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CASE REPORT

Delirium associated with only one dose of zopiclone in an older adult

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Abstract

Both insomnia and its treatment can lead to the development of delirium in older adults. In the present case, delirium occurred after a single dose of zopiclone was given for insomnia treatment in an 84-year-old patient. Considering the case, patients and caregivers should be informed about the rare complication when zopiclone is prescribed.

INTRODUCTION

Sleep complaints are common in older adults and tend to increase with age. Sleep disorders, particularly insomnia, have also been associated with decreased quality of life, daytime dysfunction, pain, cognitive impairment, depression, increased risk of falls, fractures, diabetes mellitus, and cardiovascular diseases.[1] Proper treatment of insomnia may improve the aforementioned complications.[1] Pharmacological treatment is given if non-pharmacological therapy is insufficient. 'Z drugs' are now the most commonly prescribed hypnotic agents worldwide, with proven efficacy.[1] These drugs, which bind to the GABA receptor complex, reduce sleep-onset latency and wakefulness after sleep onset, and improve total sleep time, are similar to benzodiazepines, with lower adverse effects.[1] When the literature is reviewed, case reports show that these drugs have rare side-effects, such as delirium, agitation, and falling.[2,3] However, cases related to zopiclone are quite rare and concerned with drug withdrawal.[4] In this report, delirium arising from the use of a single dose of zopiclone in an older adult is presented.

CASE REPORT

An 84-year-old woman was admitted to a geriatric center because of difficulties in initiating and maintaining sleep, and staying awake almost all night. Her medical history showed hypertension, diabetes mellitus, gastroesophageal reflux and insomnia, and she had been taking olmesartan 20 mg/day, benidipine 4 mg/day, metformin 2000 mg/day, and pantoprazole 40 mg/day for a long time. Trazodone therapy, 100 mg/day, had been started for insomnia nearly 2 weeks before. Physical examination signs, including memory, orientation, language, and perception were normal. The Insomnia Severity Index of the patient was 28 (indicating severe insomnia) and trazodone was insufficient to treat insomnia; therefore, zopiclone was prescribed. Two hours after taking the first dose of 7.5 mg zopiclone, the patient became

disoriented and agitated. Her relative expressed that she had urinary incontinence, speech disturbance and hallucinations and did not recognize her husband and, during the night, confused the rooms in the house. She was again brought to the geriatric department. Assessment of her mental condition indicated cognitive and perception problems with disturbances of memory and orientation. With psychomotor hyperactivity, she gave short, quick answers to the questions and refused to talk at interview. Based on these clinical findings and symptoms, the newly developed clinical condition was thought to be delirium.

Vital signs were stable. Examination of neurological and other systems were normal. Biochemistry showed normal liver, thyroid, and kidney functions, with no electrolyte imbalance. She had leukocytosis, and urinalysis showed no evidence of infection. Cranial computed tomography was carried out and showed cerebral atrophy and chronic ischemic alterations with no acute neurological signs. Because there were no metabolic or infectious reasons to explain her condition, it was thought that zopiclone may be associated with delirium and, therefore, it was discontinued. As her symptoms resolved within 2 days, she was not given zopiclone again. On the third day, melatonin was started for her insomnia. During outpatient follow up, the patient did not develop any further delirium.

DISCUSSION

In this case, it was presented that delirium developed after only a single dose of zopiclone in an older adult.

Delirium is characterized by distorted attention, reduced awareness of the environment, alteration in at least one cognitive area (disturbed memory, orientation, language, perception), and change in sleep cycles.[5] It is well known that severe insomnia can lead to delirium in older adults, and thus it is important to focus on preventive approaches.[5] Because of adverse effects associated with benzodiazepines, the trend in the past decade has been to use non-benzodiazepine receptor agonists, known as Z drugs.[1] Z drugs improve both subjective and objective sleep outcomes, and have a safer profile, compared with benzodiazepines.[1] However, there are rare case reports about delirium associated with zolpidem, which is one of the Z drugs.[2,3] Zolpidem may cause delirium as a result of it being highly plasma-protein bound (92.5%), its high drug–drug interaction risk by means of hepatic cytochrome P450-3A4, and its gender-based variability in plasma drug concentrations. Therefore, zopiclone was discovered with the aim of overcoming these disadvantages.[1] A study carried out in 65–85-year-old adults showed that zopiclone had no rebound or severe side-effects.[1] In one case report only, Wong *et al.* reported that a 74-year-old woman who had been taking high-dose zopiclone (112.5 mg) daily for 20 years was diagnosed with dependence and withdrawal delirium after a 2-day drugless interval.[4] In contrast to this case of delirium as a result of drug withdrawal, the present case showed that delirium could develop after only one 7.5-mg dose of zopiclone in an older adult. Because the present patient's symptoms were resolved within 2 days, it could be thought that her delirium may have been related to her persistent insomnia. However, the adverse event appeared after zopiclone was given and the adverse reaction improved when the drug was discontinued. Additionally, delirium may be prolonged in the present case, as age-related changes in pharmacokinetics and pharmacodynamics lead to a decline in the plasma half-life of drugs, and reduced functional reserve also leads to an increase in sensitivity by impairing homeostatic compensatory mechanisms in older adults.[6] These factors all support that zopiclone caused delirium, and persistent insomnia might be a strong predisposing factor for the development of delirium in the present case.

In conclusion, the present case indicates that zopiclone may cause delirium among agents used in the treatment of insomnia, as insomnia is one of the predisposing factors for delirium, which is common in the elderly. Clinicians should keep in mind this rarely occurring complication of zopiclone and ensure that patients and their relatives are adequately informed. More studies are needed to establish the effects of zopiclone in older adults in particular.

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