A Case of Zaleplon-Induced Amnestic Sleep-Related Eating Disorder

To the Editor: Sleep-related eating disorder (SRED) is a type of sleep disorder in which the individual is amnestic completely or partially to the eating episode, which occurs during NREM sleep. Several medications have been implicated in unusual sleep behaviors, and the US Food and Drug Administration (FDA) has recommended revised labeling on these medications.[1] Zolpidem has the most published data, and patients have engaged in many complex behaviors after taking this product, including sleep-eating, sleepwalking, sleep-driving, and sleep-sex.[2] In discussing the management of hypnotic-induced complex behaviors, some have postulated that switching to another nonbenzodiazepine receptor agonist (NBRA) or reducing the dose of the offending agent may decrease the possibility of these behaviors.[2]

The following case suggests that switching to another NBRA does not necessarily resolve SRED. This patient had a new onset of amnestic SRED with high-dose zolpidem that stopped when treatment was switched to zaleplon. The SRED recurred 25 months later while the patient was receiving a maximum FDA-recommended dose of zaleplon, thus highlighting the importance of dose in the occurrence of NBRA-induced complex behaviors. This is the first reported case of zaleplon-induced complex sleep behavior occurring at a recommended FDA dose.

Case report. Ms A, a 49-year-old married woman, was prescribed zolpidem 5 mg at bedtime in June 2004 after trazodone failed to treat her ongoing insomnia. She has been treated for major depression for the past 6 years, and her symptoms have been in remission for the past 2 years (since 2007) with duloxetine. She had no history of alcohol or illicit substance use (confirmed by an initial negative urine toxicology screen and blood alcohol level). She denied a history of head injuries, seizures, or loss of consciousness. Her medical history was noncontributory (she denied restless legs syndrome, sleep apnea, periodic leg movement disorder, etc). Results of a sleep study were normal.

She took zolpidem 5 mg nightly for 3 months and initially reported that it decreased sleep latency and improved quality of sleep, but over time this dose lost its efficacy. The zolpidem dose was subsequently increased to 10 mg nightly for insomnia. She initially reported improvement in her insomnia, but the effect of this dose diminished over 4 months. The zolpidem dose was then increased to 15 mg nightly in January 2005.

Five months after zolpidem was increased to 15 mg nightly, Ms A complained of eating at night. She had no memory of these behaviors, but she reported finding orange peels and/or empty potato chip bags on her nightstand in the morning. Her husband reported observing these behaviors, which occurred up to 4 times per week.

In June 2006, she was switched to zaleplon 10 mg nightly. Upon switching to zaleplon, she denied occurrence of the SRED. Zaleplon was titrated to 20 mg nightly for better symptom control in July 2006. The SRED recurred in August 2008 (25 months after initiation of zaleplon). She reported the same sleep-eating behavior that she had experienced with zolpidem in the past. These behaviors occurred 1 to 4 times per week. She found toaster pastry wrappers on the nightstand and a popcorn bowl on the headboard and did not remember eating these items. Results of a second sleep study conducted in November 2008 were also normal.

Upon further exploration, Ms A described experiencing 2 types of nocturnal eating events. On some occasions, she woke up hungry and ate volitionally (with recall). On other occasions, she could not recall engaging in these behaviors and knew that the event had occurred only because of the leftover wrappers. She denied the presence of all sleep-related behaviors prior to starting zolpidem 4 years before. She was not prescribed medications that could have interacted with either the zolpidem or zaleplon to cause these behaviors.

The zaleplon dose was reduced at the recommendation of the sleep specialist in November 2008, and the SRED has not recurred with zaleplon 10 mg nightly in the 6 months since.

A review of the literature shows that drug-induced SRED has been described primarily in association with zolpidem. Most of those articles involved patients with a previous parasomnia that was exacerbated by the zolpidem. Some had nocturnal eating syndrome that increased in frequency and/or evolved into a SRED with new amnesia for the eating.[3] Others had simple sleepwalking that evolved into more complex behaviors.[4] In one case, a patient was switched to eszopiclone without recurrence of SRED.[5] Two patients had resolution of their sleep-related eating behavior when switched back to zolpidem from zolpidem controlled-release.[6]

Noting a literature review with 15 of 17 patients having complex behaviors in association with zolpidem, one review article suggested that zolpidem has a greater propensity to cause complex behaviors than other NBRAs.[2] Dolder and Nelson's[2] review posits that an agent that inhibits cytochrome P450 (CYP)3A4 could potentially increase the level of the NBRA and thus increase the risk of complex behaviors. Their review goes as far as saying that the risk of drug interaction–induced complex behaviors for zaleplon is low because it is metabolized by a non-CYP pathway (aldehyde oxidase) plus minimal interaction at CYP3A4.[2] Although this case does not represent a drug interaction–induced

complex behavior, as duloxetine is not metabolized by CYP3A4, one must consider that an interaction at CYP3A4 may increase risk of SRED.

There is only 1 case report involving zaleplon-induced complex behavior. An adolescent patient who had taken three 10-mg tablets (which is beyond the recommended dosage) to alleviate his insomnia subsequently ingested approximately 20 additional 10-mg tablets.[7] That patient was found by his parents spilling a significant amount of gasoline on the garage floor while attempting to fill the lawnmower. Our case report was the first to describe complex behavior at a recommended dosage of zaleplon (20 mg nightly).[8]

Interestingly, in our patient, nocturnal eating with recollection of events occurred only with zaleplon. With her previous trial of zolpidem, she had only amnestic eating events. Her recollection of events with zaleplon, but not zolpidem, proffers the question, Does zolpidem cause more amnesia than zaleplon, or did the patient pay better attention to her symptoms during her recurrence? If the latter is true, is the longer half-life of zolpidem compared to zaleplon a reason for the greater amnesia? It is also possible that zaleplon's short duration of action and twice-nightly dosing could be a reason why she remembered some episodes of eating while taking this medication but had only amnestic eating episodes while prescribed zolpidem.

Lowering the dose of the NBRA is a recommended method of treating SRED. Lowering the dose of zaleplon has been effective for this patient for the past 6 months, although it is still possible that she could have a recurrence of SRED. It is important for physicians to inquire about abnormal sleep behaviors when prescribing NBRAs.

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