Persistent Psychosis after Abuse of High Dose of Zolpidem

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Case Report

Abstract

Background: Zolpidem is a non-benzodiazepine medication which selectively affects GABAA receptors and treats insomnia. There are numerous reports of psychosis following the consumption of zolpidem all of which recovered after stopping the medication.

Case Report: A 27 year old male law student, who was treated with 10 mg zolpidem due to insomnia, increased the dosage to 500 mg during 3 months. Not only was his insomnia remained untreated, but also he gradually became isolated, suspicious, and aggressive, and dropped out of university. He was then hospitalized in a psychiatric ward for 2 months, and was treated with antipsychotics and gradual discontinuation of zolpidem. With no improvement in psychosis and sleep improvement he was discharged. After two weeks he was hospitalized again and went under electroconvulsive therapy (ECT) and antipsychotic therapy, and was discharged with relative improvement. Now, after three years, he is diagnosed with schizophrenia and with modest improvements he is under care and treatment.

Conclusion: Zolpidem is a fairly useful medication for treating sleep problems, especially improving beginning of sleep. However, physicians and clinicians should consider the conditions, predispositions, and personal and family history of types of psychosis, alcohol and drug abuse in the comprehensive assessment and treatment plan for patients with insomnia.

Keywords: Zolpidem, Permanent and temporary psychosis, Insomnia

Citation: Eslami-Shahrbabaki M, Barfeh B, Nasirian M. **Persistent Psychosis after Abuse of High Dose of Zolpidem.** Addict Health 2014; 6(3-4): 159-62.

Received: 09.03.2014 **Accepted:** 05.06.2014

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Introduction

Zolpidem is one of the effective non-benzodiazepine medications for treatment of insomnia, which so-called Z-drugs. This drug, unlike benzodiazepines that activate all three specific binding sites of GABA, activates GABA receptors, causes the opening of chloride channels, reduces the firing rate of neurons and muscle fibers, and selectively binds to the subunit-specific GABA receptors. For this reason, it less sedation, muscle relaxation, and anticonvulsant effect compared to benzodiazepines, while it is sleep-improving medication.[1,2] After oral administration, this drug is rapidly absorbed, but if consumed with food, absorption is delayed by an hour. During 1.6 hours it reaches its peak plasma concentration and has a half-life of 2.6 hours.[3]

Rapid metabolism and lack of active zolpidem metabolites prevent the accumulation of potentially toxic compounds. This is also something that is contrary to the long-term use of drugs affecting benzodiazepine receptors.[4] The drug metabolism in the liver occurs by a wide range of cytochrome isoenzymes through oxidation and hydroxidation. In addition, 48 to 67% of products resulting from zolpidem metabolism are excreted in the urine and a less amount is excreted in the bile, and in the elderly it is less clear.[1,5]

Zolpidem is an effective drug for treatment of short-term insomnia. Clinically, the drug is effective, safe, and well tolerated. It has been reported that patients do not develop tolerance to zolpidem, insomnia and withdrawal syndrome after discontinuation of medication has not been observed, and the risk of drug abuse and dependence is minimal. However, cases of dependence and abuse have been reported. Patients with a history of drug abuse and drug dependence are at risk of dependence on this drug. Therefore, in prescribing this drug, like prescribing drugs affecting benzodiazepine receptors, caution should be exercised.[6,7] Zolpidem is used as a treatment for insomnia and can sometimes have irreparable effects. There are many reports of transient psychosis following the use of zolpidem, and patients recovered with drug withdrawal in these situations.[2]

Case Report

A 21 year old male law student was treated with zolpidem due to insomnia. He increased the dosage from 10 mg to 500 mg daily after 3 months. Not only was his insomnia not treated, but also he gradually became isolated, skeptical, and aggressive, laughed to himself, and dropped out of university. He was finally hospitalized in a psychiatric ward, and was treated for 2 months with risperidone 2 mg three times daily, 2 mg biperiden twice daily, trazodone 100 mg before sleeping, and gradual discontinuation of zolpidem. Patient's sleep was regulated and zolpidem use reached zero. Positive symptoms of psychosis, such as hallucinations and delusions disappeared, but social and emotional relationships of the patient remain limited and impaired. He was discharged with the same treatment and the same condition. The patient was hospitalized again after 2 weeks (because of suspiciousness, fear of food poisoning, and refusal to eat), and electroconvulsive therapy (ECT) was added to risperidone, biperidin, and trazodone with mentioned dosages. After 12 sessions of shock therapy the patient's mood, thoughts, and emotions were relatively improved. Now, after three years, the patient is under care with diagnosis of chronic schizophrenia with unfavorable response to treatment.

Discussion

High amounts of zolpidem are connected with protein in the body. Moreover, in people who have lower levels of albumin, like undernourished people, especially in association with the use of other drugs that are attached to albumin, it is possible that the amount of free zolpidem in the body increases.[8] This results in more side effects in patients taking this drug. The effects of zolpidem on the central nervous system include headache, dizziness, nightmares, confusion and dizziness, drowsiness, sensory disorders in all senses, delirium, and complex behaviors such as sleepwalking and sleep eating. In one study, the incidence of illusion and hallucination was reported to be 0.3%.[5,9,10-12]

In some studies, four factors have been reported to be effective on the increased risk of delirium or psychosis induced from zolpidem use, which include the use of this drug simultaneously with selective serotonin reuptake inhibitor medications, female gender, older age of the patient, and use of 10 mg or higher dosage of the

medication.[11,13] Delirium and hallucination was not observed in 5 mg and lower doses.[5,10] Another study reported a patient who had no history of psychosis, and due to the use of zolpidem had visual and auditory hallucinations and delusional thoughts. With withdrawal from zolpidem, these symptoms were resolved.[14]

The patient in this study, due to the use of zolpidem in the initial dose for treating insomnia, gradually became dependent and addicted to high doses of zolpidem. Subsequently, this not only caused positive psychotic symptoms (delusions and hallucinations), but also negative symptoms (limitation of emotional and social relationships), and him dropping out of university. Furthermore, even with discontinuation of the drug, psychotic symptoms continued. This was unlike the reported cases, in which incidence of psychosis have been due to zolpidem use, was observed mostly in women, and was treat improved with the drug discontinuation. Even if it can be accepted that the positive symptoms of psychosis have been resolved with discontinuation of zolpidem, zolpidem has an important role in the occurrence and persistence of negative symptoms of psychosis. In other words, this rare case might be considered to be caused due to genetic differences and the potential risk of psychosis in different individuals which should be considered when prescribing zolpidem. In addition, in people who have high probability of drug abuse, if possible, it should not be used.

Zolpidem is a relatively useful drug for improvement of sleep. Nevertheless, in the comprehensive treatment of patients, it is necessary to take into consideration the individual and family factors, such as genetic susceptibility and vulnerability to psychotic disorders, and the probability of drug abuse.

Conflict of Interests

The Authors have no conflict of interest.

Acknowledgements

We would like to thank the patient and their family for allowing the publication of this essay.

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سایکوز پایدار به دنبال بیش مصرف زولپیدم

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گزارش مورد

چکیده

مقدمه: زولپیدم داروی غیر بنزودیازپینی است که به طور انتخابی بر گیرنده‌های گابا A اثر کرده و باعث درمان بی‌خوابی می‌شود. گزارش‌های متعددی از سایکوز (روان‌پریشی) متعاقب مصرف زولپیدم وجود دارد که با قطع مصرف آن برطرف می‌گردد.

گزارش مورد: مرد ۲۷ ساله دانشجوی حقوق به علت بی‌خوابی تحت درمان با زولپیدم به میزان ۱۰ میلی‌گرم قرار گرفت. وی در طی سه ماه دوز زولپیدم را به ۵۰۰ میلی‌گرم افزایش داد و نه تنها مشکل خوابش برطرف نشد، بلکه به طور تدریجی منزوی، شکاک و پرخاشگر گردید و ترک تحصیل کرد. حدود دو ماه در بخش روان‌پزشکی بستری و تحت درمان با آنتی‌سایکوتیک و قطع تدریجی زولپیدم قرار گرفت. بدون بهبودی سایکوز و با بهبود وضعیت خواب مرخص و بعد از دو هفته دوباره بستری شد و تحت درمان با الکتروشوک و آنتی‌سایکوتیک قرار گرفت و با بهبود نسبی مرخص گردید. در حال حاضر بعد از گذشت سه سال با تشخیص اسکیزوفرنیا و با بهبود نسبی تحت مراقبت و درمان می‌باشد.

بحث: زولپیدم داروی به نسبت مفیدی برای درمان مشکلات خواب به ویژه بهبود شروع خواب است. به هر حال پزشکان و بالینگران در برنامه درمانی جامع بیماران دارای مشکل بی‌خوابی باید به شرایط، استعداد، سابقه فردی و خانوادگی انواع سایکوز و سوء مصرف مواد و الکل توجه خاصی داشته باشند.

واژگان کلیدی: زولپیدم، سایکوز دایمی و موقت، بی‌خوابی

ارجاع: اسلامی شهربابکی مهین، برفه بابک، نصیریان منصوره. **سایکوز پایدار به دنبال بیش مصرف زولپیدم.** مجله اعتیاد و سلامت ۱۳۹۳؛ ۶ (۴-۳): ۱۶۲-۱۵۹.

تاریخ دریافت: ۹۲/۱۲/۱۸ **تاریخ پذیرش:** ۹۳/۳/۱۵

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