CASE REPORT

Sleep-related eating disorder secondary to zolpidem

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SUMMARY

Sleep-related eating disorder (SRED) is characterised by eating episodes during the first period of the night sleep with partial loss consciousness, and amnesia. It can rarely be induced by some drugs, including zolpidem. We present a video report of a patient with a 1-year history of SRED caused by zolpidem causing important repercussions in the sleep structure and life quality. The night eating episodes ceased promptly with discontinuation of zolpidem. Upon the follow-up, the sleep structure improved and the daily consequences disappeared. As in few reported cases of zolpidem-induced SRED, our patient was suffering from the parasomnia for a long time before the diagnosis. Active exclusion of symptoms suggestive of SRED in patients under zolpidem treatment can avoid the deleterious effect of the sleep disorder.

supported case of zolpidem induced SRED and the related literature discussed.

CASE PRESENTATION

A 53-year-old Caucasian woman with a history of hypertension and dyslipidemia was referred by her family doctor to our sleep clinic because of a 'strange behaviour' during sleep time. She was regularly taking zolpidem 10 mg/day for the last 5 years because of situational insomnia in relation to her husband's OSA. Her other medications included simvastatin and captopril. The history was negative for any neuropsychiatric disease or drug abuse. She was adopted in early childhood and had no knowledge about her biological relatives. Her family had witnessed during the last year several episodes of eating, drinking diverse types of food, mainly milk and fruits, and sometimes cooking, during nocturnal sleep time, usually starting in the first hours of sleep. During the episodes she would remain with the eyes almost closed, usually not speaking spontaneously but when asked by the relatives she could respond incoherently. Although she reported sometimes awaking with plates, different remnants of food and knives in her bedroom, she was unable to remember almost anything of the episodes. The episodes were increasing in frequency, occurring two to three times per week in the months before the consultation. She also complained of morning nausea, reduction of appetite and fatigue. She reported gaining 6 kg during the last year. Her body mass index was 25.96 kg/m². She had a regular sleep schedule, usually going to bed at 00:30 h and waking up at 8:30 h. Although she did not complain of short sleep time, her sleep diary showed that during some days she slept less than 6 h. There were no precipitating medical and psychological events. A comprehensive questionnaire covering lifetime, sleep-wake, daytime eating habits and review of systems did not reveal any relevant fact, in particular suggesting a psychogenic dissociative disorder or nocturnal bulimia nervosa. She scored 9 in the Epworth Sleepiness Scale. Polysomnography (PSG) was scheduled. It was suggested to the patient and family to bring a home video of one of the episodes. Zolpidem was reduced

BACKGROUND

Sleep-related eating disorder (SRED) was first described in 1991 by Schenck *et al* establishing a new entity, distinct from the already known 'night-eating syndrome' (NES).¹ It is characterised by eating episodes occurring in the first period of the night sleep, often accompanied by partial consciousness and followed by limited subsequent recall. In NES, the over-eating occurs between dinner and bedtime. The patient is awake and capable of retaining full memory of the event.¹⁻³ The spectrum of the substances ingested in SRED is wide, varying from ordinary to unusual substances, generally highly caloric nutrients.¹⁻³ SRED is considered an idiopathic parasomnia appearing to be most commonly associated with other primary sleep disorders. Sleep walking is the most common associated disorder, but restless leg syndrome, periodic limb movement disorder, obstructive sleep apnoea (OSA) and circadian rhythm disorders can also occur.²⁻³ There is growing evidence of the association between the use of zolpidem and SRED.⁴⁻¹¹ Other central nervous system acting drugs such as triazolam, risperidone, olanzapine can also induce SRED.³⁻¹² Here we report the first video-

Figure 1 Evolution of the hypnogram, before (A) and after (B) stopping zolpidem.

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Video 1 Patient found in the kitchen eating. She is drowsy and staggers briefly. Responds incoherently and vague with the eyes almost closed.

to 5 mg/day, without benefit. In the following week she brought a video of one such episode (video 1). The sleep deprivation EEG was normal. During video EEG she exhibited one episode of eating with reduced level of consciousness arising from stage 1 of non-rapid eye movement (NREM) sleep. While eating she remained in stage 1. No epileptiform activity was present. In the next morning she had no memory of the episode. The metabolic panel was normal. An overnight unattended PSG showed a total sleep time of 7 h and 4 min, with decreased sleep efficiency (81.9%). The hypnogram revealed sleep instability and fragmentation, with frequent changes in the sleep phases, and excessive arousal episodes (figure 1A).

She also had a mild respiratory disturbance index (RDI) of 14.7 secondary to hypopnoeic events. Zolpidem was stopped and the night eating episodes ceased. Because of the situational insomnia she started clonazepam intermittently.

OUTCOME AND FOLLOW-UP

The follow-up PSG preformed 6 months later showed improvements, with much less sleep fragmentation (figure 1B) and reduction of the RDI to 11.6, but her sleep latency was increased (performed in the absence of clonazepam). She had lost 5 kg over 1 year and returned to her normal weight (body mass index of 23.5 kg/m²) without any particular change in the diet or physical routines.

DISCUSSION

This patient fulfilled the international classification of sleep disorder-2 (ICSD-2) criteria for SRED attested by the presence of: recurrent episodes of involuntary eating and drinking occurring in the main sleep period; direct consequences of the night eating such as morning anorexia, daytime fatigue and weight gain; and exclusion by history, examination and complementary exams of conditions such as epilepsy, psychogenic dissociative disorder, nocturnal bulimia nervosa, acute stress precipitants and drug deprivation that could explain the patient symptoms.³ There are about 37 reported cases of zolpidem-induced SRED. The largest case series of zolpidem-induced SRED was presented by Schenck *et al*,¹² who collected 19 cases in a period of 2 years. We reviewed all published cases of zolpidem induced SRED and found 18 additional cases (table 1).

Table 1 Reported cases of zolpidem-induced SRED

Case	Age of onset/gender	Dosis (mg)	Symptom onset	Possible precipitant	Frequency	Associated sleep disorder	Comorbidities	Concomitant drugs
Morgenthal and Silber ⁴	51/F	10	3 weeks after	Smoking Cessation	Daily	RLS	No	Carbidopa/levodopa, Paroxetine
	65/M	10	Soon after	No	Daily	RLS	Parkinson's disease	Trazodone, ropinerole, fluoxetine
	41/M	15–30	NA	NA	Daily	RLS, OSA	NA	Alprazolam, bupropion
	64/M	5–10	NA	NA	Daily	RLS, OSA	NA	Amitriptyline, gabapentin
	56/F	5–10	NA	NA	Daily	Somnambulism, RLS	NA	Pramipexole
Najjar ⁵	46/F	6.25	3 weeks after	No	Daily	OSA	Depression	Trazodone, paroxetine
Chiang and Krystal ⁶	75/F	12.5*	Soon after	Zolpidem*	Daily	RLS, OSA	No	Gabapentin
	70/F	12.5*	Soon after	Zolpidem*	Daily	RLS, Complex apnea	No	Pramipexole, gabapentin
Hoque and Chesson ⁷	44/F	10	Few weeks	No	Weekly	OSA, Somnambulism, Somnoliquy	Depression	Paroxetine
Dang <i>et al</i> ⁸	45/M	10	10 days after	No	Weekly	Somnambulism	No	No
Miranda <i>et al</i> ⁹	49/M	10	4 months	No	Unknown	OSA	Bipolar Disorder	Lamotrigine, clonazepam
Yun and Ji ¹⁰	45/M	10	6 months	No	weekly	RLS	No	No
Pérez-Díaz <i>et al</i> ¹¹	39/F	20	6 months after	No	Daily	Somnambulism	Major Depression	Fluoxetine
	55/F	10	9 years after	No	Daily	Somnambulism	Major Depression	Fluoxetine
	53/F	10	'Few weeks'	No	Daily	Night terror	Major Depression	Velantafaxin, alprazolam
	79/F	10	3 years after	No	Daily	No	Dysthymia	No
	27/M	10	2 months	No	Daily	Night terror Somnambulism	Sporadic use of drugs of abuse	No
Present	53/F	10	5 years	No	Weekly	No	No	No

*Expanded release form of zolpidem.
NA, information not available; OSA, obstructive sleep apnea; RLS, restless legs syndrome.

In all those subjects zolpidem was prescribed for insomnia. The age range was wide (17–79 years) with a female predominance with 73% (27/37) of cases. SRED episodes typically arise from NREM sleep stage, mostly N3, but there are cases of episodes occurring during REM.^{1–3} Our patient presented the typical characteristics found in zolpidem-induced SRED such as female gender, age of 50, eating episodes arising from NREM and prompt cessation of the episodes after stopping the drug.^{1–3} In all published cases cessation of zolpidem led to remission of the disorder, with the exception of two cases of zolpidem-induced SRED precipitated by change of regular zolpidem to expanded release form, in which reintroduction of regular zolpidem stopped the SRED.⁶ In this case the symptoms were noticed after 4 years of zolpidem use. However, we cannot exclude the presence of mild or fluctuating manifestations of SRED prior to the diagnosis. The absence of the parasomnia impact on the bed partner and the inexistence of relevant daytime symptoms until the last year can explain the diagnosis delay.¹³ Coexistence of another sleep disorder is reported in all but one of the published cases of zolpidem-induced SRED.¹¹ The patient had concomitant increase index RDI which improved in the control PSG. Changes in weight are associated with changes in the RDI.¹⁴ The loss of weight in our patient could be a consequence of SRED remission and also because of the RDI amelioration. The mechanisms underlying SRED in relation to zolpidem are unknown. It was proposed that diffuse cortical binding of zolpidem could trigger central pattern generators causing emergence of conserved primitive patterns such as walking and eating. These primitive behaviours could indeed be potentiated by the sedation-amnestic properties of zolpidem.⁷ Zolpidem is a non-benzodiazepine hypnotic γ -aminobutyric acid agonist with selective high binding affinity for the benzodiazepine $\omega 1$ receptor. It reduces time of sleep and prolongs total sleep time, without changing the sleep architecture. Somnambulism, visual hallucinations, sensory distortion and delirium are neuropsychiatric disorders also associated with zolpidem use.¹⁵ The association of SRED with dopaminergic responsive disorders such as periodic limb movement and restless leg syndrome (RLS)^{1 2}; its clinical response to dopaminergic drugs²; and major role of dopamine as a mediator of the meso-limbic reward mechanism which is fundamental in the food rewarding behaviour,¹⁰ supports a link between SRED and dopaminergic dysfunction. The completion of complex activities during sleep puts the patient and the relatives at risk of accidents. SRED is associated with sleep disturbance causing fatigue, somnolence, poor cognitive performance and irritability. Obesity is also an indirect consequence of SRED as shown by this case.^{1–3} This case highlights the importance of monitoring iatrogenic sleep disorders induced by drugs used to treat common sleep conditions. Zolpidem in particular is widely prescribed owing to its favourable pharmacological properties in comparison to other hypnotic agents used for insomnia treatment. Active exclusion of symptoms suggestive of SRED in patients under zolpidem treatment can avoid the deleterious effects of the sleep disorder.

Learning points

- The increasing use of zolpidem for insomnia and other neurological disorders can potentially increase the number sleep-related eating disorder (SRED) cases.
- SRED disturbs the sleep, decreases the quality of life and put patients and their relatives at risk of accidents.
- Interruption of zolpidem leads to cessation of SRED.
- Clinicians should ask patients and their relatives about symptoms of SRED to avoid its deleterious effects.

Competing interests None.

Patient consent Obtained.

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