PRACTICAL PSYCHOPHARMACOLOGY

Sleeping Problems in Mood, Anxiety Disorders

Make sure that primary antidepressant prescribed does not aggravate patient's sleep problems.

BY CARL SHERMAN
Contributing Writer

Nearly every psychiatric disorder has sleep disturbance as a potential symptom.

Sleep should be an object of inquiry in the initial assessment. Asking the patient about sleep is "a useful way to build rapport: Most people are quite concerned and feel comfortable talking about sleep, and the interview can then move on to other factors," said Dr. Lois Krahn, a certified sleep specialist and chair of adult psychiatry at the Mayo Clinic in Scottsdale, Ariz. The prospect of relieving sleeplessness can overcome ambivalence about treatment.

Nonpharmacologic approaches should be primary. These include basic sleep hygiene and, when available, cognitive-behavioral therapy. "[CBT is] extraordinarily effective in insomnia, and has been shown to prolong the effectiveness of hypnotics when they are used," observed Dr. Karl Doghramji, professor of psychiatry at Jefferson Medical College and director of the sleep disorders center at Thomas Jefferson University Hospital, Philadelphia.

Troubled sleep is a core symptom of depression, and although hypersomnia can occur, insomnia is far more common. Opinions differ, however, as to how aggressively to treat it directly. Unless insomnia is a major source of distress and impairs the patient's ability to function, Dr. Doghramji addresses the mood disorder first, and will consider further steps if sleep hasn't improved 4-6 weeks later.

Dr. David Neubauer, associate director of the Johns Hopkins Sleep Disorders Center in Baltimore, believes that because sleep problems can exacerbate mood disorders, "it is critical to work with patients to make sure they get adequate sleep, and to take drastic steps when necessary to achieve it."

There appears to be consensus on the need to treat sleep and mood disturbances separately, rather than seeking a single drug for both. "Otherwise, you make compromises on both ends," Dr. Neubauer said. "If you're locked into using a sedating antidepressant, you may not have chosen the best medicine for mood, and you won't have optimal sleep management."

Nor does he favor adding a low-dose sedating antidepressant at bedtime. Hypnotics are more reliable and less likely to cause daytime sedation. Orthostatic hypotension can be problematic with trazodone (Desyrel), which is commonly prescribed for this purpose, and serotonin syndrome is a danger if the primary antidepressant is a serotonin reuptake inhibitor, he said.

In choosing a primary antidepressant, "first do no harm" is the operative principle. "You don't want to aggravate sleep problems," Dr. Krahn said. Although she is disinclined to use agents that may cause insomnia, "there's none I'd absolutely avoid. Even bupropion may be used thoughtfully to provide stimulation for a patient who has daytime fatigue, although a hypnotic may be needed as well to address coexisting sleep quality issues."

Sleep problems can exacerbate mood disorders, which means 'it is critical to work with patients to make sure they get adequate sleep, and to take drastic steps when necessary to achieve it.'

There is an increasing number of hypnotics—eszopiclone (Lunesta), ramelteon (Rozerem), and zolpidem extended release (Ambien CR) were added last year—to choose from, but none has been approved specifically for insomnia of any psychiatric disorder, Dr. Doghramji said.

He generally chooses a nonbenzodiazepine benzodiazepine receptor agonist (BzRA), based on duration of action. "If the patient is having difficulty in the middle or the end of the night, something like eszopiclone or Ambien CR may be well suited," he pointed out. For initial insomnia—or if the patient awakens some nights but not others—the short half-life of zaleplon (Sonata) makes it a good choice.

The melatonin receptor agonist ramelteon represents a real departure from other hypnotics. It may be appropriate for patients with a history of drug abuse, or when the risk of overdose is a concern, or if there is worry about depressing respiratory drive, such as in a patient with chronic obstructive pulmonary disease, Dr. Doghramji said.

Although the usual caveat about using hypnotics beyond 7-10 days is absent from the labeling of all three newer drugs (and the older BzRAs apparently pose little risk of habituation), clinicians wishing to base practice on clinical trial data might note that only eszopiclone has actually been studied out to 6 months, Dr. Krahn observed.

In depressed patients with hypersomnia, modafinil (Provigil) or a psychostimulant may be useful, although not specifically indicated for this purpose, after causes like narcolepsy and sleep apnea syndrome have been addressed, she said.

Sleep and wakefulness problems are common residual symptoms when depression has otherwise remitted. Before treating these patients symptomatically with modafinil or a hypnotic, consider whether the depression itself has been undermanaged. "I see many depressives whose insomnia or fatigue resolves when the antidepressant dosage is raised," Dr. Doghramji said.

The association between anxiety disorders and insomnia is also strong. "These patients are often hyperaroused and hypervigilant, and they have considerable muscle tension. They don't fall asleep readily," Dr. Krahn said.

As with depression, treatment of the psychiatric disorder is often sufficient. If not, "I'll quite readily use a hypnotic," she said. More often than with depression, a benzodiazepine is useful. "I like short-term temazepam (Restoril) for sleep, and if an anxiolytic effect is needed both day and night, I'll think about clonazepam" for short-term treatment, Dr. Krahn said. For the long term, she would use clonazepam (Klonopin) with an SSRI.

Virtually nothing is known about ramelteon in the context of anxiety, and the lack of familiarity with this novel drug makes it more difficult to reassure a patient who is anxious about adverse effects than it would be if a BzRA were used, she said.

Bipolar disorder "is interesting from a sleep standpoint," she noted. A patient whose sleeping difficulty is cyclical may have other symptoms suggesting bipolarity, such as mood swings, which they might have been less willing to talk about. In identified bipolar patients, it is crucial to address sleep problems because they often herald—or can trigger—a manic episode.

This is one situation in which "I may strive to treat with a single agent," Dr. Krahn said, suggesting that a sedating atypical antipsychotic like quetiapine (Seroquel) might help both mood and sleep.

In other patients, particularly those with substantial anxiety, a low-dose atypical may be useful when first-line agents have been ineffective, Dr. Neubauer said. He may start with 25-50 mg of quetiapine at bedtime and move up, if necessary, to 100-200 mg.

Referral to a sleep specialist is indicated when a condition such as sleep apnea, periodic limb movements, or sleep-phase disorder may be involved. Physicians should be particularly alert for sleep apnea in heavier patients (including those who have gained weight on medication) and postmenopausal women.

Restless leg syndrome is surprisingly prevalent, particularly in older patients. "Ask if they have creepy crawly sensations in their legs," Dr. Krahn said.

Early morning awakening, which is conventionally associated with depression, can also signal sleep apnea, she said.

So can excessive daytime sleepiness, Dr. Neubauer observed.

When a comorbidity is "not readily explained by sleep deprivation or sedating medication, it makes a lot of sense to do a sleep study," he said. ■

Hallucinations Are Not 'Benign' in Parkinson's Disease

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — So-called benign hallucinations associated with dopaminergic treatment for Parkinson's disease rarely remain "benign," calling into question the accuracy of the term.

Researchers at Rush University in Chicago studied the clinical progression of 48 patients with Parkinson's disease who were diagnosed with hallucinations characterized by the patient's retention of the insight that the hallucinations are unreal. These hallucinations have been called benign, and traditionally have been associated with a Unified Parkinson Disease Rating Scale (UPDRS) Thought Disorder score of 2.

In 2 years, just 2 of the 48 patients at Rush continued to have benign hallucinations without requiring either a decrease in their dose of dopaminergic medications or an addition of neuroleptic agents to counteract the hallucinations or progressing to more serious hallucinations with loss of insight (UPDRS Thought Disorder score of 3) or delusions (UPDRS Thought Disorder score of 4).

Most, 39 of 48, progressed to scores of 3 or 4. Among nine patients who remained at a score of 2, seven required reduced dosages of dopaminergic medications in response to worsening of hallucinations and three also required neuroleptics to control the hallucinations.

Although the median time to progression of hallucinations to the point where patients were frankly delusional was less than 2 years after the onset of the study, the total length of time patients had hallucinations prior to enrollment was uncertain, noted Dr. Christopher G. Goetz, director of the Rush movement disorders center, in a poster presentation at the annual meeting of the American Neurological Association.

However, the study made clear the fact that even if hallucinations seem "benign … at the moment," they "portend serious consequences" and should not be given a label that suggests they are unimportant clinical developments, he said.

"Because hallucinations progress, the concept of benign hallucinations is prognostically misleading," Dr. Goetz and associates concluded. "The term benign hallucinations should be considered generally unsound and dropped from the operative vocabulary." ■

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