

## Case Report

# Zolpidem dependence

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## Abstract

Recently, Zolpidem dependence is rising in clinical practice. It was once thought to have low addictive potential due to its selective affinity to  $\alpha 1$ -GABA<sub>A</sub> receptors. However, contemporary studies have shown that Zolpidem may lack selectivity when used at high dose for extended periods of time and may show addictive potential similar to that of the benzodiazepines. We hereby report a case of Zolpidem dependence in a physician with insomnia, which was successfully detoxified with Diazepam to emphasize the caution while prescribing it.

**Key Words:** Dependence, Zolpidem.

## Introduction

Zolpidem is a non-benzodiazepine drug, approved by FDA for sleep induction. Earlier it was considered to be a safer hypnotic than benzodiazepines due to its lesser potentiality to cause abuse and dependence.<sup>1</sup> Therefore in past two decades its prescription started to scale up whereas benzodiazepine prescription considerably decreased.<sup>2</sup>

However, in last decade numerous cases of zolpidem abuse or dependence were reported.<sup>3</sup> As a result, on 2002, zolpidem was classified as Schedule IV controlled substance under Controlled Substances Act in the U.S. Which meant zolpidem was accounted to be equivalent to benzodiazepines in terms of abuse potential.<sup>4</sup>

These days in Nepal, Zolpidem is widely prescribed by the psychiatrist and other physicians for a variety of sleep problems. Here, we present a case of zolpidem dependence in a physician himself, emphasizing the need to be cautious while prescribing and using this drug.

## Case Presentation

The case is a 33 years old physician who developed insomnia at the age of 28, when he was doing his

residency in Internal Medicine. Patient sought consultation for his sleep problem with his supervisor at his work place. He was prescribed Zolpidem 10 mg each night for 2 weeks. Zolpidem helped him with sleep for two weeks but again experienced sleep difficulties after completion of the prescription duration. He started to buy medication by himself and continued using it for about 6 months. Gradually over time patient increased the dosage by himself initially for his persisting sleep problem and later as he developed a sense of relief and comfort during the period of use of Zolpidem. Due to this he used the medication multiple times in the day and would adjust his dose all by himself. By the time, he visited Psychiatrist, after about 5 years of regular use he was using 300 mg of Zolpidem per day in divided doses.

Patient was unaware of Zolpidem's abuse potential. Being a physician drug was easily accessible to him. He would buy drugs initially from the hospital pharmacy and later from various pharmacies. This was another contributing factor for his dependency. He had made several attempts previously to reduce the dose but failed due to resulting anxiety, restlessness, tremulousness and rebound sleep disturbances.

Finally, being motivated he visited Psychiatry service where he was admitted to Psychiatry ward for proper evaluation and management. The assessment revealed patient suffered from Primary insomnia from last 5 years then became dependent on zolpidem. He had an attack of cerebrovascular accident 3 years ago, resulting into left sided hemiparesis, but there was almost complete recovery with no major deficit. The exact cause of the event was not known however the identifiable risk factor for cerebrovascular event in the patient was smoking and newly diagnosed hypertension. Patient was then put on antihypertensive agent Losartan hydrochloride 50 mg once daily and aspirin 75 mg once daily. There was no history of any other physical, psychiatric illness or substance abuse except for nicotine dependence.

On admission, Zolpidem was stopped and switched over to equivalent dose of Diazepam. Patient was admitted for 2 weeks till the stabilization of dosage. Then, diazepam was tapered at the rate of 20% every fortnightly from outpatient basis. Mirtazapine 15 mg per day was added to curtail the sleep problem while dose was tapered and by 16 weeks diazepam was completely stopped.

## Discussion

Zolpidem is a rapid onset short acting hypnotic. It acts on GABA<sub>A</sub> receptors at the same location as Benzodiazepine but it differs in affinity to subunits of GABA<sub>A</sub> receptor. BZDs have nonselective affinity to GABA<sub>A</sub> subunits. But, Zolpidem displays high affinity to  $\alpha 1$  subunit. This  $\alpha 1$  subunit is responsible for sedative-hypnotic effect. Therefore, Zolpidem was considered to be purely hypnotic.<sup>5</sup> However, latter studies showed abuse potential similar to those of benzodiazepines.<sup>3</sup>

It has been reported that zolpidem pharmacodynamics and pharmacokinetics may have a crucial role in cases of zolpidem abuse and dependence. It is suggested that zolpidem might lose its selectivity on  $\alpha 1$ -GABA<sub>A</sub> receptors, particularly at high doses and long-term use.<sup>6</sup> It is also suggested possibility of GABA<sub>A</sub> receptor mutations which may be a predisposing factor for zolpidem dependence.<sup>7</sup> Studies have reported prior history or comorbidity of substance abuse or dependence, having other psychiatric illnesses and female gender to be other risk factors for Zolpidem dependence.<sup>3,8</sup> But in our case nicotine dependence was only the risk factor.

As, Zolpidem dependence, is a growing problem there is also need to explore different strategies for its management. Till date there is no standard pharmacological guideline for its treatment. However there are case reports that have successfully used the agents like Diazepam, Lorazepam, Quetiapine and Gabapentin for its management.<sup>9, 10, 11</sup> We treated our patient with diazepam and tapered it in 16 weeks. Our case exemplifies successful treatment of Zolpidem dependence by use of diazepam. Possible bio mechanism could be that at higher dose zolpidem might lose its selectivity on GABA<sub>A</sub> receptor and exert the same pharmacological effects as classical benzodiazepines or alcohol.<sup>6</sup>

However, as it is always better to prevent the problem, taking our case's example, we would like to emphasize that prescribers should be aware of Zolpidem's dependence potential.

**Conflict of interest: None declared.**

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