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CASE REPORT

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Quetiapine-induced sleep-related eating disorder: A case report

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Abstract

This is the first case report of two depressed Malay females prescribed quetiapine, the first patient developed sleep related eating disorder (SRED) on 200 mg per day and the second patient at 50 mg per day. Both resolved with discontinuation of the drug. Assessment for SRED should be done at every follow up.

KEYWORDS

case report, quetiapine, sleep-related eating disorder

1 | INTRODUCTION

This is the first case report to document two Malay female patients with SRED. The patient in case 1 developed SRED at a dose of 200 mg but continued to have SRED until quetiapine was discontinued and then resumed the SRED when she was put on 5 mg of olanzapine. Both patients had no recollection of their actions as is characteristic of SRED, and both patients put on considerable weight during this time. SRED as a side effect of quetiapine needs to be highlighted as it has not been given much attention by medical personnel and is not even mentioned in the packaging insert. Antipsychotics should not be freely prescribed as sleep aids. Both patients' symptoms resolved after withdrawing the antipsychotics. Some antipsychotics have greater propensity to cause SRED than others. Patients need to be educated about side effects.

Slow-wave sleep (SWS) is deep sleep and occurs in the nonrapid eye movement (NREM) stages 3 and 4.[1] Frequent arousals during this stage lead to sleepwalking (SW).[2] SW and SRED are two separate entities but both are classified as parasomnias.[3] Serotonin receptors are involved in maintaining sleep and causing muscle hypotonia during sleep.[2] Atypical antipsychotics are commonly used in psychiatric and primary care practice and place patients at risk of parasomnias such as SRED, and this condition may go undetected especially among psychotic patients where it may be mistaken for psychosis.[2]

SRED is defined as a condition which is characterized by multiple episodes of eating at the transition from nighttime sleep to arousal.[4] Quetiapine, olanzapine, chlorpromazine, and clozapine which act through serotonin receptors are often used off-label to aid in sleep.[3] Medication-induced SW and SRED have been reported with quetiapine being the most implicated.[5] The prevalence of SRED in the adult psychiatric population ranges from 1% to 5%.[6] Prevalence of SW is 6.9%.[7] Both conditions are little discussed during follow-up visits and are generally not detected.[1,2]

Quetiapine,[2,6,8-10] olanzapine,[2] and other atypical antipsychotic medications[2] have been associated with SW and have been reported to be associated with SRED. It is important to discuss this potential adverse effect with patients of these medications to prevent injuries and weight gain in the patient.

2 | CASE 1

A 26-year-old Malay woman who had been diagnosed with major depressive disorder presented with complaints of depressive symptoms for a year. She had been treated unsuccessfully on multiple antidepressants before she was prescribed duloxetine. She had been started initially on 30 mg of duloxetine which was titrated up to a dose of 60 mg. 2 mg of clonazepam was added, but she could not sleep with clonazepam, and her depressive symptoms were also poorly

controlled, hence, quetiapine was added to aid in sleep and increase the antidepressant effects. The dose of quetiapine was gradually titrated up to 200 mg at bedtime over 6 months. The diagnosis of SRED was mainly clinical. The patient walked with her eyes open, walked, and ate and had no memory of the event. She ate junk food from the refrigerator while asleep, three to four nights per week. She even cut a mango before eating it. She also ate chocolate spread from a large bottle while asleep. She finished the contents of the bottle over several nights. Normally, the patient does not like to eat chocolate as she likes to control her weight. The patient could not remember any of these events after awakening. She put on 11 kg during the 6 months. This patient had no previous history of sleep walking. Quetiapine was tapered down and olanzapine 5 mg was substituted. On olanzapine 5 mg, the frequency of SRED decreased but it did not go away completely. Hence, the olanzapine was stopped, and clonazepam was changed to 10 mg zolpidem after which the patient could sleep. Resolution of SRED after stopping quetiapine and its relapse after introduction of olanzapine in this case confirm the role of olanzapine 5 mg/day in precipitating SRED episodes. Her physical examination was unremarkable except for an elevated BMI of 34.11 kg/m^2. For her residual depressive symptoms, lithium was added and it helped alleviate the depression.

3 | CASE 2

A 23-year-old Malay woman presented with multiple depressive symptoms such as low mood, anhedonia, poor appetite, poor concentration, feeling of worthlessness, and hopelessness due to problems with her boyfriend. She also had been suffering from poor sleep for many years. I initially diagnosed her as a case of major depression and prescribed desvenlafaxine 50 mg and lorazepam 1 mg. However, as the sleep was still poor, I added quetiapine 25 mg to aid in the sleep. A few months later, she developed psychosis in the absence of mood symptoms and I revised her diagnosis to schizoaffective disorder, depressive subtype with minimal psychosis. All investigations including a computerized tomography (CT scan) scan of the brain, and connective tissue screen were normal. I increased the quetiapine to 50 mg daily. At the dose of quetiapine 50 mg/day, she developed SRED. Patient was noted to open the refrigerator and take out a jar of hazelnut chocolate cream and eat it. She was also known to finish a big bars of chocolate. The patient ate bars of chocolate mostly while asleep. In the day, she generally does not consume that quantity of chocolate. However, chocolate is one of her favorite foods. This was witnessed by her mother whom she lives with. The SRED occurred almost every night.

The quetiapine was stopped and substituted with aripiprazole 5 mg with no further episodes. Her concurrent medication was desvenlafaxine 100 mg daily and lithium 300 mg ON. During the 5 months that the patient experienced SRED, she put on 5 kg. Physical examination was unremarkable. It was the same treating doctor for both cases, and hence, the side effect in the second case was identified earlier and a more appropriate drug was administered. Unlike in the first case, the second patient did not continue to have SRED as aripiprazole and not olanzapine was used as the substitute drug. In both cases, the patients are young and female. Young females more so than males are at added risk for SRED. In both cases, SRED occurred when quetiapine dose was increased and resolved when the medication was stopped.

Both cases have insignificant medical history, with no history of sleep walking, seizure, childhood or family history of parasomnia, or alcohol abuse. Both patients were unaware of their actions of eating while asleep until informed by family members.

4 | DISCUSSION

Poor sleep is a feature of many psychiatric disorders, and quetiapine is effective in inducing and maintaining sleep even at low doses, and it does not cause dependence.[8] SRED affects both the genders, ages ranging from 18[10] to 75 years.[8] Onset of SRED was two days[9] to a few months after starting quetiapine.

Risks of developing SRED are using antipsychotics, being female, and in the twenties.[4] The above 3 risk factors are present in both our cases. Studies using polysomnogram (PSG) have found that patients with SRED are more likely to experience other sleep disorders, such as sleepwalking, periodic limb movement disorder, restless legs syndrome, obstructive sleep apnea syndrome,[11] to be obese, and suffer from narcolepsy.[12] SRED appeared to occur more among the patients suffering from mood disorder rather than schizophrenia. Most of the time, the cessation was brought about by stopping the antipsychotic. In one case, clonazepam[2] was added and in another promethazine[8] was added. Short-acting sedatives exacerbate the sleepwalking but long-acting benzodiazepines such as clonazepam (0.5-2.0 mg) successfully suppress episodes.[2] The hypothesis is that clonazepam causes an increase in 5-HT/monoamine synthesis or decrease in 5-HT receptor sensitivity mediated through the GABA system, and regulation of GABA activity, which improves sleep thus preventing sleepwalking and SRED.[2] According to Cook et al, promethazine shows potency in blocking histamine H_1 receptors and acetyl choline muscarinic receptors. Promethazine is the most potently anticholinergic of the antihistamines.[13]

SRED occurred at doses as low as 25 mg of quetiapine[8] and as in case 1, 5 mg of olanzapine. SRED appeared to be dose-dependent as reducing the dose in some cases helped in the cessation of the problem. Switching to olanzapine in

case 1 did not help, but in case 2, switching to aripirazole resolved the SRED. Possibly, there are different mechanism at work.

The mechanism for quetiapine-induced SRED may be explained by the serotonin hypothesis of parasomnia.[6] Quetiapine causes:

- 5-HT2A receptor antagonism and 5-HT1A agonism.[5]
- Blockage at 5-HT2A in the dorsal raphe nucleus inhibits sleep and leads to partial arousal. Blockage of serotonin input can decrease normal motor inhibition, enabling the person to walk and perform other physical activities.[6] This dissociation between both the state of partial arousal and muscle hypotonia enables sleepwalking.[2,14] Among the antipsychotics, SRED was found to be precipitated more commonly with quetiapine [15] It has been suggested that very low doses of quetiapine can induce SW.[8]
- Antagonism of the serotonin receptor 5-HT2C in the hypothalamus increases appetite leading to food intake and weight gain.[16]
- Patients who are on antipsychotics and gaining weight were found to have associated elevated leptin levels.[17]
- Quetiapine and olanzapine have a high degree of histamine (H1) receptor affinity. H1 receptor blockade results in sedation, increased appetite, and increased periodic limb movement (resulting in partial arousals during NREM sleep) [2]

The findings by Fihueroa et al suggest that modifying the formulation does not change the overall pharmacokinetics of quetiapine, and supports emerging clinical evidence for the use of quetiapine XR as a once daily treatment in patients initiating therapy or those established on quetiapine IR.[18] Pharmacokinetic studies show that quetiapine XR provides a lower peak and more stable plasma concentration than the IR formulation.[19]

Finally, it is important to differentiate SRED from night eating disorder. While the former is a parasomnia, the latter is an eating disorder.[20] Other differential diagnoses of SRED include nocturnal binge eating disorder, bulimia nervosa, dissociate disorder, and kleine-Levin syndrome.

4.1 | Strengths

1. Both patients had good medication adherence and premorbid function. Patient in case 1 had an undergraduate degree and patient in case 2 was pursuing an undergraduate degree. Hence, this may have made them better historians.
2. The patients had no comorbid medical conditions, concomitant medications than what is mentioned, no previous history of other parasomnia, head injury, or epilepsy. The presentation could be mimicked by other medical conditions.

4.2 | Limitations

1. Serum quetiapine was never assessed. It must be taken into consideration that serum level of quetiapine is higher when used with concomitant medication.[21] .
2. The frequency and nature of food and timing of the SRED are not well documented as this is a retrospective observation.

5 | CONCLUSION

SRED can occur at low doses of quetiapine. Possible SRED should be informed to the patient and assessed at follow-ups. Further research is necessary in assessing prevalence of SRED among various antipsychotics and similarities and differences among antipsychotics in causing SRED as well as specific patient factors.

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CONFLICT OF INTEREST
The author declares there is no conflict of interest.

AUTHOR CONTRIBUTIONS
Sharmilla Kanagasundram was solely responsible for the preparation and drafting the manuscript. She was involved in both patients' care, including diagnosing and managing the patients' conditions. She collected the patient information and revised the article critically for intellectual content as well as approved the final version of the article. Sharmilla Kanagasundram takes public responsibility for the content and is accountable for all aspects of the work.

ETHICS STATEMENT
Sharmilla Kanagasundram has been a consultant psychiatrist in the Department of Psychological Medicine, University Malaya for many years and has experience and qualifications in Psychiatry and Psychotherapy.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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