

**A CASE REPORT ON ZOLPIDEM INDUCED HALLUCINATION**

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**ABSTRACT**

Zolpidem is a newer non benzodiazepine hypnotic class of drug and it is the most widely used drug for the treatment of insomnia. Zolpidem have central nervous system related side effects such as headache(19%), depression (2%), memory difficults (1.8%), abnormal dreams (1%). This is a case on zolpidem induced hallucination in which the patient experienced at a single dose of zolpidem 10 mg. Then the dose was titrated to 5 mg but the patient was in a hallucinatory stage and after the discontinuation of the drug the patient got back to the normal stage. For the treatment of insomnia it is recommended to stick to the lowest effective dose for as short as

possible together with sleep hygiene techniques.

**KEYWORDS:** Zolpidem, Hallucination, Insomnia.

**INTRODUCTION**

According to National Institute of health consensus statement for the treatment of chronic insomnia in adult, zolpidem was considered as a hypnotic with limited risk.<sup>[1]</sup> Zolpidem is a newer non benzodiazepine hypnotic class of drug and it is the most widely used drug for the treatment of insomnia.<sup>[2]</sup> The chemical name is N, N-6-trimethyl-2-p- tolyl- imidazol and the drug is short acting imidazopyridine compound.<sup>[3, 4]</sup> It was launched in France in 1980 and approved by FDA in 1982.<sup>[5, 6]</sup> Zolpidem, Zopiclone and Zaleoplon are also called as 'Z-drugs'.<sup>[7]</sup> These group of hypnotics are clinically differ from benzodiazepines and act as agonist on a specific subset of benzodiazepine receptors and produce hypnotic amnesic action with only week anti anxiety, muscle relaxant and anti convulsant action. They have lower abuse potential than hypnotic benzodiazepines and given for the shorter duration of action.<sup>[2]</sup> Zolpidem have central nervous system related side effects such as headache(19%), depression

(2%), memory difficulties (1.8%), abnormal dreams (1%).<sup>[8]</sup> Here we present a case of zolpidem induced hallucination and delirium in a 20 year old male patient.

### CASE REPORT

This is a case on zolpidem induced hallucination which occurs with a single dose of zolpidem. A 20 yr old male patient presented to the hospital with the complaints of abdominal pain on and off for 7 days and insomnia for 10 days. He was apparently normal before 2 weeks and then he developed abdominal pain, insidious in onset. It was a colicky type of pain and progressive in nature. His USG report revealed that patient had subacute appendicitis. Patient was treated symptomatically and insomnia was treated with zolpidem 10 mg at night. Within 2 hours of administration of zolpidem the patient had abnormal speech at night. The patient spoke incorrectly using short phrases while he was sedative. There was no history of hallucination prior to the use of zolpidem. History for alcohol, tobacco or illicit drug use was negative. The patient reported no personal or family history of psychiatric or other illness. Then the dose was reduced to 5 mg but the patient was in a hallucinatory stage and finally the zolpidem was stopped. After the dechallenge of zolpidem the patient got back to the normal stage.

### DISCUSSION

Most of the cases reported in the literature were either mentally ill patients or in females. Females are more susceptible of zolpidem induced delirium because they have 45% more concentration of zolpidem.<sup>[9,10]</sup> In the psychotropic presenting guide from the physicians desk reference (PDR) the possibility of zolpidem induced hallucination is described though not shown to be frequent (between 1/100 and 1/1000 cases).<sup>[11]</sup> There is no hypothesis supporting for the zolpidem induced hallucination occurrence.<sup>[9, 12]</sup> Katz SE *et al* suggested that it was due to toxic plasma levels in susceptible patients or by the competition for the protein bond in concomitant used drugs that have high affinity with the protein such as some antidepressants.<sup>[13]</sup> But this is not consistent for the case we reported here. The rapid absorption of zolpidem may decrease the surveillance level, facilitating the occurrence of hallucinatory effect. It is clear that without any treatment after several hours of discontinuation of zolpidem the patient became normal. Ansseau *et al* reported the case of 2 patients who develop visual hallucination and anemia shortly after the intake of zolpidem.<sup>[14]</sup> Zolpidem undergoes rapid absorption from the GIT and the peak plasma concentration is about 0.5-1.6 hour.<sup>3</sup> A survey of 14029 patients treated with zolpidem for four weeks found

20 patients who reported nightmares, 1119 who reported agitation and one who developed paranoid ideation during treatment.<sup>[5]</sup>

Toner et al postulated that 4 variables should be considered before prescribing zolpidem.

**1. Gender:** women have been found to have a significantly higher serum zolpidem concentration than men.

**2. Zolpidem dose:** Zolpidem induced hallucinations occurred with doses greater than 5mg/d and were dose dependent.

**3. Protein- binding affinity:** A high proportion of zolpidem is protein bound in cases of patients with low levels of albumin, such as those suffering from malnutrition, a low serum albumin level would result in a higher level of free albumin.

**4: CYP 3 A 4 isoenzyme inhibition:** Zolpidem is metabolized via the CYP3A4 isoenzyme. Medication could decrease zolpidem metabolism leading to toxicity, especially by concomitant use with antidepressants.<sup>[9]</sup>

So many studies illustrates that patients with insomnia can be managed without drugs, limiting the use of hypnotics will limit any harmful effects.<sup>[6]</sup> Initially the insomnia patients should be practiced with sleep hygiene technique if it is not start hypnotics with lowest dose. At present, there is no good evidence that Z-drugs should be prescribed with unique precautions. If the patient is prescribed with Z-drugs should be made aware that sedation, confusion and disinhibition may occur. The hypnotic drug should be taken at night once the patient in bed, not on the way to bed.

## CONCLUSION

Zolpidem is a non benzodiazepine class of drug widely used for the treatment of insomnia. It is recommended to stick to the lowest effective dose for as short as possible together with sleep hygiene techniques. Clinicians prescribed with zolpidem should consider the risk factors and to pay attention to the effects in order to prevent drug abuse and dependence.

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