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Zolpidem Ingestion, Automatisms, and Sleep Driving: A Clinical and Legal Case Series

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SCIENTIFIC INVESTIGATIONS

Study Objectives: To describe zolpidem-associated complex behaviors, including both daytime automatisms and sleep-related parasomnias.

Methods: A case series of eight clinical patients and six legal defendants is presented. Patients presented to the author after an episode of confusion, amnesia, or somnambulism. Legal defendants were being prosecuted for driving under the influence, and the author reviewed the cases as expert witness for the defense. Potential predisposing factors including comorbidities, social situation, physician instruction, concomitant medications, and patterns of medication management were considered.

Results: Patients and defendants exhibited abnormal behavior characterized by poor motor control and confusion. Although remaining apparently interactive with the environment, all reported amnesia for 3 to 5 hours. In some cases, the episodes began during daytime wakefulness because of accidental or purposeful ingestion of the zolpidem and are considered automatisms. Other cases began after ingestion of zolpidem at the time of going to bed and are considered parasomnias. Risk factors for both wake and sleep-related automatic complex behaviors include the concomitant ingestion of other sedating drugs, a higher dose of zolpidem, a history of parasomnia, ingestion at times other than bedtime or when sleep is unlikely, poor management of pill bottles, and living alone. In addition, similar size and shape of two medications contributed to accidental ingestion in at least one case.

Conclusions: Sleep driving and other complex behaviors can occur after zolpidem ingestion. Physicians should assess patients for potential risk factors and inquire about parasomnias. Serious legal and medical complications can occur as a result of these forms of automatic complex behaviors.

Keywords: Zolpidem, sleep driving, automatism, parasomnia

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The ingestion of zolpidem and other hypnotic sedative medications for the treatment of insomnia has been associated with sleepwalking and other complex behaviors including sleep eating and sleep driving.[1-5] When ingested during the daytime, hypnotic sedatives impair cognition, memory, and motor performance.[6] There are also reports of a high frequency of blood levels of hypnotic sedatives in drivers apprehended for driving under the influence (DUI).[7-9] An advisory letter was sent and change in package insert information occurred on March 14, 2007, alerting physicians and the public to the possibility of complex behaviors with all hypnotic sedatives.

According to the prescribing information for Ambien and Ambien CR, zolpidem is an imidazopyridine chemical class agent available in the US since 1992. It is chemically unrelated to benzodiazepine and barbiturate hypnotic sedatives. Zolpidem in vitro binds the BZ1 receptor of the GABA(A) complex with high affinity ratio for the alpha1/alpha5 subunits. Mean peak concentrations were 59 (range 29 to 113) after ingestion of the 5 mg tablet and 121 (range 58 to 272) after ingestion of the 10 mg tablet (ng/mL). Time to maximum concentration was 1.6 h for both doses (but 2.2 h if taken with food) with a half-life of approximately 2.6 h (range 1.4 to 4.5) The zolpidem extended release formulation 12.5 mg tablets produced a maximum concentration of 134 (69 to 197) at 1.5 hours. Co-administration with fluoxetine increased half-life by 17%, and co-administration with sertraline increased peak concentrations by 43%.[10]

BRIEF SUMMARY

Current Knowledge/Study Rationale: Sleep driving has been noted to occur after the ingestion of hypnotic sedatives. The nature and cause of this complex behavior is not widely appreciated by clinicians.

Study Impact: This unique series describes in detail the timing of drug ingestion, patient rationale, and medication blood levels in cases of sleep driving and other complex behaviors. Because of these details, clinicians can better understand and assess risk factors, differential diagnosis, and legal ramifications for zolpidem-associated complex behaviors.

Although complex behaviors and sleep driving after zolpidem ingestion have been described, the timing of the ingestion and the legal ramifications of the behaviors are not commonly appreciated by the clinician. A recent review has highlighted the lack of specific clinical information in legal case series presently available in the literature and called for more detailed histories of sedative-related DUIs.[11] It also raised the question of whether physician and patient education could help prevent sedative-related DUIs. The case series presented here describes in detail sleep driving after zolpidem ingestion, the related clinical syndrome of daytime zolpidem-induced automatism, and identifies potential risk factors for these occurrences.

Table 1—Clinical cases

Age	Sex	BMI	Zolpidem ingestion	Behavior	Dose (mg)	Other medications	Sleep Disorder
65	M	26	Accidental during daytime	Automatism	20	Prednisone	None
50	M	24	Accidental during daytime	Automatism	10	None	None
43	M	27	Accidental during daytime	Automatism	10	None	None
28	F	30	Accidental during daytime for one week	Daily confusion	10	Sertraline	None
38	F	28	Daytime ingestion for headache	Inebriation, amnesia	5–10	Bupropion, Venlafaxine	None
65	F	22	Usual bedtime dose	Sleep driving; no accident	10	Ergotamine	Snoring, no OSA
49	F	31	Usual bedtime dose	Sleepwalking, took bath and flooded apartment	15	Temazepam, Carbamazepine	OSA on CPAP but poor adherence
54	M	27	Usual bedtime dose	Sleep eating nightly	15	None	PLMS

CLINICAL CASES

Clinical Patient 1: Acute Mental Status Change With Amnesia

A 65-year-old man presented for neurologic evaluation 2 days after a spell of strange behavior with amnesia while on vacation in rural Kenya. During breakfast he was observed by his wife to suddenly stop talking and to "stare off." He was able to give short and slow verbal responses to her questions such as a soft "yes" or "OK." He remained in this quiet, awake, but poorly responsive state for over an hour, and was then transported by jeep and by plane to a hospital in the capitol. About four hours after onset he began to ask spontaneous questions about where he was and what was going on, and he became more appropriate. He was examined in hospital and found to have a normal physical examination, brain CT scan, EKG, blood counts, and chemistries. He returned to his normal mental and physical state later that day, but with no memory of events between breakfast and the hospital. He flew home to San Diego and was again examined. He had recently been diagnosed with polymyalgia rheumatica and was on a tapering dose of prednisone (now 2 pills of 10 mg). Because of insomnia associated with the steroid, he had been prescribed zolpidem 10 mg tablets. He was found to have a normal ESR and TSH. An EEG, repeat EKG, brain MRI, and carotid duplex Doppler were normal. Upon further questioning, he had put all his pills in the same bottle for the trip to Africa. He realized that he had taken two 10 mg zolpidem tablets instead of two prednisone tablets on the morning of the illness.

Clinical Case 2: Zolpidem For Headache

A 38-year-old woman and homemaker presented with daily headache for 5 years. She had a history of chronic migraine with medication overuse. She had failed prophylactic treatments with topiramate, amitriptyline, propranolol, and botulinum toxin injections. Depression and anxiety were adequately controlled on bupropion and venlafaxine.

For about 4 years she had been taking zolpidem 5 or 10 mg to treat headache in the late afternoon. She would do this on days when her children were safe (such as with the nanny) and when the headache was severe—which was almost every day. She took some care to lock the doors and to remain in the house. After zolpidem ingestion she would stay awake and do chores such as preparing dinner for the family. She would occasionally nap, but usually would remain awake and then go to sleep at about 9 or 10 PM. The husband would arrive home and find her to be clumsy and unsteady, and she seemed inebriated. She would leave dishes strewn about and pots on the stove. He was extremely upset about her zolpidem ingestion because the next day she never remembered activities or conversations from the evening.

Substitute treatment with oral alprazolam and rapidly dissolving clonazepam were partially effective but did not adequately relieve the headache pain. She reverted to using zolpidem again. The prescribing physician was advised of the problem.

Other Clinical Cases

Table 1 shows the 2 cases described above, 3 additional cases of accidental daytime ingestion, and 3 cases of sleep-related complex behavior including one case of sleep driving. Doses of zolpidem and other medications, as well as whether the event was a daytime automatism or was sleep-related, are indicated. All cases of accidental daytime ingestion presented because of unexplained change in behavior with amnesia. Two of the daytime accidental cases were physicians (50-year-old male and 43-year-old male) who routinely put all their pills in one bottle. These patients had 3 to 5 h of amnesia, confusion, ataxia, and were looked after by spouses until the spell passed. The 28-year-old woman accidently took her sleeping pill in the morning and her antidepressant at night for several days and was brought in by family because of confusion and ataxia. In this case, the similar shape and color of Ambien 10 mg and Zoloft 100 mg led to the accidental ingestion.

The 65-year-old woman went to bed and then drove without incident to a fast food restaurant parking lot about 20 miles from her home and slept there until morning. There is no definite information on timing of the ingestion or the driving. The 49-year-old woman who flooded her apartment was also taking temazepam and had been prescribed positive airway pressure for obstructive sleep apnea (OSA), but adherence was poor. The last clinical case was a 54-year-old man who presented with weight gain after experiencing sleep eating with amnesia almost every night one hour after he took his zolpidem and retired. He was found to have generalized anxiety and severe periodic limb

Table 2—Legal defendants

Age	Sex	Behavior	Dose (mg)	Level (ng/mL)	Other Medications	Comments
42	M	Sleep driving	10	25	Medical marijuana	HIV positive; settled for lesser charge.
33	M	Sleep driving	31.25	252	Diphenhydramine	No memory of extra doses. Acquitted
34	F	Sleep driving	N/A	428	None	Took extra pills because of anxiety. Settled for lesser charge.
33	M	Sleep driving	12.5	78	Alcohol	Previous DUI. Previous sleep eating. Pled guilty to DUI.
54	M	Sleep driving	12.5	80	trazodone, paroxetine, gabapentin, levetiracetam	Took at 8 am for first time. Mistrial; settled for lesser charge.
34	F	Sleep driving	10	140	Alcohol	Drove to Burger King. Guilty of DUI

movements in sleep (PLMS). Treatment with ropinirole, low doses of clonazepam, and a cognitive behavioral program allowed him to stop zolpidem and the sleep eating disappeared.

LEGAL CONSULTATIONS

Legal cases were defended by San Diego County court-appointed public defenders. The author was compensated for expert witness evaluation of records and testimony for the defense. **Table 2** summarizes these cases.

Legal Case 1, December 2007

At 3 AM, a Toyota Sequoia struck several parked cars. Police followed skid and gouge marks for 5 blocks to an alley and found the vehicle. The driver appeared intoxicated, diaphoretic, and agitated. He would not follow commands and was handcuffed on the ground while kicking and screaming.

The 42-year-old defendant later stated that he took his usual sleeping pills at about 11 PM and remembered nothing until being in custody. At the initial police interview, after he had calmed down, he said that possibly he had driven to see his friend. He thought he might have hit a light post, but did not remember hitting vehicles or driving for several blocks on the right front wheel rim. The forensic toxicology screen was positive for zolpidem 25 ng/mL and for cannabinoids. The defendant was HIV positive and was receiving medical marijuana.

The author's written opinion was that the defendant had suffered an episode of zolpidem-associated sleep driving and that he was not in control of his behavior. Further, I did not think that he could have anticipated this problem since he had been taking zolpidem for some time, had gone to bed as usual, and was not otherwise intoxicated. He had not been alerted to the possibility of such behavior by his doctor or his pharmacist. Charges of felony DUI and resisting arrest were reduced, and the case was settled.

Legal Case 2, July 2008.

At 2:50 AM, a police officer noticed an automobile stopped at a green light. He pulled behind the car, but the car did not proceed through the light even after the use of the air horn. After activating the police car lights and siren the car began to move. The vehicle was weaving left and right at 40 MPH in both lanes and several times almost hit the curb. The vehicle turned, continued to weave at 52 MPH, stopped at a red light, waited for the green, and then made a U-turn. Two patrol cars were now behind the vehicle, which was moving at speeds up to 60 MPH. After another U-turn the vehicle hit the curb and flattened the right front tire. The driver was taken into custody and was noted to have trouble following commands, was swaying while walking, had red watery eyes, and was not making sense while speaking. He said that he was taking pain medications.

The 33-year-old defendant later made the statement that he had been prescribed Ambien CR in 2007 when on temporary disability from work with back pain. He took the medication consistently for over a year with no problems and then tapered and stopped the medication for the last month. He again developed insomnia, so he went to his doctor on the day of the accident and was prescribed Ambien CR 6.25 mg tablets. He was told that if one pill did not work to take another. He picked up his prescription at 4 PM and took one Ambien CR at approximately 9:30 PM and went to bed. He was not getting drowsy so he went downstairs to take another pill and to get a bite to eat. The next thing he remembers was being arrested in front of his car. Upon release from jail in the morning, he was surprised to find he had no wallet; just shorts, flip flops, and a tank top. When he returned home he counted the remaining pills and there were 23 of 28, suggesting that he had in fact taken 5 Ambien CR (31.25 mg).

The toxicology report from a blood sample drawn soon after the arrest, probably at about 4 AM, showed diphenhydramine and a zolpidem level of 252 ng/mL, consistent with a dose at 10 PM and additional doses after 11 PM.

I testified to the jury that the defendant was under the influence of zolpidem when he left his residence and began to drive. His behavior and rapid improvement to a normal state were typical of zolpidem effect. The jury found the defendant not guilty on all counts, including Evading Police and DUI Drugs. Some of the jurors were not as interested in whether or not the defendant was actually advised of or read the warnings about sleep-related complex behaviors because sleep driving would seem to be so rare a condition that he could not have anticipated it. Many jurors found it persuasive that he had no personal effects on him such as his wallet or cell phone, and that he was driving a route that he took every day—perhaps more likely to occur during an automatism. They also believed that he could have taken the extra pills after the first dose had taken effect.

Legal Case 3, May 2008

At 11 PM a police officer noticed a (34-year-old) woman driving about 40 MPH on the freeway drifting back and forth between lanes. She exited and stopped at a green light. As the light turned to yellow she proceeded. She later stopped at a red light but behind the limit line. She stayed at this location through one entire light cycle before proceeding and then struck a raised median with her vehicle. She continued and eventually turned into a parking lot. She was interviewed on the scene. She said that she was driving from home to her Bible study class. She said that she had one beer and that she took Lamictal. Her field sobriety tests showed that she was swaying and could not stand on one leg. There was no nystagmus. She was considered as DUI, handcuffed, and arrested. She was transported to headquarters to obtain a chemical sample.

The toxicology report showed a zolpidem level of 428 ng/mL and no other substances.

The statement from the defendant was that she remembered nothing after about 10 PM until she was in police custody. She had had dinner with her boyfriend at about 7 PM and had one beer. She decided against going to her Bible study class, but then got into an argument with her boyfriend. When alone at about 9 PM she was very anxious and even panicky. She believed that she followed the recommendation from her doctor to take two alprazolam and two zolpidem if she was having a panic attack and couldn't sleep. Her Bible was found in the car and she had parked at the Bible class location.

My written report expressed the opinion that the defendant was under the influence of a high level of zolpidem at the time of the arrest, had followed her physician's instructions, and that her behavior was consistent with an episode of zolpidem-associated sleep driving. The Public Defender was able to settle the case for a lesser charge (misdemeanor reckless driving).

Legal Case 4, April 2009

At approximately 8 PM the 33-year-old defendant's vehicle struck another car, sideswiped two parked cars, and then caused a head-on collision. The occupants of the other vehicle were seriously injured. The defendant was seen to be acting strangely (e.g., climbed out of the window of the car and staggered). He had also run a red light, was driving without headlights on, and did not stop his vehicle despite several impacts. At the hospital his zolpidem level was 78 ng/mL, his blood alcohol level was 0.23%, and field breathalyzer had been 0.182%.

The statement from the defendant and family members as well as review of his medical records indicated that he had suffered from insomnia for at least 7 years and had often been prescribed zolpidem, either 10 mg or Ambien CR 12.5 mg, using about 30 per month. An alcoholic with previous DUI conviction, the medical records indicated that he was not using alcohol in recent years. He and his family stated that in the past he had often had sleepwalking and sleep eating after taking zolpidem. His family also stated that since the previous DUI, he staunchly avoiding driving if he had been drinking.

On the afternoon before his arrest he had four rum and cokes. He wanted to sleep from about 5 or 6 PM until midnight, because the agreement with his wife was that he would take care of their newborn twins starting at midnight. He remembered taking one Ambien CR 12.5 mg at about 6 PM, and next remembers being in the hospital.

I opined that the defendant was under the influence of both zolpidem and alcohol at the time he was driving. He had a previous history of sleep eating with zolpidem suggesting a predisposition to zolpidem-associated complex behaviors. He pled guilty to DUI, the case settled and he was sentenced to probation and seven years in state prison, suspended.

Legal Case 5, June 2009

At 11:35 AM, the 54-year-old defendant's vehicle struck a parked car while turning and then rear-ended a car stopped in traffic. The defendant had wandered off briefly and was unsteady on his feet. He was making nonsensical statements to a witness (needed coffee; did not acknowledge accident) and then underwent a sobriety check by the officer. He was clearly impaired, dysarthric, had poor balance, and had difficulty making coherent sentences. He denied drinking alcohol but admitted to taking prescription drugs including pain killers and a sleeping pill. He said he was going to the store but did not remember driving or having an accident.

He was wearing pajama bottoms and his dog was in the vehicle. He was taken into custody where a blood sample was obtained. The zolpidem level was 80 ng/mL. Other medications found in his blood were trazodone (29 ng/mL), paroxetine (12 ng/mL), levetiracetam (10 mg/L), gabapentin (6 mg/L), and morphine (23 ng/mL [considered negative]). The defendant was HIV positive and had a painful peripheral neuropathy. The medical records indicated that he took Ambien CR 12.5 mg for the first time on the day of the accident.

It was my opinion that zolpidem contributed to his impairment and the accident, and that taking the medication at 8 AM, even though he hoped to sleep, had produced a state of complex automatic behavior. Later statements indicated that this defendant, after a restless and difficult night, "just wanted to get some sleep" and so took the zolpidem at 8 AM. The case went to trial for one day, a mistrial occurred, and a settlement was negotiated for a charge less than felony DUI.

Legal Case 6, October 2009

A 34-year-old woman with no criminal or civil record went through her usual routine and, after putting her 12-year-old son to bed at 9 PM, took zolpidem 10 mg. She next remembers being in police custody with disheveled clothes, no purse, and having crashed her car at 11:15 PM. She hit several parked cars over a two-block range before hers was disabled. She was incoherent and insisted that the damaged car in front of her was not hers because hers "is not crashed like that." She said that she had had 3 drinks. Her zolpidem level was 140 ng/mL and her breathalyzer alcohol level was 0.11%.

In her statement the defendant remembered putting her son to bed and taking her zolpidem as she had been doing every night for the last few years. Her son said that she later came into his room with a glass in her hand and was talking strangely.

I thought it possible that during a zolpidem-associated complex automatic state (possibly sleepwalking) she had ingested the alcohol without conscious awareness and then had driven. The jury found her guilty of misdemeanor DUI. The prosecution had emphasized the fact that she may have been drinking

Table 3—Features of zolpidem-associated complex behaviors

1. Poor motor control, dysarthria and ataxia.
2. Responsiveness to the environment; apparent wakefulness to observers
3. Confusional ideation and irrational speech
4. Impaired or absent memory for the time period, usually lasting 3 to 5 hours (anterograde amnesia)
5. Onset and offset of symptoms over 1 to 6 hours

prior to taking the sleeping pill (high alcohol level) and they noted the short time duration between her activities with the child, drinking, taking the medication, and the accident.

DISCUSSION

A clinical syndrome characterized by poor motor control, confusion, dysarthria, and anterograde amnesia occurs after zolpidem ingestion both during the daytime and at sleeping times. Whether or not the behavior can be considered a parasomnia depends on the time of ingestion, the occurrence of sleep prior to the behavior, and on patient characteristics. Both the waking and sleeping activities can, however, be termed zolpidem-associated complex behaviors, one of them an automatism and the other a parasomnia. As indicated in a review of sleep driving by Pressman, the intoxicated behavior during the arrests is often not consistent with sleepwalking alone. Pressman suggests that the onset of the event could be a parasomnia, but as the event continues the sleep-related elements disappear, leaving the person now intoxicated but not in bed.[11] This concept of an initial sleep walking episode followed by a complex automatic state is supported by the legal cases in this series based on the stated timing of ingestion, the lack of motive for driving, and the behaviors recorded at the scene.

Both the clinical and the legal cases suffer from lack of information that inhibits drawing firm conclusions. First, the medical condition of the defendants is mostly unknown. Other sleep disorders, including for example sleep apnea, could not be ruled out. Their statements, while generally under oath, were made in the context of trying to avoid DUI conviction. Even the clinical cases were reported retrospectively, and only three were studied in detail with polysomnography.

Sleepwalking does not have a well-understood pathophysiology and is considered to be a dissociative state occurring in slow wave sleep (N3), in which elements of wakefulness and sleep coexist.[12,13] Its prevalence in adults has been estimated at 0.4% in the Finnish Twin Cohort.[14] About 90% of adult cases of sleepwalking also had childhood sleepwalking in this study. In the United Kingdom, a representative telephone survey of 4972 adults found that sleepwalking was present in 2% and was associated with younger age, breathing difficulty, and sleep talking.[15] The prevalence of sleep walking suggests that there might be coincidental overlap in some patients who are prescribed hypnotic sedatives. The likelihood of sleepwalking and other NREM parasomnias is increased by factors or conditions that increase slow wave sleep (such as sleep deprivation) or cause arousals during slow wave sleep.[16] In some of the legal cases, sleep deprivation was likely present based on the statements and lifestyles of the defendants.

The selective binding of zolpidem at the BZ1 receptor may explain the relative absence of myorelaxant, anxiolytic, and anticonvulsant effects, as well as the preservation of deep sleep.[17-20] Zolpidem produces impairment of memory, motor, and cognitive functions.[21-23] Profound impairment of driving ability is present 4 hours after ingestion of both 10 and 20 mg doses, and lasts perhaps as long as 6 hours.[24-27] However, most studies of the effect of zolpidem on driving have examined the next day residual effect and have shown no impairment when conducted eight or nine hours after ingestion.[28,29]

The reason that zolpidem is often implicated in sleep-related complex behaviors is not clear, but it is the most often prescribed sleeping pill in the United States. For example, the VONA database, which captures over one-half of the US prescriptions, found that 63% of the hypnotic sedatives prescribed by primary care providers in 2007 were zolpidem or zolpidem extended release, compared to only 29% for eszopiclone and temazepam combined.[30] The West Virginia Medicaid program database indicated that in 2003, zolpidem represented 43% of claims, trazodone 46%, temazepam 10%, and triazolam, flurazepam, estazolam, and zaleplon less than 2%.[31] In Norway, a study found higher rates of zopiclone then zolpidem in drivers, reflecting the prescribing bias of the physicians in that country.[8] It is important to note that no study has prospectively studied the propensity for any hypnotic sedative to trigger a parasomnia.

It is also possible that zolpidem's receptor specificity and its rapid pharmacokinetics underlie this complication. For example, if zolpidem does not decrease anxiety at the time sleep is induced,[18] in the anxious but now asleep state, ingestion of more medication, alcohol, food, or other means of relieving anxiety might occur. It is also possible that because zolpidem appears to have less muscle relaxant properties than benzodiazepines, the motor system might remain relatively more engaged compared to the amount of sleep induction that occurs.[32] Lastly, the preservation of stage N3 that occurs with zolpidem relative to traditional benzodiazepines might increase likelihood of a parasomnia or confusional arousal based on current models that suggest deeper sleep is a risk factor for these events.[16,33]

All cases of daytime accidental ingestion in this series demonstrated rapid onset confusion, ataxia, and amnesia, which led physicians to consider the diagnoses of cerebral ischemia (stroke), partial complex seizure, or transient global amnesia. **Table 3** lists the dominant clinical findings during the episodes. Mixing pills together in the same bottle was responsible for most of the accidental cases. In addition, the similar look of different medications was responsible in one case. It is possible that use of generic equivalents might make distinction between pills more difficult for some patients. Two of the clinical cases had concomitant sleep disorders, suggesting that arousal from OSA or PLMS triggered these parasomnias. Indeed, treatment of PLMS in one patient was associated with disappearance of nightly sleep eating.

The legal cases represent complex behaviors following zolpidem ingestion intended to induce sleep, a situation that could variably be considered an altered state with amnesia (automatism) or a form of parasomnia (sleep driving), or both. It is not possible to know with certainty that the defendants ever actual-

ly slept before driving. Defendants used sleepwalking triggered by zolpidem as a defense for their DUI on the grounds that such activity could not be reasonably anticipated based on what they were told about the medication by the prescribing physician and pharmacist. The body of reports of parasomnia associated with hypnotic sedative use would seem to support such a defense, as opposed to the voluntary ingestion of alcohol.[34] Such a defense would seem to be stronger if there is a history of prior parasomnia and if the medication was used properly.

The legal cases provide some details that suggest underlying risk factors as well as real-world prescribing instructions and patient use of sleeping medications. **Table 4** lists some of these risk factors. Some cases were more likely a parasomnia in onset because of appropriate timing, dose, and bedtime behavior. In some cases the drug was combined with other medications and with varying doses of alcohol that would increase risk of automatism. The ingestion of additional doses of zolpidem (of which the person had no memory) was established in one case. In another case, the ingestion of high doses of zolpidem when upset may not have induced sleep, allowing for the expression of a state of complex automatic behavior. Similarly, the ingestion of zolpidem at 8 AM, even if exhausted and wearing pajamas, does not guarantee sleep. Lastly, it is clear that patients and physicians may not always communicate about complications of medications and use of alcohol.

One risk factor for zolpidem-associated sleep driving is suggested from this series that had not been previously noted—living alone. I suggest that this is because a spouse might notice certain behaviors and then inform the patient, for example, in the nights before sleep driving when less active parasomnias might occur such as simple sleep talking or sleep eating. The drug could then be stopped or the dose lowered. Alternatively, if there were no preceding minor events, many spouses might notice a bed partner leaving the house and starting up the car at midnight, and disaster might be averted.

CONCLUSIONS

As is obvious from the behavior in all cases, sleep driving and daytime automatism must be considered potential serious adverse effects of zolpidem ingestion with high potential for fatality. Physicians should be aware of this possibility and can perhaps minimize the likelihood of occurrence by following certain prescribing principles. These include evaluation and treatment of the underlying cause of the insomnia, assessing patient risk factors prior to prescribing, starting with very low doses, minimizing nights of patient use, asking about minor parasomnia behaviors at follow-up, and emphasizing good sleep habits and regular schedules. A cautious clinician might consider instructing the patient not only to "ingest immediately prior to going to bed," but add "at your usual bedtime only." This instruction would be implicit if all physicians included the basics of behavioral treatments and good sleep hygiene with any prescription for hypnotic sedatives.[35,36] The degree to which zolpidem-associated sleep driving in an individual case is caused by poor compliance on the part of the patient, is a rare unavoidable side effect of the drug, or is the fault of physician and pharmacist instruction might only be determined by a jury in the court room.

Table 4—Potential risk factors for zolpidem-associated automatisms and parasomnias

1. Concomitant ingestion of alcohol or sedating medications
2. Concomitant sleep disorder such as OSA or PLMS
3. A history of parasomnia
4. Hypnotic sedative ingestion at times other than habitual bedtime
5. Hypnotic sedative ingestion during agitated state with decreased likelihood of sleep
6. Hypnotic sedative ingestion when sleep deprived
7. Poor management of pill bottles
8. Living alone

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