Objective: Chronic insomnia is a common phenomenon among the elderly. Inaccurate handling and use of hypnotics in the elderly has become an important issue in patient safety. Older people who self-medicate often have a high risk for medication errors.

Methods and Results: We described here the case of a 65-year-old woman who experienced recurrent transient anterograde amnesia, anxiety, bewilderment, and repetitive questioning that lasted for 2 to 3 hours after erroneously taking zolpidem. This mistake was due to the similarity in appearance between zolpidem and her newly prescribed anticholesterol drug, ezetimibe.

Conclusions: History of medication, particularly as regards hypnotics, should be carefully reviewed when a patient presents with transient global amnesia-like symptoms. The inadvertent use of drugs may be an underestimated phenomenon among the elderly who self-medicate. When prescribing a new drug to elderly patients, especially hypnotics, physicians and pharmacists should educate them and their families about the proper use of these medications for their own safety.

Key Words: medication-use safety, elderly, hypnotics, zolpidem, amnesia

(J Patient Saf 2009;5: 00–00)

Transient global amnesia (TGA) is characterized by the abrupt onset of complete anterograde and partial retrograde amnesia, accompanied by repetitive questioning and bewilderment lasting for several hours and without impairment of consciousness and motor or sensory functions.1,2 The symptoms usually last less than 24 hours. As the amnesia resolves, the patient is left with a distinct lapse of recollection of events that happened during the attack.3 Several different causes for this syndrome have been proposed, including transient ischemic attacks, migraine, epileptic seizures, venous congestion, and psychological disturbances.2,3 However, TGA-like episodes can be observed after an intake of short-acting hypnotics.4–6

Chronic insomnia is a common phenomenon among the elderly. Inaccurate handling and use of hypnotics in the elderly have become an important issue in patient safety. Zolpidem belongs to a new class of hypnotic agents that are chemically distinct from benzodiazepines and used for the short-term treatment of insomnia.7 It is generally well tolerated in patients with insomnia, including the elderly.6,8 Although zolpidem seems to have a better safety profile than benzodiazepines, cases of amnesia associated with zolpidem have been reported.6,9,10

We report here a patient who presented with unusual TGA-like episodes caused by the mistaken intake of zolpidem instead of the cholesterol absorption inhibitor, ezetimibe.

CASE REPORT

A 65-year-old woman presented at the emergency department with 2 episodes of paroxysmal transient memory loss that occurred within the past 2 days. One day before admission, she experienced an episode of strange behavior at a market. She seemed to be puzzled and repeatedly asked the same question about the price of fish. According to her neighbor, she was still able to communicate with the clerk of the fish store and calculate the price. Two hours later, she returned to her normal behavior with residual lightheadedness, drowsiness, and blurred vision. However, she had difficulty in remembering with whom she had conversation, her whereabouts, and the subject of her conversation in the market.

Another episode occurred at approximately 9:00 A.M. on the second hospital day. She seemed bleary eyed and anxious and repeatedly asked questions concerning hospital events. Although she was hypertalkative, she was able to converse with others. There were no involuntary movements or limb convulsions during the attack. These symptoms persisted for approximately 2 hours, after which she spontaneously recovered. Nevertheless, she had difficulty recollecting her experiences during this event.

The patient had a history of hypertension, hyperlipidemia, and diabetes mellitus. She took prescription drugs that included bisoprolol, nateglinide, ezetimibe, and candesartan once a day. She also took one-half tablet of zolpidem (10 mg) twice or thrice a week for insomnia. She denied illicit drug or alcohol use and had no history of epilepsy, stroke, head injury, migraine, central nervous system infection, or psychiatric illness.

Physical and neurological examinations conducted during the attack were unremarkable. A mental status examination revealed that language function was preserved, and she was oriented to person, place, date, and situation. Attention and visual-spatial and social skills were retained. Her blood pressure was 150/90 mm Hg, body temperature was 35.8°C, heart rate was 68 beats/min, and blood glucose level was 150 mg/dL. Laboratory parameters, including complete blood cell count and estimation of alanine transaminase/aspartate transaminase, blood urea nitrogen/creatinine, serum electrolytes, thyroid hormones, cortisol level, vitamin B12, and folic acid were all within normal limits. Benzodiazepine, alcohol, and amphetamine screens and tests for syphilis, anti-nuclear antibody, and tumor markers also showed negative results.

Similar episodes occurred thrice during her admission. Long-term video-electroencephalography (EEG) recordings performed during ictus revealed mild attenuation of the alpha rhythm and a diffuse increase in beta activity, but no epileptiform discharge was recorded. In addition, no relevant arrhythmia or heart block was observed on Holter electrocardiogram monitoring during the attack. Cardiac echography, carotid and transcranial ultrasound, and brain magnetic resonance imaging findings were likewise unremarkable.

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Disclosures: None.

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J Patient Saf • Volume 5, Number 1, March 2009
Interestingly, all of the attacks occurred in the morning, particularly 30 minutes after intake of her prescription drugs. The symptoms lasted for approximately 2 to 3 hours. Because she usually took her medications by herself, we carefully examined her medication box. Surprisingly, we found that she mistakenly took zolpidem instead of her newly prescribed anticholesterol drug, ezetimibe, because of the similarity in appearance between the 2 drugs (Fig. 1). After identifying this erroneous intake, she was discharged without recurrence.

**DISCUSSION**

Transient global amnesia usually occurs in middle-aged or elderly people and manifests as paroxysmal transient loss of memory.\(^1,^2\) With the exception of amnesia, no neurological deficits or seizure phenomena is observed. Attacks usually last for minutes or hours, and the ability to lay down new memories is gradually recovered, leaving only a dense amnesic gap covering the duration of the episode.\(^3\) Our patient experienced paroxysmal transient anterograde amnesia with anxiety, bewilderment, and repetitive questioning lasting for 2 to 3 hours. Mental status, consciousness, and activity were preserved during the attack. Upon returning to baseline, there was a residual amnesic gap covering the duration of the attack. Thus, this patient fulfills the clinical criteria for TGA.

Zolpidem, an imidazopyridine, is a γ-aminobutyric acid type A agonist with selective binding affinity for the benzodiazepine α1 receptor.\(^7,^9\) Because of its safety profile, zolpidem has become

**FIGURE 1.** Tablets of both zolpidem (A) and ezetimibe (B) are wrapped in aluminum foil with black characters, which give them a similar appearance.
the most frequently used drug for the treatment of insomnia in the elderly in Taiwan.14 Associated adverse effects are usually transient and include drowsiness, dizziness, hypotonia, blurred vision, mydriasis, gait disturbances, and visual hallucinations.7,8 Memory impairment, particularly anterograde amnesia, is another important side effect and occurs at night, before sleep, or upon awakening.6,10-13 The transient anterograde amnesia that occurred in our patient in the daytime because of the mistaken intake of zolpidem could be misdiagnosed as TGA if the patient’s drug history was not thoroughly reviewed. Moreover, zolpidem has a pharmacokinetic profile of rapid sleep onset in 30 to 60 minutes and a short half-life of 1.5 to 3.2 hours after ingestion,9 which is consistent with the onset and duration of the patient’s clinical symptoms.

Chronic insomnia occurs more often among the elderly than in the young adults. However, there has been controversy regarding the safety of long-term use of hypnotics in the elderly because of the potential adverse effects of these drugs, including memory impairment.8 Inappropriate prescription of hypnotics in the elderly has become an important health issue in Taiwan,15 and the inaccurate handling and use of medication often result in potential adverse drug events.16 In fact, the elderly use more prescription and over-the-counter medications than any other age group. Because their medication regimens are often complicated and involve many drugs at different doses, times, and administration methods, older people who self-medicate have a high risk for medication errors.17 The most common include mixing over-the-counter and prescription drugs, discontinuing prescriptions, maintaining poor records, taking wrong dosages, and consuming inappropriate foods with specific medications.17 Both zolpidem and eszopiclone are wrapped in an aluminum foil with black characters that gives them a similar appearance. Our patient mistakenly ingested zolpidem several times, probably because of lack of education or information about self-management. There are many drugs that are easily confused by the elderly because the packaging looks alike, or the name looks or sounds alike. Several recommendations have been proposed to reduce the occurrence of errors from such problems.18 We believe that mistaken use of hypnotics may be an underrecognized and underreported medication error in clinical practice.

We are aware that the patient also had vascular risk factors for atherosclerosis, including hypertension, hyperlipidemia, and diabetes mellitus. Thus, transient ischemic attacks, cardiac arrhythmia, or hypoglycemic episodes was considered in the differential diagnosis. However, the absence of focal neurological signs as well as normal Holter electrocardiogram, cardiac echography, carotid and transcranial ultrasound, and brain imaging findings excluded the possibility of an ischemic/hypoxic origin of TGA. Normal blood sugar levels and the absence of an epileptiform discharge in the ictal EEG during attacks also excluded epileptic seizures or hypoglycemic episodes. It is important to note that, approximately 30 minutes after mistakenly taking zolpidem, the patient had TGA-like episodes. Furthermore, increased beta activity in ictal EEG recordings suggested the possibility of sedative/hypnotic drug ingestion. The diagnosis of drug-induced amnesia in this patient was reasonable. Therefore, a history of medication use should be carefully reviewed in a patient who presents with TGA-like symptoms.

Our case highlights the importance of increasing suspicion of medication error in senior patients. Prescribed medications are usually delivered by nursing staff during admission at our hospital. For patients who take their own medications, the nursing staff assist the patient to do so. However, in our patient, errors still occurred despite these measures. In addition to prompt alertness of possible medication error by the caring physician or nursing staff, a pharmacist review of the discrepancies between the patient's drug history and the patient’s orders as well as education of medication use can probably further reduce the occurrence of errors.19

CONCLUSIONS

The inadvertent use of zolpidem may cause TGA-like episodes. Therefore, it is important to improve the safety of medication use, particularly among the elderly, who have a poor ability to distinguish between similarly packaged drugs. When prescribing new drugs, particularly hypnotics, to older patients, physicians and pharmacists should educate them and their families about the accurate use of medicine.

REFERENCES