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증 례

고용량 졸피뎀 복용 중단 이후 발생한 경련발작 1례

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A Case of Seizures after Zolpidem Withdrawal

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The imidazopyridine, zolpidem, a non-benzodiazepine hypnotic drug, is widely-prescribed for insomnia. It is regarded as a good alternative to benzodiazepine because of the reduced possibility for abuse and development of dependence. However, more recently, due to the reduced possibility for abuse and development of dependence, it is regarded as a good alternative to benzodiazepine. adverse effects of zolpidem have been recognized. The objective of this report is to provide information on the potential for occurrence of benzodiazepine-like withdrawal seizure in patients who chronically take zolpidem continually. We present and discuss a case of seizure after sudden interruption of the protracted use of an abusively high dose of zolpidem. Zolpidem may not be the ideal drug for long-term pharmacotherapeutic management of insomnia. Clinicians should administer zolpidem at a low-dose for a short period of time for prevention of drug abuse and dependence and the potential for occurrence of benzodiazepine-like withdrawal seizure.

Key Words: Zolpidem, Seizures, Substance-related disorders, Adverse effects

Introduction

Zolpidem is a member of the imidazopyridine family and is a commonly prescribed non-benzodiazepine hypnotic drug. Zolpidem displays high affinity to the alpha-1 gamma-amino-butyric acid (GABA) A receptor, differs structurally from the benzodiazepines, and has minor axiolytic, myorelaxant, and anticonvulsant properties[1)]. It is a well-known good alternative to benzodiazepine in the treatment of insomnia because of the presumed reduced tendency for abuse and development of dependence[2)]. However, several case reports have described abusive use and dependence, with a small number of recent cases showing seizure after sudden zolpidem withdrawal.

We report here a case of a man who developed generalized seizure after sudden interruption of the sustained use of a high dose of zolpidem.

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Case Report

A 44-year-old man presented to the emergency

department following an epileptic attack. He abruptly showed facial spasm, biting of the tongue, cyanosis, tonic seizure, and loss of consciousness for about 5 minutes. On arrival at the emergency department, the patient convulsed spontaneously, necessitating admission. History gleaned from his mother revealed his use of medications for insomnia and functional gastrointestinal disorder for more than 6 years. Three years previously, he had been diagnosed with major depression and primary insomnia. At that time, the psychiatrist had prescribed a 10 mg dose of zolpidem and other anti-depressents. After taking zolpidem, the patient had the mistaken belief that the pills could palliate his symptoms. He gradually increased the dose without proper medical guidance. Two years prior to the present admission, tolerance and dependence to the hypnotic effect developed progressively. The patient was visiting several doctors to acquire the 200 mg needed each night. His need for zolpidem escalated to the point where he was using stolen identities at several hospitals. He suffered an epileptic attack after abruptly stopping zolpidem because of the inability to acquire a prescription. He hid the incident and was successful in securing further prescriptions. However, another forced withdrawal resulted in another seizure. Hours prior to the current admission, he had discontinued the medication for the same reason. The present withdrawal symptoms included anxiety and restlessness. The latest seizure occurred 8 hours without taking zolpidem. His mother denied history of smoking, alcohol, and illegal drugs.

Blood pressure was 130/70 mmHg, respiratory rate 15 breaths/min, pulse rate 88 beats/min, temperature 36.2°C, and oxygen saturation 97%. The patient was conscious without any anticonvulsant management. The neuropsychological evaluation showed full spatial and temporal orientation, but with no recall of the events of the day before. Brain computed tomography scan, electrocardiogram, arterial blood gas analysis, cell blood count, liver enzyme, and biochemical measures were normal. An electroencephalogram was not acquired because of the patient's refusal for the procedure. He had no further withdrawal symptoms and was discharged the next day for admittance to another hospital.

Discussion

Adverse effects have curtailed the use of benzodiazepines in the treatment of insomnia over the past 30 years. During the same period, prescriptions of non-benzodiazepine hypnotics have been increasing[3]. Zolpidem, an imidazopyridine agent with hypnotic properties, is a common agent for treating insomnia as an alternative to benzodiazepine[1]. The effect of the drug is associated with an agonistic affinity to the GABAA receptor, which comprises α1, α2, α3, α4, and α5 subunit receptors. The α1 receptors are associated with the sedation and sleeping mechanism, α2 receptors contribute to anxiolytic action, and α5 receptors are involved in cognition and memory[4]. All GABAA receptors have non-selective affinity to benzodiazepine, whereas zolpidem binds preferably to the α1-GABAA receptor. This is considered the main mechanism of zolpidem's pure hypnotic effect.

The present case highlights the potential adverse effect after high-dose, long-term use of non-benzodiazepine hypnotics. Cases of pure zolpidem withdrawal seizure are extremely rare, with a few reports in the last 30 years[4-7]. Our case indicates that zolpidem may also have a pharmacologic side effect similar to benzodiazepine and that a new pharmacologic explanation of zolpidem effect is needed.

The present case documents a seizure in a patient taking 200 mg zolpidem per night. The usual adult dose for insomnia is 10 mg orally once before bedtime. Most cases of seizure after zolpidem withdrawal involve medication doses ranging between 160 mg/day to 600 mg/day. A patient taking a zolpidem dose of up to about 150 mg may have the potential of seizure after abruptly ceasing medication. Gender is an important factor associated with adverse effect of zolpidem. Most seizures after zolpidem withdrawal zolpidem have occurred in women, who manifest a higher(40%) serum zolpidem concentration than men at equivalent dosages[1].

Conclusion

Zolpidem remains a safer alternative medication to benzodiazepine in insomnia management[3]. Although withdrawal seizure is related to the use of benzodiazepine, some recent reports and this case demonstrate the discrete potential of seizures from zolpidem withdrawal. Emergency physicians should keep in mind the potential of seizure on abrupt cessation after high-dose and long-term use of zolpidem.

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