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Case Report

# Zolpidem dependence with frontal lobe syndrome: a case report

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## ABSTRACT

Zolpidem is a non-benzodiazepine sedative hypnotic that binds to the benzodiazepine binding site on the gammaaminobutyric acid type A (GABA-A) receptors. It is the most commonly prescribed sleep medication which has been shown to be effective for treating insomnia on a short-term basis with fewer side effects than traditional benzodiazepines, which are feared for their abuse and dependence potential. Many studies have reported efficacy and safety of zolpidem in treatment of insomnia keeping in mind about its low abuse, and dependence capability. We present a case of zolpidem dependence in a 36-year-old male to emphasize that zolpidem also should be judiciously prescribed under supervision so that it does not develop tolerance, abuse and dependence.

**Keywords:** Dependence, Frontal lobe syndrome, Insomnia, Zolpidem

## INTRODUCTION

Insomnia disorder is the most prevalent sleep disorder, diagnosed when there is difficulty getting to sleep and/or staying asleep, with distress regarding sleep issue and/or daytime impairment. Zolpidem is the most commonly prescribed sleep medication, where almost 39 million prescriptions written in the United States in 2011.[1,2] However, in contrast to BDZs, zolpidem shows selectivity for the V1 receptor subtype, which corresponds to GABA A receptors containing the a1 subunit1. Zolpidem is able to produce sedation without interfering with the BDZ properties linked to other receptor subtypes.[3] So zolpidem was considered a safer hypnotic than benzodiazepines because of a lesser liability for abuse and dependence.

However, in recent years, new evidence has revealed that the behavioral effects of zolpidem at higher than recommended doses are generally similar to those of BDZs. As the use of benzodiazepines (BDZs) in the treatment of insomnia has been declining in recent years as a result of studies documenting a series of deleterious effects (addiction, rebound insomnia, etc.), the prescription of non-BDZ hypnotics, such as zolpidem has been increasing substantially. There is some indication that zolpidem can have an anxiolytic effect at higher doses and that with increasing dose of zolpidem for sleep can lead to withdrawal side effects during the daytime.[4] The guideline also states that the duration of treatment should usually vary from a few days to two weeks with a maximum of four weeks, including tapering off where appropriate.[5] However, recently concern has been raised regarding the dependence potential of these Z-drugs.[6] In the last few

years, several cases of misuse of the Z-drugs characterized by significant dose escalation, dependence, abuse and withdrawal symptoms have been reported.[7-10] We present a case of zolpidem dependence in a 36-year-old male to highlight the need for caution when prescribing this drug.

## CASE REPORT

The patient 32 years old married male from urban setting, teacher by profession presented to the psychiatry outpatient facility of our institute with sleep disturbances and inability to stop zolpidem use. He started to use spasmo-proxyvon (dextropropoxyphene) tablets recreationally since 2011 while after about 1 year he started abusing the same with a daily intake of 16 tablets per day. Nearly one and a half year back in 2015 one day he consumed a relatively higher dose of tablets than usual (nearly 30 tablets) and had a fainting attack followed by head injury with extradural hemorrhage which required prompt neurosurgical intervention.

During discharge he was prescribed tablet zolpidem 10mg for insomnia. Despite using usual dose of Zolpidem he couldn't initiate sleep at night and could sleep for a maximum duration of 3-4 hours with frequent awakenings. Hence he started self medication and increased taking 2-3 tablets of zolpidem. Following that he could sleep better and had a sense of euphoria. He enjoyed the high and gradually started increasing the dose to 2-3 tablets every 7-10 days and during presentation he was taking 24-26 tablets (240-260mg) of Zolpidem 10mg in 4 divided doses over 24 hours. Whenever he didn't consume zolpidem he developed insomnia, irritability, generalized weakness, excessive desire to take the same every after 4-6 hours which went on increasing day by day.

Despite knowing the harmful effects of consuming unsupervised higher dose of the drug he couldn't stop himself from taking it. His family, socio-occupational and cultural life was impaired to great extent and gradually he spent most of his time in procuring the drug from pharmacies. Since last 15-18 months he also developed persistent low mood present almost whole day for most of the days, generalized lack of interest in pleasurable activities and his teaching job, easy fatigability, lack of motivation and dizziness off and on.

He was assessed and admitted in psychiatric ward and detoxification was started with Diazepam 20mg tablet with Clobazam 10mg tablet in divided doses. Gradually the benzodiazepines were tapered off over 15 days. 6 sessions of motivational enhancement therapy were provided along with relapse prevention. After detoxification he was educated about sleep hygiene measures and the need to abstain from benzodiazepines and other hypnotics. He has till date been on follow-up for more them 2 months. He is having normal sleep and is abstinent from zolpidem and other hypnotics.

## DISCUSSION

Zolpidem is a non-benzodiazepine hypnotic. Its mechanism of action is selective benzodiazepine type 1 receptor agonist. However, other studies suggest at higher does it loses selectivity and may have addictive potential similar to benzodiazepines.[10] Rappa et al described a case of zolpidem dependence detoxified using a 7 days tapering regime of diazepam. Our patient was also treated with a 15 weeks tapering dose of diazepam and clobazam. It has been proposed that possible GABA-A receptor mutations may be a predisposing factor in zolpidem dependency.[11] Literature suggests that patients with a history of drug abuse or dependence or those with psychiatric disorders are at increased risk of abuse of zolpidem and other Z-drugs, which is also consistent with our study.[12]

In view of several case reports of Z-drugs dependence in the last few years, it is suggested that the same stringent precautions as with benzodiazepines should be adhered to while prescribing these Z-drugs. Since there are presently no clear-cut guidelines for the treatment of Z-drugs dependence, prevention is probably the best form of treatment. There is also an urgent need to study the range of treatment options for dependent patients, but it would be expected that gradual withdrawal would be as prominent as with benzodiazepines.

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