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CASE REPORT

TOXICOLOGY

Henry A. Spiller,[1] *M.S. and Dennis J. Siewert,*[2] *M.S.*

Drug-Facilitated Sexual Assault Using Tetrahydrozoline

ABSTRACT: Drug-facilitated sexual assault (DFSA) has been defined as the use of a chemical agent to facilitate a sexual assault. We report two cases of the use of tetrahydrozoline for DFSA. We believe this is the first report with urinary quantification of tetrahydrozoline levels postassault. Blood and urine were obtained *c.* 20 h postexposure in two cases of reported DFSA. Tetrahydrozoline was not detected in blood but was identified in urine in both victims. After initial identification in the urine using the 2010 update to the AAFS mass spectrometry database library, tetrahydrozoline was quantified at 114 and 150 ng/mL, respectively, using GC/MS. Two unique clinical features reported in these cases were intermittent periods of consciousness and postexposure vomiting. Use of GC/MS was successful in identifying tetrahydrozoline in the 100 ng/mL range up to 20 h postexposure. For victims with late presentation, urine may be a better sample for evaluation for tetrahydrozoline.

KEYWORDS: forensic science, drug-facilitated sexual assault, tetrahydrozoline, poisoning, urine quantification, gas chromatography mass spectrometry

Drug-facilitated sexual assault (DFSA) has been defined as the use of a chemical agent to facilitate a sexual assault (1). While the true incidence of DFSA is not known, the U.S. Department of Justice estimates that 44% of sexual assaults are perceived to occur under the influence of drugs or alcohol. Often the primary intoxicant appears to be alcohol, a benzodiazepine, or another hypnotic (1–5). Additionally, other substances have been used including over-the-counter medications such as antihistamines, cough remedies, and ocular medications (1,6–8).

The primary reason for the use of a substance in DFSA is to produce a victim unable to resist the attacker. Several other factors may come into play in the choice of a substance in DFSA including: (i) to impair memory, so the victim is less likely to accurately recall the circumstances, (ii) to impair judgment coupled with reduced inhibition, giving the attacker the impression of collaboration or submission by the victim, (iii) to produce a period of unconsciousness so the victim will be unable to resist, (iv) selection of a substance that is not routinely detected on standard drug analysis screens, if after the assault the victim seeks medical/forensic help, and (v) availability of the substance to the perpetrator. A number of substances commonly used for DFSA are widely available and easily detected on routine drug screens such as benzodiazepines, opiates, barbiturates, and alcohol. Other substances such as rohypnol are not legally available in the United States, can only be obtained on the illicit market, and are not commonly found during postassault testing. In recent years, there have been two reports of the use of a widely available over-the-counter medication, tetrahydrozoline, in cases of DFSA (6,7). We report two additional cases of the use of tetrahydrozoline for DFSA. We believe this is the first report with urinary quantification of tetrahydrozoline levels postassault.

[1]Kentucky Regional Poison Control Center, PO Box 35070, Louisville, KY 40232.
[2]Toxicology Section, Florida Department of Law Enforcement, 500 West Robinson Street, Orlando FL 32801.

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Case Reports

Case One

A 19-year-old female was invited to watch a movie at the home of an adult male. While there she consumed one drink of vodka with cranberry juice from a 6- to 8-ounce cup. Less than 30 min later, a second drink was prepared for her by the adult male. The second drink was described to her as a special concoction, was noted to have a different taste, and because of this the female ingested less than half of this drink, refusing to finish it. Within 15–20 min, the adult female began to feel lightheaded, groggy, and lost consciousness. Following this, there were several brief periods of intermittent consciousness where the victim was able to remember and describe certain events including: waking up during active involuntary vaginal intercourse, waking up feeling she could not breathe and recognizing the male's hands on her throat, and waking up to vomit. She woke again *c.* 9 h postingestion and found herself partially clothed in the male's bed. She dressed herself and left. Within 30 min of leaving she attempted to go to work, where she had two more episodes of spontaneous emesis and was noted to be drowsy. She was sent home from work after 1 h. At home she slept three more hours, where she was woken by a friend and brought to the hospital for medical help and forensic documentation of the assault. Blood and urine samples were obtained 20 h postingestion.

No drugs or alcohol were detected in the blood. The urine was screened for amphetamines, antidepressants, antihistamines, barbiturates, benzodiazepines, cannabinoids, cocaine, dextromethorphan, lidocaine, narcotic analgesics, opiates, gamma-hydroxybutyrate,

phencyclidine, phenothiazines, sympathomimetic amines, and verapamil by gas chromatography, color tests, and enzyme-linked immunosorbent assay. Tetrahydrozoline was initially detected in the urine by gas chromatography during initial screening and confirmed by gas chromatography/mass spectroscopy (GC/MS) at 114 ng/mL utilizing appropriate quality control practices.

Case Two

A 31-year-old female stated she was visiting the Orlando area with her family. After a domestic dispute, her husband was removed from the resort and the victim was offered a place to stay and a job by the subject, acting as a manager of the resort. After a week, in which the subject and victim went on a few dates, the victim was moved to a room at another resort. At that time, the subject took the victim's debit cards and removed all of her money out of the accounts so that he could buy cocaine. The subject told the victim that if she left the room he would kill her and her family with a firearm he possessed. With no money or communications, the victim remained confined in the apartment.

During the second week, the subject would either use a syringe to inject an unknown liquid or pour an unknown powder over the victim's face. Whenever she would get the injection, her heart rate accelerated, lose consciousness, and could not remember any events. After receiving the powder, the victim also lost consciousness and had no concept of time. While she was unconscious, the subject would dress her in different clothing, cut her hair, apply makeup, and perform pedicures.

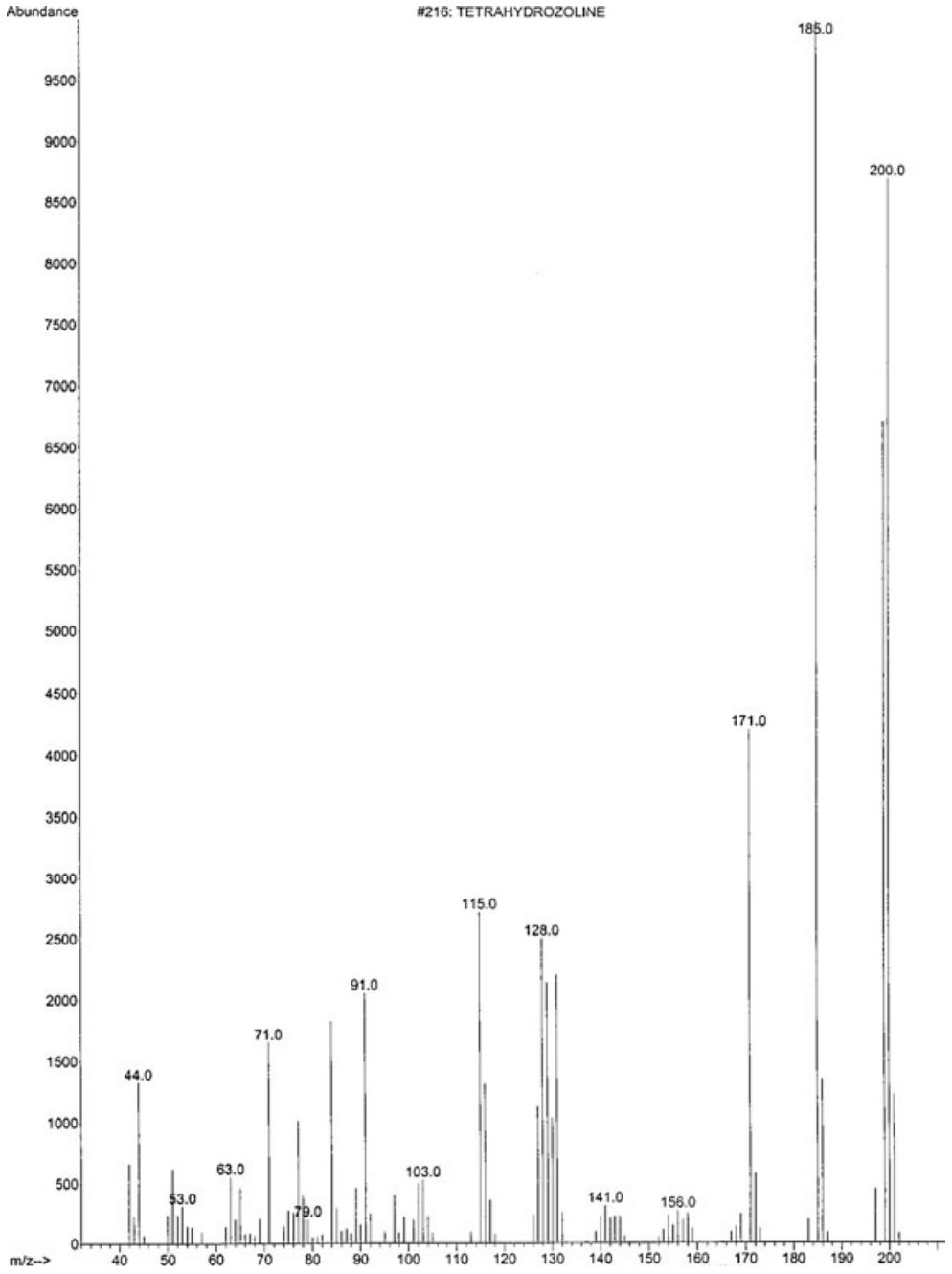

FIG. 1—*Mass spectrum of tetrahydrozoline.*

On one particular morning, the victim awoke in the morning hours and had the feeling of being raped and sodomized. She was also vomiting and experiencing body tremors. She noticed that she was wearing different clothing and her face had a burning sensation. The victim left the room and made contact with an individual in an adjoining room. This witness took the victim to the nearest hospital for treatment. Not knowing exactly what incident had occurred, a sexual assault kit was obtained at 10:10 PM that same night.

The toxicological sample within the sexual assault kit consisted of two gray-stopped blood tubes and a urine specimen cup. There were *c.* 7 mL of blood total and 90 mL of urine. Information within the kit stated that the victim took several types of prescription medication, none of which were identified in the below testing.

The blood was tested for ethyl alcohol using headspace gas chromatography with flame ionization detectors, yielding negative results. The urine was screened for amphetamines, antidepressants, antihistamines, barbiturates, benzodiazepines, carisoprodol, cocaine metabolite, methadone, opiates, oxycodone, propoxyphene, marijuana metabolite, and other drugs by enzyme-linked immunosorbent assay and GC/MS.

Tetrahydrozoline was initially identified with the 2010 update to the AAFS mass spectrometry database library (Fig. 1). A reference standard of the drug was ordered from Sigma-Aldrich Chemical Company (St. Louis, MO) and was prepared for the same extraction procedure. Blank urine was spiked with a prepared methanolic solution of tetrahydrozoline at concentrations of 50, 250, and 500 ng/mL. These spiked samples along with a second aliquot of the victim's urine was extracted and analyzed with GC/MS. The presence of tetrahydrozoline was confirmed at a quantitative value of *c.* 150 ng/mL. The victim's blood was analyzed using a similar procedure for tetrahydrozoline with negative results. Marijuana metabolite, cocaine, benzoylecgonine, alprazolam, alpha-hydroxyalprazolam, citalopram, and diphenhydramine were also identified in the urine.

Discussion

Our report provides further evidence of tetrahydrozoline use in DFSA. Urine quantification of tetrahydrozoline in our cases suggests detection in urine up to at least 20 h postingestion may be expected. GC/MS has previously been reported as an appropriate methodology for tetrahydrozoline (9). This information is helpful as victims of sexual assault may not seek help for a number of hours after the assault. It is unclear from our data how long postingestion tetrahydrozoline would be detected in the urine, but it appears reasonable to assume up to 24 h. There is a dearth of information on the kinetics of tetrahydrozoline. A half-life of 4.4 h has been postulated based on serum clearance in two young children (2 and 3 years old) with an unintentional ingestion (10). However, small children are not adults and kinetics may be significantly different (11). We could locate no further information on the kinetics or metabolism of tetrahydrozoline in humans. Tetrahydrozoline was not detected in the blood of our two cases. But both samples were obtained >16–22 h postexposure, suggesting urine may be a better sample in late presentations of tetrahydrozoline exposure. In contrast, the published reports of tetrahydrozoline ingestion have consistently noted duration of clinical effects of 8–24 h postingestion (12–17). The half-life of tetrahydrozoline and detection in blood may not match its duration of clinical effects.

Tetrahydrozoline is an alpha-2 receptor agonist. Stimulation of the alpha-2 receptor decreases cellular cyclic-AMP production with subsequent decreased neuronal activity. Stimulation of postsynaptic alpha-2 receptors produces local vasoconstriction with reduced blood flow and subsequent decreased tissue swelling which is the basis for therapeutic use as a decongestant (18–20). Owing to its lipophilic properties, there is limited systemic absorption after ocular or nasal use with no significant cardiovascular effects (18,20). However, after ingestion, tetrahydrozoline readily crosses the blood–brain barrier and produces presynaptic alpha-2 stimulation (21). Clinical effects from central alpha-2 receptor agonism from tetrahydrozoline are similar to other imidazoline derivatives such as clonidine, tizanadine, and naphazoline (12–16,22). Reported effects include drowsiness, coma, respiratory depression, bradycardia, hypotension, hypotonia, muscle flaccidity, and hypothermia (12–16,22).

There are a number of reasons tetrahydrozoline might be chosen for DFSA. It is an easily obtained, inexpensive medication widely available without a prescription. A bottle of an over-the-counter "eye drops" (e.g., Visine®; Johnson & Johnson, SKillman, NJ) may not raise suspicions of a potential victim or police investigators (6). It is a potent CNS depressant with a rapid onset (13). Use of tetrahydrozoline would produce a flaccid, obtunded, or comatose victim, potentially unable to resist an attacker. Concomitant use of tetrahydrozoline with another CNS depressant (e.g., ethanol) may have potential additive effects, possibly decreasing the dose of tetrahydrozoline necessary for CNS depression. As a colorless, odorless, and tasteless liquid, it can easily be added or dissolved into drinks or food (18). Tetrahydrozoline will not be detected by common urine immunoassays if postassault testing occurs.

There are two unique clinical features that deserve mention. Previous reports of unintentional ingestion of tetrahydrozoline alone have not reported vomiting. However, in both cases of this report and in one previous report, multiple episodes of spontaneous vomiting occurred (7). In one of our cases, as well as the report by Stillwell et al. (7), ethanol was a coingestant and this may have a synergistic role. Additionally in our cases and a previous report, there were intermittent periods of consciousness reported (7). Similar alternating periods of intermittent consciousness have been previously reported with tetrahydrozoline (16,23). Victims of DFSA using tetrahydrozoline may have brief periods of return to consciousness secondary to vigorous stimulation during the assault.

In summary, we report two additional cases of the use of tetrahydrozoline in DFSA, with quantified urine tetrahydrozoline levels. Use of GC/MS was successful in identifying tetrahydrozoline in the 100 ng/mL range up to 20 h postexposure.

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Additional Information and reprint requests:
Henry A. Spiller, M.S.
Kentucky Regional Poison Control Center
PO Box 35070
Louisville, KY 40232
E-mail: Henry.spiller@nortonhealthcare.org