Suvorexant for Primary Insomnia in a Patient at High Risk for Hypnotic Dependence

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Despite primary reports of zolpidem safety and minor abuse and dependency capability,[1,2] subsequent reports showed that zolpidem can lead to abuse and dependency.[3–8] Also, the elderly and women have decreased clearance capacity to zolpidem, which can possibly predispose patients to zolpidem dependence.[6,9]

Suvorexant is an orexin 1 and 2 receptor antagonist that is US Food and Drug Administration (FDA) approved for the treatment of primary insomnia. Animal studies[10–15] report orexin 1 antagonism to decrease craving and orexin 2 receptor antagonism to improve sleep. Zolpidem is commonly prescribed for the treatment of insomnia with a risk of tolerance and dependence. Such tolerance and dependence can lead to worsening of insomnia. Here, we present the case of a patient dependent on zolpidem for chronic insomnia, who was treated with suvorexant, which improved sleep and decreased craving for zolpidem.

Case Report

The patient was a 50-year-old woman who presented with a 5-year history of difficulty falling (latency > 30 minutes) and staying asleep (< 5 hours). There was a history of snoring but no observed apnea. She presented with subjective daytime sleepiness with decreased attention and concentration and feeling sleepy at work. The baseline habits were established based on patient self-report to providers, which included a primary care physician (PCP) and subsequently sleep clinic providers (initially an outside provider and then later a provider at our clinic).

She scored 4/24 on the Epworth Sleepiness Scale.[16] She had a hyperactive mind, thinking about day-to-day issues, which prevented her from napping or dozing off during the daytime. Her past medical history was significant for episodic worsening of major depressive disorder with 1 inpatient hospitalization for suicidal behavior (overdose) about 10 years before this presentation. Her depression was managed by her PCP and treated with quetiapine 200 mg and fluoxetine 60 mg. Other medical issues included obesity with a body mass index of 30 kg/m^2 for which she was not on any active treatment. She did not smoke, denied using alcohol or other drugs for recreation, and drank about 1 cup of coffee and two 16-ounce sodas per day.

Her family physician prescribed various hypnotics including trazodone (up to 150 mg) at night, temazepam 10 mg, alprazolam 1 mg, doxepin 6 mg, zaleplon 10 mg, and quetiapine 200 mg over 5 years. The sleep physician (outside provider) recommended a polysomnogram with multiple sleep latency test for evaluation of daytime sleepiness. On the overnight polysomnogram, she had a sleep latency of 42 minutes and a total sleep time of 330 minutes with a sleep efficiency of 65% (Table 1). On the multiple sleep latency test, she did not have sleep or sleep onset rapid eye movement periods during any of the naps (Table 2). On recommendation of the sleep clinic (outside provider), she was started on an initial dose of zolpidem 10 mg, on which she slept for 3 to 4 hours. She took an additional tablet of zolpidem 10 mg with her awakenings at night. She later increased the dosage to 3 to 4 tablets of zolpidem 10 mg at night, as she woke up every 2 hours and was awake for at least 30 minutes each time. She used to crave zolpidem 10 mg when she woke up at night. She ran out of her medications before she was due for the next prescription and was having self-limiting withdrawal symptoms including shaking, shivering, and sweating for 1 to 2 nights, which was suggestive of dependence. With deterioration in her sleep, she experienced worsening depression with passive suicidal thoughts.

She had a second sleep physician evaluation (at our clinic) 1 year after her initial sleep evaluation. She was started on suvorexant 10 mg with partial response and later increased to 15 mg at night within 1 week, resulting

Table 1. Sleep Study Results

Measure	Result
Sleep latency, min	42.0
REM latency, min	340.0
Time in bed, min	466.0
Total sleep time, min	330.0
Sleep efficiency, %	65.0
Stage N1, %	38.3
Stage N2, %	57.3
Stage N3, %	0.0
REM, %	4.4
Apnea Hypopnea Index	0.0
Periodic Leg Movement Index	0.0

Abbreviation: REM = rapid eye movement.

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Table 2. Mean Sleep Latency Test Results

Start Time	Stop Time	Sleep Latency	REM Latency	Total Sleep
8:48 PM	9:08 PM	20.0	No Sleep	0.0
10:44 PM	11:04 PM	20.0	No Sleep	0.0
12:44 AM	1:04 AM	20.0	No Sleep	0.0
2:45 AM	3:05 AM	20.0	No Sleep	0.0
Average		20.0	No REM	0.0

Abbreviation: REM = rapid eye movement.

in further improvement in sleep. This improvement was as reported by the patient and charted on the sleep diary. Her sleep latency was reduced (less than 30 minutes) with increase in total sleep time (to 6 1/2 hours), increased sleep efficiency, and overall sleep quality. Her Epworth Sleepiness Scale score decreased to 0/24. She did not crave zolpidem, and her daytime functioning improved. She reported falling asleep within 30 minutes and slept for 6 1/2 to 7 hours with occasional short (less than 1 minute) awakening in the middle of the night. She reported improvement in her mood with no further passive suicidal ideations. She was more awake and alert with improved concentration at work. This improvement persisted for 3 weeks while she was taking suvorexant. She stopped suvorexant after 3 weeks due to insurance coverage issues. She was again prescribed zolpidem, on which she had sleep fragmentation as before and started taking it multiple times at night with cravings for the medication. She also reported worsening of mood symptoms. She was referred for a second opinion again by her primary care and was prescribed suvorexant 15 mg at night for the second time, which again (approved by insurance) led to remission of insomnia, craving, and associated mood symptoms as described previously. Her treatment regimen for depression remained unchanged throughout this period.

Discussion

Suvorexant is an orexin 1 and 2 receptor antagonist FDA approved for the treatment of primary insomnia. The American Academy of Sleep Medicine recommends suvorexant for the treatment of sleep onset and sleep maintenance.[17] In our case report, suvorexant decreased sleep latency (to less than 30 minutes), improved total sleep time (to 6 1/2 to 7 hours), and decreased awakenings (from 3 to 4 to 1).

Despite preliminary reports of zolpidem safety and minor abuse and dependency capability,[1,2] subsequent reports showed that zolpidem can lead to abuse and dependency.[3–8] Also, the elderly and women have decreased clearance capacity to zolpidem, which can possibly predispose patients to zolpidem dependence.[6,9]

Orexins are known to have a variety of functions, most notably in regulating arousal, appetite, and reward.[12] Previous studies[13–15] reported orexin 1 receptors to be involved in craving and orexin 1 receptor antagonists to decrease craving in animal models. Orexin 2 receptors are involved in sleep, and orexin 2 receptor antagonists improve sleep as shown in animal models.[3] Suvorexant, a dual receptor antagonist, improved sleep and decreased craving for zolpidem in our patient. In our case, improved sleep was associated with improved daytime functioning and mood and decreased passive suicidal ideations, which further reinforces the role of sleep in daytime functioning, regulation of mood, and self-injurious behavior.[18,19]

This is the first case report, to our knowledge, of suvorexant decreasing craving and improving sleep in a patient dependent on zolpidem. Further studies should explore the effectiveness of suvorexant on sleep and craving in substance use disorder patients, elderly patients, patients experiencing craving and dependence, and patients at higher risk of abuse while on other traditional hypnotics widely used to treat sleep disturbance.

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