Questions and Answers

The Role of Pharmacotherapy in the Clinical Management of Insomnia

In the Questions and Answers section of this PSYCHIATRY IN BRIEF, the chair, William M. Glazer, M.D., and the faculty, Paul P. Doghramji, M.D., and Milton K. Erman, M.D., first discuss a case that Dr. Doghramji presents and then answer questions that participants in the live telecast of their meeting submitted to them via telephone or e-mail.

Dr. Glazer: Dr. Doghramji, please describe a typical insomnia case from your practice.

Dr. Doghramji: A 50-year-old man came into my office primarily for acute sinusitis. As I was finishing my examination, he said, "Doctor, what are you going to do about my sleep problems?" I started to delve into it, even though I did not have much time left with him. Nonetheless, I was able to ascertain that he was having trouble getting to sleep, but especially staying asleep. He smoked 2 to 3 packs of cigarettes daily, and he had recently stopped drinking alcohol. He was diagnosed with generalized anxiety disorder (GAD) in his 20s, but he had quit taking his medication several years earlier due to side effects. His wife was with him, and she said that he was snoring a lot lately, which was common when his sinuses were bothering him. He had used over-the-counter nose spray for his sinus trouble in the past but had stopped the sprays recently.

Dr. Glazer: Dr. Erman, what are the issues you see related to this case?

Dr. Erman: This is a great example because there are a tremendous number of elements that are contributing to the insomnia. Here is a fellow who snores—might he have sleep apnea? The cigarette smoking—when he gets up at night, is he having a cigarette when he wakes up, and is the nicotine addiction waking him? We need to ask about these issues and be open to thinking about all the potential causes that may be there.

Dr. Doghramji: So many things could be causing insomnia, and I had very little time to fully explore his problems.

Dr. Erman: In the time you had, you elicited the fact that the patient had GAD. That certainly could be a contributing factor—as well as the sinus problems, the acute medical condition. Pain and discomfort disrupt sleep and can lead to insomnia.

Dr. Glazer: In medicine, diagnosis is rarely straightforward. With all these different possible reasons for insomnia that have been mentioned, we are going to select one of them as the critical issue. The live-telecast participants will vote on 1 of 4 options presented to them and then the faculty will discuss the results. So the question is, what is the critical issue for this patient in this case?

The majority of live-telecast participants—65%—chose "insomnia caused by GAD," and 22% of participants said "insomnia making GAD worse." Eighteen percent chose "sinus condition causing insomnia." Finally, 5% chose "OTC medications causing insomnia." Gentlemen, what do you think? Do you agree with the principal answer?

Dr. Doghramji: It does not surprise me to see these results, because this patient's main problem did turn out to be GAD. Do you agree, Dr. Erman?

Dr. Erman: I do. What we need to emphasize now is the concept of comorbidity, that illness is not always simple cause and effect. It is true, the probable primary cause here was the GAD. But beyond that, the insomnia was probably making the GAD worse.

Dr. Doghramji: At the first visit, the patient and I discussed the fact that we had to resolve his sinus infection. I also gave him a sleep diary to use and then come back and talk with me about how he was doing so that we could have more details about his sleep and how he was feeling the next day.

Once his sinus infection improved, it became clearer that his GAD was the factor contributing most to the insomnia. I ended up treating him for his GAD at the same time as his insomnia, and he has done very well.

Dr. Glazer: Did you treat the insomnia and GAD with one medication, or use separate agents?

Dr. Doghramji: His main medicine for GAD turned out to be venlafaxine. But along with that, I did prescribe a medication for sleep, and he has continued to take that since then.

Dr. Erman: Another point to emphasize is that these are long-term problems. We are talking about an accrual

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of symptoms that takes time to build up. We have to follow them over time, work on sleep hygiene, and help patients get better over time.

Dr. Glazer: Dr. Doghramji, what did you think about this patient's sleep disorder? What conceptual thinking did you do, given the short amount of time that you had to treat him in a visit?

Dr. Doghramji: Remember that this patient was having some trouble getting to sleep, but he was also frequently waking up in the middle of the night, with difficulty falling asleep again. That was his most pressing insomnia symptom. And so, what I really needed was something that was effective for sleep maintenance. And that was one of the main aspects of the medications that I considered when I chose a medication for his sleep.

Dr. Glazer: We will now take questions from the audience.

Participant: Is ramelteon indicated for short-term use or is it indicated only for long-term use?

Dr. Doghramji: Ramelteon is indicated for sleep initiation insomnia—that is, to help people get to sleep. A 1-year open-label study *[DeMicco M, et al. Sleep 2006;29(suppl):A234 and Richardson G, et al. Sleep 2006;29(suppl):A233]* has been conducted on ramelteon that suggests that it can be used for either short-term insomnia or long-term insomnia. The indication for ramelteon does not limit it to short-term use.

Dr. Erman: The newer insomnia medications can be used for short-term treatment, but there is not the restriction to short-term use that has accompanied sleep medications in the past.

Participant: I am treating a 52-year-old woman with chronic insomnia and restless legs syndrome. Currently, I treat both problems with zolpidem. I was wondering about trying ropinirole but have some concerns about the side effects. Would you try ropinirole and stop zolpidem, try them together, or continue treating with zolpidem alone?

Dr. Doghramji: The first thing I would do is to make sure that the restless legs syndrome is not secondary to another disorder. It is very important to try to identify primary causes, possibly iron deficiency, diabetes, or even neuropathy, when restless legs syndrome is present.

Dr. Erman: I agree. The next question is, how well is the current medication working? I have to assume, based on the question, that treatment with zolpidem is not fully covering the symptoms. Ropinirole is the first agent that is approved by the U.S. Food and Drug Administration for the treatment of restless legs syndrome, and so it would certainly be an option. The side effects that are associated with it are a source of concern. Ropinirole is a dopamine agonist, so the physician should watch for exacerbation of psychosis, anxiety disorders, and bad dreams. However, the dosage for restless legs syndrome is fairly low compared to that ordinarily used for the treatment of Parkinson's disease, so the side effect profile tends to be fairly benign. It is best to start with treatment at a low dose, escalate, and see if there is symptomatic relief. Many patients who have had long-standing insomnia problems related to restless legs syndrome with periodic limb movements in their sleep get relief with dopamine agonist compounds.

Participant: I practice general psychiatry, mainly geriatric. What would you recommend instead of trazodone for Alzheimer's patients who stay awake in the night at nursing homes with severe agitation?

Dr. Doghramji: I see a lot of patients in nursing homes, and it is a difficult question, because on the one hand, you want to help patients get to sleep and stay asleep at night, yet you do not want to give elderly patients something that will cause them to fall if they need to get up in the middle of the night. What I have done in many nursing homes is to first address the condition that is causing the insomnia. I consult with my psychiatry colleagues, and they have been using atypical antipsychotics to treat the patients' psychosis, which sometimes helps them get to sleep. This is off-label use, and there are cautions to be regarded with usage of these medications in the elderly. Other times, we also still have to use the benzodiazepine receptor agonists, which I do not have much of a problem doing when I know the patient will not be getting up in the middle of the night. What do you think, Dr. Erman?

Dr. Erman: I agree. A study *[Avidan AY, et al. J Am Geriatric Soc 2005;53:955–962]* looked at the factors that contribute to falls in nursing homes. The single greatest contributor was insomnia. If you do not get up in the middle of the night, you are not likely to fall. We do not want the orthostasis that occurs sometimes with trazodone.

Dr. Glazer: We were hoping that atypical antipsychotics might be helpful, but with the black box warnings that they have now, there are many concerns about giving them to an older population.

Dr. Erman: If we have the capacity to improve the patients' cognition, we should, but if not, we should treat the insomnia. We may have been overly concerned about some of the safety issues with benzodiazepine receptor agonists. The newer benzodiazepine receptor agonists are safe and effective in promoting sleep.

We should also work with the patients' situations in the nursing homes and make sure that they are getting to sleep at reasonable hours, which means not going to bed at 8:00 p.m. and waking up at 4:00 a.m. Physicians and caregivers need to consider circadian rhythm issues as well.

Participant: My question is about the expense of the newer agents for insomnia, such as the nonbenzodiazepines. If patients do not have insurance plans, what medication would you suggest in order for them to get

a good night's sleep—maybe the older, generic benzodiazepines?

Dr. Doghramji: This is a common problem. A lot of our patients are struggling with choosing the best medication for themselves versus the most affordable one. I am a major advocate in my state to make sure that patients get the best medication. Anything that I can do to help patients get the best medicine I will do, whether it is using prior authorization forms for their insurance companies, giving them samples, or getting medications directly from the pharmaceutical company because they are indigent. I have one person in my office in charge of getting patients the right medications. Especially in the field of insomnia, it is important to have the patient get the best treatment, because we are finding out that treatment of insomnia is very important to the overall health of the patient.

Dr. Erman: What about the use of some of the older compounds that may be generic? These are not necessarily bad drugs—drugs like triazolam, which is a very potent drug with a short half-life, or a drug like temazepam, with an intermediate half-life and a long duration of action. However, we also have to think about the context. Some people do not have a problem with buying a $3.50 latte every morning, but spending $3 for a sleeping pill out of pocket bothers them. I agree these are often somewhat expensive medications, particularly for people who do not have drug plans, but we also have to look at what the benefit is and how people feel and function the next day. Compared with older sleep medications, the newer medications are safer and as effective.

Participant: I have a question with regard to using pregabalin, gabapentin, and tiagabine for insomnia. These medications are slow-wave sleep inducers, and they cause growth hormone release, but do they have a role in the treatment of severe insomnia in patients for whom no other treatment has been effective?

Dr. Erman: I think these agents have potential. They are currently being investigated as primary sleep-promoting agents, and preliminary research suggests that they may benefit some patients. There is interest in looking at compounds that promote slow-wave sleep. These medications do not have the same flexibility across the board as other medications for insomnia, but they may be more appropriate for patients with severe insomnia. Patients with less severe insomnia often have problems with residual sedation when taking these agents, so physicians need to be careful when prescribing these medications.

Dr. Doghramji: Patients will come to me with severe insomnia that has been going on for a long time and is really resistant. I have to take my time with these patients. Often, in the initial phase of treatment, I see them every week or every other week, with telephone calls between visits. In some cases, patients may need 2 forms of treatment, one usually of the type that we are discussing, as well as cognitive-behavioral therapy, to help them get through the difficult times.

Participant: What is your insight into children with insomnia?

Dr. Doghramji: The whole field of pediatric insomnia is wide open. One of the drug companies is just now starting a clinical trial with insomnia in adolescents. Treating insomnia in children and adolescents is difficult, and all medication that has been used has been off-label, so it has been done by intuition and our best guess.

Dr. Erman: The pharmaceutical companies may have held back from performing more research with children because they did not want to be perceived as pushing these medications on children. We want to use the behavioral treatments that are available—sleep hygiene education, cognitive-behavioral therapy, and exploring the child's family situation. But, what I hear from psychiatrists who work with children and adolescents is that children may have sleep problems as a primary disorder. The medications available now are safe and effective in adults, and we can extrapolate about their use in children. I prefer these newer agents to the older compounds that are sedating and possibly risky.

Dr. Glazer: Is there any epidemiology research on this? Do we have any idea how common sleep disorder in children is?

Dr. Doghramji: Insomnia is distressing to parents. The parents of at least half of child patients with insomnia know about it and want to do something about it, but they do not know what to do. Their physicians are often not sure what to do, either. Along with the insomnia, one thing we need to address is any comorbid disorders—to know what exactly is going on with the patient.

Participant: What is the role of modafinil in the treatment of insomnia?

Dr. Doghramji: Modafinil is an alerting agent but is not a classic stimulant—it does not cause widespread energizing of the brain. It works by turning on the alertness centers. It has proved useful for the treatment of narcolepsy, residual daytime sleepiness in treated sleep apnea, and shift work sleep disorder. It is a class IV scheduled agent, with limited restrictions on its use. It has been an important addition to our medical armamentarium.

Dr. Glazer: Those were great questions and answers. Please give us a summary to conclude this discussion.

Dr. Erman: We have learned a lot about insomnia in recent years. In a recent NIH report on insomnia *[Buscemi et al. Agency for Healthcare Research and Quality, Publication 05-E021. (http://www.ahrq.gov/clinic/epcsums/insomnsum.htm)]*, chronic insomnia was recognized as a significant problem that does not just affect patients in the short term. There is evidence that cognitive-behavioral therapy and the benzodiazepine receptor agonists are effective in the treatment of insomnia. The most important point that was made in the NIH Con-

ference Statement on insomnia *[http://consensus.nih.gov/2005/2005InsomniaSOS026html.htm]* was that we need to address this disorder with more education for physicians.

Dr. Doghramji: Physicians need to know more about insomnia because it is highly prevalent, but patients often do not report insomnia to their physicians. It is up to us as physicians to identify patients with insomnia even when they do not talk about it. We have many effective ways of identifying and treating this problem.

Drug names: gabapentin (Neurontin and others), modafinil (Provigil), pregabalin (Lyrica), ramelteon (Rozerem), ropinirole (Requip), temazepam (Restoril and others), tiagabine (Gabitril), trazodone (Desyrel and others), triazolam (Halcion and others), venlafaxine (Effexor), zolpidem (Ambien).

Disclosure of off-label usage: The meeting chair has determined that, to the best of his knowledge, gabapentin, modafinil, pregabalin, tiagabine, and trazodone are not approved for the treatment of insomnia; and zolpidem is not approved for the treatment of restless legs syndrome. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.