Long Term Zolpidem Dependency Exceeding 100 Times the Maximum Dose: A Case Report of Severe Withdrawal Syndrome and Detoxification

Derek Kohler, DO; Maha Gaber, OMS-4; Janny Rivera, DO

Arnot Ogden Medical Center, Department of Psychiatry

Introduction

Zolpidem is a nonbenzodiazepine hypnotic medication indicated for short-term use in patients with insomnia and has the potential for misuse. It is thought that adaptive changes over time in the GABA-A receptors play a role in the development of tolerance and dependence.[1] Severe withdrawal symptoms from zolpidem are rare with a reported incidence of 1% or less.[2] This incidence is likely higher with misuse. Abruptly discontinuing chronic use at high doses has the potential for severe symptoms that can resemble withdrawal from benzodiazepines.[3] This can include anxiety, gastrointestinal issues, and seizures. Symptoms frequently occur within 48 hours following the last dose of zolpidem.

Case Presentation

The patient is a 46-year-old Caucasian female with a history of hypothyroidism, insomnia, depression, anxiety, and two decades of escalating zolpidem misuse with daily doses ranging from 300 to 1200 mg and six reported incidents of withdrawal seizures in the past year from unsuccessful discontinuation. Due to the extent of her abuse, she had been unable to return to work for several months out of fear of having more seizures. She attempted inpatient rehab on several occasions with subsequent relapse. She went through cycles of self-escalating her doses due to difficulty sleeping as well as anxiety over trying to prevent withdrawal seizures. The patient only had a prescription for zolpidem 10 mg daily, however she was able to sustain her habit through illicit means: She reported having pills shipped internationally, buying from local dealers, and having friends obtain their own prescriptions on her behalf. She presented to the hospital on transfer from inpatient rehab after being unsuccessfully managed with several doses of diazepam 5 mg. She reported that she took 400 mg of zolpidem over the course of the past 24 hours. Her initial presentation included visible discomfort, anxiety, slight confusion, photosensitivity, body aches, abdominal discomfort, nausea, diarrhea, mild tremor, and piloerection.

Hospital Course

Day 1:

In the ED, Poison Control was contacted and the patient was started on a three-day phenobarbital taper to prevent withdrawal due to its long half-life and auto tapering after discontinuation. She also received levetiracetam 1000 mg for seizure prophylaxis. She was admitted to the hospital for further observation.

Psychiatry consult revealed no history suggestive of bipolar disorder, psychosis, depression, or posttraumatic stress disorder. The patient had denied anxiety except for related to worrying at night whether or not she would be able to fall asleep. Trazodone 50 mg was started at bedtime for insomnia, and gabapentin 100 mg was started at bedtime for anxiety related to not being able to fall asleep.

Day 2:

She was able to sleep approximately 4 to 5 hours total the first night. Her withdrawal symptoms were improving, as she was better able to tolerate stimuli such as light and noise. Trazodone was increased to 100 mg at bedtime for insomnia. She reported a delayed sleep onset of about three hours on Day 2, but once falling asleep she stayed asleep for 6.5 hours.

Hospital Course (Cont…)

Day 3:

She reported that her anxiety had been minimal overnight. Her withdrawal symptoms such as gastrointestinal side effects were resolving. She did not want to return to inpatient rehab and was discharged on hospital day three with addiction psychiatrist outpatient follow-up.

3-Day Phenobarbital Protocol Taper for Withdrawal

	Dosage	Frequency	Total Doses
Day 1:	130mg PO	Q4	6
Day 2:	130mg PO	Q6	4
Day 3:	130mg PO	Q8	3

Discussion

- The objective of this case report is to educate clinicians about zolpidem tolerance, abuse potential, and withdrawal management. Clinicians should question the necessity of continuing their patients on zolpidem for insomnia long-term due to tolerance. They should also be aware of the typical symptoms of withdrawal.
- Serious zolpidem withdrawal is not commonly encountered but more cases are being documented.[4,5] The most significant issue related to withdrawal is seizures, which can be life-threatening.
- Our case outlines management of the acute withdrawal period and seizure prevention with the administration of phenobarbital, levetiracetam, trazodone, and gabapentin.
- In literature of a similar patient misusing zolpidem 1200 mg per day, successful treatment involved tapering off high-dose zolpidem and replacing it with clonazepam, sertraline, and pregabalin.[6] A gradual cross-taper method may be ideal as a means to prevent seizures and allow the patient to better tolerate discontinuation.

References

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For additional information please contact:
Derek Kohler, DO: dkohler@arnothealth.org
Maha Gaber, OMS-4: mgaber90617@med.lecom.edu
Janny Rivera, DO: jrivera@arnothealth.org