



Short communication

Unexpected effect of Zolpidem in a patient with attention deficit hyperactivity disorder

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ABSTRACT

Sleep-related eating disorder (SRED) is characterized by recurrent episodes of eating during the night, accompanied by partial consciousness and followed by limited recall.

Zolpidem is a sedative-hypnotic drug commonly used to treat sleep disorders. Zolpidem reduces sleep latency and increases the total time of sleep. Here, we described a case of a patient with attention-deficit/hyperactivity disorder (ADHD) who suffered from zolpidem-induced SRED. The symptoms disappeared when the use of zolpidem as discontinuation. To the best of our knowledge, this is the first documented case of SRED induced by the use of zolpidem in a patient with ADHD.

1. Introduction

SRED is characterized by recurrent episodes of feeding after arousal from nighttime sleep. According to the International Classification of Sleep Disorders, Second Edition (American Academy of Sleep Medicine, 2005), SRED is classified as parasomnia and characterized by recurrent episodes of involuntary eating and drinking in the middle of sleep periods with problematic consequences. Patients insist that the eating is involuntary, and cohabitants report that patients are difficult to awaken completely. Because nocturnal food consumption in SRED is highly caloric, this behavior may lead to morning bloating, embarrassment, and weight gain. The exact etiology of SRED is not clear. However, SRED has been described in connection with and said to be triggered by the use of hypnotic drugs, especially zolpidem. The chemical structure of zolpidem is unrelated to that of benzodiazepines, barbiturates, or other hypnotic drugs. Zolpidem is a nonbenzodiazepine receptor agonist, and a highly effective hypnotic with a short half-life. Compared with other hypnotics, zolpidem induces a pattern of sleep more similar to natural sleep. Several clinical trials examining the use of zolpidem for the treatment of chronic insomnia have demonstrated that it is well tolerated and remains effective for up to 12 months without any evidence of significant tolerance or rebound insomnia on discontinuation (Bomalaski et al., 2017). In addition, zolpidem appears to have low abuse liability at doses commonly prescribed for insomnia.

Attention-deficit/-hyperactivity disorder (ADHD) is a lifelong developmental disorder that leads to cognitive, social, and emotional impairments (Kessler et al., 2009). The symptoms range in severity from mild to severe and usually persist throughout the lifespan

(Faraone et al., 2006). It is now known that individuals with ADHD are vulnerable to a number of various psychiatric and neurological disorders. In addition, ADHD in adults is often associated with high rates of comorbidities. Sleep problems are one of the most common comorbid conditions experienced by individuals with ADHD. Previous studies have showed that individuals with ADHD have longer sleep latency, more frequent nocturnal awakenings, and lower sleep efficiency. These symptoms of adult ADHD lead to poor outcomes (Hirvikoski et al., 2011).

Here, we present a case report of patient with ADHD who developed zolpidem-induced SRED.

2. Case report

A 21-year-old female university student was referred to our clinic for difficulties of initiating sleep. She was previously diagnosed with inattentive type ADHD at the age of 20 years old. She discontinued going to the hospital after being diagnosed with ADHD and was not taking any medications. She had no co-occurring substance use disorders or eating disorders. She lived alone after entering university, and her daily patterns were irregular due to her ADHD. She was prescribed with zolpidem 10 mg at bedtime. After prescribing zolpidem, her difficulties initiating sleep improved. After 2 months, she complained of morning nausea, reduction of appetite, and a 3-kg weight gain. She also reported finding evidence of having eaten cookies, bread, or snacks after awakening. Because she lived alone, no one saw her eating behaviors under impaired consciousness. There was clear evidence that she ate, such as leftover food and residue in her mouth. She was unable

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to recall details of the nocturnal eating episodes. This behavior was never noted prior to imitating the use of zolpidem. The dose of this drug was tapered to 5 mg for 1 week and then discontinued. After stopping the use of zolpidem, 0.5 mg clonazepam was prescribed for her insomnia. At follow-up more than 6 months, she did not have any recurrence of SRED symptoms while stop of zolpidem.

3. Discussion

The diagnostic criteria for SRED include recurrent episodes of involuntary eating and drinking during arousal from sleep with problematic consequences. Because our patient's SRED symptoms started only after the use of zolpidem was started and disappeared after its discontinuation. This case shows a clear temporal association between the use of zolpidem and SRED. To our knowledge, this is the first case report of zolpidem-induced SRED in a patient with ADHD.

In patients with adult ADHD, both long and short sleep duration are associated with inattentive symptoms, whereas only short sleep duration is associated with hyperactive symptoms. As a result, adult ADHD and sleep disturbance symptoms show strong associations (Wynchank et al., 2018). In addition, insomnia is associated with significantly worse daily function and adverse health outcomes in patients with adult ADHD (Ten Have et al., 2016). Thus, it is important that insomnia is recognized and treated in patients with adult ADHD.

Zolpidem is associated with minimal rebound insomnia and continues to be a useful therapeutic option for the pharmacological treatment of insomnia. Although action of zolpidem at GABA_A receptor is similar to benzodiazepines, zolpidem has more selectivity for the α_1 subunit, which could tentatively explain the difference in its effects on sleep architecture and the lower incidence of adverse events (Monti et al., 2017). However, there are several reports suggesting that the use of zolpidem is associated with SRED. For example, Nzwalo et al. (2013) reported 18 cases of zolpidem-induced SRED. Nevertheless, the prevalence of zolpidem-induced SRED remains unknown and the mechanism underlying the association between the use of zolpidem and SRED is unclear. Some possible risk factors have been hypothesized, which include zolpidem dosage, sex, drug-drug interactions with serotonin reuptake inhibitors, protein-binding competition, body weight, and a combination of a history of sleepwalking, medication increasing delta sleep, and a precipitating stimulus.

Polypharmacy with concurrent medication usage is another risk factor for SRED. The uniqueness of zolpidem in comparison with other benzodiazepine or nonbenzodiazepine hypnotics with regard to precipitating SRED remains unclear. Therefore, further studies of the pathophysiology of SRED are necessary. To confirm the association of

zolpidem and SRED, the resolution of SRED on stopping the use of zolpidem should be demonstrated.

4. Conclusion

Zolpidem is an effective hypnotic with a short half-life compared with other benzodiazepine. However, general practitioners should be cautious while prescribing zolpidem for the treatment of insomnia and should ask patients and their relatives regarding SRED.

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Declaration of Competing Interest

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