found to be efficacious with no significant issues of abuse or tolerance in a 24-week open-label study. The literature for longer use of hypnotics is scarce.

Anxiety disorders are frequently comorbid with alcohol or substance use disorders. Consider ramelteon or low-dose sinequan to avoid potential issues of abuse and addiction. Nonbenzodiazepines are preferred over benzodiazepines; there is evidence that the former have decreased potential for abuse and a better adverse-effect profile.

In some patients with insomnia, benzodiazepines are clearly necessary. The other hypnotics may not be as effective for some patients, and the anxiolytic properties of benzodiazepines may be helpful.

When hypnotics are used (particularly, benzodiazepines and nonbenzodiazepines), their use should be reassessed—every 3 to 4 weeks. Many patients with insomnia do not experience sleep disturbances nightly. Therefore, the use of hypnotics on an as-needed basis or a few times a week helps cut down on the amount and exposure to medication.

Trazodone and mirtazapine are also widely used for insomnia, as are atypical antipsychotics and herbal preparations. Unfortunately, these agents have not been rigorously studied for insomnia and thus their effectiveness and safety remain unclear.

### Nonpharmacological interventions

CBT-I is an important, widely accepted, multimodal treatment for insomnia and the best-studied of the nonpharmacological approaches for this disorder. It is a manualized treatment that focuses on various components of CBT (ie, cognitive restructuring and the use of psychological interventions, such as the practice of good sleep hygiene, stimulus control, sleep restriction, and relaxation therapy). These methods address negative and distorted cognitions and behaviors that initiate and perpetuate insomnia. Treatment duration is relatively short. It is administered for 5 hours divided over 4 to 6 weeks and can subsequently be used as a maintenance treatment in monthly sessions. There are approximately 12 well-designed CBT-I trials that have clearly demonstrated that it is a highly effective intervention for insomnia for 1 year or longer.

Studies that compared CBT-I with pharmacotherapy found equivalent efficacy. This has led the NIH Consensus and State of the Science Statement to conclude that CBT-I is “as effective as prescription medications are for short-term treatment of chronic insomnia. Moreover, there are indications that the beneficial effects of CBT, in contrast to those produced by medications, may last well beyond the termination of active treatment.” In contrast to hypnotics, learned CBT-I skills may persist even when active treatment ends. Furthermore, some patients may prefer CBT-I over hypnotic drugs because of their possible adverse effects or because of concerns about drug interactions or taking a drug during pregnancy.

In general, CBT-I is underutilized—only about 1% of patients with chronic insomnia receive this therapy. To increase the availability of CBT, it can be administered via self-help strategies (eg, educational books and materials) and in group formats. In addition, the use of the Internet to provide CBT has been shown to be effective. Nonetheless, patients frequently prefer face-to-face contact.

Besides CBT-I, a number of other nonpharmacological therapies, such as bright light, physical exercise, acupuncture, tai chi, and yoga, have been used to treat insomnia. Unfortunately, the results have been inconsistent.

### Combination therapy

Is a combination of pharmacotherapy and nonpharmacotherapy more effective than either alone in the treatment of anxiety disorders with insomnia? Combination therapy has not been addressed in studies of this particular patient population. Furthermore, the question has been minimally
addressed even in the treatment of insomnia per se. Study findings suggest only modest differences in outcomes with a combination of therapies. Similar results were seen in a study that compared CBT with CBT plus zolpidem. The 6-week acute study demonstrated a 60% response rate and a 40% remission rate; the group with the combination treatment did have a significant increase in sleep time of 15 minutes, but the researchers question the clinical significance of this isolated finding.\textsuperscript{29}

**Summary**

Anxiety disorders with comorbid insomnia are highly prevalent with potential negative consequences. Therefore, assess for insomnia with self-rating scales and careful clinical interviews. When appropriate, refer patients for polysomnography.

Insomnia should be treated aggressively with pharmacotherapy, nonpharmacotherapy (particularly CBT-I), or a combination. Some of the hypnotic treatments actually appear to facilitate successful therapy for the anxiety disorder.

Benzodiazepines and nonbenzodiazepines have a number of adverse effects and can lead to abuse and dependence. Patients with an anxiety disorder may be particularly vulnerable, especially those with a history of alcohol and drug abuse. Treatment with benzodiazepine and nonbenzodiazepine hypnotics needs to be reassessed monthly. Alternatively, ramelteon, low-dose sinequan, and CBT-I should be considered because they have minimal adverse effects and no risk of abuse.

Successful treatment of insomnia is an important goal in patients with anxiety disorders. Both pharmacological and nonpharmacological interventions have response rates of approximately 60%.

**References:**


Source URL: http://www.psychiatrictimes.com/sleep-disorders/treatment-insomnia-anxiety-disorders

Links: