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A Case Report on Zolpidem Abuse:Dependence and Withdrawal Syndrome

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ABSTRACT

This case report presents a 25-year-old male with a history of insomnia and depression, who developed zolpidem abuse, dependence, and withdrawal syndrome. The patient had been consuming high doses of zolpidem—up to 150 mg per day—for eight months. Following abrupt discontinuation of the drug, he experienced seizures within 24 hours. The seizures were managed using phenytoin, and detoxification was carried out with diazepam. This case highlights the importance of proper counseling about zolpidem, including its appropriate dosage, potential adverse effects, and the risks associated with sudden withdrawal. Clinical pharmacists play a crucial role in educating patients to prevent such complications.

Keywords: Zolpidem, abuse, dependence, withdrawal syndrome, seizures

Zolpidem, chemically known as *N,N,6-trimethyl-2[4-methyl-phenyl] imidazo[1,2-a]pyridine-3-acetamide hemitartrate*, is a hypnotic medication classified under the imidazopyridine group. It is widely prescribed for the management of insomnia. Zolpidem was first introduced in Europe in 1986 for insomnia treatment, followed by its launch in France in 1987 and in the United States in 1993.

During the 1970s, benzodiazepines emerged as a treatment option for insomnia and various sleep disorders. However, due to their adverse effects—such as drowsiness, dizziness, confusion, fatigue, and rebound insomnia—as well as issues of tolerance and abuse, their use declined. This prompted the development of non-benzodiazepine alternatives, including cyclopyrrolones (like zopiclone and eszopiclone), imidazopyridines (such as zolpidem), and pyrazolopyrimidines (like zaleplon), all of which are now commonly used to treat insomnia.

Zolpidem works by enhancing the inhibitory activity of the GABA_A receptors in the brain, leading to sleep induction. It is known to maintain deep sleep stages (Stage 3 and Stage 4) and improve slow-wave sleep more effectively than traditional benzodiazepines. The standard therapeutic dosage ranges from 5 to 10 mg, and the drug has a half-life of approximately 1.4 to 4.5 hours. Zolpidem is metabolized into inactive forms and eliminated via the urinary system.

Reported side effects of zolpidem include dizziness, fatigue, agitation, headaches, hallucinations, vivid dreams, and nausea. In rare cases, it has also been linked to suicidal ideation, as documented in a report by Hejiri et al. involving a 24-year-old male who consumed 20 mg of zolpidem. Although numerous studies highlight the potential for abuse and dependence associated with zolpidem, instances of seizures resulting from its abrupt discontinuation are relatively rare.

The withdrawal effects of zolpidem closely resemble those of benzodiazepines and may include insomnia, tremors, anxiety, palpitations, and seizures. Additional symptoms can involve fatigue, nausea,

flushing, dizziness, vomiting, abdominal cramps, panic attacks, nervousness, and gastrointestinal discomfort.

This paper presents a clinical case involving a patient who misused high doses of zolpidem (150 mg daily), developed dependency, and experienced seizures following sudden withdrawal.

Case Report

A 25-year-old male with a known history of psychiatric illness presented to Vishwa Bharathi Superspeciality Hospital with generalized tonic-clonic seizures. The patient had previously been diagnosed with multiple personality disorder in 2008 and was under psychiatric care for two years, after which he showed improvement. However, he later developed depression and insomnia, reportedly due to social isolation.

To manage his symptoms, he was prescribed zolpidem 10 mg for insomnia, in addition to trazodone and divalproex for depression. Over time, the patient began abusing zolpidem, escalating the dose to 150 mg/day, and had been using it at this high dose for approximately eight months.

During this period of high-dose usage, the patient experienced hallucinations and suicidal ideation. His parents eventually became aware of the zolpidem abuse and intervened by abruptly discontinuing the medication. Within 24 hours of stopping zolpidem, the patient developed generalized tonic-clonic seizures, accompanied by drooling of saliva. He remained unconscious for around 30 minutes, followed by a phase of postictal confusion.

Other withdrawal symptoms observed included insomnia, anxiety, restlessness, and a heavy headache. Following the seizure episode, the patient was admitted to the hospital. The seizures were managed with phenytoin, and detoxification from zolpidem was initiated using diazepam.

Discussion

Zolpidem, a non-benzodiazepine hypnotic agent, was developed by Synthelábo Recherche in the early 1980s for the management of insomnia. It primarily acts on the ω1 subunit (alpha-1) of the GABA_A benzodiazepine receptor complex in the central nervous system, leading to sedative and hypnotic effects. However, at higher doses (above 10 mg), zolpidem can lose its receptor selectivity, potentially interacting with other benzodiazepine receptor subtypes, thereby mimicking classical benzodiazepine-like pharmacological effects.

Zolpidem is frequently prescribed for sleep disorders, making it one of the most commonly misused hypnotic medications. Due to its widespread use and rapid onset of action, the risk of dependency and abuse is significantly high. In the present case, the patient consumed an excessive dose of 150 mg per day for eight months, developing a clear pattern of dependence and abuse. During this period, the patient reported hallucinations, experienced suicidal ideation, and even attempted suicide.

Similar findings have been reported in prior literature. Singh et al. documented a case of hallucinations in a 20-year-old female receiving 10 mg zolpidem for insomnia. Another report by Hejri et al. described a young male who, after ingesting 20 mg of zolpidem, exhibited altered thought processes and later attempted suicide by consuming 60 mg. Additionally, Susan et al. presented two cases of zolpidem-related suicides, both resulting in fatal outcomes.

Zolpidem withdrawal is known to produce symptoms akin to benzodiazepine withdrawal, including insomnia, anxiety, tremors, palpitations, and seizures. In this case, the patient experienced generalized tonic-clonic seizures following abrupt discontinuation of zolpidem, along with anxiety and severe

insomnia. A similar episode was reported by Chang et al., where a 40-year-old married woman developed generalized seizures after stopping zolpidem used for sleep disturbances.
This case reinforces the need for cautious prescribing practices, patient education, and close monitoring of zolpidem, particularly in individuals with psychiatric vulnerabilities.

Conclusion

Zolpidem abuse, dependence, and withdrawal can significantly impact a patient's overall quality of life, particularly in individuals being treated for insomnia. Misuse of this medication is becoming increasingly common among such patients, leading to serious psychological and neurological complications. To prevent these adverse outcomes, it is essential to provide thorough patient counseling regarding the appropriate dosage, frequency of administration, potential side effects, and the risks associated with abrupt discontinuation. Clinical pharmacists hold a critical responsibility in this educational process, ensuring safe and informed use of zolpidem.

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