کارکاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی

- کارکاه آنلاین کاربرد نرم افزار SPSS در پژوهش
- کارکاه آنلاین اصول تنظیم قراردادها
- کارکاه آنلاین پروپوزال نویسی
Zolpidem Dependency and Withdrawal Seizure: A Case Report Study

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Introduction: Zolpidem is a short acting inducer of sleep and thought to lack benzodiazepine properties such as anxiolysis, anticonvulsion, muscle relaxation and side effects such as dependency. Recently, some cases of Zolpidem abuse and dependency have been reported. In review of literature, we found that the lowest reported dosage of Zolpidem, which caused dependency, was 160 mg daily.

Case Presentation: We reported a 30-year-old unmarried Iranian woman with dysthymic disorder and chronic insomnia treated with Zolpidem irregularly. She started to use Zolpidem with 5 mg per day irregularly since a year ago but augmented its daily dosage gradually to 100 to 150 mg per day in divided doses. After a period of 16 hours without taking Zolpidem she developed a withdrawal syndrome, with generalized tonic-clonic seizures for two times. She was managed with supportive care and recovered completely.

Conclusions: Zolpidem dependency and withdrawal seizure can occur with a dosage under last reported doses. Therefore, possibility of mentioned problems cannot be excluded at any dosage and physicians should pay more attention to potential of Zolpidem to create these adverse effects.

Keywords: Zolpidem; Dependence; Benzodiazepine

1. Introduction

Zolpidem (an imidazopyridine derivative agent) is a non-benzodiazepine hypnotic drug with a high affinity to a subunit of gamma amino butyric acid-A (GABA-A) receptor and minor anxiolytic and anti-convulsant effects which is indicated for short-term management of insomnia (1). Zolpidem is thought to be a safer drug than benzodiazepines (BZD) because of no evidence of abuse or dependence potential and a less liability for abuse and dependence (2). Against so many studies indicating no evidence regarding abuse or dependence potential by Zolpidem, case reports of Zolpidem abuse or dependence (3-5) and epileptic-seizure related to Zolpidem withdrawal (6-8) are increasing. To our knowledge, most of these case reports have been reported from Western countries (9) and in the Asian population, one case of Zolpidem dependence (10) and one case of Zolpidem withdrawal seizure (6) were reported. Nonetheless, in Iranian people, we did not find any similar report. Moreover, withdrawal seizure in our case with 100 to 150 mg/day of Zolpidem is the minimum dosage reported up to now.

2. Case Presentation

On October 2013, a 30 year-old unmarried Iranian woman (known case of dysthymic disorder) was admitted to Emergency Department (ED) of 22-Bahman Psychiatric Hospital (Qazvin, Iran) with seizure without any history of head trauma. No medications were administered en route to the hospital. For about five minutes early after admission, she had seizure one time again, thus she suddenly had tonic-clonic seizure (full body “shaking” movements lasting approximately two minutes) with upward gaze and loss of consciousness. Then, postictal confusion with clouded consciousness, regressed attitude and behavior and psycho-motor retardation happened for about two hours. After postictal phase, she indicated to use Zolpidem for a year due to insomnia and not receiving any other medication. She started to use Zolpidem with 5 mg per day irregularly since a year ago but augmented its daily dosage gradually from three months before to 100-150 mg per day in divided doses. She used this dosage for about one month prior to her seizure. She had drug tolerance, abuse and dependence and if she had not used tablets, she would become irritable with decreased energy, feeling of weakness and tremor of hands and feet. In the day of admission, she had not used Zolpidem to maintain her alertness for an important ceremony and after a period of 16 hours without taking Zolpidem, she developed an abstinence syndrome, with generalized tonic clonic seizures. In her medical history, she did not have any systemic, organic, metabolic or endocrine problems unless a history of adenoidecotomy 25 years ago and dysthymic disorder from one year ago. She had not experienced any seizure already. In her drug history, she just had used Zolpidem with the mentioned dosage. Some of patient’s characteristics were summarized in Table 1.
3. Discussion

During the last decade, Zolpidem (a non BZD hypnotic drug) was considered a new way for treatment of patients with insomnia as it was suggested that it has the efficacy of BZDs for insomnia but without many side effects. It was suggested that Zolpidem lacked muscle relaxant, anticonvulsant and anxiolytic properties and poor potential for abuse or dependence (11). GABA-A receptors include α₁, α₂, α₃, α₄, and α₅ subunits receptors. The α₁ subunit involves in sleeping mechanisms and α₂ subunit contributes to anxiolytic action. BZDs have nonselective affinity to GABA-A subunits along with α₁ subunits (12). Therefore, high-dose Zolpidem can potentially lead to dependence and withdrawal seizure in Iranian population, also can occur with a dosage under last reported doses. Besides, the possibility of mentioned problems cannot be excluded at any dosage. We suggest physicians to pay more attention to the potential of Zolpidem to create dependence and withdrawal seizure. Besides, they should always keep its effects in their mind and subtilize during prescription of Zolpidem for any patients and at any doses, especially for those with a previous history of drug or substance abuse and at high doses. This study presented a new dosage of Zolpidem that causes withdrawal seizure. However, this is a case study and it needs further studies to conclude about adverse effects of Zolpidem.

Authors' Contributions

Seyed Alireza Haji Seyed Javadi and Farid Hajiali were involved in acquisition of clinical data and reviewing the scientific literature. Farid Hajiali and Marjan Nassiri-Asl wrote the manuscript. All authors read and approved the final manuscript.
References


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