



Case Report

Zolpidem Abuse in a Patient with Breathing Pattern Disorder

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Abstract

Introduction: Zolpidem is a nonbenzodiazepine sedative-hypnotic agent which binds selectively to the benzodiazepine ω_1 -receptor subtype in the central nervous system.

Case Presentation: This is case of 56-year old woman suffering from Breathing Pattern Disorder. Her symptoms of insomnia as well as her craving for anxiolytic effect of zolpidem, that helped her to cope with everyday activities, transformed her into a zolpidem abuser. The patient discontinued zolpidem use and respiratory function improved. Treatment with antidepressant improved her psychosocial state.

Discussion: Zolpidem is an interesting alternative to benzodiazepines in the treatment of insomnia under a range of cautious medical supervision and prescription.

Keywords

Zolpidem; Breathing Pattern Disorder (BPD); Respiratory failure; Suicide; Overdose; Coma; Depression

Introduction

Zolpidem is a nonbenzodiazepine sedative-hypnotic agent which binds selectively to the benzodiazepine ω_1 -receptor subtype in the central nervous system but possesses low affinities for ω_2 - or ω_3 -receptor subtypes [1]. Zolpidem is one of the most commonly prescribed hypnotics because of its rapid onset, and short duration of action. In the literature there are some cases of individuals without a history of substance abuse, who started receiving zolpidem for stimulation and anxiolysis rather than sedation and developed a serious dependence of it after a short period of time [2]. Zolpidem may reduce oxygen intake in patients with sleep apnea. Studies in baboons have shown that the drug may reduce cerebral blood flow and oxygen consumption [3]. Incidence of allergic manifestations in hyperventilators is high and is related to the known increase in histamine production provoked by hyperventilation [4]. Hyperventilation pertains with abnormal respiratory patterns in relation to overbreathing known as Breathing Pattern Disorder (BPD). Breathing Pattern Disorder is a combination of individual symptoms which, on their own, may all be attributed to other causes, but collectively may make up of a breathing pattern disorder. This is not a considered a disease process, but simply alterations in breathing patterns that interfere with normal respiratory processes

[5]. However, they can, co-exist with disease such as COPD (Chronic Obstructive Pulmonary Disease) or heart disease, and in some cases they can mimic cardiac symptoms. These symptoms are all actually due to low levels of CO₂ (carbon dioxide), as opposed to the common misconception that the cause is insufficient intake of oxygen [6]. We present a case of a woman who was suffering from allergies and from BPD and developed mild zolpidem dependence. Zolpidem use enabled her to deal with her insomnia and due to anxiolytic effect it helped her to cope with everyday activities.

Case Presentation

This is case of a 56-year old woman who used five years ago chemical treatment against house dust who mite in her mattress. She immediately developed swelling of the nose and throat, tightness of the chest and shortness of breath. She visited the emergency hospital and she was treated with oxygen and steroids. From that point on wards she became clearly allergic to perfumes but she practiced avoidance and the sensitivity gradually decreased. However, three years later on she was exposed by inhalation to chlorine bleach and this triggered the same respiratory symptoms again. Since then, there were several similar incidences that perpetuated and worsened the chemical sensitivity. During the last six months her exposure to most airborne chemical fumes but particularly to perfumes detergents and formaldehyde caused swelling and burning of the nose and throat, cough and tightness of the chest, headache fatigue, shivering and chattering of teeth. She also manifested a localized oral reaction to citrus fruits and abdominal bloating reaction to eating dairy products. Due the allergic reaction she had breathing problems like nasal congestion, asthmatic symptoms, coughing wheezing and chest tightness.

The patient used a mask on a daily basis in order to minimize the inhalation of chemicals. She had taken currently, fefolate, paracetamol, aflun, aneva sativa, and intermittently vitamin and mineral supplements. The toxicology panel showed two important findings: Dichlorophenol at two intracellular locations, and lymphocyte sensitivity to dichlorophenol but also to bleach and to mould products. The hematology and biochemistry panel also showed borderline anemia related to prolonged heavy menstruation presumed to be caused by a fibroid. A diagnosis of Breathing Pattern Disorder was established on the grounds of evidence emanating from the following instruments: Nijmegen questionnaire had high scores and the Breath Holding Test, the Breathing Wave Technique, the Seated Lateral Expansion Technique and Breath Holding Test were Positive. Respiratory Induction Plethysmography confirmed the diagnosis. The patient was suffering from breathing discomfort, disturbed sleep, erratic heartbeats, chest pain and fatigue. Because of the somatic symptoms, she developed mild depressive symptoms and intense insomnia. Her general practitioner prescribed 10mg/day p.o. zolpidem. The patient by trying to alleviate the symptoms, she started receiving zolpidem and reached to almost five tables daily (50 mg/day p.o.). She increased the dose because, as she stated, zolpidem improved her mood, calmed her down, obtained energy, and increased her energy levels enabled her to cope with every day activities. According to her claim the primary gain to use of zolpidem was to reduce the intensity of the dysfunctional breathing. Under

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regular psychiatric monitoring she managed to reduce the use of zolpidem, started receiving antidepressant medication (zolpidem 50 mg per day) and her psychosocial status improved. On the Beck Depression Inventory (BDI) she had a score of 24. Her score on BDI was mainly shaped by the reported symptoms in the subscale that measures somatic-vegetative performance complaints (consisting from the last eight items of the BDI). Two months later her emotional state improved progressively and the score in BDI was reduced to 14. The patient reported on her last assessment that she could enjoy her daily activities, be more active, and be less fearful of her breathing problems that now were milder.

Discussion

This case illustrates the role of zolpidem in achieving a relief of allergic and depressive symptoms in a patient with Breathing Pattern Disorders (BPD) (or Dysfunctional Breathing). BPD consist of an abnormal respiratory patterns in relation to over breathing which range from simple upper chest breathing to, the extreme end of the scale, hyperventilation. BPD influences the whole person especially if it has, a long duration, as the dysfunctional breathing can destabilize mind and muscles, mood and metabolism, BPD can play a part in, for instance, premenstrual syndrome, chronic fatigue, neck, back and pelvic pain, fibromyalgia and some aspects of anxiety and depression [7]. The anxiolytic effect of zolpidem in high doses is related to the loss of its selectivity and by acting on α_2 , α_3 and α_5 subunit-containing GABA_A receptors; while the stimulating and euphoric effect pertains to the activity of the drug on dopaminergic pathways [8]. The absorption rate and peak concentration levels in benzodiazepines is approximately 1 hour, likewise zolpidem has a similar absorption rate than is achieved within 0.8 to 2.6 hours. This rapid rate of absorption is directly related to the reinforcing effects seen in abuse [9]. Although data from other studies has shown that zolpidem taken at recommended doses is not addictive and does not exhibit withdrawal effects upon discontinuation; we demonstrated that this is not always the case. We believe that there is possibility for a patient to develop zolpidem dependence even if it is consumed in recommended doses by a person without a substance abuse history [3]. Hamad et al. [10] reported a 44-year old white male with no significant past medical history except for major depression. He presented to the emergency room with drowsiness after swallowing 20 tablets zolpidem and developed respiratory depression with hypoxia (PO₂ of 70mmHg) and mild hypercapnia (PCO₂ of 46mmHg). Benzodiazepines are frequently used in the management of breathlessness in advanced diseases and are regularly recommended in textbooks for palliative medicine or clinical guidelines [11]. The most common drugs are diazepam, midazolam, alprazolam, and lorazepam, zolpidem. However, there are more than 40 different benzodiazepines. Benzodiazepines belong to the group of hypnotics and sedatives. Their core chemical structure is a fusion of the benzene and the diazepine ring with various modifications which are responsible for the different compounds of the drug. The interaction of benzodiazepines with specific subunits of GABA (gamma-aminobutyric acid) receptors is responsible for their mechanism of action. The central and main effects of benzodiazepines are sedative-hypnotic, muscle-relaxant, anxiolytic, and anticonvulsant. Side effects include impairment of mental and motor function, light-headedness, and nausea [12].

Conclusion Section

Zolpidem overdose is related to its ability to produce a satisfactory anxiolytic effect and psychiatrist should be particularly

careful in prescribing zolpidem in patients with double diagnosis like respiratory failure or allergic diseases and depression.

Conflict of interests

The authors declare that they have no conflict of interests.

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