

# New-Onset Visual Hallucinations With Eszopiclone

**To the Editor:** Eszopiclone is a nonbenzodiazepine hypnotic.<sup>1</sup> Hallucinations have been frequently described with other nonbenzodiazepine hypnotics (“Z-drugs”) such as zolpidem and zaleplon but not with eszopiclone.<sup>2–10</sup>

**Case report.\*** Ms A, a 38-year-old woman with suicidal ideation, presented for psychiatric inpatient admission in February 2014. She had a history of bipolar disorder with 2 previous suicide attempts. Her medication regimen prior to admission included alprazolam extended release 1 mg/d, vortioxetine 10 mg/d, oxcarbazepine 600 mg twice daily, divalproex extended release 1,500 mg/d, bumetanide, dextansoprazole, enalapril, loratidine, tizanidine, vitamin B complex, and an oral contraceptive. The patient weighed 325.3 lb, and she was 5 feet 4 inches tall with a body mass index of 56. She presented with depressed mood without auditory or visual hallucinations and crying spells stating, “I just want to sleep and never wake up.” Ms A complained of poor sleep initiation with frequent awakenings during the night and early morning awakening. She had received an outpatient prescription for eszopiclone 3 mg but had never filled it. The medication was continued for inpatient use by the admitting physician. Medication allergies included paroxetine, citalopram, sulfa drugs, and hydrocodone. Her history was significant for abuse of oxycodone, and her urine drug screen was positive for benzodiazepines and oxycodone. Results from her laboratory tests were within normal limits with the exception of a mildly elevated aspartate aminotransferase at 54 IU/L.

Vortioxetine was discontinued, and Ms A was initiated on venlafaxine extended release 75 mg daily. Alprazolam was stopped, and an approximately equivalent dose of lorazepam was started at 1 mg twice daily. Tizanidine, the oral contraceptive, and dextansoprazole were discontinued at admission. Two days after admission, Ms A received her first dose of eszopiclone 3 mg. She reported awakening at 1:00 AM and experiencing vivid visual hallucinations of snakes and spiders on the bathroom floor that made her fearful of getting up to use the restroom. She reported that this was her first episode of visual hallucinations and denied any subsequent hallucinations. The next day, her thinking was organized and logical, and she denied any suicidal ideation. Eszopiclone was discontinued and trazodone at bedtime was initiated. The patient reported no visual hallucinations after discontinuation of eszopiclone.

This report is only the second in the literature to describe hallucinations associated with eszopiclone.<sup>2</sup> Our patient reported no visual hallucinations prior to eszopiclone initiation or any subsequent hallucinations after discontinuation. The patient received 3 mg based on the outpatient prescription that she had received for insomnia. The prescribing information<sup>11</sup> suggests a starting dose of 1 mg before bedtime that may be increased to 3 mg if clinically indicated and lists the incidence of hallucination with 2 mg and 3 mg as 1% and 3%, respectively. It is possible that our patient experienced hallucinations because the higher dose was administered.

The patient maintained an organized thought pattern, orientation to time and place, and the ability to clearly describe her hallucinations. Therefore, it is unlikely that the episode was due to a primary psychotic disorder. She exhibited no signs or symptoms of opioid or benzodiazepine withdrawal during her stay, and she was initiated on a dose of lorazepam approximately

equivalent to the alprazolam she had been taking, making this switch in benzodiazepines a highly unlikely cause of her visual hallucinations. Furthermore, it is unlikely that any of her other medications induced the hallucinations, as the patient had been stable on these medications and the hallucinations occurred as an isolated event after administration of eszopiclone.

Her Naranjo adverse drug reaction probability score was 6, indicating a probable adverse drug reaction.<sup>12</sup> A literature search using MEDLINE and key words *eszopiclone*, *Lunesta*, and *hallucinations* was conducted, yielding one case report.<sup>2</sup> Literature has suggested that hallucinations with the Z-drugs may occur primarily with zolpidem.<sup>13,14</sup> For instance, a review<sup>15</sup> of spontaneous reports of adverse events with zolpidem in Australia found higher odds of parasomnia, amnesia, hallucination, and suicidality for zolpidem compared to other drugs in the analysis.

Our case highlights the need for continued patient and clinician education regarding the potential neuropsychiatric adverse effects of eszopiclone. In addition, clinicians are encouraged to report cases such as ours, which may allow the identification of predictive factors.

\*Written informed consent was obtained from the patient prior to submission.

## REFERENCES

- Morin AK, Willett K. The role of eszopiclone in the treatment of insomnia. *Adv Ther*. 2009;26(5):500–518.
- Duggal HS. New-onset transient hallucinations possibly due to eszopiclone: a case study. *Prim Care Companion J Clin Psychiatry*. 2007;9(6):468–469.
- Elko CJ, Burgess JL, Robertson WO. Zolpidem-associated hallucinations and serotonin reuptake inhibition: a possible interaction. *J Toxicol Clin Toxicol*. 1998;36(3):195–203.
- Bhatia SC, Arora M, Bhatia SK. Perceptual disturbances with zaleplon. *Psychiatr Serv*. 2001;52(1):109–110.
- Stone JR, Zorick TS, Tsuang J. Dose-related illusions and hallucinations with zaleplon. *Clin Toxicol (Phila)*. 2008;46(4):344–345.
- Markowitz JS, Rames LJ, Reeves N, et al. Zolpidem and hallucinations. *Ann Emerg Med*. 1997;29(2):300–301.
- Tsai MJ, Huang YB, Wu PC. A novel clinical pattern of visual hallucination after zolpidem use. *J Toxicol Clin Toxicol*. 2003;41(6):869–872.
- van Puijenbroek EP, Egberts AC, Krom HJ. Visual hallucinations and amnesia associated with the use of zolpidem. *Int J Clin Pharmacol Ther*. 1996;34(7):318.
- Markowitz JS, Brewerton TD. Zolpidem-induced psychosis. *Ann Clin Psychiatry*. 1996;8(2):89–91.
- Manfredi G, Kotzalidis GD, Lazano S, et al. Command hallucinations with self-stabbing associated with zolpidem overdose. *J Clin Psychiatry*. 2010;71(1):92–93.
- Lunesta [package insert]. Marlborough, MA; Sunovion Pharmaceuticals Inc; 2014.
- Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239–245.
- Gunja N. The clinical and forensic toxicology of Z-drugs. *J Med Toxicol*. 2013;9(2):155–162.
- Gunja N. In the Zzz zone: the effects of Z-drugs on human performance and driving. *J Med Toxicol*. 2013;9(2):163–171.
- Ben-Hamou M, Marshall NS, Grunstein RR, et al. Spontaneous adverse event reports associated with zolpidem in Australia 2001–2008. *J Sleep Res*. 2011;20(4):559–568.

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