

# **Zolpidem Dependence Syndrome- A report of Two Cases**

**Ajeet Sidana, Priti Arun, Sachin Rai**

## **ABSTRACT**

*Many drugs (hypnotics) are prescribed for sleep disorders. Benzodiazepines have been the most widely used but they carry the risk of abuse and dependence. Some drugs like zolpidem were manufactured as having no or very low dependence potential but in the recent times cases of zolpidem dependence syndrome have been reported. The authors report two cases of zolpidem dependence syndrome.*

**Key words:** zolpidem dependence syndrome

## **INTRODUCTION**

Recent large scale epidemiological studies have confirmed the importance of insomnia as an extremely prevalent condition in the general population.<sup>1</sup> Approximately every second patient seeing a general physician in routine care has significant sleep complaints, and every fourth patient fulfils the DSM-IV criteria for insomnia.<sup>2</sup>

The short-acting imidazopyridine hypnotic Zolpidem was introduced in clinical practice in 1988 and is now prescribed widely by the psychiatrists and other health professionals globally. It has been suggested that it acts selectively on alpha1 subunit-containing GABA benzodiazepine (BZ1) receptors presenting (contrary to classic benzodiazepines) low or no affinity for other subtypes of receptors. Therefore, it has been proposed that it lacks the benzodiazepines-like side-effects, having minimal abuse and dependence potential. Nevertheless, there is considerable number of zolpidem dependence case reports in the literature.<sup>3</sup>

Here the authors report 2 cases of Zolpidem dependence who were using very high doses of Zolpidem (up to 300mg/day) with atypical withdrawal syndrome.

## **CASE I**

Mr. PS is 44 Years married male, farmer by occupation, hailing from middle socioeconomic status family and is a known case of Obsessive Compulsive Disorder (OCD) for last 18 years. His OCD symptoms were partially controlled with Serotonin Specific Reuptake Inhibitor.

Patient started taking tab. Zolpidem 10mg for sleep disturbances without any prescription from from doctor since last 1 year. Initially he used to take Zolpidem 30-40 mg/day but increased it to 30 tabs (Zolpidem 300mg)/day since last 3 months. Whenever he missed the Zolpidem, he experienced withdrawal in the form of restlessness, palpitation, dryness of mouth, irritability, choking sensations and would also have blurring of vision, increased frequency of micturition, sneezing and intense craving for Zolpidem. He tried to stop Zolpidem many times unsuccessfully. He was admitted in psychiatry ward and treated symptomatically.

## **CASE-II**

Mr. RK is 43 years, widowed, bank employee, from middle socioeconomic status family, with history of multiple stressors in the recent past,

presented with chief complaints of sleep disturbance in onset and intermittent awakenings and intermittent sadness of mood since 1 year. The onset of the illness was acute and was precipitated by his wife's death and had a continuous course. He went to a private psychiatrist and was started on tab. zolpidem 10mg at night time. The patient started taking 20-30mg of Zolpidem for getting sleep. After about 1 month, he started taking zolpidem to 20-30 mg during daytime because of craving for it. After about 2 months, he developed anxiety with restlessness, tremors in hands and pain in the calves which would subside after taking 20-30mg of zolpidem. Over the next few weeks, zolpidem intake increased to 100mg per day because of craving, and fear of withdrawals. At times, he took 40-50tablets of 10mg zolpidem at one time and then became confused along with redness of eyes, slurred speech, difficulty in walking straight, drowsiness without any sleep. With a diagnosis of zolpidem dependence syndrome, he was admitted in the psychiatry ward. The last intake of zolpidem 30mg was on the day of admission. In the indoor setting, no other psychiatric diagnosis could be made. He reported anxiety, pain in calves and craving for zolpidem. He was prescribed tab. clonazepam 6 mg/day. On the 5<sup>th</sup> day in the ward, other withdrawal symptoms in the form of running nose, lacrimation and yawning were seen. All the symptoms subsided by the 8<sup>th</sup> day of admission.

## DISCUSSION

Previous reports of withdrawal symptoms of oral zolpidem abuse/dependence are those of Benzodiazepine-like withdrawal symptoms i.e. tremors, agitation, anxiety and seizure.<sup>4,5</sup> Ours is the first report of oral zolpidem dependence with mixed kind of withdrawals i.e. Benzodiazepine and opiate-like( yawning, lacrimation, sweating, running of nose and body aches).

Animal studies have shown that withdrawal of zolpidem induces changes in GABA<sub>A</sub>-receptors gene expression<sup>6,7</sup> and stimulation of GABA<sub>A</sub>- receptors reduces yawning. Other possible explanation for opiate-like withdrawal could be that zolpidem may have indirect effect on the opiate system through GABA<sub>A</sub>- receptors and animal studies shows co expression of opioid system and GABA<sub>A</sub>- receptors by the same neuron in the rat brain.<sup>6,7</sup>

Third possibility can be that Nucleus ceruleus is under inhibitory control of GABA and reduced GABA levels are responsible for increased adrenergic activity in the form of lacrimation, sweating, running of nose etc.

Whatever may be the mechanism, but its clear that zolpidem shows abuse/dependence potential and sometimes can have physical withdrawal symptoms as in our case. Thus these reports suggest that zolpidem should be used cautiously.

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