Lorazepam and Driving Impairment*

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Abstract

Lorazepam (Ativan®), is a benzodiazepine frequently used to manage anxiety, presurgically, and as a sedative. Common side effects include sedation, dizziness, weakness, unsteadiness, and disorientation. Consequently, lorazepam can have a significant effect on driving ability. We reviewed all positive lorazepam drug-impaired driving cases submitted to the Washington State Toxicology Laboratory between January 1998 and December 2003. The mean concentration found in the blood of these drivers (n = 170) was 0.048 mg/L (std. dev. = 0.06, median = 0.03). Concentrations ranged from < 0.005 to 0.39 mg/L. Eighty-six percent of these drivers tested positive for other drugs in addition to lorazepam that may have contributed to their impairment. There were 23 cases in which lorazepam was the only drug detected. The mean concentration found in the blood of these drivers was 0.051 mg/L (median = 0.03, range < 0.01-0.38). This population was 56% male, with a mean age of 39.5 years, (range 16-72). We obtained Drug Recognition Expert reports containing details of events surrounding arrest and performance on field sobriety tests for 10 of the remaining cases in which no drugs other than lorazepam were present. Lorazepam concentrations in these cases averaged 0.050 mg/L (median = 0.04, range 0.01-0.13 mg/L). This review of these subjects indicates that lorazepam is capable of causing significant impairment to driving and psychomotor abilities, independent of the concentration detected.

Introduction

Lorazepam (Ativan®) is a 3-hydroxy benzodiazepine, belonging to the same family as oxazepam and temazepam. It has an intermediate half-life of 9–16 h and is metabolized by glucuronidation and excretion. It has no active metabolites. The drug is used most frequently via the oral route for the management of anxiety disorders, for relief of the symptoms of anxiety associated with depression, and for insomnia. It is administered intravenously as an anticonvulsant medication for treatment of epileptiform seizures and is often given intravenously as a presurgical sedative, where it produces sedation, anxiolysis, and decreased ability to recall events related to the day of surgery. It can be used as a chemical restraint agent for combative patients in the emergency department. The main effect profile of lorazepam, as with the other benzodiazepines, is one of sedation, producing classical symptoms associated with CNS depression; consequently, lorazepam can have a significant effect on driving ability.

The ability of laboratories to detect lorazepam in biological samples depends heavily on the screening technology used. Although lorazepam is structurally similar to oxazepam, and oxazepam is frequently used as the immunogen for immunoassay antibodies, lorazepam has poor cross-reactivity with enzyme multiplied immunoassay technique (EMIT), ELISA, and FPIA immunoassay screening tests, although it appears to react much better with CEDIA technology (1,2). These authors also note that β-glucuronidase hydrolysis of the glucuronide conjugate significantly improves the detectability of the drug in urine. Laboratories relying on EMIT or FPIA benzodiazepine assays will likely fail to detect lorazepam in samples from drug positive drivers.

Lorazepam has been tested for and detected with increasing frequency in impaired drivers in Washington state (Figure 1). This series of cases was reviewed to identify the circumstances, demographics, patterns of use, signs and symptoms of intoxication, effects on driving, and the lorazepam concentrations associated with drug-impaired driving.

Methods

Blood samples from drug-impaired drivers in Washington State are first subject to testing for alcohol. In general, if a driver has more than 0.10 g/100 mL of ethanol and will not be charged with vehicular homicide or assault, no additional testing is performed. If additional testing is required, samples are screened for drugs of abuse and several prescription drug classes using an EMIT assay. Blood specimens (1 mL) undergo protein precipitation with methanol (1 mL) and acetonitrile (5 mL) while vortex mixing. The samples are centrifuged and the supernatant evaporated to 50 µL, then reconstituted to 350 µL with methanol/EMIT buffer (1:1). The EMIT procedure screens for cocaine metabolites (cutoff limit 0.15 mg/L), opiates (0.3 mg/L), amphetamines (0.5 mg/L), carboxy tetrahydrocannabinols (0.02 mg/L), methadone (0.3 mg/L), phencyclidine (0.025 mg/L), propoxyphene (0.3 mg/L), barbiturates (0.2 mg/L), benzodiazepines (0.2 mg/L), and tricyclic antidepressants (0.3 mg/L). Cutoff limits were determined experimentally by the laboratory.

Samples are also tested by gas chromatography (GC) and gas chromatography–mass spectrometry (GC–MS) for volatiles including ethanol, basic drugs, and neutral and weakly acidic drugs. Samples testing positive for drugs by EMIT were confirmed by GC–MS.

Cases were further subjected to GC–MS analysis for benzodiazepines, including lorazepam, when a benzodiazepine immunoassay–positive screening result was obtained and/or when circumstances indicated the involvement of lorazepam either through medications found in the vehicle or in the subject’s possession, statements by the subject, or other investigative information. Additionally in cases where other drugs with CNS depressant effects, such as tricyclic antidepressants, barbiturates, GHB, and narcotic analgesics had been ruled out. Every effort is made to cover drugs frequently used, however not every drug can be detected in our laboratory. Specific to this study, some of the subjects may have had lithium present, but it would not have been detected in our analysis.

The GC–MS benzodiazepine procedure used was as follows. Urine samples are first hydrolyzed (2-mL sample, 100 µL β-glucuronidase, 50 µL internal standard, and 2 mL of pH 6.8 phosphate buffer (0.1M); then the sample is heated for 2 h at 37°C prior to extraction. Blood or hydrolyzed urine (2 mL), internal standard solution (diazepam-d₅, 200 µL of a 10 g/mL solution in methanol), and pH 7.0 phosphate buffer (1 mL) are mixed, then extracted with n-butyl chloride (6 mL) and rotated slowly for 15 min. The organic layer is transferred to a conical tube and evaporated to dryness, then reconstituted with acetone (200 µL), and vortex mixed. Heptane (500 µL) is added as a wash, vortex mixed, and the heptane discarded. The acetone layer is evaporated to dryness then reconstituted and derivatized using acetone/MTBSTFA+ 1% TBDMS (3:1) (75 µL). Samples are allowed to derivatize in a 70°C oven for 30 min, then transferred to an autosampler vial for GC analysis. Samples are quantitated using a selected ion monitoring (SIM) mode (Figure 2) and confirmed using a full scan mode. This assay is currently used in the laboratory to detect diazepam, nordiazepam, flurazepam, N-desalkylflurazepam, midazolam, oxazepam, temazepam, flunitrazepam, 7-aminojunitrazepam, alprazolam, α-hydroxy-alprazolam, clonazepam, and 7-aminoclonazepam. For lorazepam, the limit of detection and lower limit of quantitation is 0.003 mg/L, typically reported to two significant digits. The upper limit of linearity is 1.5 mg/L.

Lorazepam-positive cases in the Washington State Toxicology Laboratory’s database were reviewed. There were 170 drivers testing positive for lorazepam detected between the years 1998 and 2003. Two drivers were counted twice in this study, due to multiple arrests for driving under the influence. One subject was arrested for driving under the influence of lorazepam (0.01 mg/L) and was then stopped two months later for driving under the influence of lorazepam (0.02 mg/L) and mirtazapine (0.41 mg/L). The other subject was arrested for driving under the influence of lorazepam (0.39 mg/L) and ethanol (0.18 g/100 mL), then again six months later for driving under the influence of lorazepam (0.04 mg/L).

For the purposes of further review, cases were assigned into groups of drivers in which lorazepam was present with other drugs (n = 147) or cases in which lorazepam was the only drug detected (n = 23). The later group includes a subset of lorazepam-only cases in which a Drug Recognition Expert (DRE) examined the subject (n = 10).

The Drug Evaluation and Classification program (DEC) was developed in response to the increasing problem of the drug-impaired driver. The program uses officers specifically trained in diagnostic tests (Drug Recognition Experts, DRE) to evaluate suspects in a 12-step standardized battery of tests, including interview, field sobriety tests, eye exams in both light and dark, vital signs, and a subsequent blood draw submitted for toxicoc-
logical examination. The officer concludes the class or classes of impairing drugs, and when the toxicological analysis confirms the officers' conclusion, the two are used in court to establish the impairment of the suspect. Non-DRE officers may have specific training to recognize drug-impaired drivers but have not had the extensive training of the DRE and do not perform the 12-step examination of the suspect. Blood draws from the latter cases are identified at the WSTL as DUI cases. Those cases which were evaluated by a DRE were matched up with their reports to create a more detailed account of events surrounding arrest and performance on field sobriety tests.

### Table II. Other Drugs Most Frequently Found in Combination with Lorazepam

<table>
<thead>
<tr>
<th>Drug or Metabolite</th>
<th>Total Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>meprobamate</td>
<td>26</td>
</tr>
<tr>
<td>carboxy-THC (THC detected in 5 cases)</td>
<td>23</td>
</tr>
<tr>
<td>ethanol</td>
<td>23</td>
</tr>
<tr>
<td>carisoprodol</td>
<td>18</td>
</tr>
<tr>
<td>diphenhydramine</td>
<td>16</td>
</tr>
<tr>
<td>venlafaxine</td>
<td>16</td>
</tr>
<tr>
<td>methadone</td>
<td>16</td>
</tr>
<tr>
<td>nordiazepam (diazepam detected in 5 cases)</td>
<td>16</td>
</tr>
<tr>
<td>promethazine</td>
<td>14</td>
</tr>
<tr>
<td>hydrocodone</td>
<td>13</td>
</tr>
</tbody>
</table>

### Table III. Case Information on Drivers Testing Positive for Lorazepam Alone (Includes Caffeine and/or Nicotine)

<table>
<thead>
<tr>
<th>Case #</th>
<th>Age</th>
<th>Gender</th>
<th>mg/L</th>
<th>Accident</th>
<th>Circumstances Resulting in Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>m</td>
<td>&lt; 0.01</td>
<td>no</td>
<td>Lane travel</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>f</td>
<td>&lt; 0.01</td>
<td>no</td>
<td>Speeding</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>f</td>
<td>0.007</td>
<td>no</td>
<td>Traffic violations</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>f</td>
<td>0.01</td>
<td>yes</td>
<td>Failed to negotiate a curve and struck a semi-trailer</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>f</td>
<td>0.01</td>
<td>no</td>
<td>Speeding and lane travel</td>
</tr>
<tr>
<td>6</td>
<td>44</td>
<td>m</td>
<td>&lt; 0.02</td>
<td>yes</td>
<td>Hit and run accident</td>
</tr>
<tr>
<td>7</td>
<td>47</td>
<td>m</td>
<td>0.02</td>
<td>no</td>
<td>Potential DUI</td>
</tr>
<tr>
<td>8</td>
<td>47</td>
<td>m</td>
<td>0.02</td>
<td>no</td>
<td>Erratic driving through a DOT paving project</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>m</td>
<td>0.02</td>
<td>yes</td>
<td>Called in as a potential DUI—resulted in a two-car collision</td>
</tr>
<tr>
<td>10</td>
<td>53</td>
<td>m</td>
<td>&lt; 0.025</td>
<td>unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>11</td>
<td>33</td>
<td>m</td>
<td>&lt; 0.025</td>
<td>yes</td>
<td>Single car accident</td>
</tr>
<tr>
<td>12</td>
<td>16</td>
<td>m</td>
<td>0.03</td>
<td>yes</td>
<td>Speeding, lane travel, hit a mailbox, lost a tire, and drove on the rim</td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>f</td>
<td>0.04</td>
<td>no</td>
<td>Observed running stop signs and hitting curbs, front tire was flat</td>
</tr>
<tr>
<td>14</td>
<td>26</td>
<td>f</td>
<td>0.04</td>
<td>yes</td>
<td>Fell asleep at the wheel and hit a parked car</td>
</tr>
<tr>
<td>15</td>
<td>35</td>
<td>f</td>
<td>0.04</td>
<td>yes</td>
<td>Involved in two separate rear-end collisions and additional traffic violations</td>
</tr>
<tr>
<td>16</td>
<td>36</td>
<td>m</td>
<td>0.04</td>
<td>yes</td>
<td>Single car accident</td>
</tr>
<tr>
<td>17</td>
<td>17</td>
<td>m</td>
<td>0.05</td>
<td>yes</td>
<td>Struck a street sign</td>
</tr>
<tr>
<td>18</td>
<td>24</td>
<td>m</td>
<td>0.05</td>
<td>yes</td>
<td>Multi car accident</td>
</tr>
<tr>
<td>19</td>
<td>58</td>
<td>m</td>
<td>0.07</td>
<td>yes</td>
<td>Rear ended another vehicle</td>
</tr>
<tr>
<td>20</td>
<td>39</td>
<td>f</td>
<td>0.09</td>
<td>no</td>
<td>Traffic violations</td>
</tr>
<tr>
<td>21</td>
<td>72</td>
<td>f</td>
<td>0.09</td>
<td>no</td>
<td>Called in as a potential DUI</td>
</tr>
<tr>
<td>22</td>
<td>37</td>
<td>m</td>
<td>0.13</td>
<td>yes</td>
<td>Struck two parked cars, jersey barrier and rear-ended another vehicle</td>
</tr>
<tr>
<td>23</td>
<td>35</td>
<td>f</td>
<td>0.38</td>
<td>yes</td>
<td>Single car accident</td>
</tr>
</tbody>
</table>

* This individual tested negative for ethanol in the laboratory, but gave a 0.04 g/210 L of breath reading on a portable breath test instrument used in the field.

### Results

The frequency with which lorazepam has been detected in drug-impaired drivers has increased markedly over the last eight years (Figure 1). Several factors have contributed to this increase, most notably the introduction in 1995 of a DRE program, followed by provision of an 8-h training course for most law enforcement officers in the state, providing guidance on how to recognize drug impairment in drivers. This training provided officers with probable cause to initiate many more drug impaired driving arrests. The second significant factor was the introduction in 1997 of an enhanced GC–MS method for measuring benzodiazepines, including lorazepam, with low limits of detection (< 0.003 mg/L). We have no independent indicators of any increase in either the licit or illicit use of lorazepam in Washington state during this period.

In the course of this review we identified 170 cases of impaired drivers who tested positive for lorazepam after a targeted GC–MS test was administered. The mean lorazepam concentration found in the blood of these drivers was 0.048 mg/L (S.D. 0.06, median 0.03 mg/L) (Table I). Eighty-six percent of these drivers tested positive for other drugs in addition to lorazepam that may have contributed to their impairment. In cases in which other drugs were present, the most frequently detected drugs were muscle relaxants or painkillers (Table II), suggesting that these patients may be taking lorazepam to treat anxiety associated with depression secondary to chronic pain or as a presurgical sedative. Ethanol was also frequently detected in these cases.

Because of the difficult nature of isolating the impairing effects of lorazepam in poly-drug cases, we further considered those cases (n = 23) in which lorazepam alone was present (Table III). The circumstances which resulted in testing were obtained from the police report, or taken from the request for analysis form sent in with the sample for those cases in which a copy of the police report was not available.

Lorazepam concentrations detected in drivers with no other drugs present (n = 23) ranged from 0.01 to 0.38 mg/L (mean 0.051,
median 0.03 mg/L (Table I). These concentrations range from
the sub therapeutic to higher than steady state concentrations
associated with a 10-mg daily dose. The concentration range in
cases in which lorazepam was the only drug detected (n = 23),
was very similar to the group as a whole (n = 170). These data
suggest that adverse effects on driving can be associated with
subtherapeutic, therapeutic, and supratherapeutic dosing. The
population with lorazepam alone was 56% male, with a mean
age of 39.5 years (median 37 years, range 16–72). Ten of the lo-
razepam alone cases were evaluated by a DRE.

Lorazepam-only DRE cases
In the 10 cases in which lorazepam was the only drug present,
and for which DRE information was available, concentrations
averaged 0.05 mg/L (median = 0.04, range 0.01–0.13 mg/L)
(Table I). The subjects reported various reasons for their lo-
razepam use. Three were using it as a sleep aid or a sedative,
three were using it for non-prescribed purposes, two did not
specify their reason for taking the drug, one individual used lo-
razepam as an anxiolytic, and one to treat heroin withdrawal
symptoms (Table IV).

In these 10 subjects, the reasons for the initial traffic stops
were attributed to involvement in an accident (7 cases) or err-
erratic driving (3 cases). Despite the wide range of lorazepam
concentrations detected, the subjects’ behaviors were highly
consistent. Speech was slow, thick, low, and/or slurred in all but
1 of the 10 cases. Attitudes were cooperative in all cases. Coor-
dination was poor in all but one case, and this individual was in-
stead noted as being lethargic. Blood pressures and pulse rates
were unremarkable, and temperatures were on the low side of
normal (mean 96.4°F, median 96.5°F, range 93.6–98.4°F) (Table
V). There was a wide range in the subject’s estimation of the pas-
sage of 30 s (mean = 38.9 s, range 13–90+ s). Swaying 2–6 in.
during the Romberg test was observed in all but one subject
(mean sway 3 in., median sway 2 in.). The Romberg test was
stopped short for two individuals because they were unable to
maintain balance and the officers were concerned for their
safety. All subjects did poorly on the modified finger-to-nose
test. There appeared to be no correlation between standard-
ized field sobriety test (SFST) performance and the concentra-
tion of lorazepam detected. Horizontal Gaze Nystagmus (HGN)
was observed in all drivers. Five of the 10 subjects had vertical
nystagmus, which is normally associated with dissociative drugs
such as LSD, but is frequently anecdotaly reported in subjects
heavily intoxicated with CNS depressants. All subjects per-
formed poorly on the walk-and-turn and one-leg-stand tests
(Table VI).

### Table IV. Reasons Cited by Subjects for using Lorazepam
During the DRE Evaluations (n = 10)

<table>
<thead>
<tr>
<th>Reason for Use</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep-aid/sedative</td>
<td>3</td>
</tr>
<tr>
<td>Misuse</td>
<td>3</td>
</tr>
<tr>
<td>Unspecified</td>
<td>2</td>
</tr>
<tr>
<td>Anxiolytic</td>
<td>1</td>
</tr>
<tr>
<td>Treat heroin withdrawal</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table V. Results of Physical Exam Performed by Drug Recognition Experts (n = 10)

<table>
<thead>
<tr>
<th>Physical Exam</th>
<th>Range</th>
<th>Mean</th>
<th>Median</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse (beats per min)</td>
<td>66–116</td>
<td>91</td>
<td>97</td>
<td>60–90</td>
</tr>
<tr>
<td>Blood pressure-systolic (mmHg)</td>
<td>108–160</td>
<td>125</td>
<td>120</td>
<td>120–140</td>
</tr>
<tr>
<td>Blood pressure-diastolic (mmHg)</td>
<td>56–94</td>
<td>80</td>
<td>84</td>
<td>70–90</td>
</tr>
<tr>
<td>Temperature (degrees Fahrenheit)</td>
<td>93.6–98.4</td>
<td>96.4</td>
<td>96.5</td>
<td>97.6–99.6</td>
</tr>
</tbody>
</table>

### Table VI. Results of Standardized Field Sobriety Tests (n = 10)

<table>
<thead>
<tr>
<th>Standardized Field Sobriety Tests</th>
<th>range</th>
<th>mean</th>
<th>median</th>
<th>scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal Gaze Nystagmus</td>
<td>2–6</td>
<td>4</td>
<td>3.5</td>
<td>6 clues max.</td>
</tr>
<tr>
<td>One-Leg Stand</td>
<td>3–4</td>
<td>3.5</td>
<td>3</td>
<td>4 clues max.</td>
</tr>
<tr>
<td>Walk-and-Turn</td>
<td>4–8</td>
<td>6</td>
<td>6</td>
<td>8 clues max.</td>
</tr>
</tbody>
</table>

### Case Histories

Three cases in which lorazepam was the only drug detected,
and one where the driver was under the influence of lorazepam
and other drugs is presented here. For the lorazepam-only
cases, a case from a subtherapeutic, therapeutic, and suprather-
apeutic concentration was chosen, based on the amount of de-
tail provided by the officer.

**Subject 1**

A cell phone caller reported that a car had pulled into a
parking lot, struck some curbing, and the 44-year-old male
driver appeared to pass out. When the officer arrived, he saw a
car awkwardly parked, taking up two stalls. While examining the
vehicle, he observed the subject approaching. He was stag-
gering and appeared somewhat slumped over. The officer asked
if he was having problems driving, and the subject admitted to
being involved in a two car accident prior to hitting the curb
and pulling into the parking lot. He was returning from a med-
ical appointment where he had been prescribed lorazepam to
take an hour prior to his magnetic resonance imaging (MRI)
procedure to help him relax. The subject stated that his stomach
was bothering him (he had been vomiting before the officer ar-
rived), and he was having difficulty concentrating and felt
sleepy. He was surprised at how the medication affected him.

The officer noticed that the subject’s speech was thick and
slurred and his movements were sluggish, uncoordinated, and
"drunk-like". He had droopy, red, watery eyes. All six clues of
HGN were present. The subject also did poorly on the one-leg-
stand, swaying, raising his arms, and putting his feet down. On
the walk-and-turn test, he was unable to follow directions, had
seven of the eight clues, and fell to his side and had to grab a
wall to regain posture. He displayed a slow internal clock on the Romberg balance and the one-leg stand.

Toxicology revealed a lorazepam concentration of < 0.02 mg/L and caffeine. No alcohol or other drugs were detected.

Subject 2
A witness observed a 17-year-old male speeding and driving all over the road and shoulder. He noticed that the car had been in an accident, tire rubber was "flying everywhere," and the car was being driven on its rims. The caller followed the vehicle, watched it miss a turn, stop, back up, and then speed past a group of pedestrians. When the car pulled into a driveway, the driver stumbled out, appearing drunk, and muttered an expletive. The caller asked the subject if he knew he was driving on his rims and if he was okay, but the subject acted confused and mumbled, so the caller notified the police.

When officers arrived, they saw damage to the vehicle, including front-end damage containing dark-brown wood splinters. It was later discovered that the subject had hit a mailbox, but he denied having hit anything but a curb. The subject's parents told the officer that they felt their son was on drugs, and that he had attempted to overdose on some of their pills (including lorazepam) in the past. He had also used other recreational drugs.

Upon contact with the subject, the officer immediately observed him to have droopy eyes and he was swaying and stumbling while trying to maintain a stationary position. He claimed that he was daydreaming and had hit a curb, then sped home so that he could fix his flat tire. The subject had all six clues of HGN and had vertical nystagmus. He did poorly on the one-leg stand and walk-and-turn. He was unable to maintain balance, had to grab on to the wall, and was unable to follow directions. The only drug the subject admitted to using was fluoxetine. No other drugs or alcohol were detected.

Toxicology revealed a lorazepam concentration of 0.03 mg/L. No other drugs or alcohol were detected.

Subject 3
A 35-year-old woman drove her vehicle off the road and into the bushes. She was not injured and was trying to free her vehicle when the officer arrived. There was an odor of intoxicants coming from the car and the officer noted a beer bottle on the floor of the vehicle. The subject stated that she may have been drinking in the car.

The officer noted that she appeared to be in a dazed state. She was slow to respond to basic questions. She had poor balance and could not stand still without swaying. The officer was unable to test for HGN; the subject would not hold her head still and would only follow the pen with her head, not her eyes. He did notice that her eyes were watery and bloodshot. She had to put her foot down after several seconds on the one-leg stand and she did not touch heel to toe, stumbled on her turn, and used her arms to balance as she performed the walk-and-turn test. Her movements throughout the testing phase were noted as being slow and unsteady, she had difficulty following and remembering directions, and at times she was described as having a blank stare. The arresting officer further noted the subject as having slurred and mumbled speech. The subject stated she was taking Afrin® (nasal spray) and "some mental health drugs."

When the subject gave a negative reading for ethanol on the breath test instrument, she was taken to a hospital for blood draw.

Toxicology revealed 0.38 mg/L of lorazepam. This concentration is in excess of the recommended therapeutic concentration and most likely represents abuse of the drug. No other drugs or alcohol were detected.

Subject 4
A 45-year-old woman lost control of her vehicle, traveled off the road, then came back across both lanes of travel and hit a tree. She was initially observed to have poor coordination, difficulty standing, and was laughing. She later became disoriented, restless, and paranoid. Her voice was low and raspy and she complained of a dry mouth and displayed body tremors. This subject had six clues of HGN, performed poorly on the other Field Sobriety Tests, had an elevated pulse, low blood pressure, little reaction to light, and hippus was observed.

Toxicology indicated a lorazepam concentration of 0.06 mg/L. No ethanol was detected, but carboxy-THC 14 ng/mL, meprobamate 7.5 mg/L, carisoprodol < 2.5 mg/L, fentanyl < 0.05 mg/L, oxycodone < 0.05 mg/L, acetaminophen 20.5 mg/L, and caffeine were all detected.

Discussion
In a sample of about 3500 anxious patients being treated for anxiety, the most frequent adverse reaction to lorazepam was sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%), and unsteadiness (3.4%). Less frequent adverse reactions include disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye-function disturbance, together with various gastrointestinal symptoms, and autonomic manifestations. The incidence of sedation and unsteadiness increased with age. Patients taking lorazepam are at greatest risk for adverse effects on their psychomotor skills when they begin taking the drug for the first time, have their dosage adjusted, or take the drug in combination with alcohol or other drugs with CNS depressant properties (3).

The recommended dose of lorazepam for treatment of anxiety starts at 2–3 mg/day increasing to 2–6 mg/day in divided doses, although in practice dosing can go much higher depending on the patient’s ability to tolerate the side effects. For insomnia the recommended dose is 2–4 mg.

Average peak plasma concentrations occur about 2 h after administration of a single oral 2-mg dose at 0.018 mg/L, declining to 0.009 mg/L by 12 h (4). Patients receiving a chronic 10 mg/day dose developed a steady-state plasma concentration of 0.181 mg/L (range 0.140–0.240 mg/L) (5). The drug has a half life of 9–16 h although this can be longer in the elderly, requiring the use of lower doses. Use in an elderly patient of what might be appropriate doses of lorazepam in a younger patient can result in long-term marked sedation and apparent dementia.

In comparison, the concentrations detected in Washington
state drivers, both those taking lorazepam alone and those using it in combination with other drugs, represented sub-therapeutic, therapeutic, and supratherapeutic concentrations. This review of these subjects confirms that lorazepam is capable of causing significant impairment to driving and psychomotor abilities, independent of the concentration detected, but likely related to the patient’s tolerance of the sedating side effects.

Other authors have evaluated the effects of lorazepam on driving either in the laboratory or on closed course driving courses. A study of 18 patients administered a twice daily 1.5-mg dose of lorazepam for 7 consecutive days exhibited a pronounced impairing effect on lateral position control and induced daytime sleepiness. The authors concluded that lorazepam administered under this regimen would be hazardous for drivers engaged in daily driving (6).

Other workers have also demonstrated marked and pervasive driving impairment following the administration of lorazepam. (7-9).

A committee of European toxicologists and pharmacologists have developed a system for characterizing drugs according to their potential for causing impairment (10). They recommended a classification of III for any dose of lorazepam, that is, likely to produce severe impairment or presumed to be potentially dangerous, equivalent to a BAC > 0.04 g/100 mL. The findings in the cases underscore the importance of ensuring that patients taking lorazepam and other sedating drugs receive and understand warnings regarding the potential effects of the drug on their driving. As illustrated by the cases in this review, patients are evidently driving after taking the drug, even when prescribed legitimately by their physician. Various prescribing information sources in the United States state that “patients receiving lorazepam should be warned not to drive or operate heavy machinery” or “not to operate dangerous machinery or motor vehicles, and that their tolerance for alcohol and other CNS depressants will be diminished.” (3).

Better structured warnings such as those developed in Europe related to dose dependence, tolerance to effects, and the time frame in which the risk of impairment is greatest, would better serve patients and should be investigated for implementation in the United States (10,11).

Conclusions

Many laboratories may currently not detect lorazepam in their routine screening procedures; however this is a drug that has been shown to be capable of causing driving impairment, and an effort should be made to test for it, particularly in cases where symptoms suggest intoxication with a CNS depressant, and other CNS drugs have been ruled out. The detrimental effects of lorazepam on driving, including sedation, poor motor coordination, and an inability to divide attention, are similar to those observed with other CNS depressants like alcohol. Although lorazepam concentrations cannot currently be correlated to a degree of impairment, this and other studies support the fact that impairment can result from therapeutic use as well as abuse. Furthermore, these cases show that this drug is most frequently taken with other CNS depressants that are likely to have a compounding effect on driving performance, and physicians should take care to stress the risks to patients taking this medication alone, and especially in combination with other drugs.

References

9. ROSITA Deliverable D1. Drugs and medicines that are suspected to have a detrimental impact on road user performance. A. Verstraete, Project coordinator. ROSITA 1999.