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CASE REPORTS

Two Cases of Sleep-Related Eating Disorder Responding Promptly to Low-Dose Sertraline Therapy

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We report two cases of adult males with sleep-related eating disorder (SRED), with durations of 3 and 7 years, and without associated psychiatric history. In both cases, the use of low-dose (25 mg) sertraline taken at bedtime resulted in immediate, full and sustained resolution of symptoms at the latest follow-ups. The sertraline efficacy was of particular benefit for the patient reported on in case 2 who was a commercial airline pilot subjected to a highly restricted list of Federal Aviation Administration-approved medications. Risk factors for SRED included smoking cessation and work-related stress in case 1, and a history of sleepwalking and work-related circadian disruptions and partial sleep deprivations in case 2. Sertraline therapy of SRED is considered within a review of all current pharmacologic therapies of SRED.

Keywords: night eating syndrome, non-REM parasomnia, sleep-related eating, sleepwalking

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INTRODUCTION

Sleep-related eating disorder (SRED) is a parasomnia characterized by clinically consequential involuntary eating emerging from sleep with partial or full unconsciousness.[1] SRED is considered to be a "final common pathway disorder," with sleepwalking (SW) being the most common predisposing condition,[1–6] followed by restless legs syndrome (RLS), narcolepsy type 1, obstructive sleep apnea (OSA), and hypnotic medication use (particularly zolpidem).[1,4,7–9] SRED is a complex parasomnia[4,6,10,11] that warrants further study of its associated features and the underlying mechanisms for its initiation and perpetuation. Treatment of SRED can also be challenging, so additional effective therapies are needed. We present two cases of patients with severe, high-frequency, chronic SRED who responded promptly and in sustained fashion to low-dose sertraline therapy.

REPORT OF CASES

Case 1

A 36-year-old male software developer presented to one author (RV) with a complaint of nightly sleep-related eating that began 7 years previously. Symptoms began after a stressful work week, and also soon after quitting smoking. He had no prior history of SW, other parasomnia, or RLS symptoms.

Early in the nocturnal eating process, his wife would awaken and witness these events, estimating the frequency to be in the range of 2 to 5 times per night. His Fitbit also provided similar information on estimated awakenings. He only had partial recall for about a quarter of these events, with no recall for about 75% of the events. He denied any dangerous or injurious behaviors during these events, such as eating unpalatable food, using the stove or oven, or driving to get food. Locking up food cabinets did not deter the sleep-related eating.

Upon awakening in the morning, he felt "exhausted" and did not have any appetite for breakfast or even for lunch, but still ate these meals per his diet book recommendations. In an attempt to lose weight, he jogged 3 days a week and reported feeling exhaustion afterwards, with increased SRED events later those nights. Similarly, on days he worked late nights at the office, he reported more SRED events.

Medication trials to treat his SRED prior to presentation included trazodone and melatonin, which he felt helped his sleep quality but did not affect sleep-related eating frequency. He also tried clonazepam, which increased the frequency of sleep eating and was promptly discontinued.

The patient filled out a comprehensive sleep questionnaire. Epworth Sleepiness Scale (ESS) score was 5/24. Apart from situational stress and mild anxiety, the patient did not exhibit any mood or anxiety disorder per the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) criteria. Psychiatric questionnaires were not used, but he was evaluated by a board-certified psychiatrist and sleep physician (RV).

Body mass index (BMI) was 38.5 kg/m^2, with obesity being in part due to his SRED with an estimated 50 lb weight gain despite diet and exercise. Medical history was otherwise unremarkable. There was no family history of parasomnia. He had

never used zolpidem. He denied RLS symptoms. He stopped smoking 2–3 packs daily just before the onset of SRED. He denied using alcohol.

He underwent technologist-attended video polysomnography (PSG) to rule-out a primary sleep disorder potentially contributing to abnormal arousals with eating. Sleep architecture was unremarkable: stage N1 sleep 9%, stage N2 sleep 54%, stage N3 sleep 14.5%, and stage R sleep 22.5%. Sleep latency was 16.5 minutes. Sleep efficiency was 85%. Total sleep time was 416 minutes. Wake after sleep onset (WASO) was 52 minutes. Arousal index was 11 events/h. Stage N3 sleep was observed without arousals. The AHI was 2.8 events/h. The RDI was 7 events/h. The oxyhemoglobin desaturation nadir was 86%. Mild snoring was noted. Periodic limb movement (PLM) index was 0 events/h. Complex sleep-related behaviors were not observed.

Initial recommendations were to optimize sleep hygiene and increase total sleep time, which he reported helped but not completely stop sleep-related eating. While topirimate therapy was considered, because of mild anxiety features, low dose (25 mg) sertraline was prescribed to be taken at bedtime. He reported that all amnestic sleep-related eating stopped on the first night of sertraline therapy, and that this effect was full and sustained for weeks after beginning sertraline, which had been maintained at 19-month follow-up. Additionally, he also remarked that his mild anxiety had noticeably reduced immediately the next day after starting sertraline, and this anxiolytic benefit was also sustained.

Case 2

A 37-year-old divorced commercial airline pilot presented to an author (JRC) with a complaint of sleep-related eating of 3 years duration. There was a history of childhood SW with the last episode of isolated SW (ie, not associated with eating) occurring at age 11 years.

At the time of presentation, SW included wandering to the kitchen, opening the refrigerator and compulsively eating. Events were episodic and not associated with increased sex drive. The events clustered every 2–4 months and more frequently when he had a cumulative sleep debt associated with his job as a pilot. He had partial recall of the events. At times he has ingested large quantities of uncooked food causing gastric upset the next morning. He has burned food on the stovetop and on one occasion he wandered out of his hotel room, and took an elevator to the hotel kitchen in search of food. Hotel employees awakened him.

Medical and chemical dependency histories were unremarkable. He did not smoke. There was no family history of parasomnias.

His Hamilton Depression Rating Scale score was 11, suggestive of mild depression. The patient otherwise did not have a contributory psychiatric history. ESS score was 8/24. BMI was 25.5 kg/m^2.

Due to Federal Aviation Administration (FAA) regulations, medication options for the pilot were limited, but while on vacation he was prescribed clonazepam 1 mg, which achieved control of SW with SRED. Clonazepam was stopped at least 10 days before returning to work.

Video PSG results were within normal limits. Sleep architecture showed stage N1 sleep 3%, stage N2 sleep 49%, stage N3 sleep 20%, and stage R sleep 28%. Sleep latency was 13 minutes. Sleep efficiency was 92%. Total sleep time was 414 minutes. WASO was 52 minutes. Arousal index was 20 events/h. The PLM index was 0 events/h. The AHI was 1 event/h. The RDI was 13 events/h. The oxyhemoglobin desaturation nadir was 90%. Mild snoring was noted, and no parasomnia behavior was observed.

Initial recommendations that complied with FAA regulations were to optimize sleep hygiene, and improve bedroom safety including using door and window alarms. After previously consulting with one of the authors (CL) about this case, followed by consulting with another author (CHS) who recommended either topiramate or sertraline therapy, sertraline was chosen since topiramate is on the prohibited list in the FAA regulations. After sertraline 25 mg at bedtime was started, the patient noted immediate, full and sustained remission of SRED and associated SW. Additionally, the patient also noted an overall enhanced feeling of well-being. However, at a follow-up appointment 4 months after starting sertraline, the patient complained of erectile dysfunction and diminished libido that were then substantially reversed with sildenafil therapy, 100 mg prn, while maintaining the nightly 25 mg dose of sertraline that continued to fully suppress the SRED. The dual benefit of sertraline, 25 mg at bedtime for controlling SRED, and sildenafil, 100 mg prn for controlling sexual dysfunction was maintained at the next follow-up 3 months later.

DISCUSSION

To our knowledge, these are the first two reported cases of successful sertraline therapy of SRED. What is notable is that in both cases there was an immediate and complete response to low-dose (25 mg) bedtime sertraline in controlling longstanding, high-frequency SRED, with the benefit sustained for 19 and 7 months in case 1 and case 2, respectively. A similar immediate and sustained (3 years) response to selective serotonin reuptake inhibitor (SSRI) therapy of SRED was reported with 40 mg fluoxetine therapy of a non-depressed 32 year-old female.[4] Three other cases of SRED responding to fluoxetine monotherapy or combined with clonazepam have been reported,[4,12] although two cases of fluoxetine non-responders have also been reported.[4,13] In a SRED case series study of 4 patients involving SSRI therapy,[14] 3 patients had SRED reduction beginning a few days after starting paroxetine, and 1 patient a few days after starting fluvoxamine. Sustained remission was maintained at 2–7 week follow-ups.

Our two patients tolerated sertraline therapy, with the only side effect being diminished libido and erectile dysfunction from low-dose sertraline in case 2, which was substantially reversed with sildenafil therapy. Both patients also reported an immediate sense of well-being after starting sertraline therapy, which could have been due to immediate control of their SRED and/or an immediate SSRI effect. Case 1 had two prior unsuccessful medication trials (trazodone, melatonin), lessening the probability of a placebo effect with sertraline.

Serotonergic therapy is also reported to be effective for another disorder of abnormal nocturnal eating—night eating syndrome (NES)—which is an insomnia disorder with recurrent full awakenings from all stages of sleep, as documented by video PSG in two published studies in which there was prompt food ingestion after the awakenings, with most episodes lasting between 30 seconds and 3 minutes.[15,16] Anxiety and depressive symptoms are common in NES.[15,17] NES involves a circadian shift in the timing of eating,[17,18] Sertraline therapy of NES in a double-blind, randomized, placebo-controlled trial lasting 8 weeks demonstrated sertraline efficacy in 71% of 17 patients at a mean daily dose of 126 ± 50 mg; these patients with NES did not have an immediate response to sertraline.[17] In another study of patients with NES, D-fenfluramine, an appetite suppressant with serotonergic activity, controlled NES in 6 of 7 treated patients, with benefit maintained for 6–15 months at the latest follow-up.[15] (D-fenfluramine is no longer available). Therefore, sleep-related serotonergic dysregulation may be a promoting factor for both SRED and NES. In this context, the proposed mechanism of action of serotonergic therapy of NES has been discussed.[18]

Our two cases had several notable clinical features of SRED apart from the dramatic therapeutic response to sertraline. The lack of any PLM during sleep in both cases supported the lack of any RLS history. Also, there was no clinically significant sleep-disordered breathing in either case, despite the greatly elevated BMI in case 1. Each case had recognized risk factors for SRED,[1–6] including smoking cessation and work-related stress in case 1, and a history of SW and work-related circadian disruptions in case 2. In a series of 38 consecutive cases of SRED,[4] cessation of cigarette smoking triggered SRED onset in 2 cases, and major stress triggered SRED onset in 6 cases. In case 2, the SRED history in a patient with SW was typical in that once eating emerged with SW, it became the only SW behavior.[1] Also, in case 2, circadian rhythm disruptions and recurrent partial sleep deprivation related to being a commercial airline pilot played an exacerbating role for his often clustered SRED episodes. Case 2 also had major adverse and potentially dangerous consequences from his SRED, including gastric upset, burning food, and wandering outside his hotel room in search of food. Furthermore, ingestion of harmful or toxic substances can occur in SRED,[1] in contrast to NES.

There was also a divergent prior response to clonazepam therapy of SRED in the two cases. Whereas clonazepam exacerbated SRED in case 1, it was effective in case 2, but could not be continued given his job as a commercial pilot. In the previously cited series of 38 SRED cases,[4] 50% (7/14) patients with SW and SRED treated with bedtime clonazepam had control of their SRED, with a dose range of 0.5–2.0 mg. However, there is a variable response rate to clonazepam therapy of SRED in published reports, with benefit often obtained in combined therapy.[4,12,19] Additionally, clonazepam can worsen SRED, as described in case 1.

Topiramate and dopaminergic agents are other firstline therapies of SRED besides SSRIs. The current-perspective treatments for SRED are primarily based on findings from case series and case reports. Topiramate efficacy, based on two case series, was reported in approximately two-thirds of treated patients.[20,21] Dopaminergic therapy of either SRED associated with RLS, or with idiopathic SRED, can be effective as monotherapy or as combined therapy with codeine, benzodiazepines, bupropion and/or trazodone, in various combinations.[4,19,22] The dopaminergic agents with reported efficacy include levodopa (usually controlled-release carbidopa/L-dopa), bromocriptine, and pramipexole.

In a randomized, double-blind, placebo-controlled crossover trial of 11 patients with SRED, using actigraphy-based and visual analog-based outcome measures, pramipexole-treated patients had significantly reduced nocturnal motor activity and a significantly increased number of nights with good self-reported sleep.[23] This was the first study objectively evaluating the efficacy of pramipexole in SRED. It should be noted that FAA regulations allow the use of dopaminergics "on a case-by-case basis," and so this would be another therapeutic option for case 2. Finally, nortriptyline, a tricyclic antidepressant, has been reported to be partially effective in controlling SRED in a 31-year-old woman.[24]

Similar to the treatment for most parasomnias, SRED management is based on whether the presentation is idiopathic or secondary to a condition associated with arousals from sleep such as SW, OSA, RLS/PLM, or the use of sedative-hypnotics. Therapeutic protocols for the pharmacologic management of SRED have been developed,[4,19] initially involving levodopa (or bromocriptine), codeine and clonazepam (or other benzodiazepine) in various combinations in 18 patients (with 72% efficacy), and "the rationale for this therapeutic approach was based on the successful control of problematic nocturnal eating in patients with [combined] RLS/PLMD/SRED."[19] In other words, the generally successful therapy of SRED comorbid with RLS/PLMD was then applied to idiopathic SRED or SRED associated with SW. However, this therapeutic approach is cumbersome, especially in light of the subsequent recognition of topiramate monotherapy efficacy in idiopathic SRED or SRED associated with SW, with the total number of reported cases currently being 45.[20,21,25] Similarly, SSRI monotherapy of SRED, as reported in 10 cases (n = 6, fluoxetine; n = 3, paroxetine; n = 1, fluvoxamine)[4,12–14] represents another noncumbersome treatment approach. Nearly 40 cases have been reported of dopaminergic therapy of SRED, involving levodopa, pramipexole, and bromocriptine, either as monotherapy or combined therapy with other agents.[4,19,25]

Therefore, given what was just cited and discussed, a therapeutic approach for managing idiopathic SRED/SW-SRED cases, would first involve topiramate or SSRI monotherapy, or dopaminergic therapy, either alone or in combination with codeine and/or clonazepam. In cases where RLS is present, treatment with dopaminergic agents (at times with combined therapy) is the preferred treatment. The use of hypnotics, especially zolpidem, can induce amnestic SRED,[8,26,27] especially in cases with occult RLS.[26] Benzodiazepines have been implicated in inducing or worsening SRED, and clonazepam increased the frequency of SRED in case 1. However, in selected cases, clonazepam therapy (alone or combined), can help suppress SRED.

In conclusion, SRED is a parasomnia that can be part of complex clinical scenarios, including comorbid sleep

disorders; psychiatric, eating and chemical dependency disorders; and medical disorders. Furthermore, SRED may exist on a spectrum of mixed clinical features with NES,[11] which merits further study. Low-dose bedtime sertraline therapy, as another SSRI option, can be added to the list of effective therapies of SRED.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
DSM, Diagnostic and Statistical Manual of Mental Disorders
ESS, Epworth Sleepiness Scale
FAA, Federal Aviation Administration
HAM-D, Hamilton Depression Rating Scale
NES, night eating syndrome
OSA, obstructive sleep apnea
PLM, periodic limb movement
PSG, polysomnography
RDI, respiratory disturbance index
RLS, restless legs syndrome
SRED, sleep-related eating disorder
SSRI, selective serotonin reuptake inhibitor
SW, sleepwalking
WASO, wake after sleep onset

REFERENCES

1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
2. Whyte J, Kavey NB. Somnambulistic eating: a report of three cases. *Int J Eat Disord.* 1990;9(5):577–581.
3. Schenck CH, Hurwitz TD, Bundlie SR, Mahowald MW. Sleep-related eating disorders: polysomnographic correlates of a heterogeneous syndrome distinct from daytime eating disorders. *Sleep.* 1991;14(5):419–431.
4. Schenck CH, Hurwitz TD, O'Connor KA, Mahowald MW. Additional categories of sleep-related eating disorders and the current status of treatment. *Sleep.* 1993;16(5):457–466.
5. Winkelman JW. Clinical and polysomnographic features of sleep-related eating disorder. *J Clin Psychiatry.* 1998;59(1):14–19.
6. Brion A, Flamand M, Oudiette D, Voillery D, Golmard JL, Arnulf I. Sleep-related eating disorder versus sleepwalking: a controlled study. *Sleep Med.* 2012;13(8):1094–1101.
7. Provini F, Antelmi E, Vignatelli L, et al. Association of restless legs syndrome with nocturnal eating: a case-control study. *Mov Disord.* 2009;24(6):871–877.
8. Howell MJ, Schenck CH. Restless nocturnal eating: a common feature of Willis-Ekbom syndrome (RLS). *J Clin Sleep Med.* 2012;8(4):413–419.
9. Palaia V, Poli F, Pizza F, et al. Narcolepsy with cataplexy associated with nocturnal compulsive behaviours: a case-control study. *Sleep.* 2011;34(10):1365–1371.
10. Vetrugno R, Manconi M, Ferini-Strambi L, Provini F, Plazzi, Montagna P. Nocturnal eating: sleep-related eating disorder or night eating syndrome? a videopolysomnographic study. *Sleep.* 2006;29(7):949–954.
11. Winkelman JW. Sleep-related eating disorder and night eating syndrome: sleep disorders, eating disorders, or both? *Sleep.* 2006;29(7):876–877.
12. Willmer J, Warnes H. Somnambulistic bulimia: evaluation and treatment of 4 patients [abstract]. *Sleep Res.* 1990;19:310.
13. Winkelman JW. Nocturnal binge eating is a familial disorder [abstract]. *Sleep Res.* 1993;22:290.
14. Miyaoka T, Yasukawa R, Tsubouchi K, et al. Successful treatment of nocturnal eating/drinking syndrome with selective serotonin reuptake inhibitors. *Int Clin Psychopharmacol.* 2003;18(3):175–177.
15. Spaggiari MC, Granella F, Parrino L, Marchesi C, Melli I, Terzano MG. Nocturnal eating syndrome in adults. *Sleep.* 1994;17(4):339–344.
16. Iranzo A, Santamaria J, Sureda B, Carrasco E, de Pablo J. El sindrome de la cena durante el sueño. *Neurologia.* 2000;15(6):226–230.
17. O' Reardon JP, Allison KC, Martino NS, Lundgren JD, Heo M, Stunkard AJ. A randomized, placebo-controlled trial of sertraline in the treatment of night eating syndrome. *Amer J Psychiatry.* 2006;163(5):893–898.
18. Milano W, De Rosa M, Milano L, Capasso A. Night eating syndrome: an overview. *J Pharm Pharmacol.* 2012;64(1):2–10.
19. Schenck CH, Mahowald MW. Dopaminergic and opiate therapy of nocturnal sleep-related eating disorder associated with sleepwalking or unassociated with another nocturnal disorder [abstract]. *Sleep.* 2002;25(abstract suppl):A249–A250.
20. Winkelman JW. Treatment of nocturnal eating syndrome and sleep-related eating disorder with topiramate. *Sleep Med.* 2003;4(3):243–246.
21. Schenck CH, Mahowald MW. Topiramate therapy of sleep related eating disorder (SRED) [abstract]. *Sleep.* 2006;29(abstract suppl):A268.
22. Schenck CH, Mahowald MW. Combined bupropion-levodopa-trazodone therapy of sleep-related eating and sleep disruption in two adults with chemical dependency. *Sleep.* 2000;23(5):587–588.
23. Provini F, Albani F, Vetrugno R, et al. A pilot double-blind placebo-controlled trial of low-dose pramipexole in sleep-related eating disorder. *Eur J Neurol.* 2005;12(6):432–436.
24. De Ocampo J, Foldvary N, Dinner DS, Golish J. Sleep-related eating disorder in fraternal twins. *Sleep Med.* 2002;3(6):525–526.
25. Chiaro G, Caletti M, Provini F. Treatment of sleep-related eating disorder. *Curr Treat Options Neurol.* 2015;17(8):361.
26. Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. *Sleep Med.* 2002;3(4):323–327.
27. Schenck CH, Connoy DA, Castellanos M, et al. Zolpidem-induced sleep-related eating disorder (SRED) in 19 patients [abstract]. *Sleep.* 2005;28(abstract suppl):A259.

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DISCLOSURE STATEMENT

Work for this study was performed at the Minnesota Regional Sleep Disorders Center (case 1) and the Departamento de Medicina, Escuela de Medicina, Universidad Peruana Cayetano in Lima, Peru (case 2). All authors have seen and approved the manuscript. The authors report no conflicts of interest.