A Case Report of Zolpidem-Induced Somnambulism

Sir: The physiology of sleep, memory, awareness, and arousal can be influenced by different drugs.[1] Zolpidem tartrate is a nonbenzodiazepine hypnotic agent of the imidazopyridine group with a rapid onset and short duration of action. Its side effect profile is milder than those of benzodiazepines and barbiturates used for treating insomnia.[2] To our knowledge, there are 5 published articles[3–7] related to zolpidem-induced somnambulism. Somnambulism, or sleepwalking, could be dangerous due to the possibility of accidental injury. Here, we present a case of somnambulism associated with zolpidem use.

Case report. Mr. A, a 19-year-old white man, had a history of and current diagnoses of DSM-IV schizoaffective disorder and impulse-control disorder. The patient lived with his parents and a younger brother. He worked as a volunteer at a university hospital and had received a general equivalency diploma. Mr. A had no current or past history of substance abuse and did not smoke or drink alcohol. His medical history was unremarkable. The patient had a history of 2 psychiatric hospitalizations for worsening of his symptoms. He had no personal or family history of sleepwalking.

In the past, olanzapine and paroxetine had been tried without successful results. Mr. A was stable on his medications, which included aripiprazole 15 mg once per day, venlafaxine extended release 150 mg once per day, and quetiapine 50 mg once per day. He received no other medications, including herbal supplements.

During the course of his treatment, Mr. A began complaining of insomnia, for which brief zolpidem treatment was prescribed. He was started on treatment with zolpidem 10 mg orally at bedtime on an as-needed basis for insomnia. Within a few days of the initiation of zolpidem treatment, the patient's family noticed the patient waking up in the middle of night and walking into their room with a staring expression and some incoherent speech. The patient had no memory of this event in the morning. This sleepwalking episode was attributed to zolpidem, as no medication change was made besides initiating zolpidem and the patient had no history of such episodes in the past. Zolpidem treatment was stopped, and since then, no complaints of sleepwalking have been reported.

Somnambulism, or sleepwalking, generally occurs during stages 3 and 4 of slow-wave sleep.[8] During an episode of somnambulism, the normal arousal mechanism is altered, which results in partial arousal without full consciousness.[9] Electroencephalographic changes associated with the use of zolpidem include suppression of REM sleep.[10] It has been suggested that some drugs produce a physiologic state during slow-wave sleep that can present clinically as somnambulism.[8] A definitive diagnosis of somnambulism usually requires all-night sleep recordings,[8] which were not performed on our patient. We suggest that when seeking an etiology of somnambulism in a patient, a careful review of the patient's current medications should be performed.

The authors report no financial affiliation or other relationship relevant to the subject matter of this letter.

REFERENCES

1. Huapaya LV. Seven cases of somnambulism induced by drugs. Am J Psychiatry 1979;136:985–986
2. Toner LC, Tsambiras BM, Catalano G, et al. Central nervous system side effects associated with zolpidem treatment. Clin Neuropharmacol 2000;23:54–58
3. Yanes Baonza M, Farrer Garcia-Borras JM, Cabrera Majada A, et al. Sleep-walking linked to zolpidem [letter] [in Spanish]. Aten Primaria 2003;32:438
4. Sattar SP, Ramaswamy S, Bhatia SC, et al. Somnambulism due to probable interaction of valproic acid and zolpidem. Ann Pharmacother 2003;37:1429–1433
5. Harazin J, Berigan TR. Zolpidem tartrate and somnambulism. Mil Med 1999;164:669–670
6. Iruela LM. Zolpidem and sleepwalking [letter]. J Clin Psychopharmacol 1995;15:223
7. Mendelson WB. Sleepwalking associated with zolpidem [letter]. J Clin Psychopharmacol 1994;14:150
8. Charney DS, Kales A, Soldatos CR, et al. Somnambulistic-like episodes secondary to combined lithium-neuroleptic treatment. Br J Psychiatry 1979;135:418–424
9. Kawashima T, Yamada S. Paroxetine-induced somnambulism [letter]. J Clin Psychiatry 2003;64:483
10. Feinberg I, Maloney T, Campbell IG. Effects of hypnotics on the sleep EEG of healthy young adults: new data and psychopharmacologic implications. J Psychiatr Res 2000;34:423–438

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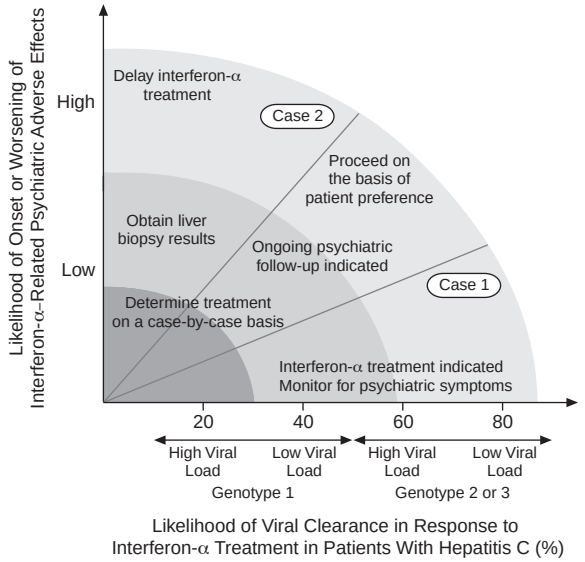
Interferon-α Treatment of Hepatitis C Patients With Psychiatric Illness: Evidence-Based Risk-Benefit Assessment

Sir: The clinical management of individuals with comorbid chronic hepatitis C virus (HCV) infection and psychiatric illness is a substantial public health problem.[1] At least 50% of patients with HCV suffer from at least 1 psychiatric illness.[2,3] Furthermore, the prevalence of HCV in patients with psychiatric illness (10%–20%)[1] is 5 to 10 times that in the general U.S. population (2%). Recent advances in the treatment of HCV and the introduction of interferon-α–based therapies in combination with ribavirin have resulted in viral clearance (complete eradication of HCV; absent HCV viral load 6 months after HCV treatment is completed) rates of 50% to 59% of patients with HCV genotype 1 (70% of the U.S. HCV-infected population) and 80% to 90% of patients with HCV genotypes 2 and 3 (20%–30% of the U.S. HCV-infected population).[4,5] These viral clearance rates, however, may not be applicable to the HCV-infected population with comorbid psychiatric illness, since most large HCV treatment trials[4,5] have excluded patients with any history of psychiatric or substance use disorders. The practice of excluding patients with HCV and psychiatric illness from interferon-α treatment is stigmatizing and will result in substantial morbidity and mortality for a vulnerable population no less deserving of treatment than HCV patients without psychiatric illness.

Recently, gastroenterologists have started evaluating patients with HCV and comorbid psychiatric illness and

Figure 1. Risk-Benefit Model for Interferon-α Treatment of Hepatitis C Patients Integrating the Risks of Neuropsychiatric Adverse Events and the Likelihood of Viral Clearance



making a risk-benefit assessment for interferon-α treatment. Fearing the precipitation or worsening of preexisting psychiatric illness with interferon-α treatment, gastroenterologists call upon consultant psychiatrists to assist in making a risk assessment regarding the probability of interferon-α–induced neuropsychiatric adverse effects. Several risk factors are thought to increase the probability of interferon-α–emergent neuropsychiatric adverse effects[6]: a history of any psychiatric illness, a history of substance abuse, a family history of psychiatric illness, and a history of suicidal ideation. The ability to predict the variable interferon-α–induced neuropsychiatric adverse effects, however, remains modest at best due to the lack of systematic large-scale data and the exclusion of patients with psychiatric illness from HCV clinical trials.[7] In contrast to the variable influence of these psychiatric risk factors, the decreased likelihood of viral clearance in response to interferon-α is associated with several well-established predictive and additive factors including male gender, African American race, increased body mass index, advanced age (> 40 years), higher HCV viral load, coinfection with human immunodeficiency virus, and HCV genotype 1.[8]

I propose a comprehensive clinical risk-benefit model (Figure 1) integrating factors pertaining to the likelihood of viral clearance in response to interferon-α and the probable risk of interferon-α–induced neuropsychiatric adverse effects.

A 35-year-old slender white woman with no history of psychiatric illness who is infected with a low HCV viral load of either genotype 2 or 3 would be a candidate for interferon-α treatment (represented by case 1 in Figure 1). In the case of a 50-year-old obese African American man with a history of psychosis and a substance use disorder who is infected with a high viral load of HCV genotype 1 (represented by case 2 in Figure 1), interferon-α should be delayed in the absence of advancing cirrhosis. While these 2 cases present clinical scenarios at the opposite ends of the risk-benefit spectrum, the risk-benefit profile in the majority of patients with HCV and psychiatric comorbidities is in an intermediate zone. Prophylactic treatment with psychotropics might be offered if the woman in case 1 had a history of major depressive disorder and was infected with a low viral load of HCV genotype 1. Biopsy-demonstrated cirrhosis might be a compelling reason to attempt interferon-α treatment in case 2. Ongoing psychiatric follow-up is certainly indicated when a patient has 1 or more of the psychiatric risk factors listed above. In cases in which a low estimated likelihood of viral clearance of HCV is combined with an intermediate to low probability of psychiatric adverse effects, an evaluation incorporating the patient's interferon-α treatment preference and available psychosocial support can influence the treatment decision.

Use of an evidence-based approach in selecting patients for interferon-α treatment is paramount when endeavoring to treat patients with HCV and comorbid psychiatric illness in order to minimize the morbidity and mortality associated with interferon-α (i.e., suicide). This model is intended to assist clinicians in making an individualized and balanced risk-benefit analysis incorporating HCV–disease specific factors as well the potential for psychiatric complications prior to offering interferon-α treatment.

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REFERENCES

1. Rosenberg SD, Swanson JW, Wolford GL, et al. The five-site health and risk study of blood-borne infections among persons with severe mental illness. Psychiatr Serv 2003;54:827–835
2. Rifai MA, Moles JK, Van Der Linden BJ. The prevalence of psychiatric disorders in patients with chronic hepatitis C [abstract]. Psychosomatics 2003;44:142–143
3. Yovtcheva SP, Rifai MA, Moles JK, et al. Psychiatric comorbidity among hepatitis C–positive patients. Psychosomatics 2001;42: 411–415
4. Hadziyannis SJ, Sette H Jr, Morgan TR, et al. Peginterferon-α2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. Ann Intern Med 2004; 140:346–355
5. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med 2002; 347:975–982
6. Dieperink E, Ho SB, Thuras P, et al. A prospective study of neuropsychiatric symptoms associated with interferon-α-2b and ribavirin therapy for patients with chronic hepatitis C. Psychosomatics 2003; 44:104–112
7. Schaefer M, Schmidt F, Folwaczny C, et al. Adherence and mental side effects during hepatitis C treatment with interferon alfa and ribavirin in psychiatric risk groups. Hepatology 2003;37:443–451
8. Strader D, Wright T, Thomas DL, et al. Diagnosis, management, and treatment of hepatitis C. Hepatology 2004;39:1147–1171

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