



# Zolpidem-Induced Acute Altered Level of Consciousness: A Report of Two Cases

Abdolhamid Parsa<sup>1</sup>, Seyyed Ali Tabaeian<sup>2</sup>, Sadra Einizadeh<sup>3</sup> and Mohammad Babaeian<sup>1,\*</sup>

<sup>1</sup>School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding author: School of Pharmacy, Shahid Beheshti University of Medical Sciences, P.O. Box: 14155-6153, Vali-e-Asr Ave., Niayesh Junction, Tehran, Iran. Tel/Fax: +98-2188873704, Email: babaeianm@gmail.com

Received 2016 December 09; Revised 2017 July 09; Accepted 2017 October 02.

## Abstract

**Introduction:** The Z-drug zolpidem is an imidazopyridine hypnotic that is prescribed widely for short-term treatment of sleeping problems. However, there have been various cases affected by the side effects of this medication.

**Case Presentation:** Further to the extant reports of zolpidem adverse reactions, in the current manuscript, two cases of zolpidem toxicity in 2016 in Tehran are presented. They had both taken 20 mg of zolpidem and as a result, they began to develop an altered level of mentality.

**Conclusions:** Zolpidem use may affect the mental status and results in performing unconscious behaviors.

**Keywords:** Altered Mental Status, Case Report, Insomnia, Somnambulism, Zolpidem

## 1. Introduction

The Z-drug zolpidem (ZLP) is an imidazopyridine hypnotic that is prescribed widely for short-term treatment of sleeping problems (1). It has attained popularity as an alternative to benzodiazepines due to the claims regarding its milder and fewer problematic side effects although they have been refuted in recent studies (2-4). Side effects related to ZLP have been frequently reported. Nausea, dizziness, malaise, hallucination, nightmares, agitation, and headache are some of the most frequently reported adverse effects of ZLP (5). Several systematic descriptive reviews of ZLP dangerous side effects including psychotic types have been undertaken (6, 7). Although ZLP appears to be well tolerated in adults (8), there are so many reports of abuse, dependence, and withdrawal syndrome of ZLP. It merits mentioning that a larger number of these cases had used ZLP more than the prescribed dose and most of these people had a history of substance or drug abuse and/or psychiatric disorders (6, 9).

Further to the extant reports of adverse reactions related to zolpidem use, hereby two cases with zolpidem intoxication effects are presented.

## 2. Case Presentation

Two 29-year-old single males who were graduated in pharmacy, sharing an apartment in Tehran, without any di-

agnosed mood disorder or neuropsychiatric disease, went to another pharmacist friend's house to have dinner together.

Being fully alert and free of any drug at that night, the host declared the following statements:

Case 1: He had been using ZLP often but irregularly throughout the past 2 years. He had not any history of using another drug. He used to use ZLP for his sleeping problems, but in the repercussion of repetitive use, he became interested in the pleasurable and felicitous mental encounters of ZLP. He also had a history of an unsuccessful suicide attempt upon taking ZLP. Within the recent 2 years, he had been taking 10-80 mg of ZLP on an irregular basis and he had entirely forgotten the happenings of the nights when he took ZLP.

Case 2: He had only used ZLP for a few times and he did not have any history of continuous use of this drug. He was free of any other medication.

As both cases declared later, they suffered a dramatically gloomy night on 3rd November 2016. Unbeknown to the host, as they arrived at his house, they each took four pills of ZLP 5 mg with a full glass of water. After a few minutes, they were invited to a dining room to have the meal. Case 1 started eating food voraciously and non-stop while opining around music for about 30 minutes. Case 2 had less attention to the food. He just drank a lot of water and talked about a mixture of religious, romantic, and philo-

sophical topics. In the middle of the dinner, the second case started to fancy that several people with deformed faces and winding bodies were gazing through the room window.

The first case demanded some more ZLP tablets. He got prepared for buying ZLP and case 2 decided to accompany him.

The host tried his best to prevent them from going out, but they remained utterly determined. He joined them towards a 24-hour pharmacy in case any unexpected problem occurred. Along the way, both cases 1 and 2 were unable to navigate the pathway to the pharmacy and their balance was impaired. Case 2 said that some people were hiding behind the trees and were watching them. Case 1 entered the pharmacy and bought a full package of ZLP 10 mg with a package of atorvastatin 10 mg tablets. He stated, "I did not want to seem suspicious".

After returning to the house, case 1 and case 2 attempted to use 60 mg of ZLP apiece. They were advised to go to sleep by the host. After a short time, they fell asleep fast while breathing normally. The host checked their pulse rate and their blood pressure with an automatic sphygmomanometer and they were normal. Both of them reacted to loud voice and had movement on the bed during their sleep. Their pupils started to contract as the host flashed the torch into their eyes.

They woke up easily at eight in the morning after; however, they were feeling dizziness, headache, lightheadedness, and gastrointestinal discomfort.

### 3. Discussion

Due to the tolerance, dependence, and associated adverse effects, the abuse of benzodiazepines and Z-drugs has become a serious public health problem (10, 11). ZLP as a very commonly prescribed Z-drug has the potential for both medical misuse -when it is taken for the long term without or against medical advice- and recreational use -when is abused to achieve a "high"- (11-13).

There have been reports of some life-threatening complications associated with ZLP overdose, such as suicidal attempts, seizure, and coma (13, 14). There have also been some other reports in which the cases experienced altered mental status (AMS) and as a result, expressed dangerous behaviors (15-17).

AMS as a condition, in which the levels of consciousness and/or cognition are altered, has myriad causes (18). The term is used to describe various disorders of mental functioning that can range from slight confusion to coma (18, 19).

Sleepwalking, as a sleep-related disorder, also known as somnambulism, is a phenomenon of combined sleep and wakefulness (20). It performs activities that are usually performed during a state of full consciousness. These activities can be as benign as sitting up in the bed, walking

to a bathroom, and cleaning, or as critical as cooking, driving, rubbery, violent gestures, or even suicide or homicide (21, 22).

Although both cases were responsive to stimuli, the occurred case cannot be identically classified as a serious AMS or simple and benign somnambulism.

By and large, the following points are worth mentioning:

Due to its contribution to abnormal and hazardous behavior, the case should be considered as a potentially dangerous situation in an intoxicated person.

As underlined by FDA (23), it is suggested to use ZLP at the lowest effective dose for the shortest period of time, as necessarily needed.

As observed in these cases and based on the clinical evidence (24), ZLP has a very rapid onset of action. It is highly suggested to administer and use ZLP just before bedtime.

As described in the case presentation section and based on some evidence, ZLP may cause an acute change in eating behavior (25). Due to the altered level of consciousness, to prevent the blockage of the airway during eating, it is highly recommended advising patients to avoid eating or drinking after taking ZLP.

### 3.1. Conclusions

Since this case was based on personal declarations, further studies are suggested to disclose the true outcomes of the zolpidem-induced altered level of consciousness. On the other hand, dose modification and potentially dangerous consequences of zolpidem intoxication are necessary to be publicized.

### Acknowledgments

We would like to acknowledge Mr. Majid Ghobadi for his tremendous help and valuable suggestions.

### Footnotes

**Authors' Contribution:** Abdolhamid Parsa performed the critical revision of the manuscript for important intellectual content. Mohammad Babaeian collected and interpreted the clinical data, study concept, and design and prepared the manuscript.

**Declaration of Interest:** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

**Funding/Support:** No funding was received for this research.

## References

- Langtry HD, Benfield P. Zolpidem. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential. *Drugs*. 1990;**40**(2):291-313. doi: [10.2165/00003495-199040020-00008](https://doi.org/10.2165/00003495-199040020-00008). [PubMed: [2226217](https://pubmed.ncbi.nlm.nih.gov/2226217/)].
- Ganzoni E, Santoni JP, Chevillard V, Sebillé M, Mathy B. Zolpidem in insomnia: A 3-year post-marketing surveillance study in Switzerland. *J Int Med Res*. 1995;**23**(1):61-73. doi: [10.1177/030006059502300108](https://doi.org/10.1177/030006059502300108). [PubMed: [7774760](https://pubmed.ncbi.nlm.nih.gov/7774760/)].
- Kang DY, Park S, Rhee CW, Kim YJ, Choi NK, Lee J, et al. Zolpidem use and risk of fracture in elderly insomnia patients. *J Prev Med Public Health*. 2012;**45**(4):219-26. doi: [10.3961/jpmph.2012.45.4.219](https://doi.org/10.3961/jpmph.2012.45.4.219). [PubMed: [22880153](https://pubmed.ncbi.nlm.nih.gov/22880153/)]. [PubMed Central: [PMC3412984](https://pubmed.ncbi.nlm.nih.gov/PMC3412984/)].
- Wang PS, Bohn RL, Glynn RJ, Mogun H, Avorn J. Zolpidem use and hip fractures in older people. *J Am Geriatr Soc*. 2001;**49**(12):1685-90. doi: [10.1111/j.1532-5415.2001.49280.x](https://doi.org/10.1111/j.1532-5415.2001.49280.x). [PubMed: [11844004](https://pubmed.ncbi.nlm.nih.gov/11844004/)].
- Hajak G, Bandelow B. Safety and tolerance of zolpidem in the treatment of disturbed sleep: A post-marketing surveillance of 16944 cases. *Int Clin Psychopharmacol*. 1998;**13**(4):157-67. doi: [10.1097/00004850-199807000-00002](https://doi.org/10.1097/00004850-199807000-00002). [PubMed: [9727726](https://pubmed.ncbi.nlm.nih.gov/9727726/)].
- Inagaki T, Miyaoka T, Tsuji S, Inami Y, Nishida A, Horiguchi J. Adverse reactions to zolpidem: Case reports and a review of the literature. *Prim Care Companion J Clin Psychiatry*. 2010;**12**(6). doi: [10.4088/PCC.09r00849bro](https://doi.org/10.4088/PCC.09r00849bro). [PubMed: [21494350](https://pubmed.ncbi.nlm.nih.gov/21494350/)]. [PubMed Central: [PMC3067983](https://pubmed.ncbi.nlm.nih.gov/PMC3067983/)].
- Garnier R, Guerault E, Muzard D, Azoyan P, Chaumet-Riffaud AE, Efthymiou ML. Acute zolpidem poisoning analysis of 344 cases. *J Toxicol Clin Toxicol*. 1994;**32**(4):391-404. doi: [10.3109/15563659409011040](https://doi.org/10.3109/15563659409011040). [PubMed: [8057398](https://pubmed.ncbi.nlm.nih.gov/8057398/)].
- Darcourt G, Pringuey D, Salliere D, Lavoisy J. The safety and tolerability of zolpidem an update. *J Psychopharmacol*. 1999;**13**(1):81-93. doi: [10.1177/026988119901300109](https://doi.org/10.1177/026988119901300109). [PubMed: [10221362](https://pubmed.ncbi.nlm.nih.gov/10221362/)].
- Swainston Harrison T, Keating GM. Zolpidem: A review of its use in the management of insomnia. *CNS Drugs*. 2005;**19**(1):65-89. [PubMed: [15651908](https://pubmed.ncbi.nlm.nih.gov/15651908/)].
- Cardinali DP, Golombek DA, Rosenstein RE, Brusco LI, Vigo DE. Assessing the efficacy of melatonin to curtail benzodiazepine/Z drug abuse. *Pharmacol Res*. 2016;**109**:12-23. doi: [10.1016/j.phrs.2015.08.016](https://doi.org/10.1016/j.phrs.2015.08.016). [PubMed: [26438969](https://pubmed.ncbi.nlm.nih.gov/26438969/)].
- Keuroghlian AS, Barry AS, Weiss RD. Circadian dysregulation, zolpidem dependence, and withdrawal seizure in a resident physician performing shift work. *Am J Addict*. 2012;**21**(6):576-7. doi: [10.1111/j.1521-0391.2012.00273.x](https://doi.org/10.1111/j.1521-0391.2012.00273.x). [PubMed: [23082842](https://pubmed.ncbi.nlm.nih.gov/23082842/)]. [PubMed Central: [PMC3744365](https://pubmed.ncbi.nlm.nih.gov/PMC3744365/)].
- Griffiths RR, Johnson MW. Relative abuse liability of hypnotic drugs: A conceptual framework and algorithm for differentiating among compounds. *J Clin Psychiatry*. 2005;**66 Suppl 9**:31-41. [PubMed: [16336040](https://pubmed.ncbi.nlm.nih.gov/16336040/)].
- Paradis CM, Siegel LA, Kleinman SB. Two cases of zolpidem-associated homicide. *Prim Care Companion CNS Disord*. 2012;**14**(4). doi: [10.4088/PCC.l2br01363](https://doi.org/10.4088/PCC.l2br01363). [PubMed: [23251862](https://pubmed.ncbi.nlm.nih.gov/23251862/)]. [PubMed Central: [PMC3505131](https://pubmed.ncbi.nlm.nih.gov/PMC3505131/)].
- Mortaz Hejri S, Faizi M, Babaeian M. Zolpidem-induced suicide attempt: A case report. *Daru*. 2013;**21**(1):77. doi: [10.1186/2008-2231-21-77](https://doi.org/10.1186/2008-2231-21-77). [PubMed: [24359886](https://pubmed.ncbi.nlm.nih.gov/24359886/)]. [PubMed Central: [PMC3878174](https://pubmed.ncbi.nlm.nih.gov/PMC3878174/)].
- Hamad A, Sharma N. Acute zolpidem overdose leading to coma and respiratory failure. *Intensive Care Med*. 2001;**27**(7):1239. doi: [10.1007/s001340100972](https://doi.org/10.1007/s001340100972). [PubMed: [11534578](https://pubmed.ncbi.nlm.nih.gov/11534578/)].
- Behrouz R, Godoy DA, Azarpazhooh MR, Di Napoli M. Altered mental status in the neurocritical care unit. *J Crit Care*. 2015;**30**(6):1272-7. doi: [10.1016/j.jcrc.2015.07.021](https://doi.org/10.1016/j.jcrc.2015.07.021). [PubMed: [26315655](https://pubmed.ncbi.nlm.nih.gov/26315655/)].
- Shuaib W, Beatrice C, Abazid AG. Zolpidem overdose: A medical and ethical dilemma. *Am J Ther*. 2016;**23**(6):e1956-7. doi: [10.1097/MJT.0000000000000380](https://doi.org/10.1097/MJT.0000000000000380). [PubMed: [26539907](https://pubmed.ncbi.nlm.nih.gov/26539907/)].
- Lehman RK, Mink J. Altered mental status. *Clin Pediatr Emerg Med*. 2008;**9**(2):68-75. doi: [10.1016/j.cpem.2008.02.003](https://doi.org/10.1016/j.cpem.2008.02.003).
- Murty S. Altered mental status. In: David SS, editor. *Clinical pathways in emergency medicine*. Springer; 2016.
- World Health Organization. *ICD-11 beta draft*. 2015. Available from: <http://apps.who.int/classifications/icd11/browse/l-m/en>.
- Judd SJ. Sleepwalking. *Sleep disorders sourcebook*. Omnigraphics; 2010.
- Singhal S, Jain PC. *Wireless health monitoring system for sleepwalking patients*. 2015 39th National Systems Conference (NSC), IEEE; 2015. doi: [10.1109/natsys.2015.7489083](https://doi.org/10.1109/natsys.2015.7489083).
- U.S. Food and Drug Administration (FDA). *Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem (Ambien, Ambien CR, Edluar, and Zolpimist)*. 2014.
- Yaripour S, Nezami Rashid S, Alibakhshi H, Mohammadi A. Development and validation of a stability-indicating reversed phase HPLC method for the quality control of Zolpidem in bulk and tablet dosage forms. *J Anal Chem*. 2015;**70**(6):738-43. doi: [10.1134/s1061934815060143](https://doi.org/10.1134/s1061934815060143).
- Najjar M. Zolpidem and amnesic sleep related eating disorder. *J Clin Sleep Med*. 2007;**3**(6):637-8. [PubMed: [17993047](https://pubmed.ncbi.nlm.nih.gov/17993047/)]. [PubMed Central: [PMC2045714](https://pubmed.ncbi.nlm.nih.gov/PMC2045714/)].